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SYSTEMATIC REVIEW OF ORAL JANUS KINASE INHIBITORS IN ALOPECIA AREATA: INSIGHTS FROM 2020 TO 2025 STUDIES

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ABSTRACT

Background: Alopecia areata (AA) is an autoimmune, non-scarring hair loss disorder with variable clinical presentations. Its pathogenesis involves immune privilege collapse of the hair follicle, CD8+ T-cell activation, and cytokine signaling—particularly IFN-γ and IL-15—via the JAK/STAT pathway. Recent studies highlight Janus kinase (JAK) inhibitors as promising therapeutic agents for moderate-to-severe AA.
Objectives: This systematic review aimed to evaluate the efficacy and safety of oral JAK inhibitors in the treatment of adolescent and adult patients with AA based on studies published between 2020 and 2025.
Material and Methods: Following PRISMA 2020 guidelines, a comprehensive search of PubMed, Cochrane Library, and ClinicalTrials.gov was conducted for studies assessing oral JAK inhibitors (e.g., baricitinib, ritlecitinib, deuruxolitinib) in AA. Inclusion criteria encompassed RCTs, observational studies, and interventional trials involving patients ≥12 years old with moderate-to-severe AA.
Results: Ten studies met the criteria, including seven RCTs. Efficacy was measured predominantly by the Severity of Alopecia Tool (SALT) score. Baricitinib and deuruxolitinib consistently demonstrated superior outcomes compared to placebo and traditional therapies, with up to 41.5% of patients achieving SALT ≤20 at 24 weeks. Long-term data confirmed sustained benefits. Adverse events were mostly mild (e.g., URTI, headache, acne); serious events and discontinuations were rare.
Conclusions: Oral JAK inhibitors represent an effective and generally well-tolerated option for treating moderate-to-severe AA. Their targeted mechanism offers advantages over traditional immunosuppressants, and accumulating long-term data support their integration into therapeutic guidelines.

KEYWORDS

Alopecia Areata, Janus Kinase Inhibitors, SALT, Treatment Outcome

CITATION

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Introduction

Alopecia areata (AA) is a chronic, immune-mediated, nonscarring hair loss disorder with an estimated lifetime prevalence of 2% globally, affecting all age groups, genders, and ethnicities. [1,2] While the annual incidence is approximately 20.9 per 100,000 person-years, clinical manifestations vary from localized patches of hair loss to complete scalp involvement (alopecia totalis, AT) or total body hair loss (alopecia universalis, AU). [3]

AA is frequently associated with other autoimmune diseases such as autoimmune thyroiditis, vitiligo, systemic lupus erythematosus, and atopic dermatitis. [4,5] Psychiatric comorbidities like anxiety and depression are also common due to the visible nature of hair loss and its negative impact on self-image and quality of life. Indeed, more than half of patients report a significant psychosocial burden, often exacerbated by the unpredictable course of the disease and frequent relapses. [1,3]

The etiology of AA is multifactorial and remains only partially elucidated. At the core of its pathogenesis lies a complex interplay between genetic predisposition, immune system dysregulation, and environmental influences. Genetic studies, including genome-wide association studies (GWAS), have identified several susceptibility loci related to immune modulation (e.g., IL2RA, CTLA4, IL15, ULBP3, HLA-DQA1) and hair follicle biology (e.g., STX17, PRDX5), indicating that both immune and structural components contribute to disease susceptibility. [5,6]

Environmental triggers are considered key in activating the disease in genetically predisposed individuals. These include infections, vaccinations, trauma, hormonal changes, and even psychosocial stress, which may act via activation of the hypothalamic–pituitary–adrenal (HPA) axis, modulating cytokine production and impairing immune tolerance. [3,5] Alterations in gut microbiota composition have also been implicated, supporting the role of the gut-skin-immune axis in AA pathogenesis. [4]

One of the earliest events in AA is thought to be the collapse of the immune privilege (IP) of the hair follicle. Under normal conditions, the anagen hair follicle maintains IP through low MHC expression and the local secretion of immunosuppressive cytokines (e.g., TGF-β1, IL-10, α-MSH). Breakdown of this protective barrier leads to enhanced antigen presentation, recruitment of autoreactive CD8+ NKG2D+ T-cells, and secretion of IFN-γ and IL-15, initiating a cytotoxic cascade that targets the follicular epithelium. [4-6]

This convergence of genetic, immunologic, and environmental factors forms the rationale for the use of targeted therapies, particularly Janus kinase (JAK) inhibitors, which act by blocking downstream signaling of multiple cytokines involved in AA pathogenesis. These agents represent a promising direction in the treatment of this often relapsing and psychologically burdensome disease.

