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Efficacy and Safety of Ritlecitinib in Severe Alopecia Areata: A Systematic Review

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Abstract

Severe alopecia areata (AA), including alopecia totalis and alopecia universalis, is a devastating autoimmune condition that causes widespread hair loss. Ritlecitinib, a selective Janus kinase 3 (JAK3) and TEC family kinase inhibitor, is emerging as a systemic therapy for severe AA. This systematic review looked at the efficacy and safety of ritlecitinib in people with severe AA. We systematically searched PubMed/MEDLINE (Medical Literature Analysis and Retrieval System Online), Embase, Scopus, and the Cochrane Library from the databases' inception through August 31, 2026. Eligible studies assessed ritlecitinib in adolescents or adults with severe AA, typically defined by a baseline Severity of Alopecia Tool (SALT) score of ⩾50. Study selection and data extraction were done manually with standardized Google Sheets (Google LLC, Mountain View, California, United States), while Rayyan (Rayyan, Cambridge, Massachusetts, United States) and Zotero (Corporation for Digital Scholarship, Vienna, Virginia, United States) were utilized for screening and reference management. The risk of bias was assessed using RoB 2 (Cochrane Collaboration, London, United Kingdom) for randomized trials, ROBINS-I (Risk Of Bias In Non-randomized Studies - of Interventions) (Cochrane Collaboration) for non-randomized intervention studies, and the Newcastle-Ottawa Scale (Ottawa Hospital Research Institute, Ottawa, Canada) for observational cohorts. Because of significant clinical and methodological variation, findings were presented narratively. Five studies, totaling 483 patients, were included. High-stringency responses were seen. The mean SALT score declined consistently across investigations. Eyebrow and eyelash enhancements were also recorded. Adverse-event rates ranged from 44.4% to 67% in 24-week studies and reached 97.4% during three-year follow-up; serious adverse events occurred in 6.8% during long-term treatment. In clinical and real-world tests, ritlecitinib showed persistent scalp hair regeneration and improvement in brow and eyelash involvement, with generally controllable adverse effects. Long-term safety and efficacy studies suggest long-term clinical benefit, although interpretation was hampered by variability and the prevalence of non-randomized evidence.

Categories: Pharmacology, Allergy/Immunology, Dermatology
Keywords: alopecia areata, alopecia totalis, alopecia universalis, hair fall, jak3 inhibitor, janus kinase inhibitor, ritlecitinib, salt score, severe alopecia areata

Introduction And Background

Alopecia areata (AA) is a long-term, immune-mediated, nonscarring hair loss condition marked by abrupt, frequently unpredictable hair loss from the scalp and other hair-bearing areas, such as the eyebrows, lashes, and nails. Its clinical spectrum includes alopecia totalis, alopecia universalis, and restricted patchy illness. AA results from a loss of immune privilege within the hair follicle; cytotoxic T-cell activation and interferon-ɣ-associated inflammatory signaling cause follicular damage and disrupt the normal hair-growth cycle [1,2]. Extensive AA can have significant psychological repercussions beyond its outward manifestations, such as diminished quality of life, social challenges, and emotional discomfort [2,3].

Although reported incidence varies among populations and study approaches, the estimated lifetime risk of AA is about 2% [4]. Because spontaneous persistent regrowth is less predictable and standard treatments sometimes result in incomplete or transient responses, severe illness, which is often characterized by ⩾50% scalp hair loss, poses a particularly difficult therapeutic profile [3,5]. In the past, systemic corticosteroids, methotrexate, cyclosporine, azathioprine, and other immunomodulatory treatments have been used for more extensive disease, whereas topical or intralesional corticosteroids have been used for limited disease. However, recurrence, inconsistent effectiveness, side effects, and a lack of long-term disease control frequently restrict these therapies [5,6].

The Janus kinase (JAK)-signal transducer and activator of transcription pathway has been identified as a key therapeutic target due to growing knowledge of AA pathophysiology. Targeting signaling pathways implicated in the immunological dysregulation that underlies AA, ritlecitinib is an oral inhibitor of JAK3 and the TEC family of tyrosine kinases. The ALLEGRO phase 2b/3 trial showed that ritlecitinib significantly outperformed placebo in achieving Severity of Alopecia Tool (SALT) ⩽20 at Week 24, demonstrating clinically significant scalp hair regrowth with targeted treatment. Afterward, ritlecitinib was approved as a systemic treatment for severe AA in adults and adolescents who were at least 12 years old [12].

Long-term extension studies and real-world cohorts are examples of more recent research that goes beyond randomized trials and offers more details about sustained scalp regrowth, eyebrow and eyelash healing, nail involvement, and safety. However, differences in follow-up duration, study design, and outcome assessment may complicate the interpretation of treatment efficacy and long-term safety across the available evidence. A synthesis of findings from randomized trials, long-term extension studies, and real-world cohorts is therefore valuable for providing a broader assessment of clinical outcomes.

This systematic review aimed to comprehensively evaluate the efficacy and safety of ritlecitinib in patients with severe AA by synthesizing evidence from randomized controlled trials, long-term extension studies, and real-world cohorts. The review assessed treatment efficacy across clinically meaningful scalp hair regrowth endpoints, longitudinal SALT score changes, stringent regrowth outcomes (SALT ⩽10 and SALT 0), eyebrow and eyelash regrowth, and nail involvement. Safety outcomes included the incidence of adverse events, serious adverse events, and treatment discontinuations. By integrating evidence across different study designs and follow-up periods, this review provides a comprehensive assessment of the clinical benefits and safety profile of ritlecitinib in severe AA.

Review

Methods

This systematic review aimed to assess the efficacy and safety of ritlecitinib treatment in patients with severe AA. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 [8] statement was followed in conducting the review. The review was registered with the International Prospective Register of Systematic Reviews (PROSPERO) (registration number: CRD420261517203). The methodological approach was guided by recommendations from the Cochrane Handbook for Systematic Reviews of Interventions [9] for literature searching, study selection, data extraction, risk of bias assessment, and evidence synthesis.

Information Sources and Search Strategy

A comprehensive electronic literature search was conducted in PubMed/MEDLINE (Medical Literature Analysis and Retrieval System Online), Embase, Scopus, and the Cochrane Library from database inception to August 31, 2026. The search strategy combined controlled vocabulary (Medical Subject Headings (MeSH)/Emtree terms) with free-text and MeSH entry terms to maximize sensitivity and identify studies evaluating ritlecitinib in patients with AA. Search concepts comprised terms related to AA and ritlecitinib, including its development code PF-06651600. Controlled vocabulary included 'Alopecia Areata,' 'Alopecia Areata/drug therapy,' 'Protein Kinase Inhibitors,' and 'Janus Kinase 3,' supplemented by free-text/MeSH entry terms such as 'alopecia areata,' 'alopecia totalis,' 'alopecia universalis,' 'severe alopecia areata,' 'ritlecitinib,' 'PF-06651600,' 'JAK3 inhibitor,' and 'Janus kinase 3 inhibitor.' The search strategy was adapted for other databases using equivalent Emtree terms and keywords (see Appendices).

Eligibility Criteria

Inclusion criteria: Studies were eligible for inclusion if they met the PICOS (Population, Intervention, Comparator, Outcomes, Study design) criteria given in Table *1*.

