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Therapeutic Ranking of Oral Janus Kinase (JAK) Inhibitors for Severe Alopecia Areata: A Bayesian Network Meta-Analysis of Five Agents Across 10 Randomized Trials

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Abstract

This systematic review and Bayesian network meta-analysis (BNMA) evaluated the efficacy of five oral Janus kinase (JAK) inhibitors approved for the treatment of severe alopecia areata (AA) in one or more major regulatory markets. The study synthesized placebo-controlled randomized controlled trials (RCTs) evaluating baricitinib, ritlecitinib, deuruxolitinib, ivarmacitinib, and upadacitinib in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (International Prospective Register of Systematic Reviews (PROSPERO) registration number: CRD420261461735).

Primary and secondary outcomes were Severity of Alopecia Tool (SALT) score ⩽20 and SALT ⩽10 at week 24. Arm-level BNMA analyses were conducted using binomial likelihoods with logit links and random-effects models. Treatment effects were expressed as odds ratios (ORs) with 95% credible intervals (CrIs). In addition to relative treatment effects, placebo-adjusted response differences were calculated for each active treatment at week 24. Posterior rank probabilities, probabilities of occupying each rank, and surface under the cumulative ranking curve (SUCRA) values were estimated for each treatment.

Ten RCTs (N=5,276) contributed 26 eligible treatment arms. For SALT ⩽20, the largest effect was observed with upadacitinib 30 mg (OR 36.50; 95% CrI 16.53-83.18), followed by upadacitinib 15 mg (OR 24.68; 95% CrI 11.27-56.16) and deuruxolitinib 8 mg (OR 17.96; 95% CrI 8.05-42.79). Ritlecitinib 50 mg (OR 10.74; 95% CrI 3.80-34.94), baricitinib 4 mg (OR 10.23; 95% CrI 5.59-19.88), ivarmacitinib 8 mg (OR 6.13; 95% CrI 2.31-15.42), ivarmacitinib 4 mg (OR 4.82; 95% CrI 1.81-12.33), and baricitinib 2 mg (OR 3.67; 95% CrI 1.94-7.39) demonstrated more modest efficacy. For SALT ⩽10, upadacitinib 30 mg again produced the largest effect (OR 69.03; 95% CrI 26.14-221.38), followed by upadacitinib 15 mg (OR 43.83; 95% CrI 16.57-141.77) and deuruxolitinib 8 mg (OR 39.80; 95% CrI 12.46-172.80). The remaining treatments showed smaller effects.

Placebo-adjusted response differences for SALT ⩽20 supported the relative treatment effects, with the greatest improvements for upadacitinib 30 mg (52.14%), upadacitinib 15 mg (42.4%), and deuruxolitinib 8 mg (29.28%). Other treatments showed smaller effects. A similar pattern was observed for SALT ⩽10.

Posterior rank probabilities and SUCRA values for SALT ⩽20 similarly indicated that upadacitinib 30 mg had the highest probability of being the most effective treatment (82.7%). SUCRA rankings placed upadacitinib 15 mg second and deuruxolitinib 8 mg third. Ranking results for SALT ⩽10 mirrored those for SALT ⩽20.

All oral JAK inhibitors improved SALT outcomes. Upadacitinib 30 mg generated the largest efficacy estimates, followed by upadacitinib 15 mg and deuruxolitinib 8 mg, while ritlecitinib, baricitinib, and ivarmacitinib were associated with more modest efficacy. Placebo-adjusted response differences and treatment-ranking metrics supported these findings. Overall, the results indicate that upadacitinib may occupy a higher efficacy tier for severe AA within the JAK inhibitor class. Safety events were generally uncommon across trials, although reporting completeness varied and findings should be interpreted descriptively.