Pathogenesis of Alopecia Areata

The pathogenesis of alopecia areata (AA) revolves around the collapse of the hair follicle's immune privilege (IP), a local immunosuppressive microenvironment that normally prevents autoimmune responses against follicular antigens. [7,8] Under physiological conditions, the proximal anagen hair bulb expresses low levels of MHC class I molecules and is devoid of antigen-presenting cells. In addition, local production of immunomodulatory cytokines such as TGF-β1, IL-10, and α-MSH contributes to maintaining this immune privilege. [7,9]

Disruption of IP leads to the aberrant expression of major histocompatibility complex (MHC) class I and II molecules on follicular epithelial cells, enabling antigen presentation. Simultaneously, ligands for activating receptors on immune cells, such as NKG2D ligands—including MICA and ULBP3—are upregulated in the hair follicle epithelium. [7,9,10] The identification of MICA and ULBP3 upregulation in AA patients has also been supported by genome-wide association studies (GWAS). [7,8,10]

This altered immunological environment facilitates infiltration of cytotoxic CD8+ NKG2D+ T lymphocytes into the peribulbar region, leading to the destruction of anagen hair follicles. These T cells release proinflammatory cytokines, primarily interferon-gamma (IFN-γ), which further exacerbate the inflammatory process and enhance local IL-15 production by follicular keratinocytes. [5,7,9] IL-15, a key cytokine in AA pathogenesis, promotes survival and activation of autoreactive memory CD8+ T cells via JAK1 and JAK3 signaling pathways. [8-10]

Together, IFN-γ and IL-15 create a pathogenic feedback loop in which follicular epithelial cells and immune cells reinforce each other's activation, thereby sustaining chronic inflammation and hair follicle destruction. This self-perpetuating circuit has been demonstrated in both human tissue and animal models of AA. [6,7,11]

These molecular insights have paved the way for targeted therapies, particularly Janus kinase (JAK) inhibitors, which block intracellular signaling cascades initiated by IFN-γ, IL-2, IL-7, IL-15, and other γ-chain cytokines implicated in AA pathophysiology. [7,9,10]

Materials and Methods

This systematic review was conducted in accordance with the PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. A comprehensive literature search was performed across PubMed, the Cochrane Library, and ClinicalTrials.gov databases between January 2020 and April 2025. The search strategy incorporated a combination of keywords and controlled vocabulary, including MeSH (Medical Subject Headings) and EMTREE terms, to enhance sensitivity and specificity. Search terms included: "alopecia areata", "Janus kinase inhibitors", "treatment outcome", "Severity of Alopecia Tool (SALT)", "tofacitinib", "baricitinib", "ritlecitinib", and "deuruxolitinib". The search strategy was tailored for each database and designed to identify studies evaluating the efficacy and/or safety of oral JAK inhibitors in the treatment of alopecia areata.

Studies were included if they met all of the following criteria: (1) involved adolescents (aged ≥12 years) or adults diagnosed with alopecia areata (AA), regardless of disease subtype (including patchy AA, alopecia totalis, or alopecia universalis), with diagnosis confirmed clinically or according to recognized diagnostic criteria; (2) involved systemic treatment with oral Janus kinase (JAK) inhibitors—such as tofacitinib, baricitinib, ritlecitinib, deuruxolitinib, or other JAK inhibitors—regardless of dose, treatment duration, or treatment line; (3) utilized a study design that included randomized controlled trials (RCTs), post-hoc analyses of RCTs, integrated safety analyses, or observational studies (both prospective and retrospective); and (4) were published between January 1, 2020, and July 1, 2025, in peer-reviewed journals or were listed in clinical trial registries (e.g., ClinicalTrials.gov) as completed studies with publicly available results. Only original studies reporting efficacy and/or safety outcomes were included, and publications were limited to English language.

Exclusion criteria included studies reporting conducted solely in pediatric populations (<12 years), case reports or case series with fewer than 10 patients, narrative reviews, editorials, or letters to the editor, studies

published in non-English languages, conference abstracts or unpublished studies without accessible full text and results, and duplicate publications, including overlapping data from the same clinical trial.

Two independent reviewers screened titles, abstracts, and full texts for eligibility. Discrepancies were resolved by discussion or consultation with a third reviewer. Data extraction was performed using a standardized form. Extracted data included: author and year, study population, type of article, JAK inhibitor used, treatment outcome, and reported side effects or adverse events. A total of ten studies met all eligibility criteria and were included in the final analysis. Key findings were summarized in a structured table format.

Results

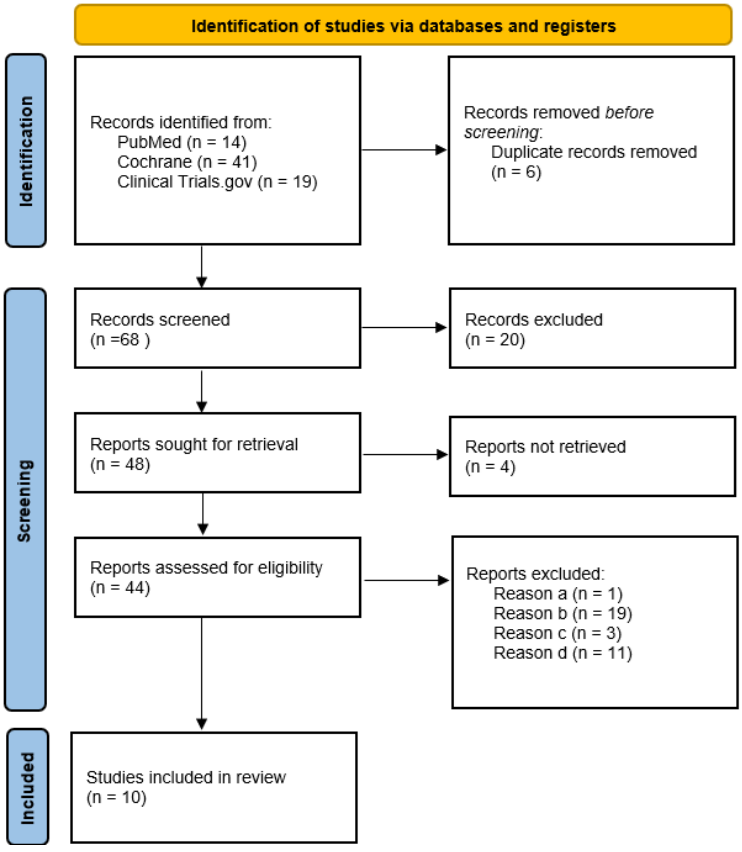
A total of ten clinical studies were included in this systematic review (Figure 1. [PRISMA]) after applying the predefined inclusion and exclusion criteria. These studies collectively evaluated the efficacy and safety of various oral Janus kinase (JAK) inhibitors in the treatment of moderate to severe alopecia areata (AA) in adolescent and adult populations. The final set of studies comprised seven randomized controlled trials (RCTs), one RCT with long-term follow-up, one retrospective observational study, and one open-label, single-arm, phase 4 interventional study.