Parameter	Criteria
Population	Adolescents aged ≥12 years and adults aged ≥18 years with a proven clinical diagnosis of severe AA, alopecia totalis, or alopecia universalis. Severe illness was classified as a baseline SALT score ≥50, indicating at least 50% scalp hair loss. Patients with at least six months of persistent hair loss may be eligible, as may those who have previously undergone or failed other therapy such as topical treatments, corticosteroids, or other JAK inhibitors.
Intervention	Oral ritlecitinib monotherapy, including the recommended maintenance dose of 50 mg once daily, with or without an initial loading phase. Eligible studies included those with a treatment duration of ≥24 weeks, as well as open-label extension studies with up to 3 years of follow-up.
Comparator	In randomized controlled trials, the comparator can be a placebo or another control group. For single-arm open-label extension studies and observational cohorts, within-patient longitudinal or baseline-to-follow-up comparisons were permitted.
Outcomes	Studies had to report at least one efficacy or safety result. The efficacy endpoints were SALT ≤20, SALT ≤10, SALT30, SALT90, SALT 0/complete scalp regrowth, change in mean SALT score, brow and eyelash responses, nail outcomes, trichoscopic findings, patient-reported outcomes, and quality-of-life measures. Safety results included adverse events, major adverse events, therapy withdrawal due to adverse events, and laboratory abnormalities
Study Design	Eligible studies included randomized controlled trials, phase 2/3 interventional studies, open-label extension studies, and prospective or retrospective real-world observational cohorts.

TABLE 1: PICOS framework for inclusion of studies

PICOS: Population, Intervention, Comparator, Outcomes, Study design; SALT: Severity of Alopecia Tool; JAK: Janus kinase

Exclusion criteria: Studies involving patients with non-severe AA (SALT <50) or other forms of hair loss without separately extractable data for severe AA were excluded. This included cases with concomitant scarring or non-scarring alopecias or active inflammatory scalp disorders. Studies evaluating ritlecitinib in combination with other systemic immunosuppressive treatments, systemic corticosteroids, or biologic drugs were excluded because the independent effect of ritlecitinib could not be determined. Studies with insufficient washout periods following previous AA therapy were also excluded.

Studies involving patients with severe uncontrolled systemic infections, clinically significant hepatic or renal impairment, significant baseline laboratory abnormalities, active malignancy or premalignant conditions, pregnancy or breastfeeding, or other major conditions precluding ritlecitinib treatment were excluded.

Case reports, reviews, systematic reviews, meta-analyses, editorials, commentaries, guidelines, animal or laboratory studies, and conference abstracts lacking sufficient extractable clinical data were excluded. Duplicate or overlapping publications were also excluded when they did not provide additional relevant outcome data. When multiple reports originated from the same cohort, the publication providing the most complete or relevant data was retained.

Screening Process and Study Selection

All records identified through the electronic database searches were imported into Zotero (Corporation for Digital Scholarship, Vienna, Virginia, United States) for reference management and duplicate identification. After removal of duplicate records, the remaining studies were transferred to Rayyan (Rayyan, Cambridge, Massachusetts, United States) for systematic screening. During the primary screening stage, titles and abstracts were independently reviewed against the predefined eligibility criteria, and clearly irrelevant records were excluded. Potentially eligible studies were then subjected to secondary screening, during which the full texts were manually assessed against the inclusion and exclusion criteria. We documented screening decisions and reasons for full-text exclusion in a standardized Google Sheets spreadsheet (Google LLC, Mountain View, California, United States). Reference lists of included studies and relevant systematic reviews were also manually screened to identify additional potentially eligible studies. The overall study-selection process was documented using a PRISMA 2020 flow diagram.

Data Extraction

Data from all relevant studies were manually extracted using a standard Excel sheet (Microsoft Corporation, Redmond, Washington, United States) data extraction form. The extracted information included the first author and publication year, study design and setting, sample size, patient age and demographic characteristics, definition and severity of alopecia areata, baseline SALT score, ritlecitinib dose and treatment regimen, treatment duration and follow-up period, efficacy and safety outcomes, adverse events,

serious adverse events, treatment discontinuations, study limitations, and risk-of-bias or methodological quality assessment. When multiple publications arose from the same clinical study or cohort, we thoroughly examined the papers to avoid double-counting individuals. The article with the most complete or relevant outcome data was selected for the associated analysis, and companion publications were reviewed if they provided additional non-overlapping information.

Outcomes

The primary effectiveness endpoint was clinically relevant scalp hair regeneration, namely achieving a SALT score ⩽20, as described. Secondary efficacy outcomes included SALT ⩽10, SALT90, SALT 0 or total scalp hair regeneration, decrease in mean SALT score, brow and eyelash responses, and nail results. Safety outcomes comprised the occurrence of any adverse event, significant adverse events, therapy discontinuation due to adverse events, and individual adverse events reported by the included studies. Because the included studies used different definitions, assessment methodologies, and follow-up time points, outcome definitions were kept as close to the original study reports as possible.

Risk of Bias and Methodological Quality Assessment

The risk of bias and methodological quality were evaluated based on the design of each included study. The Cochrane Risk of Bias 2 (RoB 2) tool [10] was used to assess the randomized controlled trial across five domains: bias arising from the randomization process, bias due to deviations from intended interventions, bias due to missing outcome data, bias in outcome measurement, and bias in reported result selection. We evaluated the non-randomized, open-label extension study using the Non-randomized Studies of Interventions (ROBINS-I) (Cochrane Collaboration, London, United Kingdom) [11] tool, which covers seven domains: confounding, participant selection, intervention classification, deviations from intended interventions, missing data, outcome measurement, and result selection. The Newcastle-Ottawa Scale (NOS) (Ottawa Hospital Research Institute, Ottawa, Canada) [12], with a maximum score of 9 stars, was used to evaluate the real-world observational cohort studies.

Data Synthesis

Because of the clinical and methodological heterogeneity among the included studies, such as differences in study design, patient populations, baseline disease severity, treatment duration, follow-up periods, outcome definitions, and reporting methods, the findings were synthesized using a narrative approach. Efficacy results were summarized using the reported treatment-response thresholds and follow-up time points. Continuous outcomes, such as changes in SALT scores, were described using reported means, standard deviations, mean changes, or other appropriate statistical estimates. In contrast, dichotomous outcomes, such as treatment responses and adverse events, were provided as proportions or percentages. Results from randomized controlled trials, open-label extension studies, and real-world observational cohorts were evaluated individually where possible to avoid considering diverse study designs as equivalent evidence. When comparing findings between studies, special care was taken to account for differences in follow-up time and outcome definition. There was no quantitative meta-analysis because of significant variability in study design and outcome reporting, as well as a small number of studies reporting comparable outcomes. The narrative summary thus concentrated on the direction, magnitude, consistency, and clinical relevance of the reported effectiveness and safety results.

Results

Study Selection Process

The database search identified a total of 846 records, including 204 from PubMed, 298 from Embase, 338 from Scopus, and six from the Cochrane Library. After removal of 192 duplicate records, 654 records remained for title and abstract screening. Of these, 612 records were excluded based on the predefined eligibility criteria, leaving 42 reports for full-text retrieval. We could not retrieve three reports, and the remaining 39 reports were assessed for eligibility. During full-text assessment, 34 reports were excluded, including 20 for wrong population, seven for wrong intervention, three for wrong comparator, two for wrong outcomes, and two for other reasons. Ultimately, five studies [13-17] met all eligibility criteria and were included in the systematic review (Figure *1*).