Categories: Therapeutics, Allergy/Immunology, Dermatology
Keywords: alopecia areata, baricitinib, deuruxolitinib, ivarmacitinib, jak inhibitors, network meta-analysis, ritlecitinib, severity of alopecia tool, systematic review, upadacitinib

Introduction And Background

Alopecia areata (AA) is a nonscarring, organ-specific autoimmune disorder characterized by the collapse of

hair follicle immune privilege leading to hair loss affecting the scalp, face, and body, with a reported global prevalence of approximately 0.1-2% [1,2]. Severe scalp involvement, defined as ⩾50% hair loss according to the Severity of Alopecia Tool (SALT) score, is frequently associated with psychological distress, social isolation, reduced quality of life, workplace and school absenteeism, reduced academic performance, and financial burden [2-5]. Immune-mediated comorbidities, including allergic rhinitis, asthma, atopic dermatitis, Hashimoto's thyroiditis, inflammatory bowel disease, psoriasis, systemic lupus erythematosus, and vitiligo, further contribute to disease burden [6]. AA is driven by autoimmune targeting of hair follicles mediated by cytotoxic T lymphocytes and proinflammatory cytokines that activate the Janus kinase (JAK) signal transducer and activator of transcription (JAK-STAT) pathway [7,8]. Pharmacologic inhibition of this pathway with JAK inhibitors has therefore emerged as a major therapeutic advance capable of reducing autoimmune activity, facilitating the restoration of hair-follicle immune privilege to allow safe re-entry into anagen phase, and promoting hair regrowth [8].

Upadacitinib, baricitinib, ritlecitinib, deuruxolitinib, and ivarmacitinib are approved JAK inhibitors indicated for severe AA in one or more major regulatory markets. Baricitinib, ritlecitinib, and deuruxolitinib were commercialized in the United States for severe AA in 2022, 2023, and 2025, respectively, and ivarmacitinib was commercialized in China for severe AA in 2025 [9-14].

Upadacitinib was approved in 2026 by the European Medicines Agency (EMA) for adolescents and adults with severe AA [15] and is under review by the Food and Drug Administration (FDA) [16]. Upadacitinib is also approved in most major regulatory markets for several immune-mediated inflammatory diseases, including atopic dermatitis and rheumatoid arthritis [17]. It selectively inhibits JAK1, producing dose-dependent suppression of IL-6-induced STAT3 and IL-7-induced STAT5 phosphorylation. This reversible blockade of JAK1-dependent cytokine signaling is relevant in AA because interruption of gamma chain cytokine pathways, including IL-15 and IL-7, reduces the activation and survival of autoreactive cytotoxic T cells that drive follicular inflammation [15,17,18]. Recent randomized controlled trials (RCTs) have demonstrated clinically meaningful scalp hair regrowth with upadacitinib 15 mg and 30 mg once daily, supporting its potential as an additional treatment option for severe AA [15,18].

Baricitinib is a selective JAK1 and JAK2 inhibitor that suppresses inflammatory cytokine signaling pathways implicated in AA pathogenesis, particularly interferon gamma-mediated immune activation [11,19-21]. Ritlecitinib is an irreversible inhibitor of JAK3 and members of the TEC kinase family, blocking their adenosine triphosphate binding sites and suppressing downstream signaling. By targeting JAK3-dependent cytokine receptors, it reduces STAT phosphorylation and dampens lymphocyte-driven inflammatory pathways. Ritlecitinib also interferes with TEC-mediated immune receptor signaling. In patients with AA, treatment leads to reductions in total lymphocyte counts, including CD3-positive T cells, CD4-positive and CD8-positive subsets, and CD16/56-positive natural killer cells [9,22-25]. Baricitinib and ritlecitinib have received approval for the treatment of severe AA in adults in the United States, the United Kingdom, the European Union, China, and Japan. Ritlecitinib is also approved for use in adolescents in these same regions. Baricitinib has recently been approved in the United States and the European Union for adolescents with severe AA [11,26-28].

Deuruxolitinib, a deuterated JAK1 and JAK2 selective inhibitor, was approved in the United States and the United Kingdom following phase 3 trials demonstrating efficacy and acceptable safety [10,29-32]. It shows greater inhibitory potency for JAK1, JAK2, and tyrosine kinase 2 (TYK2) relative to JAK3 [10].