The reviewed trials investigated multiple JAK inhibitors, including baricitinib, ritlecitinib, deuruxolitinib, tofacitinib, brepocitinib, and CTP-543 (a selective JAK1/JAK2 inhibitor). Across studies, treatment outcomes were predominantly measured using the Severity of Alopecia Tool (SALT) score, a validated and standardized tool for assessing the extent of scalp hair loss. Key efficacy endpoints included the proportion of patients achieving SALT scores ≤20 (indicating ≤20% hair loss), as well as relative improvements from baseline defined as SALT50, SALT75, or SALT90, corresponding to ≥50%, ≥75%, or ≥90% improvement in scalp hair coverage, respectively.

Secondary outcomes often included patient-reported outcome measures, eyebrow and eyelash regrowth, and overall treatment satisfaction. Most studies demonstrated favorable therapeutic responses, particularly with higher dosages and longer treatment durations. Adverse events (AEs) were commonly reported but generally mild to moderate in severity, with upper respiratory tract infections (URTI), acne, and headache among the most frequent. Serious AEs were rare, and discontinuation rates due to side effects remained low.

A detailed summary of each study's design, study population, JAK inhibitor used, treatment outcomes, and reported side effects is presented in Table 1 below.

Figure 1. PRISMA flow diagram detailing the search and selection process for studies evaluating treatment with oral JAK inhibitors for alopecia areata.



Reports excluded: a) Studies focusing on pediatric populations (<12 years) and cell lines; b) Ineligible study type or stage for inclusion; c) Studies published before 2020; d) Duplicate reporting of clinical trial results.

Table 1. Summary of Literature on the relationship between Alopecia Areata and treatment with oral JAK inhibitors

Author and year	Study population	Type of the article	JAK Inhibitor Used	Treatment Outcome	Side effects/ AEs
Dash et al., 2025 [12]	84 patients with severe AA (≥50% scalp hair loss, AT or AU) baricitinib 4 mg daily n=42, methotrexate 15 mg weekly n=42	Randomized Controlled Trial	Baricitinib	After 6 months: SALT90 (complete response) in 57.1% (vs. 0% in MTX group), SALT75 in 19%, SALT50 in 14.3%; statistically significant superiority of baricitinib over methotrexate.	-common: URTI (14.3%), acne (7.1%), headache (4.8%), hyperlipidaemia (11.9%) -no serious AEs or treatment discontinuations reported
Vignoli et al., 2025 [13]	96 patients with severe AA from 11 Italian dermatology centers (baricitinib 4 mg/day)	Retrospective Observational Study	Baricitinib	After 52 weeks, 61.5% of patients achieved SALT ≤ 20; among those with very severe AA, 56% reached this goal. Eyebrow and eyelash regrowth were also significant, with 67.6% and 69.7% of patients showing ≥2-point improvements in ClinRO EB and EL, respectively. Improvements were steady over time.	-common: URTI, headache, acne, asthenia, hypercholesterolemia -mild or moderate
Mesinkovska et al., 2024 [14]	718 patients with ≥50% scalp hair loss due to AA(supgroups AT, AU, AT/AU, non-AT/AU); (placebo n = 131, Ritlecitinib 30mg/day n=132, Ritlecitinib 50mg/day n=130, Ritlecitinib 200/30mg daily n=130, Ritlecitinib 200/50mg daily n=132)	Randomised Controlled Trial	Ritlecitinib	At week 24: 7–21% of AT and 4–10% of AU patients treated with ritlecitinib (≥30 mg) achieved SALT ≤20 vs. 0% in placebo; results increased to 11–41% at week 48. PGI-C improvement and satisfaction with hair growth generally increased or were maintained through week 48 across all AA subgroups.	-common: nasopharyngitis, URTI, folliculitis, headache, acne -serious AEs (e.g., pulmonary embolism, sepsis, breast cancer) rare -discontinuation due to AEs ≤5%