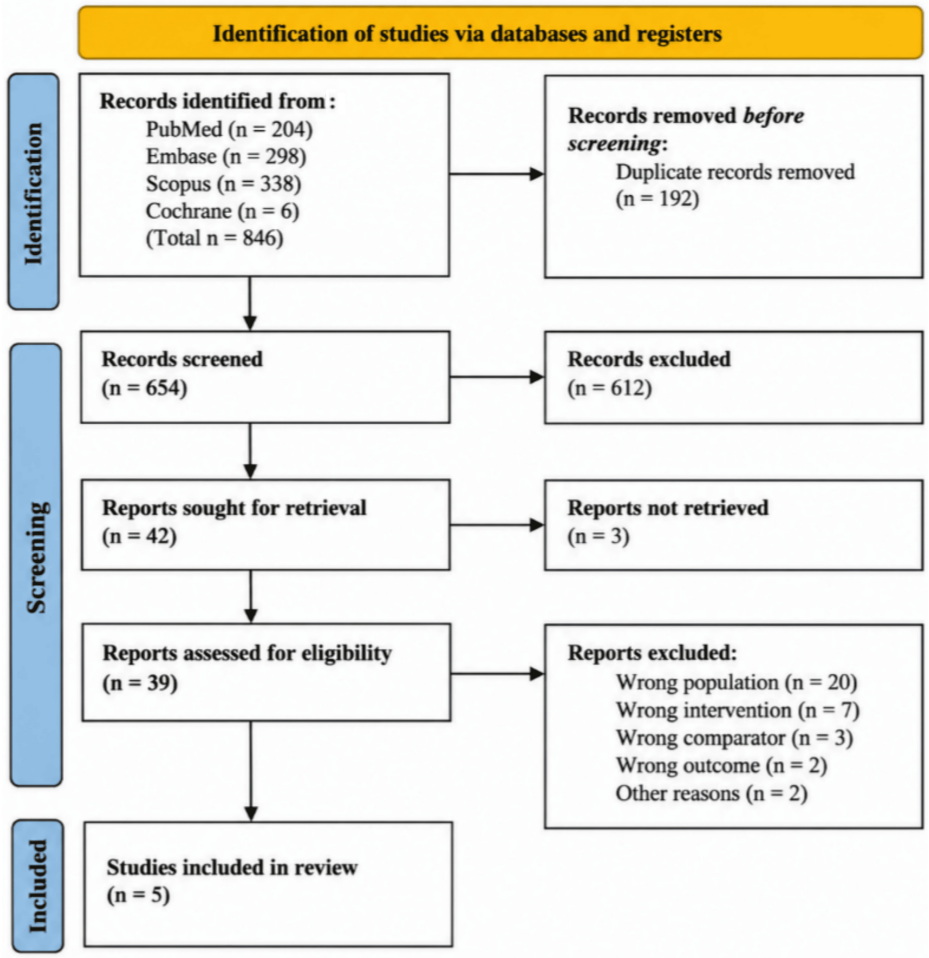


FIGURE 1: PRISMA flow diagram

A total of 846 records were identified from PubMed, Embase, Scopus, and the Cochrane Library. After removing duplicates, screening titles and abstracts, assessing full texts, and excluding ineligible reports, five studies were ultimately included in the review.

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Baseline Characteristics and Patient Demographics

The five studies included varied in their clinical context and study design and included randomized, long-term extension, and real-world observational data [13-17]. Patient samples ranged from 18 to 191 patients. King et al. reported activity data from a Phase 2a randomized controlled trial of ritlecitinib [13], and Senna et al. published long-term results from the ALLEGRO-LT Phase 3 open-label extension [14]. The studies by Starace et al. [15] and Perrotta et al. [16] were real-world data from Italian cohorts. In contrast, Huang et al. assessed patients who had failed previous JAK inhibitor therapy for AA [17].

Studies also varied widely in age distribution. Mean ages ranged from 23.9 years [15,17] to 37.0 years [13]. The study by Starace et al. included the largest number of adolescents (70/102 patients, 68.6%) [15], compared to 14.1% in the studies by Senna et al. [14] and zero in King et al. [13], which only included adults in the 50-mg treatment arm. In four studies, the majority of participants were female: 77.1% in King et al.'s study [13], 56.0% in the Senna et al.'s study [14], 70.0% in the Perrotta et al.'s study [16], and 61.1% in Huang et al.'s study. [17] However, Starace et al. found a slightly higher percentage of male participants (53.9%) [15].

Disease levels were high in all groups. The reported mean baseline SALT scores ranged from 68.1 to 89.4 and the highest mean score was reported by King et al. [13] and the lowest by Huang et al. [17] The proportion of patients having combined alopecia totalis or alopecia universalis varied from 22.2% in the study by Huang et al. [17] to 86.7% in Perrotta et al. [16] 41.7% in King et al. [13] 45.0% in Senna et al. [14] and 55.9% in Starace et al. [15]. Disease duration was usually longer. Starace et al. (2026) reported a median disease duration of 6.7 years [15], and Senna et al. reported 6.9 years [14], while Perrotta et al. reported a median duration of

five years [16]. Current episode duration was also longer in two studies, with a median of 2.2 years in Senna et al. [14] and 2.6 years in King et al. [13]. Starace et al. reported a mean current episode duration of 49.3 months [15]. The extent of exposure to past treatment was unevenly distributed across cohorts. A majority of the patients in the real-world cohorts of Starace et al. [15] and Perrotta et al. [16] were previously treated with topical or intralesional corticosteroids (97.1% and 80.0%, respectively). In contrast, 16.7% of patients in the study by Perrotta et al. [16] and 5.9% in the study by Starace et al. [15] had prior exposure to systemic JAK inhibitors, while all patients in the Huang et al.'s study [17] had prior exposure to systemic JAK inhibitors, including tofacitinib or baricitinib (Table *2*).

Characteristic	King et al. (2021) [13]	Senna et al. (2026) [14]	Starace et al. (2026) [15]	Perrotta et al. (2026) [16]	Huang et al. (2025) [17]
Study design and setting	Phase 2a RCT; United States, Canada, Australia	ALLEGRO-LT Phase 3 OLE; Global	Retrospective multicenter cohort; Italy, 20 centers	Prospective single-center cohort; Italy	Retrospective refractory cohort; China
Sample size	48 (50-mg arm); 142 total RCT	191	102	30 completers	18
Age (years), mean±SD	37.0±13.0	33.2±14.4	23.9±15.3	33.5±17.9	23.9±10.7
Age (years), median (range/IQR)	NR	31.0 (12–70)	NR	31.5 (16–52.5)	21.0 (12–47)
Adolescents, n (%)	0 (0%)	27 (14.1%)	70 (68.6%)	NR	NR
Adults, n (%)	48 (100%)	164 (85.9%)	32 (31.4%)	Predominantly adults	Predominantly adults
Female, n (%)	37 (77.1%)	107 (56.0%)	47 (46.1%)	21 (70.0%)	11 (61.1%)
Male, n (%)	11 (22.9%)	84 (44.0%)	55 (53.9%)	9 (30.0%)	7 (38.9%)
Baseline SALT, mean±SD	89.4±15.8	83.3±15.4*	86.2±18.5	79.7±22.0	68.1±30.2
Baseline SALT, median (IQR)	NR	NR	NR	90 (50–100)	NR
SALT 50–94, n (%)	28 (58.3%)	105 (55.0%)	45 (44.1%)	4 (13.3%)	14 (77.8%)†
Alopecia totalis, n (%)	7 (14.6%)	Combined with AU	Combined in severe category	14 (46.7%)	NR
Alopecia universalis, n (%)	13 (27.1%)	Combined with AT	Combined in severe category	12 (40.0%)	NR
Combined AT/AU, n (%)	20 (41.7%)	86 (45.0%)	57 (55.9%)‡	26 (86.7%)	4 (22.2%)§
Disease duration (years), median (IQR)/mean±SD	6.7 (0.6–52.3)	6.9 (0.3–58.2)	8.9 ± 8.9	5.0 (2–10)	Age at diagnosis: 18.6 ± 11.4
Current episode duration, median (IQR)/mean±SD	2.6 (0.3–7.5) years	2.2 (0.04–10.0) years	49.3 ± 83.0 months	NR	36 (12–180) months
Topical/intralesional steroid exposure, n (%)	NR	NR	99 (97.1%)	24 (80.0%)	NR
Systemic corticosteroid exposure, n (%)	NR	NR	68 (66.7%)	NR	NR
Prior systemic JAK inhibitor exposure, n (%)	Excluded if <12 weeks	NR	6 (5.9%)	5 (16.7%)	18 (100%)
Prior topical immunotherapy, n (%)	NR	NR	24 (33.3%)	6 (20.0%)	NR

TABLE 2: Baseline demographic and clinical characteristics of included studies

*Mean SALT reported for the non-AT/AU subgroup. †S2/S3 severity tiers. ‡SALT ≥95%. §S4 severity tier. The table preserves the values and reporting formats provided in the uploaded source.