Ivarmacitinib, a selective JAK1 inhibitor, was approved in China for AA in July 2025 following a phase 2 study conducted in China, Australia, and the United States and a phase 3 study in China, each demonstrating efficacy and tolerability in adults with AA. Ivarmacitinib is also approved in China for ankylosing spondylitis, rheumatoid arthritis, and atopic dermatitis. It is occasionally referred to as amaxitinib (or aimaxitinib), a phonetic rendering derived from its Chinese name which more closely approximates the original developer's designation than the internationally adopted generic name ivarmacitinib. It exhibits significantly greater inhibitory potency for JAK1 over JAK2, JAK3, and TYK2 [13,14,33,34].

Although oral JAK inhibitors represent an important advance in the management of severe AA, clinical trials show that approximately half of treated patients fail to achieve clinically meaningful scalp hair regrowth, defined as SALT ⩽20, after 24, 48, or 52 weeks of therapy [9-11,13,19-25,27-37]. Durability of response also remains a challenge. In patients who achieve meaningful hair regrowth, discontinuation of baricitinib has been associated with early loss of benefit in a subset of responders and substantial loss of benefit over longer follow-up, although many but not all patients regain improvement when treatment is restarted [35]. Discontinuation of ritlecitinib shows a similar pattern, with only a portion of responders recapturing improvement after retreatment [37]. Variability in individual treatment trajectories further highlights this limitation, emphasizing the need for therapies with more consistent and sustained effects.

In the absence of a new pharmacologic class with a differentiated mechanism and an approved indication for severe AA, suboptimal efficacy or tolerability will likely require switching among available oral JAK inhibitors to take advantage of interindividual or intraclass differences, as suggested in recent clinical experience reports [38-45].

Despite the therapeutic advance represented by oral JAK inhibitors, direct RCTs comparing baricitinib, ritlecitinib, deuruxolitinib, ivarmacitinib, and upadacitinib are lacking, resulting in uncertainty regarding their relative effectiveness.

Several systematic reviews and network meta-analyses have attempted to synthesize evidence comparing JAK inhibitors and other agents for the treatment of AA. However, many included investigational, off-label, demonstrably ineffective, or abandoned agents, subtherapeutic doses or regimens exceeding established safety margins, combination therapies, and populations with baseline SALT scores <50 [46]. These factors limit the clinical applicability and comparability of their findings. Moreover, JAK inhibitors that were recently approved or are under active regulatory review have not been incorporated into previous evidence networks [47,48].

This systematic review and Bayesian network meta-analysis (BNMA) compared five oral JAK inhibitors in patients ⩾12 years with severe AA: once-daily baricitinib 2 mg and 4 mg, ritlecitinib 50 mg, ivarmacitinib 4 mg and 8 mg, and upadacitinib 15 mg and 30 mg, as well as twice-daily deuruxolitinib 8 mg. The primary outcome was the proportion of patients achieving SALT ⩽20 at week 24, and the secondary outcome was the proportion achieving SALT ⩽10 at week 24. Safety outcomes were summarized descriptively. By focusing on clinically relevant doses, placebo-controlled RCTs, and consensus SALT-based measures of treatment success, this analysis aims to inform evidence-based clinical decision-making and identify priorities for future head-to-head and long-term studies.

Review

Methods

Protocol and Reporting

This systematic review and BNMA was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) extension for Network Meta-Analyses [49]. A protocol was developed prior to study initiation and prospectively registered with the International Prospective Register of Systematic Reviews (PROSPERO; registration number: CRD420261461735).

Eligibility Criteria

Placebo-controlled RCTs evaluating JAK inhibitors in male or female patients aged ⩾12 years with severe AA involving ⩾50% scalp hair loss (baseline SALT score ⩾50) in any geographic location were eligible. Studies enrolling patients with alopecia totalis or alopecia universalis were also eligible because these conditions represent severe forms of AA. The inclusion of placebo comparators enabled the construction of an indirect evidence network.