King et al., 2024 [15]	706 patients with ≥50% scalp hair loss due to AA (placebo n = 140, Deuruxolitinib 8 mg BID n = 351, Deuruxolitinib 12 mg BID n = 215)	Randomised Controlled Trial	Deuruxolitinib	At week 24, significantly higher proportions of patients treated with deuruxolitinib achieved a SALT score ≤20 (29.6% with 8 mg BID; 41.5% with 12 mg BID) compared to placebo (0.8%). Patient satisfaction (SPRO responders) was also higher in both treatment groups (42.1% and 53.0% vs. 4.7%). Treatment was generally well tolerated.	-mild or moderate in severity -common: headache, acne, and elevated creatine phosphokinase
Senna et al., 2024 [16]	Patients with AA from BRAVE-AA1 and BRAVE-AA2 Phase 3 trials continuing treatment (Week-52 responders; 2-mg: n=65; 4-mg: n=129) (Week-52 mixed responders; N=110)	Randomised Controlled Trial (long-term follow-up)	Baricitinib	Among Week-52 responders treated with baricitinib 4 mg and 2 mg, 90.7% and 89.2%, respectively, maintained a SALT score ≤20 at Week 104. In the group of Week-52 mixed responders, 39.1% achieved a SALT score ≤20 by Week 104. Continued improvement in eyebrow and eyelash regrowth was observed across all groups.	-common: COVID-19, URTI, headache, nasopharyngitis, acne, UTI, ↑CPK -mostly mild or moderate -serious AEs rare (~5%) -discontinuation due to AEs: ~3%
Kwon et al., 2023 [17]	855 adult patients with ≥50% scalp hair loss due to AA (BRAVE-AA1 n = 465, BRAVE-AA2 n = 390) Baricitinib (2 mg/day and 4 mg/day)	Randomised Controlled Trial	Baricitinib	After 52 weeks of continuous treatment, 40.9% (4 mg) and 21.2% (2 mg) of patients in BRAVE-AA1, and 36.8% (4 mg) and 24.4% (2 mg) in BRAVE-AA2 achieved a SALT score ≤20, indicating ≤20% scalp hair loss. Improvements in eyebrow and eyelash regrowth were also observed. Clinical responses increased steadily throughout the 52-week period, suggesting that long-term treatment may be necessary to achieve optimal outcomes.	-common: URTI, headache, acne, nasopharyngitis, UTI, ↑CPK, COVID-19 - mostly mild or moderate - serious AEs rare
King et al., 2022 [18]	149 patients with ≥50% scalp hair loss due to AA (placebo n=44, CTP-543 4 mg BID n=30, CTP-543 8 mg BID n=38,CTP-543 12 mg BID n=37)	Randomised Controlled Trial	CTP-543 (JAK1/ JAK2 Inhibitor)	At week 24, ≥50% SALT improvement was observed in 21% (4 mg BID), 47% (8 mg BID), and 58% (12 mg BID) vs. 9% in placebo. SALT90 achieved in 0% (4 mg), 16% (8 mg), 36% (12 mg) vs. 2% in placebo. Patient-reported outcomes and quality of life measures improved significantly in 8 and 12 mg groups.	-common: headache, nasopharyngitis, acne, URTI -mostly mild or moderate -no dose-dependent trend -one serious AE (cellulitis) in 12 mg group

King et al., 2021 [19]	142 patients with ≥50% scalp hair loss due to AA (Ritlecitinib n = 48, Brepocitinib n = 47, placebo n = 47)	Randomised Controlled Trial	Ritlecitinib, Brepocitinib	At week 24, SALT30 was achieved by 50% (ritlecitinib) and 64% (brepocitinib) vs. 2% in placebo. SALT90 was achieved by 25% (ritlecitinib) and 34% (brepocitinib) vs. 0% in placebo. Treatment was generally well tolerated.	-common: headache, nasopharyngitis, acne, URTI -two serious AEs (rhabdomyolysis) in brepocitinib group
Concert Pharmaceuticals, 2021 [20]	517 patients with ≥50% scalp hair loss due to AA	Randomised Controlled Trial	CTP-543 (JAK1/ JAK2 Inhibitor)	After 24 weeks, 38.3% of patients in the 12 mg twice-daily group and 33.0% in the 8 mg twice-daily group achieved a SALT score of less than 20, compared to only 0.8% of patients receiving placebo (P < 0.0001). Treatment was generally well tolerated.	-common: headache, acne, nasopharyngitis, increased creatine kinase levels -mild or moderate -discontinuation due to AEs was low
Institute of Dermatology, Thailand, 2021 [21]	19 patients with extensive and recalcitrant AA (Tofacitinib 5 mg BID)	Open-Label, Single-Arm, Phase 4 Interventional Study	Tofacitinib	Baseline SALT: 95.11 (±14.24); 9 patients (47.4%) achieved ≥50% SALT improvement (responders); 10 patients (52.6%) had <50% improvement (non-responders)	-dyslipidemia,URTI, acne, tuberculosis, myalgia, weight gain, constipation