NR: not reported; RCT: randomized controlled trial; OLE: open-label extension; SALT: Severity of Alopecia Tool; AT: alopecia totalis; AU: alopecia universalis; JAK: Janus kinase.

Risk of Bias Assessment using ROB 2.0

The RoB 2 tool was used to evaluate the risk of bias of King et al.'s study [13]. The study was deemed to have a minimal risk of bias across all five domains, as seen in Figure 2 and Figure 3. Bias resulting from the randomization process (D1), bias resulting from variations from intended interventions (D2), bias resulting from missing outcome data (D3), bias in outcome assessment (D4), and bias in the selection of the reported result (D5) were all found to be low risk. As a result, the study was rated as having a low risk of bias overall. The randomized, controlled, and blinded design, proper management of end data, objective outcome assessment, and prespecified reporting all contributed to a minimal possibility of systematic bias in the study findings, as seen by the consistent low-risk judgments across all domains.

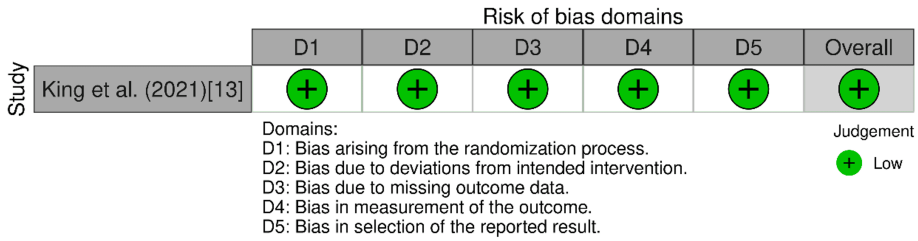


FIGURE 2: Traffic plot of risk of bias assessment using ROB 2.0.

Traffic plot illustrating the domain-specific risk of bias assessment for the randomized controlled trial by King et al. (2021) [13]. The assessment covers all five RoB 2 domains: bias arising from the randomization process, bias due to deviations from intended interventions, bias due to missing outcome data, bias in measurement of the outcome, and bias in selection of the reported result. The study was judged to have a low risk of bias across all five domains.

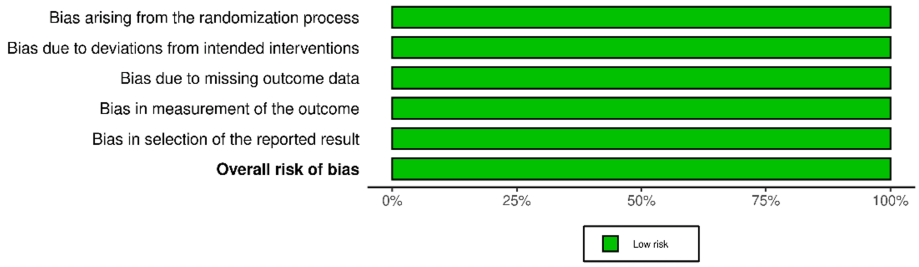


FIGURE 3: Summary plot of risk of bias assessment using ROB 2.0

Summary plot presenting the overall risk of bias judgments for the study by King et al. (2021) [13] across the five RoB 2 domains. All domains were assessed as low risk of bias, resulting in an overall low risk of bias judgment for the study.

Risk of Bias Assessment Using ROBINS-I

The ROBINS-I method was used to evaluate the non-randomized extension study by Senna et al. [14] for risk of bias. The study was deemed to have an overall serious risk of bias, as illustrated in Figure 4 and Figure 5. Bias resulting from confounding (D1) and bias resulting from missing data (D5) were determined to be a serious risk. Bias resulting from participant selection (D2), deviations from planned interventions (D4), and outcome measurement (D6) was shown to be of moderate concern. On the other hand, bias in the selection of the reported result (D7) and bias in the classification of interventions (D3) were deemed to be of moderate risk. The serious risk of confounding was primarily related to the single-arm, open-label design without a concurrent control group. In contrast, the serious risk related to missing data reflected substantial attrition during long-term follow-up. Overall, these methodological limitations indicate that the findings from the Senna et al. extension study should be interpreted with caution.

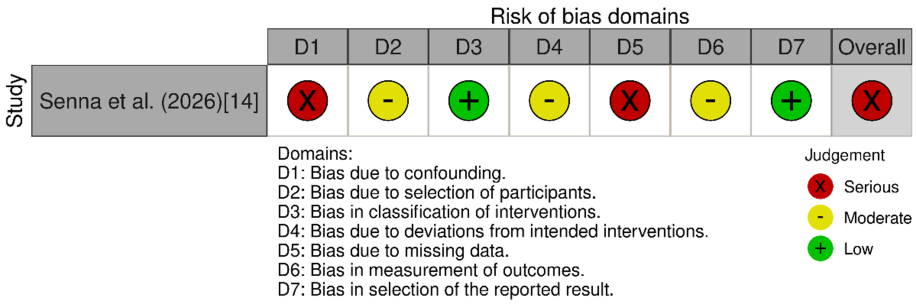


FIGURE 4: Traffic plot of risk of bias assessment using ROBIN-I

Traffic plot illustrating the domain-specific risk of bias assessment for the non-randomized extension study by Senna et al. (2026) [14]. The assessment covers seven ROBINS-I domains, including bias due to confounding, participant selection, classification of interventions, deviations from intended interventions, missing data, outcome measurement, and selection of the reported result.

ROBINS-I: Risk Of Bias In Non-randomized Studies - of Interventions

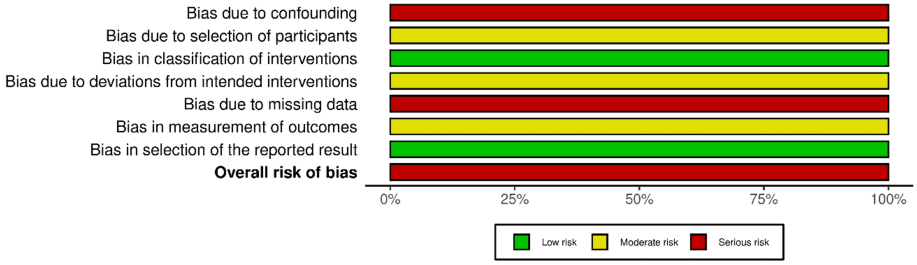


FIGURE 5: Summary plot of risk of bias assessment using ROBIN-I

Summary plot presenting the overall distribution of risk of bias across the seven ROBINS-I domains for the Senna et al. (2026) [14] non-randomized extension study. The study was judged to have an overall serious risk of bias, with the greatest concerns related to confounding and missing data. At the same time, other domains demonstrated moderate or lower concerns as detailed in the assessment.