The interventions of interest comprised any oral JAK inhibitors approved in one or more major regulatory markets, including the United States, the United Kingdom, the European Union, Japan, or China, for the treatment of severe AA at regulator-specified doses and schedules. For dose-ranging studies, only regulator-approved doses for AA were included in the primary network. Pharmacokinetic-only doses, unapproved loading-dose regimens, and doses not relevant for the indication were excluded. The eligible treatment nodes were baricitinib 2 and 4 mg once daily [11,27,28,36], deuruxolitinib 8 mg twice daily [10,29-32], ivarmacitinib 4 and 8 mg once daily [13,14,34], ritlecitinib 50 mg once daily [9,22,23], and upadacitinib 15 and 30 mg once daily [15,18].

All studies were placebo-controlled RCTs evaluating an eligible oral JAK inhibitor. Each eligible active dose and dosing regimen was treated as a separate treatment node. Phase 2, phase 2/3, phase 2b/3, and phase 3 RCTs with extractable aggregate outcome data at arm level were included. Studies were limited to RCTs of ⩾24-week duration, published in English. Full-text publications, conference abstracts from major dermatology congress proceedings, trial-registry results, regulatory documents, and other reports containing sufficient numerical data were considered. Non-randomized studies, single-arm studies, case reports, case series, narrative reviews, systematic reviews, and studies without extractable data were excluded. Complete study-specific eligibility criteria are available in the original publications.

Subgroup reports and secondary analyses were used to obtain supplementary information but were not included alongside the corresponding complete trial population when this would have resulted in participant double-counting. Multiple reports describing the same trial were treated as a single study.

Information Sources and Search Strategy

A systematic literature search was conducted in MEDLINE/PubMed, Embase, the Cochrane Library, and ClinicalTrials.gov from database inception through July 26, 2026. Data from the two upadacitinib RCTs had been publicly available and identified before completion of the search. Following publication of the full peer-reviewed report of both trials on August 12, 2026 [18], the previously available data were verified

against the published results, with no discrepancies identified [18]. The reference lists of the included studies and relevant systematic reviews were also screened manually. The search strategy combined controlled vocabulary and free-text terms related to AA and JAK inhibitors. Individual drug names, drug codes, and commonly used synonyms were included. The complete search strategy for each database is provided in Table *1*.