AEs – Adverse Events, AA – Alopecia Areata, n – number of patients, BID – *Bis in die* (twice daily), SALT – Severity of Alopecia Tool, SALT90 – At least a 90% improvement from baseline in SALT score, SALT75 – At least a 75% improvement from baseline in SALT score, SALT50 – At least a 50% improvement from baseline in SALT score, SALT30 – At least a 30% improvement from baseline in SALT score, URTI – Upper Respiratory Tract Infection, AT – alopecia totalis, AU – alopecia universalis, AT/AU – alopecia totalis/alopecia universalis, non-AT/AU – patients with AA who do not have complete scalp hair loss or do not meet the clinical criteria for AT or AU, PGI-C – Patient Global Impression of Change, ClinRO EB – Clinician-Reported Outcome (Eyebrow Hair Loss), EL – Eyelash Hair Loss, SPRO – Satisfaction of Hair Patient-Reported Outcome, ↑CPK – elevated creatine phosphokinase, COVID-19 – Coronavirus Disease 2019, UTI – Urinary Tract Infection, ↑AST/ALT – elevated liver enzymes (Aspartate/Alanine Aminotransferase), GI – Gastrointestinal

Discussion

In recent years, oral Janus kinase (JAK) inhibitors have revolutionized the therapeutic approach to alopecia areata (AA), especially in its severe forms. Until recently, treatment largely relied on corticosteroids and non-specific immunosuppressants such as methotrexate, which were limited in efficacy and often associated with adverse effects.

The most extensive clinical data regarding the efficacy and safety of baricitinib come from the BRAVE-AA1 and BRAVE-AA2 trials. After 52 weeks of treatment with baricitinib 4 mg daily, 40.9% of patients in BRAVE-AA1 and 36.8% in BRAVE-AA2 achieved a SALT score ≤20. For the 2 mg dose, the respective outcomes were 21.2% and 24.4%. [17] At 104 weeks, 90.7% of 4 mg and 89.2% of 2 mg responders maintained a SALT ≤20, while among the Week-52 mixed responders, 39.1% reached this threshold. [16]

These findings indicate that baricitinib's therapeutic response may be gradual and cumulative, with maximal benefit potentially requiring more than one year of continuous treatment. Long-term therapy was not associated with emergent safety signals; the most commonly reported adverse events (AEs) included mild upper respiratory tract infections, headache, acne, and elevated creatine kinase levels. [16]

A randomized controlled trial from Bangladesh compared baricitinib with methotrexate in patients with severe AA. After 6 months, patients receiving baricitinib demonstrated significantly greater SALT score reductions (from 71.1 to 13.2) than those on methotrexate (from 65.4 to 51.3), with 57.1% achieving SALT90 versus 0% in the methotrexate group. [12] These results strongly support the superior efficacy of baricitinib in this clinical context.

Further confirmation comes from a real-world, retrospective, multicenter study conducted in Italy, in which 61.5% of patients achieved SALT ≤20 after 52 weeks of baricitinib 4 mg daily. [13] These real-life data align closely with clinical trial findings, validating the utility of baricitinib outside controlled research environments.

Ritlecitinib, a selective JAK3/TEC family inhibitor, has also demonstrated promise in AA management. In the ALLEGRO-2b/3 study, among patients with alopecia totalis or universalis, SALT ≤20 was achieved by 11–41% by Week 48 depending on dose and subgroup. [14] Earlier data from the ALLEGRO-2a trial showed that 50% of patients on ritlecitinib and 64% on brepocitinib reached SALT30 at 24 weeks, although serious adverse events (e.g., rhabdomyolysis) occurred in the brepocitinib arm. [19]

Deuruxolitinib (CTP-543), a selective JAK1/2 inhibitor, yielded similarly encouraging results in both Phase 2 and 3 trials. In the THRIVE-AA1 trial, 29.6% of patients receiving 8 mg twice daily and 41.5% of those receiving 12 mg twice daily achieved SALT ≤20 after 24 weeks, with significant improvements in patient-reported outcomes. [15] Dose-response data from Phase 2 further support its efficacy, with SALT50 reached by 47% and 58% of patients at 8 mg and 12 mg twice daily, respectively. [18]

In addition to the published THRIVE-AA1 Phase 3 trial, another pivotal randomized controlled trial - THRIVE-AA2 further confirmed the efficacy of deuruxolitinib in patients with ≥50% scalp hair loss. After 24 weeks of treatment, 38.3% of patients receiving 12 mg BID and 33.0% receiving 8 mg BID achieved a SALT score <20, compared to only 0.8% in the placebo group ($P < 0.0001$), underscoring a robust dose-dependent response to treatment.

The safety profile remained favorable, with most adverse events classified as mild to moderate. The most frequently reported events included headache, acne, nasopharyngitis, and elevated creatine kinase levels. Importantly, treatment discontinuation due to adverse events was low, reinforcing the tolerability of deuruxolitinib across dosing regimens. [20]

A Phase 4 open-label study conducted by the Institute of Dermatology in Thailand evaluated tofacitinib 5 mg twice daily in 19 patients with extensive and treatment-resistant AA. A clinical response, defined as ≥50% improvement in SALT scores, was observed in 47.4% of patients, while 52.6% showed less than 50% improvement. Adverse events were more diverse compared to other JAK inhibitors and included dyslipidemia, upper respiratory tract infections, acne, myalgia, weight gain, constipation, and a single case of tuberculosis. While most events were manageable, these findings highlight the importance of patient monitoring and individualized risk assessment when considering tofacitinib for recalcitrant AA. [21]