ROBIN-I: Risk Of Bias In Non-randomized Studies - of Interventions

Quality Assessment using NOS

NOS was used to evaluate the methodological quality of the three real-world studies. The study by Starace et al. [15] received 6 stars, and 6 of 9 points were assigned, indicating high methodological quality. The study was rated as having adequate follow-up, adequate cohort follow-up, outcome assessment, comparability, outcome not present at baseline, ascertainment of exposure, and representativeness of the exposed cohort. Tbhe studies by Perrotta et al. [16] and Huang et al. [17] were both rated with 5 out of 9 stars and were of moderate methodological quality. Both studies received star ratings for cohort representativeness, exposure ascertainment, baseline outcome assessment, outcome measurement, adequate follow-up duration, and adequate follow-up. All three studies were single-arm, and none selected a non-exposed cohort, so none received a score for selecting a non-exposed cohort. Moreover, the studies by Perrotta et al. [16] and Huang et al. [17] were not awarded any stars of comparability due to the absence of a comparative control group. In conclusion, the quality of the included real-world studies was generally high to moderate, with the primary limitation of the studies being the single-arm design and lack of non-exposed comparison groups (Table 3).

Study (Author, Year)	Exposed Cohort	Non-exposed Cohort	Exposure Ascertainment	Outcome Absent at Baseline	Comparability	Outcome Assessment	Adequate Follow-up Duration	Adequate Cohort Follow-up	Total NOS Score
Starace et al. (2026) [15]	★	—	★	★	★	★	★	★	6/9
Perrotta et al. (2026) [16]	★	—	★	★	—	★	★	★	5/9
Huang et al. (2025) [17]	★	—	★	★	—	★	★	★	5/9

TABLE 3: Newcastle–Ottawa Scale (NOS) quality assessment of observational studies

★: Indicates adherence to the criteria. Numbers in parentheses () represent the maximum possible score for each criterion.

The total score reflects the overall quality assessment of each study. The total score reflects the overall quality assessment of each study. A maximum 9 is high quality; 6 and above is good quality; Below 6 is low quality

Systematic Review of Outcomes

SALT ⩽20 responder rates: Five studies (one Phase 2a RCT, one long-term OLE study, one multicenter retrospective real-world cohort, one prospective single-center cohort, and one retrospective cohort of patients with previous JAK inhibitor treatment failure) reported outcomes related to achieving a Severity of Alopecia Tool (SALT) score ⩽20 [13-17]. Due to differences in research design, patient characteristics, follow-up duration, and outcome reporting, quantitative pooling of this endpoint was not possible.

In a Phase 2a randomized controlled trial, King et al. compared ritlecitinib 50 mg to placebo for 24 weeks [13]. The study did not provide SALT ⩽20 as a separate endpoint, but instead included SALT30 and SALT90 answers. The study's results cannot be directly compared to those reporting SALT ⩽20. Senna et al. presented three-year results from the ALLEGRO Phase 2b/3 and ALLEGRO-LT Phase 3 trials [14]. At Month 36-38, 65.1% of patients achieved SALT ⩽20 in the observed analysis, compared to 47.1% with LOCF (95% CI, 40.0%-54.3%). In Month 12, the rates were 45.1% and 40.3%, respectively. Patients with baseline SALT 50- < 95 had higher Month 36-38 response rates (78.0% observed and 66.7% last observation carried forward (LOCF)) than those with baseline SALT 95- 100 (57.4% and 36.8%, respectively). In a retrospective real-world cohort by Starace et al., 41/102 (40.2%) patients had SALT ⩽20 by Week 24 [15]. The between-response rate was 48.6% (34/70) among teenagers and 21.9% (7/32) among adults, with a statistically significant difference in age groups ($\chi^2 = 4.01$, $P = 0.045$). Perrotta et al. observed an increase in SALT ⩽20 responses after 24 weeks of treatment in a real-world sample [16]. The response rate rose from 30.0% (9/30; 95% CI, 16.7%-47.9%) in Week 12 to 43.3% (13/30; 95% CI, 27.4%-60.8%) in Week 24. Huang et al. studied individuals with severe AA who had previously failed or were resistant to JAK inhibitor treatment. SALT ⩽20 was reached by 16.7% (3/18) in Week 4, 22.2% (4/18) in Week 8, 22.2% (4/18) in Week 12, and 44.4% (8/18) in Week 24 [17].

High-stringency regrowth endpoints (SALT ⩽10, SALT90, and SALT 0): All five studies contributed data to the scalp hair regrowth endpoints of high stringency (SALT ⩽10, SALT90, or complete scalp hair regrowth [SALT 0]) [13-17]. These outcomes were summarized descriptively because there were not enough common data points to pool them quantitatively due to differences in endpoint definitions and follow-up periods. In the Phase 2a randomized controlled trial, King et al. reported SALT90 response at Week 24 [13]. Among patients receiving ritlecitinib 50 mg, 25% (90% CI, 15%-37%) achieved SALT90 compared with 0% (90% CI, 0%-6%) in the placebo group. The longest time series data was from Senna et al., in which 191 patients were followed up till Month 36-38 [14]. At this time point, 52.3% achieved SALT ⩽10 in the observed analysis, compared with 36.7% (95% CI, 29.9%-43.6%) using LOCF. The observed analysis showed that 31.2% of patients achieved complete hair regrowth (SALT 0), compared with 22.5% in the LOCF analysis. Starace et al. reported that 32/102 patients (31.4%) achieved SALT ⩽10 at Week 24 [15]. The response rate was 27/70 (38.6%) among adolescents and 5/32 (15.6%) among adults. Perrotta et al. assessed SALT ⩽20, but not as separate endpoints of SALT ⩽10, SALT90, or SALT 0 [16]. Thus, this study provided no direct comparison of response rates with high stringency. Huang et al. reported that 5/18 patients (27.8%) achieved SALT ⩽10 and 3/18 (16.7%) achieved complete scalp hair regrowth (SALT 0) at Week 24 [17].

Continuous scalp hair loss trajectory (mean SALT scores): Four studies reported SALT scores as continuous and described longitudinal changes [13-16]. King et al. reported a baseline mean SALT score of 89.4 ± 15.8 [13]. The least-squares mean difference for ritlecitinib versus placebo was −31.1 points (95% CI, −43.5 to −18.8; $P < 0.0001$); the mean change in the placebo group was about +1.4 points at Week 24. Among patients who did not have alopecia totalis or alopecia universalis at baseline, the baseline mean SALT score was 83.3 ± 15.4, according to Senna et al. [14]. The mean change from baseline was −49.9 points at Month 12 (observed

analysis) and −45.5 points (LOCF). With longer treatment, the mean reduction was −62.1 ± 35.6 points (observed) and −47.4 ± 39.3 points (LOCF) at Month 36-38. Starace et al. reported a baseline mean SALT score of 86.2 ± 18.5, which decreased to 81.4 ± 21.9 at Week 4, 58.3 ± 33.9 at Week 12, and 40.8 ± 37.1 at Week 24 [15]. The overall mean difference between baseline and Week 24 was -45.4 points (P < 0.001). Perrotta et al. reported a baseline mean SALT score of 79.7 ± 22.0, decreasing to 67.7 ± 30.8 at Week 4, 54.7 ± 34.0 at Week 12, and 44.5 ± 37.2 at Week 24 [16]. This was a mean decrease of 35.2 points at Week 24 (P < 0.001). This treatment-refractory population had a baseline mean SALT score of 68.1 ± 30.2, dropping to 50.1 ± 31.7 at Week 12 and 37.1 ± 31.9 at Week 24, for an overall 31.0-point reduction from baseline.