Database	Search string	Hits
PubMed	("Alopecia Areata"[Mesh] OR "alopecia areata"[Title/Abstract] OR "alopecia totalis"[Title/Abstract] OR "alopecia universalis"[Title/Abstract]) AND (baricitinib[Title/Abstract] OR Olumiant[Title/Abstract] OR LY3009104[Title/Abstract] OR INCB028050[Title/Abstract] OR ritlecitinib[Title/Abstract] OR Litfulo[Title/Abstract] OR PF-06651600[Title/Abstract] OR deuruxolitinib[Title/Abstract] OR Leqselvi[Title/Abstract] OR CTP-543[Title/Abstract] OR upadacitinib[Title/Abstract] OR Rinvoq[Title/Abstract] OR ABT-494[Title/Abstract] OR ivarmacitinib[Title/Abstract] OR SHR0302[Title/Abstract] OR "Janus Kinase Inhibitors"[Mesh] OR "Janus kinase inhibitor*"[Title/Abstract] OR "JAK inhibitor*"[Title/Abstract]) AND (randomized controlled trial[Publication Type] OR controlled clinical trial[Publication Type] OR clinical trial[Publication Type] OR random*[Title/Abstract] OR placebo*[Title/Abstract] OR trial[Title/Abstract] OR blind*[Title/Abstract]) NOT (animals[MeSH Terms] NOT humans[MeSH Terms])	185
Cochrane Library	("alopecia areata" OR "alopecia totalis" OR "alopecia universalis") AND (baricitinib OR Olumiant OR LY3009104 OR INCB028050 OR ritlecitinib OR Litfulo OR PF-06651600 OR deuruxolitinib OR Leqselvi OR CTP-543 OR upadacitinib OR Rinvoq OR ABT-494 OR ivarmacitinib OR SHR0302 OR "Janus kinase inhibitor" OR "JAK inhibitor")	192
Embase	('alopecia areata'/exp OR 'alopecia areata':ti,ab,kw OR 'alopecia totalis':ti,ab,kw OR 'alopecia universalis':ti,ab,kw) AND ('baricitinib'/exp OR baricitinib:ti,ab,kw OR olumiant:ti,ab,kw OR 'ly3009104':ti,ab,kw OR 'incb028050':ti,ab,kw OR 'ritlecitinib'/exp OR ritlecitinib:ti,ab,kw OR litfulo:ti,ab,kw OR 'pf-06651600':ti,ab,kw OR 'deuruxolitinib'/exp OR deuruxolitinib:ti,ab,kw OR leqselvi:ti,ab,kw OR 'ctp-543':ti,ab,kw OR 'upadacitinib'/exp OR upadacitinib:ti,ab,kw OR rinvoq:ti,ab,kw OR 'abt-494':ti,ab,kw OR 'ivarmacitinib'/exp OR ivarmacitinib:ti,ab,kw OR 'shr0302':ti,ab,kw OR 'janus kinase inhibitor'/exp OR 'janus kinase inhibitor*':ti,ab,kw OR 'jak inhibitor*':ti,ab,kw) AND ('randomized controlled trial'/exp OR 'controlled clinical trial'/exp OR 'clinical trial'/exp OR 'phase 2 clinical trial'/exp OR 'phase 3 clinical trial'/exp OR random*:ti,ab,kw OR placebo*:ti,ab,kw OR trial:ti,ab,kw OR blind*:ti,ab,kw) NOT ('animal'/exp NOT 'human'/exp)	493
ClinicalTrials.gov	Alopecia Areata AND (Baricitinib OR Ritlecitinib OR Deuruxolitinib OR Upadacitinib OR Ivarmacitinib)	55
Total hits	-	925

TABLE 1: Database-specific search strategies for the systematic literature search

Search strategies used to identify potentially eligible studies across the specified databases. The table presents the database-specific search strings and the number of records retrieved from each database before duplicate removal.

Study Selection

All retrieved records were imported into EndNote (Clarivate, Philadelphia, Pennsylvania, United States), and duplicate records were removed. The titles and abstracts were independently screened against the prespecified eligibility criteria by the lead author and a second, non-author individual. Potentially eligible reports were retrieved in full and independently assessed by the same two reviewers. Disagreements were resolved through discussion or consultation with a third reviewer. Reasons for exclusion at the full-text stage were recorded, and the study-selection process was presented using a PRISMA flow diagram. Multiple reports describing the same trial were consolidated to avoid double-counting.

Data Extraction

Data were independently extracted by the lead author and the same non-author individual using a standardized extraction form to include author, publication year, trial name, registration number, study phase, country or region, study design, eligibility criteria, sample size, participant age, sex distribution, baseline SALT score, prevalence of alopecia totalis or universalis, previous treatments, intervention, dose, dosing frequency, comparator, treatment duration, outcome definitions, assessment time points, number of responders, number of participants analyzed, safety events, analysis population, and methods used to address missing outcome data.

For dichotomous outcomes, the number of participants experiencing the outcome and the corresponding number analyzed in each treatment arm were extracted. When responder counts were not reported directly,

they were derived from the reported percentage and denominator when the calculation was unambiguous. All derived values were independently verified. When multiple reports described the same trial, information was collated across reports, and the most complete and relevant source was used for each outcome. Any discrepancies across reports were resolved through consensus.