Current Therapeutic Guidelines and the Role of JAK Inhibitors

According to the recommendations of the Polish Dermatological Society, the severity of AA—measured using tools such as the SALT score—should directly inform therapeutic decisions, ranging from topical corticosteroids for mild cases to systemic therapy for more severe forms. [22] Although JAK inhibitors are not yet universally recognized as first-line treatments in many countries, growing clinical trial data and real-world evidence strongly support their superiority over traditional therapies. [23,24]

A recent network meta-analysis (NMA) comparing the relative efficacy of monotherapies found that FDA-approved JAK inhibitors—baricitinib, deuruxolitinib, and ritlecitinib—ranked among the most effective treatments for achieving SALT ≤20 at week 24. Deuruxolitinib 12 mg BID was the top-performing regimen (SUCRA = 92.6%). [25]

Limitations of Traditional Therapies

While topical and intralesional corticosteroids remain commonly used, especially for mild-to-moderate AA, their efficacy is limited, and relapses after discontinuation are frequent. [26] A retrospective study showed that baricitinib outperformed both topical immunomodulators and conventional systemic immunosuppressants (e.g., methotrexate), demonstrating better outcomes in SALT score reduction and achieving SALT ≤10. [23]

The Microbiome in AA Pathogenesis

Emerging evidence strongly supports the involvement of both gut and skin microbiota in the pathogenesis of alopecia areata (AA), aligning with patterns seen in other autoimmune diseases. Dysbiosis —

a microbial imbalance — may disrupt immune homeostasis and contribute to the collapse of immune privilege at the hair follicle level. This breakdown facilitates $CD8^{+}NKG2D^{+}$ T-cell infiltration and activation, with increased production of pro-inflammatory cytokines such as interferon-γ (IFN-γ) and interleukin-15 (IL-15), primarily via the JAK–STAT pathway. [27,28]

Alterations in the scalp and follicular microbiome of AA patients have been documented, including a decreased abundance of *Staphylococcus epidermidis* and *Acinetobacter*, and an increased presence of *Cutibacterium acnes* and *Neisseria* spp.. [28,29] Additionally, intestinal dysbiosis has been associated with AA, with specific bacterial markers such as *Parabacteroides distasonis*, *Clostridiales vadin BB60*, and *Ruminococcus bicirculans* identified in stool samples of AA patients. [27]

Interestingly, microbiota-modulating interventions — including probiotics and fecal microbiota transplantation (FMT) — have led to unexpected improvements in hair regrowth in some AA patients, indicating a potential therapeutic role. [29,30]

Furthermore, mechanistic links between the microbiome and key inflammatory signaling pathways in AA (e.g., JAK–STAT, TGF-β, and Wnt/β-catenin) suggest that microbial metabolites may influence immune responses and hair follicle cycling. [27] As research progresses, individualized microbiome profiling may facilitate tailored treatments and enhance prediction of therapeutic responses — especially for immunomodulatory agents such as JAK inhibitors. [28]

Topical JAK Inhibitors

Topical JAK inhibitors (JAKi) are gaining attention as a localized treatment option for alopecia areata (AA), offering potential efficacy with reduced systemic side effects. As noted by Solimani et al. (2019), the JAK/STAT pathway is central to AA pathogenesis, and targeting it topically may modulate local inflammation without broader immunosuppression. [31]

In a phase I double-blind study, Bokhari and Sinclair evaluated 2% tofacitinib and 1% ruxolitinib ointments in patients with alopecia universalis. Partial hair regrowth was observed in areas treated with both agents, with tofacitinib showing slightly better outcomes. No significant adverse effects were reported, and generalized regrowth in two patients suggested possible systemic absorption. [32]

These early results support the further investigation of topical JAKi as a safe and potentially effective alternative for patients with localized or treatment-resistant AA.

Conclusions

Between 2020 and 2025, a growing body of evidence has firmly established oral Janus kinase (JAK) inhibitors as a transformative therapeutic option in the management of moderate to severe alopecia areata (AA). Data from multiple randomized controlled trials, long-term extension studies, and real-world observational cohorts consistently demonstrate that agents such as baricitinib, deuruxolitinib, and ritlecitinib not only significantly improve scalp hair regrowth—as measured by SALT outcomes—but also enhance patient-reported satisfaction and quality of life. Among these, baricitinib and deuruxolitinib exhibit the most robust and sustained responses, particularly at higher doses and over prolonged treatment durations.

Although adverse events are relatively common, they are generally mild to moderate in severity, and the incidence of treatment discontinuation remains low. Nonetheless, ongoing vigilance regarding long-term safety is essential, especially when considering tofacitinib or higher-risk patient populations.

Despite promising results, several challenges remain. Traditional therapies still dominate first-line treatment, and access to JAK inhibitors is often limited by cost. Furthermore, heterogeneity in study populations and endpoints complicates direct comparisons across trials.

Looking ahead, integrating microbiome research, refining patient selection criteria, and expanding studies on topical formulations may further optimize treatment strategies. Ultimately, oral JAK inhibitors represent a major advancement in AA therapy, offering new hope to patients previously unresponsive to conventional modalities.