Secondary anatomical outcomes (eyebrows, eyelashes, and nails): All five included studies reported outcomes related to eyebrow, eyelash, and/or nail involvement [13-17]. These outcomes were not quantitatively pooled because of differences in assessment instruments, responder definitions, and reporting methods across the included studies. In the Phase 2a RCT by King et al., 51% (21/41) of patients receiving ritlecitinib 50 mg achieved a ⩾1-grade improvement in eyebrow assessment (EBA) at Week 24, compared with 15% (6/40) receiving placebo [13]. For eyelashes, a ⩾1-grade improvement was observed in 60% (22/37) of patients in the ritlecitinib group compared with 14% (5/35) in the placebo group. A standardized standalone nail outcome was not reported. In the long-term extension study by Senna et al., eyebrow and eyelash responses were assessed through Month 36-38 using the EBA and Eyelash Assessment (ELA), with response defined as a ⩾2-grade improvement or a score of 3 [14]. EBA response was achieved by 63.2% of patients in the observed analysis and 48.7% using LOCF. Corresponding ELA response rates were 60.4% and 49.6%, respectively. Standardized nail outcomes were not reported. Among real-world studies, Starace et al. assessed eyebrow, eyelash, and nail involvement using Clinician-Reported Outcome (ClinRO) scales [15]. Mean ClinRO eyebrow scores decreased from 1.9 ± 1.3 at baseline to 0.7 ± 1.0 at Week 24 (P < 0.001), while mean eyelash scores decreased from 1.7 ± 1.3 to 0.7 ± 1.0 (P < 0.001). Overall mean ClinRO Nail Appearance scores also decreased from 0.3 ± 0.7 to 0.1 ± 0.4 (P = 0.006). Among the 14 patients with baseline nail involvement, the mean nail score decreased from 1.6 ± 0.8 to 0.6 ± 0.8 at Week 24 (P = 0.002). Perrotta et al. clinically monitored eyebrow and eyelash involvement during follow-up but did not provide separate numerical responder rates or mean changes [16]. Similarly, Huang et al. reported that 61.1% (11/18) of patients had eyebrow and/or eyelash alopecia at baseline but did not provide separate numerical outcomes for eyebrow, eyelash, or nail regrowth [17].

Safety, adverse events, serious adverse events, and discontinuations: All five included studies reported safety outcomes after ritlecitinib therapy [13-17]. In King et al.'s 24-week Phase 2a randomized controlled study, adverse events occurred in 67% (32/48) of patients who received ritlecitinib 50 mg, with no major adverse events (0/48) [13]. Treatment was discontinued due to adverse events in 4.2% (2/48). The most common adverse effects were nasopharyngitis (13%), headache (13%), acne (10%), upper respiratory tract infection (8%), and diarrhea (8%). Senna et al. reported the longest safety follow-up in the open-label ALLEGRO-LT extension research, which tracked 191 patients on ritlecitinib 50 mg for up to three years [14]. At least one adverse event was documented in 97.4% (186/191) of patients, with major adverse events occurring in 6.8% (13/191). Permanent treatment discontinuation due to adverse events occurred in 11.0% (21/191) over the three-year follow-up. The most frequently reported events were positive SARS-CoV-2 testing (24.1%), headache (19.9%), COVID-19 (18.3%), nasopharyngitis (17.8%), cough (15.7%), pyrexia (15.2%), upper respiratory tract infection (15.2%), and acne (12.0%). Starace et al. found that in real-world cohorts, adverse events were mainly minor across 24 weeks, with no major occurrences [15]. Treatment was stopped in 1.0% (1/102) of patients due to severe anemia (hemoglobin 9.6 g/dL). Reported adverse events included acneiform rash (4.9%), headache (3.9% at Week 4), upper respiratory tract infection (2.9% at Week 4), constipation (2.0%), fatigue (2.0%), and labial herpes simplex infection. Perrotta et al. documented adverse effects in a small proportion of patients over 24 weeks, with no significant adverse events or treatment discontinuations [16]. Acneiform responses (n = 2), transient myalgias (n = 2), asthenia (n = 1), and palpitations (n = 1) were among the reported occurrences. Huang et al. reported adverse events in 44.4% (8/18) of patients with previous JAK inhibitor treatment failure, with no serious adverse events or treatment discontinuations [17]. The most frequently reported events were acne (27.8%), urticaria (11.1%), weight gain (5.6%), fatigue (5.6%), and headache (5.6%).

Discussion

Summary of Findings

This meta-analysis assessed the efficacy and safety of ritlecitinib in patients with severe alopecia areata across five studies [13-17] with a total of 483 patients (including real-world prospective and retrospective, randomized, and long-term extension studies). Overall, ritlecitinib was clinically meaningful and progressive in scalp hair regrowth and was generally more effective as treatment was extended. In the extended study, the proportion of patients with SALT ⩽20 at Week 24 was higher (65.1%) with observed data and was between 40.2% and 44.4% across the studies in the real-world cohorts at Week 24. High-stringency regrowth was also seen, with 27.8% to 31.4% of patients in available 24-week cohorts regrowing at the highest level in the long-term study (SALT ⩽10); 52.3% regrew at the highest level in the long-term study (SALT ⩽10). In one cohort, 16.7% reported complete scalp regrowth (SALT 0) at Week 24, and 31.2% in the longer-term study.

Comparison with Previous Literature

The results of the present review are confirmed by the controlled evidence that Alfahl and Alzolibani summarized in a systematic review and meta-analysis of randomized controlled trials that assessed ritlecitinib in SALT ⩽20 [18]. Their aggregated analysis showed significant differences between ritlecitinib and placebo at Weeks 12 and 24 in SALT scores, which is clinically meaningful scalp hair regrowth in the present review. Similarly, Piliang et al. performed an integrated analysis of the ALLEGRO Phase 2b/3 and Phase 3 long-term studies and found that the efficacy of SALT ⩽20 continued to improve through Month 24, suggesting progressive improvement in efficacy with longer exposure to the treatment [19]. Tziotzios et al. reported sustained efficacy through Month 24 across patients with varying baseline scalp hair loss results in the ALLEGRO-LT Phase 3 open-label study, supporting the progressive response seen in our review [5]. This growing response to SALT ⩽20 observed over time with ritlecitinib treatment is consistent with the overall clinical development program for ritlecitinib.

Furthermore, the results are also consistent with the previous evidence provided by JAK inhibitors for high-stringency scalp regrowth (SALT ⩽10, SALT90 and SALT 0). A systematic review and meta-analysis by Yan et al. showed that the majority of JAK inhibitors exhibited acceptable short-term safety profiles [20]. Another systematic review and meta-analysis found that JAK inhibitors were associated with hair regrowth compared with placebo [21]. Mao et al. assessed six randomized controlled trials and 26 observational studies in their systematic review and meta-analysis and found that the SALT50 and SALT90 were higher in patients on JAK inhibitors, with an overall trend for notable scalp regrowth shown from the observational studies compared with baseline [22]. These analyses included several JAK inhibitors and not ritlecitinib specifically, but these analyses offer supporting evidence that more scalp regrowth may be possible with JAK-pathway inhibition. This is consistent with the cumulative progression of SALT ⩽10 and SALT 0 responses in long-term ritlecitinib treatment in our review.

Additionally, previous literature also supports the findings of the continuous improvement of SALT. In their systematic review and meta-analysis of controlled trials, Alfahl and Alzolibani reported pooled mean changes in SALT score in favor of ritlecitinib over placebo at both Week 12 and Week 24 [18]. Phan and Sebaratnam, in their meta-analysis including multiple JAK inhibitors and treatment regimens, found that the oral route was significantly associated with response to treatment compared to topical therapy [23]. The overall results of these studies corroborate the overall drop in mean SALT scores seen in the cohorts in the current review.