Outcomes

SALT is a standardized measure of scalp hair loss ranging from 0 (no scalp hair loss) to 100 (complete scalp hair loss) [50]. The primary efficacy outcome was the proportion of participants achieving SALT ⩽20 at week 24. SALT ⩽20, corresponding to ⩾80% scalp hair coverage, was selected as the primary efficacy threshold based on its established use in clinical trials and evidence supporting it as a clinically meaningful treatment-success threshold in severe AA [51,52]. Qualitative validation involving patients with ⩾50% scalp hair loss and expert clinicians identified ⩾80% scalp hair coverage as an appropriate threshold for treatment success [50]. The secondary efficacy outcome was the proportion of participants achieving SALT ⩽10 at week 24.

Safety outcomes included any adverse event, serious adverse events, serious infections, treatment discontinuation due to adverse events, conjunctivitis, herpes infections, and death. Other safety outcomes were evaluated when they were consistently reported across eligible trials. Safety outcomes were summarized descriptively because event definitions, reporting completeness, and follow-up reporting varied across trials. The number and percentage of participants experiencing each event were presented by study and treatment arm; no statistical analysis of safety outcomes was performed. Safety findings were therefore interpreted qualitatively rather than through comparative modeling.

Data Preparation and Network Geometry

Before analysis, interventions, doses, dosing frequencies, trial identifiers, outcome definitions, and assessment time points were standardized. Placebo formulations judged to be clinically equivalent were combined into a single placebo node, whereas each active dose and dosing regimen was retained as a distinct treatment node.

The geometry and connectivity of the evidence network were examined separately for each outcome. Network plots were generated with node size proportional to the number of participants receiving each treatment and edge thickness proportional to the number of studies contributing the corresponding direct comparison. Networks were inspected to confirm adequate connectivity for valid indirect comparisons.

The transitivity assumption was evaluated by comparing the distribution of potential effect modifiers across comparisons, including age, baseline SALT score, disease duration, alopecia totalis or universalis, previous treatment, trial phase, geography, outcome definition, analysis population, and handling of missing outcome data. Potential imbalances were documented to inform interpretation of indirect comparisons.

Statistical Analysis

For each outcome, an arm-level BNMA was performed using a binomial likelihood with a logit link [53,54]. Treatment effects were expressed as odds ratios (OR) with 95% Bayesian credible intervals (CrIs), with placebo serving as the reference treatment. Correlations arising from multi-arm trials were accounted for directly within the model without splitting or duplicating shared comparator groups.

Both fixed-effects and random-effects consistency models were fitted. The random-effects model assumed a common between-study heterogeneity parameter across all treatment comparisons. Weakly informative priors were assigned to study-specific baseline effects and relative treatment effects, and a weakly informative half-normal prior was used for the between-study standard deviation. Zero-event treatment arms were retained within the arm-based binomial model without applying continuity corrections. Trials with zero events in all arms were considered to contribute limited information on relative treatment effects.

Analyses were conducted using R version 4.5.2 (R Foundation for Statistical Computing, Vienna) in RStudio version 2026.06.0+242 (Posit Software, PBC, Boston, Massachusetts, United States), using the gemtc package version 1.1.1 [55-58]. Markov chain Monte Carlo sampling was performed using four parallel chains with dispersed initial values. The number of adaptation, burn-in, and sampling iterations was increased as needed to achieve stable convergence and adequate effective sample sizes.

Convergence was considered adequate when visual inspection of the trace plots demonstrated satisfactory mixing and potential scale reduction factors below 1.05 and effective sample sizes were sufficient for stable posterior estimation. Model fit was assessed using the posterior mean residual deviance (Dbar), the ratio of residual deviance to the number of unconstrained data points, the effective number of parameters (pD), and the deviance information criterion (DIC). Lower DIC values indicated a comparatively better balance between model fit and complexity, although small differences were not considered clinically meaningful. The random-effects model was prespecified as the primary model when the network contained sufficient

studies to estimate heterogeneity reliably. Sensitivity analyses were conducted using a fixed-effects model for SALT ⩽20 and SALT ⩽10. For SALT ⩽10, an additional sensitivity analysis was performed using a wider prior distribution for the treatment effects to assess the influence of prior specification in the relatively sparse network. Treatment estimates, CrIs, model-fit statistics, and the overall direction of findings were compared across model specifications. In sparse networks where heterogeneity could not be estimated reliably, the fixed-effects model was used with appropriate caution. Residual deviance and leverage plots were used to examine the contribution of individual study arms to model fit, and arms with relatively large residual deviance values were evaluated as potential sources of poor fit or disproportionate influence.