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REFERENCES

1. Strazzulla, L. C., Wang, E. H. C., Avila, L., Lo Sicco, K., Brinster, N., Christiano, A. M., & Shapiro, J. (2018). Alopecia areata: Disease characteristics, clinical evaluation, and new perspectives on pathogenesis. *Journal of the American Academy of Dermatology, 78*(1), 1–12. https://doi.org/10.1016/j.jaad.2017.04.1141
2. Lee, H. H., Gwillim, E., Patel, K. R., Hua, T., Rastogi, S., Ibler, E., & Silverberg, J. I. (2020). Epidemiology of alopecia areata, ophiasis, totalis, and universalis: A systematic review and meta-analysis. *Journal of the American Academy of Dermatology, 82*(3), 675–682. https://doi.org/10.1016/j.jaad.2019.08.032
3. Abarca, Y. A., Scott-Emuakpor, R., Tirth, J., Moroz, O., Thomas, G. P., Yateem, D., & Alhusayen, R. (2025). Alopecia areata: Understanding the pathophysiology and advancements in treatment modalities. *Cureus, 17*(1), e78298. https://doi.org/10.7759/cureus.78298
4. Sterkens, A., Lambert, J., & Bervoets, A. (2021). Alopecia areata: A review on diagnosis, immunological etiopathogenesis and treatment options. *Clinical and Experimental Medicine, 21*(2), 215–230. https://doi.org/10.1007/s10238-020-00673-w
5. Zhou, C., Li, X., Wang, C., & Zhang, J. (2021). Alopecia areata: An update on etiopathogenesis, diagnosis, and management. *Clinical Reviews in Allergy and Immunology, 61*(3), 403–423. https://doi.org/10.1007/s12016-021-08883-0
6. Lensing, M., & Jabbari, A. (2022). An overview of JAK/STAT pathways and JAK inhibition in alopecia areata. *Frontiers in Immunology, 13*, 955035. https://doi.org/10.3389/fimmu.2022.955035
7. Park, H., Yu, D. A., & Kwon, O. (2019). Janus kinase inhibitors: An innovative treatment for alopecia areata. *Journal of Dermatology, 46*(8), 724–730. https://doi.org/10.1111/1346-8138.14986
8. Barati Sedeh, F., Michaelsdóttir, T. E., Henning, M. A. S., Jemec, G. B. E., & Ibler, K. S. (2023). Comparative efficacy and safety of Janus kinase inhibitors used in alopecia areata: A systematic review and meta-analysis. *Acta Dermato-Venereologica, 103*, adv00855. https://doi.org/10.2340/actadv.v103.4536
9. Shah, R. J., Banerjee, S., Raychaudhuri, S., & Raychaudhuri, S. P. (2023). JAK-STAT inhibitors in immune mediated diseases: An overview. *Indian Journal of Dermatology, Venereology and Leprology, 89*(5), 691–699. https://doi.org/10.25259/IJDVL_1152_2022
10. Favoino, E., Prete, M., Catacchio, G., Ruscitti, P., Navarini, L., Giacomelli, R., & Perosa, F. (2021). Working and safety profiles of JAK/STAT signaling inhibitors: Are these small molecules also smart? *Autoimmunity Reviews, 20*(3), 102750. https://doi.org/10.1016/j.autrev.2021.102750
11. Rakowska, A., Rudnicka, L., Olszewska, M., Bergler-Czop, B., Czuwara, J., Brzezińska-Wcisło, L., & Adamski, Z. (2023). Alopecia areata: Diagnostic and therapeutic recommendations of the Polish Dermatological Society. Part 2: Treatment. *Dermatology Review, 110*(2), 101–120. https://doi.org/10.5114/dr.2023.127811
12. Dash, P. S., Khondker, L., Khan, M. A., Talukder, M. S., Jahan, S., & Lubna, E. K. (2025). Comparison of efficacy of baricitinib versus methotrexate therapy in the treatment of severe alopecia areata. *Journal of Population Therapeutics and Clinical Pharmacology, 32*(3), 402–411. https://doi.org/10.53555/9n99h371
13. Vignoli, C. A., Gargiulo, L., Ibba, L., Balato, A., Barbareschi, M., Barruscotti, S., & Pellacani, G. (2025). Baricitinib for the treatment of severe alopecia areata: Results from a 52-week multicenter retrospective real-world study. *Journal of Dermatological Treatment, 36*(1), 2444494. https://doi.org/10.1080/09546634.2024.2444494
14. Mesinkovska, N., King, B., Zhang, X., Guttman-Yassky, E., Magnolo, N., Sinclair, R., & Senna, M. (2024). Efficacy and safety of ritlecitinib, an oral JAK3/TEC family kinase inhibitor, in adolescent and adult patients with alopecia totalis and alopecia universalis. *Journal of Dermatology, 51*(11), 1414–1424. https://doi.org/10.1111/1346-8138.17442
15. King, B., Senna, M. M., Mesinkovska, N. A., Lynde, C., Zirwas, M., Maari, C., & Guttman-Yassky, E. (2024). Efficacy and safety of deuruxolitinib, an oral selective Janus kinase inhibitor, in adults with alopecia areata: Results from the phase 3 randomized, controlled trial (THRIVE-AA1). *Journal of the American Academy of Dermatology, 91*(5), 880–888. https://doi.org/10.1016/j.jaad.2024.06.097
16. Senna, M., Mostaghimi, A., Ohyama, M., Sinclair, R., Dutronc, Y., Wu, W. S., & King, B. (2024). Long-term efficacy and safety of baricitinib in patients with severe alopecia areata: 104-week results from BRAVE-AA1 and BRAVE-AA2. *Journal of the European Academy of Dermatology and Venereology, 38*(3), 583–593. https://doi.org/10.1111/jdv.19665
17. Kwon, O., Senna, M. M., Sinclair, R., Ito, T., Dutronc, Y., Lin, C. Y., & King, B. (2023). 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). *American Journal of Clinical Dermatology, 24*(3), 443–451. https://doi.org/10.1007/s40257-023-00764-w
18. King, B., Mesinkovska, N., Mirmirani, P., Bruce, S., Kempers, S., Guttman-Yassky, E., & Sinclair, R. (2022). Phase 2 randomized, dose-ranging trial of CTP-543, a selective Janus kinase inhibitor, in moderate-to-severe alopecia areata. *Journal of the American Academy of Dermatology, 87*(2), 306–313. https://doi.org/10.1016/j.jaad.2022.03.045