The present results align with findings from the literature on ritlecitinib and other JAK inhibitors for eyebrow and eyelash efficacy. Piliang et al. analyzed both the EBA and ELA responses in their integrated 24-month assessment and showed clinically meaningful improvement over long-term treatment with ritlecitinib [19]. A systematic review of controlled trials of ritlecitinib and a meta-analysis conducted by Alfahl and Alzolibani also found improvement in the condition of the eyebrows and eyelashes of ritlecitinib-treated patients [18]. The results corroborate the notion that ritlecitinib may offer more than just hair regrowth. This is clinically significant because eyebrow/eyelash loss is readily apparent and can be a nuisance even when scalp hair starts to regrow.

There is less evidence of nail involvement than for scalp, eyebrow, and eyelash outcomes. However, few studies have evaluated extracranial manifestations of AA consistently across JAK-inhibitor studies, and there is significant variability in the definitions of outcomes and the outcomes reported in these studies. Thus, while the present review found that there was some improvement in nail scores in one real-life population, there were few comparable nail-specific outcomes available to assess consistency and/or magnitude of this effect fully.

A scoping review by Xia et al. highlighted substantial heterogeneity in clinician-reported and patient-reported outcome measures used in clinical research [24]. SALT was identified as the most frequently used clinician-reported measure, although inconsistencies in outcome assessment across studies remained evident. These findings emphasize the importance of standardized and reliable outcome measures when evaluating treatment efficacy. In this context, the positive SALT improvements observed in our review, along with the increasing number of stringent treatment responses, provide clinically relevant evidence of hair regrowth following ritlecitinib treatment.

Overall, the safety profile of ritlecitinib was similar to the known safety profile of the compound. In an integrated analysis of the ALLEGRO clinical program involving 1294 patients, King et al. reported most adverse events were not serious, with commonly reported events including headache, SARS-CoV-2 positivity, and nasopharyngitis [25]. They found no safety profile differences for the various exposure durations. Piliang et al. performed an integrated safety analysis of ritlecitinib in a post hoc analysis of the ALLEGRO phase 2b/3 trial; the proportion of patients developing adverse events was 87.1% with or without the loading dose of ritlecitinib 50 mg; serious adverse events were 6.8%, and adverse events resulting in discontinuation were 8.1% [26]. The higher incidence of adverse events seen in the longer-term study in our review as compared to the shorter 24-week studies is relevant to the findings above.

Alfahl and Alzolibani, in their systematic review and meta-analysis of controlled trials, identified that headache, acne, and nasopharyngitis occurred more commonly with ritlecitinib while serious adverse events were seen more in the placebo groups [18]. Likewise, Mao et al. examined randomized and observational studies of JAK inhibitors [22]. They reported that side effects were noted during treatment, but the safety profile was deemed acceptable for the studies that were reviewed. The results corroborate the overall positive short-term tolerability reported from the 24-week studies we reviewed.

The BRAVE-AA1 and BRAVE-AA2 Phase 3 randomized trials of baricitinib in adults with severe AA showed that baricitinib was associated with significantly more scalp hair regrowth than placebo [27]. Later, Kwon et al. assessed the 52-week results of the BRAVE-AA program, demonstrating that continued scalp hair treatment could maintain or enhance scalp hair responses [28]. The results of this other JAK inhibitor align with the overall notion that perhaps more sustained pathway inhibition is needed to keep hair regrowth and further strengthen it in severe AA; but the data cannot be directly compared to ritlecitinib because of the differences between the two trials in terms of population, dose, endpoints, and trial design.

Finally, evidence of JAK-inhibitor withdrawal reinforces the need for continuing treatment for maintenance of response. In the randomized clinical trial BRAVE-AA1, King et al. compared treatment withdrawal with treatment retreatment and observed significant loss of previously achieved hair regrowth in a significant number of patients who discontinued treatment [27]. These findings are for baricitinib and cannot be directly translated to ritlecitinib, but highlight an important point for chronic AA: therapeutic response may require ongoing pathway suppression. Based on the progressive efficacy seen with prolonged ritlecitinib exposure in this review, it is important to consider treatment effectiveness on a longitudinal basis, not just by early response milestones.

Strengths

There are several strengths to this review. It used evidence from randomized, long-term extension, prospective, and retrospective studies with real-world evidence, which enables the evaluation of controlled efficacy as well as longer-term clinical outcomes. We conducted a comprehensive search of four major databases up to August 31, 2026, followed by manual screening and standardization of the results. Specific tools for assessing risk of bias were used based on study design, such as RoB2, ROBINS-I, and NOS. Multiple clinically relevant outcomes were also assessed in the review, such as SALT response thresholds, continuous SALT changes, EBA, ELA, nail outcomes, and safety.

Limitations

Importantly, a gradual response was seen with prolonged treatment duration, suggesting that longer treatment may not be optimal; continued treatment and follow-up evaluation are justified in patients. Some of the limitations of these findings should be noted. Few studies met the inclusion criteria (483 patients in total), and few were randomized, which limited conclusions about causality. There was significant variation in study design, patient populations, duration of follow-up, and outcome definitions and reporting. The long-term open-label study had a high risk of bias due to the lack of a concurrent control group, and it had substantial missing data; real-world cohorts were single-arm studies without non-exposed comparison groups.

Clinical Implications

This systematic review has a few implications for the management of severe alopecia areata. Ritlecitinib achieves clinically meaningful scalp hair regrowth, with substantial and almost complete regrowth in a subset of patients, and benefits the involvement of the eyebrows and eyelashes. Importantly, a gradual response was seen with prolonged treatment duration, suggesting that longer treatment may not be optimal; continued treatment and follow-up evaluation are justified in patients who are showing some or gradual improvement rather than deeming them treatment failures. Treatment decisions should be based on the individual patient and their specific baseline disease severity, duration of alopecia, treatment response, tolerability, and patient preference. The safety results are supportive of the use of ritlecitinib when properly monitored, especially in long-term treatment.

More adverse events and more serious adverse events were reported with longer exposure, although most adverse events were not serious. Monitoring should be continued during therapy and should focus on infections, laboratory abnormalities, and clinically important adverse events. Collectively, the evidence suggests that ritlecitinib might offer advantages other than scalp hair regrowth, such as improving eyebrows and eyelashes, which could be of special interest to those with high or cosmetically significant disease.

Conclusions

Based on this systematic review, ritlecitinib is a clinically effective treatment for severe AA that results in meaningful scalp hair regrowth and improvements in the extent of eyebrow and eyelash involvement, including potential for continued improvement with extended treatment. In a small proportion of patients,

high-stringency regrowth (SALT ≤10) and complete scalp regrowth were seen, and continuous SALT scores showed consistent improvement across the available evidence. Overall, it was generally acceptable, with most adverse events reported as non-serious, but cumulative adverse events increased with longer treatment duration.

As a whole, the results indicate that patients treated with ritlecitinib should be followed over time and treated on a patient-by-patient basis. In summary, the small number of studies, variability in study design and reporting of efficacy and safety outcomes, and lack of long-term real-world data highlight the need for larger prospective studies with standardised efficacy and safety outcomes to further define the long-term effectiveness and safety of ritlecitinib in severe AA.