In addition to relative treatment effects, observed placebo-adjusted response differences were calculated for each treatment at week 24. For treatments evaluated in more than one trial, the numbers of responders and participants were summed across the relevant treatment arms, and the corresponding concurrent placebo data were similarly pooled. The pooled observed response percentage for placebo was then subtracted from the pooled observed response percentage for the active treatment and expressed as a percentage-point difference. These descriptive estimates were not interpreted as Bayesian model-based risk differences.

Assessment of Heterogeneity and Inconsistency

Clinical and methodological heterogeneity were assessed by comparing study, participant, intervention, and outcome characteristics. Statistical heterogeneity was summarized using the posterior median of the between-study standard deviation (τ) with its 95% CrI. Heterogeneity was also expressed as I^2 using the corresponding model-based estimate.

Local inconsistency was planned to be evaluated using node-splitting analyses when a treatment comparison had sufficient independent direct and indirect evidence. The magnitude, direction, and uncertainty of disagreement between direct and indirect estimates were to be examined. When no eligible comparison contained sufficient direct and indirect evidence, node splitting was not performed, and inconsistency was considered not formally assessable. Global inconsistency was also monitored through overall model fit to ensure that the consistency assumption was reasonable for the available evidence.

Risk of Bias

The risk of bias in the included RCTs was independently assessed by two reviewers using the Cochrane Risk of Bias 2 (RoB 2) tool [59,60]. Judgments were made across the 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. Domain-specific and overall judgments were classified as low risk, some concerns, or high risk. Disagreements were resolved through discussion.

Treatment Ranking

Posterior rank probabilities, probabilities of occupying each rank, and surface under the cumulative ranking curve (SUCRA) values were estimated for each treatment [61]. Rankings were interpreted alongside the magnitude and uncertainty of relative treatment effects and were not considered independently as evidence of treatment superiority. Rank metrics were used only as supportive summaries and were not treated as stand-alone indicators of comparative efficacy.

Results

Study Selection

The database and trial-register searches identified 925 records, including 185 from PubMed, 493 from Embase, 192 from the Cochrane Library, and 55 from ClinicalTrials.gov. After removing 432 duplicates, 493 records underwent title and abstract screening, of which 401 were excluded. The full texts of 92 reports were assessed for eligibility, and all were successfully retrieved. Following the exclusion of 82 reports because of non-randomized designs, non-AA populations, or absence of a placebo comparator, 10 RCTs were included in the review [18,22,28-31,34,36]. These comprised three trials of baricitinib (BRAVE-AA1 [36], BRAVE-AA2 [36], and BRAVE-AA-PEDS [28]), three of deuruxolitinib ([29], THRIVE-AA1 [30], and THRIVE-AA2 [31]), two of upadacitinib (UP-AA1 [18] and UP-AA2 [18]), one of ritlecitinib (TRIAL AA-1 [22]), and one of ivarmacitinib [34] (Figure *1*). No additional eligible studies were identified through manual reference screening. Some of the included data are also reported in the United States Prescribing Information, China's Drug Insert Sheet, the European Medicines Agency Summary of Product Characteristics (SmPC), and the United Kingdom SmPC [9-11,13,15,27,32].