19. King, B., Guttman-Yassky, E., Peeva, E., Banerjee, A., Sinclair, R., Pavel, A. B., & Zangrilli, J. G. (2021). 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. *Journal of the American Academy of Dermatology, 85*(2), 379–387. https://doi.org/10.1016/j.jaad.2021.03.050
20. Concert Pharmaceuticals, Inc. (2021). *Protocol CP543.3002: A double-blind, randomized, placebo-controlled study to evaluate the efficacy and safety of CTP-543 in adult patients with moderate to severe alopecia areata.* Concert Pharmaceuticals, Inc.
21. Institute of Dermatology, Thailand. (2019). *Effectiveness and safety of tofacitinib in patients with extensive and recalcitrant alopecia areata. ClinicalTrials.gov.* https://clinicaltrials.gov/study/NCT03800979
22. Rakowska, A., Rudnicka, L., Olszewska, M., Bergler-Czop, B., Czuwara, J., Brzezińska-Wcisło, L., & Adamski, Z. (2023). Alopecia areata: Diagnostic and therapeutic recommendations of the Polish Dermatological Society. Part 1: Diagnosis and severity assessment. *Dermatology Review, 110*(2), 89–100. https://doi.org/10.5114/dr.2023.127704
23. Stefanis, A. J., Dolezal, T., Gkalpakiotis, S., & Arenberger, P. (2025). Comparative efficacy and safety of baricitinib against traditional therapies in severe alopecia areata: A retrospective cohort study. *Journal of Cosmetic Dermatology, 24*(2), e16666. https://doi.org/10.1111/jocd.16666
24. Almutairi, N., Nour, T. M., & Hussain, N. H. (2019). Janus kinase inhibitors for the treatment of severe alopecia areata: An open-label comparative study. *Dermatology, 235*(2), 130–136. https://doi.org/10.1159/000494613
25. Gupta, A. K., Bamimore, M. A., Mirmirani, P., Piguet, V., & Talukder, M. (2025). The relative efficacy and safety of monotherapies for alopecia areata: A network meta-analysis study. *Journal of Cosmetic Dermatology, 24*(4), e70185. https://doi.org/10.1111/jocd.70185
26. Gregoire, S., McIntosh, B., Sanchez, K., Biba, U., & Mostaghimi, A. (2025). Local corticosteroids for alopecia areata: A narrative review. *Dermatology and Therapy, 15*(7), 1607–1631. https://doi.org/10.1007/s13555-025-01421-2
27. Liu, Z., & Liu, X. (2023). Gut microbiome, metabolome and alopecia areata. *Frontiers in Microbiology, 14*, 1281660. https://doi.org/10.3389/fmicb.2023.1281660
28. Sánchez-Pellicer, P., Navarro-Moratalla, L., Núñez-Delegido, E., Agüera-Santos, J., & Navarro-López, V. (2022). How our microbiome influences the pathogenesis of alopecia areata. *Genes, 13*(10), 1860. https://doi.org/10.3390/genes13101860
29. Carrington, A. E., Maloh, J., Nong, Y., Agbai, O. N., Bodemer, A. A., & Sivamani, R. K. (2023). The gut and skin microbiome in alopecia: Associations and interventions. *Journal of Clinical and Aesthetic Dermatology, 16*(10), 59–64.
30. Mahmud, M. R., Akter, S., Tamanna, S. K., Mazumder, L., Esti, I. Z., Banerjee, S., & Rahman, M. M. (2022). Impact of gut microbiome on skin health: Gut-skin axis observed through the lenses of therapeutics and skin diseases. *Gut Microbes, 14*(1), 2096995. https://doi.org/10.1080/19490976.2022.2096995
31. Solimani, F., Meier, K., & Ghoreschi, K. (2019). Emerging topical and systemic JAK inhibitors in dermatology. *Frontiers in Immunology, 10*, 2847. https://doi.org/10.3389/fimmu.2019.02847
32. Bokhari, L., & Sinclair, R. (2018). Treatment of alopecia universalis with topical Janus kinase inhibitors: A double blind, placebo, and active controlled pilot study. *International Journal of Dermatology, 57*(12), 1464–1470. https://doi.org/10.1111/ijd.14192