Appendices

Databases	PubMed	Embase	Scopus	Cochrane
Number of records	204	298	338	6
Search Terms	("Alopecia Areata"[MeSH Terms] OR "alopecia areata/drug therapy"[MeSH Terms] OR "Alopecia Areata"[Title/Abstract] OR "alopecia totalis"[Title/Abstract] OR "alopecia universalis"[Title/Abstract] OR "severe alopecia areata"[Title/Abstract]) AND ("ritlecitinib"[Title/Abstract] OR "PF-06651600"[Title/Abstract] OR "JAK3 inhibitor"[Title/Abstract] OR "Janus kinase 3 inhibitor"[Title/Abstract] OR "TEC family kinase inhibitor"[Title/Abstract] OR "JAK-3 inhibitor"[Title/Abstract])	('alopecia areata'/exp OR 'alopecia areata':ti,ab,kw OR 'alopecia totalis':ti,ab,kw OR 'alopecia universalis':ti,ab,kw) AND (ritlecitinib:ti,ab,kw OR 'pf-06651600':ti,ab,kw)	(TITLE-ABS-KEY ("alopecia areata" OR "alopecia totalis" OR "alopecia universalis") AND TITLE-ABS-KEY (ritlecitinib OR "PF-06651600"))	#1 MeSH descriptor: [Alopecia Areata] explode all trees #2 (alopecia areata OR alopecia totalis OR alopecia universalis):ti,ab,kw #3 (ritlecitinib OR PF-06651600):ti,ab,kw #4 #1 OR #2 #5 #4 AND #3

TABLE 4: Search terms used

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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References

1. Pratt CH, King LE Jr, Messenger AG, Christiano AM, Sundberg JP: Alopecia areata. Nat Rev Dis Primers. 2017, 3:17011. 10.1038/nrdp.2017.11
2. Trüeb RM, Dias MF: Alopecia areata: a comprehensive review of pathogenesis and management . Clin Rev Allergy Immunol. 2018, 54:68-87. 10.1007/s12016-017-8620-9
3. Strazzulla LC, Wang EH, Avila L, Lo Sicco K, Brinster N, Christiano AM, Shapiro J: Alopecia areata: disease characteristics, clinical evaluation, and new perspectives on pathogenesis. J Am Acad Dermatol. 2018, 78:1-12. 10.1016/j.jaad.2017.04.1141
4. Mirzoyev SA, Schrum AG, Davis MD, Torgerson RR: Lifetime incidence risk of alopecia areata estimated at 2.1% by Rochester Epidemiology Project, 1990-2009. J Invest Dermatol. 2014, 134:1141-2. 10.1038/jid.2013.464
5. Tziotzios C, Sinclair R, Lesiak A, et al.: Long-term safety and efficacy of ritlecitinib in adults and adolescents with alopecia areata and at least 25% scalp hair loss: results from the ALLEGRO-LT phase 3, open-label study. J Eur Acad Dermatol Venereol. 2025, 39:1152-62. 10.1111/jdv.20526
6. Rudnicka L, Arenbergerova M, Grimalt R, et al.: European expert consensus statement on the systemic treatment of alopecia areata. J Eur Acad Dermatol Venereol. 2024, 38:687-94. 10.1111/jdv.19768
7. Blair HA: Ritlecitinib: first approval. Drugs. 2023, 83:1315-21. 10.1007/s40265-023-01928-y
8. Page MJ, McKenzie JE, Bossuyt PM, et al.: The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021, 372:n71. 10.1136/bmj.n71
9. Cumpston MS, McKenzie JE, Welch VA, Brennan SE: Strengthening systematic reviews in public health: guidance in the Cochrane Handbook for Systematic Reviews of Interventions, 2nd edition. J Public Health (Oxf). 2022, 44:e588-92. 10.1093/pubmed/fdac036
10. Sterne JA, Savović J, Page MJ, et al.: RoB 2: a revised tool for assessing risk of bias in randomised trials . BMJ. 2019, 366:l4898. 10.1136/bmj.l4898
11. Sterne JA, Hernán MA, Reeves BC, et al.: ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ. 2016, 355:i4919. 10.1136/bmj.i4919
12. Stang A: Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol. 2010, 25:603-5. 10.1007/s10654-010-9491-z
13. King B, Guttman-Yassky E, Peeva E, et al.: A phase 2a randomized, placebo-controlled study to evaluate the efficacy and safety of the oral Janus kinase inhibitors ritlecitinib and brepocitinib in alopecia areata: 24-week results. J Am Acad Dermatol. 2021, 85:379-87. 10.1016/j.jaad.2021.03.050
14. Senna M, Soung J, Figueras I, et al.: Long-term efficacy and safety of ritlecitinib in adults and adolescents with alopecia areata: 3-year results from the ALLEGRO Phase 2b/3 and ALLEGRO-LT Phase 3 clinical studies. Am J Clin Dermatol. 2026, 27:1091-105. 10.1007/s40257-026-01029-y
15. Starace M, Rapparini L, Pampaloni F, et al.: Ritlecitinib for severe alopecia areata: a 24-week, multicentre, real-world study. Am J Clin Dermatol. 2026, 27:621-30. 10.1007/s40257-026-01022-5
16. Perrotta N, Fiorito LA, Vescovo R, et al.: Trichoscopic markers and clinical response patterns with ritlecitinib in severe alopecia areata: 24-week outcomes from a prospective real-world cohort. Dermatol Ther. 2026, 2026:1771776. 10.1155/dth/1771776
17. Huang J, Jian J, Li M, et al.: Use of ritlecitinib in patients with alopecia areata refractory to tofacitinib or baricitinib: a single-center retrospective cohort study. J Am Acad Dermatol. 2026, 94:351-3. 10.1016/j.jaad.2025.09.053
18. Alfahl SO, Alzolibani A: Safety and efficacy of ritlecitinib for the treatment of patients with alopecia areata: a systematic review and meta-analysis of controlled trials. J Clin Med. 2025, 14:1817. 10.3390/jcm14061817
19. Piliang M, Soung J, King B, et al.: Efficacy and safety of the oral Janus kinase 3/tyrosine kinase expressed in hepatocellular carcinoma family kinase inhibitor ritlecitinib over 24 months: integrated analysis of the ALLEGRO phase IIb/III and long-term phase III clinical studies in alopecia areata. Br J Dermatol. 2025, 192:215-27. 10.1093/bjd/ljae365
20. Yan T, Wang T, Tang M, Liu N: Comparative efficacy and safety of JAK inhibitors in the treatment of moderate-to-severe alopecia areata: a systematic review and network meta-analysis. Front Pharmacol. 2024, 15:1372810. 10.3389/fphar.2024.1372810
21. Liu M, Gao Y, Yuan Y, Yang K, Shen C, Wang J, Tian J: Janus kinase inhibitors for alopecia areata: a systematic review and meta-analysis. JAMA Netw Open. 2023, 6:e2320351. 10.1001/jamanetworkopen.2023.20351
22. Mao MQ, Ding YX, Jing J, et al.: The evaluation of JAK inhibitors on effect and safety in alopecia areata: a systematic review and meta-analysis of 2018 patients. Front Immunol. 2023, 14:1195858. 10.3389/fimmu.2023.1195858
23. Phan K, Sebaratnam DF: JAK inhibitors for alopecia areata: a systematic review and meta-analysis . J Eur Acad Dermatol Venereol. 2019, 33:850-6. 10.1111/jdv.15489
24. Xia E, Li SJ, Drake L, Reyes-Hadsall S, Mita C, Drucker AM, Mostaghimi A: An assessment of current clinician-reported and patient-reported outcome measures for alopecia areata: a scoping review. J Invest Dermatol. 2023, 143:1133-7.e12. 10.1016/j.jid.2023.02.020
25. King B, Mirmirani P, Lo Sicco K, et al.: Patterns of clinical response in patients with alopecia areata treated with ritlecitinib in the ALLEGRO clinical development programme. J Eur Acad Dermatol Venereol. 2025,

39:1163-73. 10.1111/jdv.20547

26. Piliang M, Lynde C, King B, 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, 92:276-84. 10.1016/j.jaad.2024.09.064
27. King B, Ohyama M, Kwon O, et al.: Two phase 3 trials of baricitinib for alopecia areata . N Engl J Med. 2022, 386:1687-99. 10.1056/NEJMoa2110343
28. 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, 24:443-51. 10.1007/s40257-023-00764-w