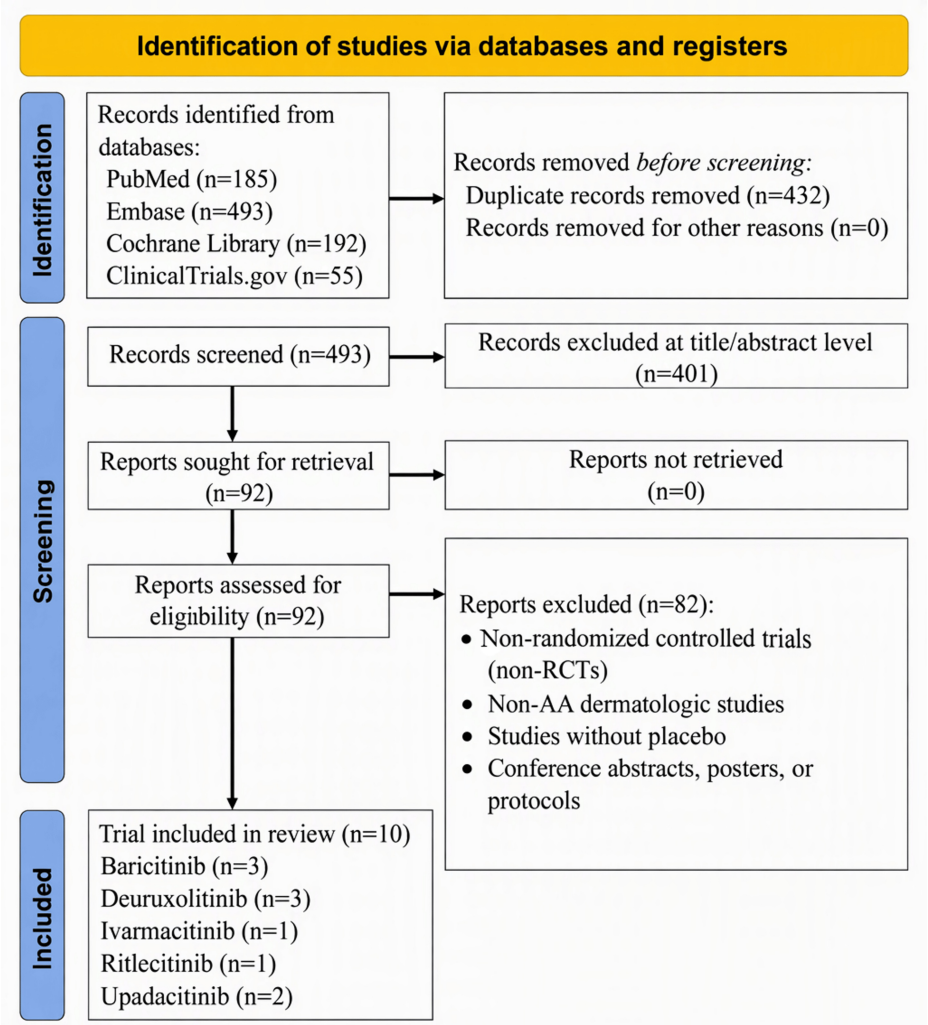

FIGURE 1: PRISMA flow diagram of study selection

Sources: Mostaghimi et al., 2026, upadacitinib [18]; King et al., 2023, ritlecitinib [22]; Passeron et al., 2025, baricitinib [28]; King et al., 2022, deuruxolitinib [29]; King et al., 2024, deuruxolitinib [30]; Tsianakas et al., 2026, deuruxolitinib [31]; Zhou et al., 2026, ivarmacitinib [34]; and King et al., 2022, baricitinib [36]

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; AA: alopecia areata

Characteristics of the Included Studies

The 10 included RCTs collectively enrolled 5,276 participants and were published between 2022 and 2026 [18,22,28-31,34,36]. The studies included one phase 2 trial, one phase 2b/3 trial, and eight phase 3 trials. All studies were multicenter, randomized, double-blind, and placebo-controlled, reporting efficacy outcomes at week 24, the common assessment time used in the network meta-analysis. The trials evaluated baricitinib 2 or 4 mg once daily, deuruxolitinib 8 mg twice daily, ivarmacitinib 4 or 8 mg once daily, ritlecitinib 50 mg once daily, and upadacitinib 15 or 30 mg once daily. Most studies were conducted across multiple countries. The phase 2 trials for deuruxolitinib [29] and the phase 3 trials for ivarmacitinib [34] were conducted solely in the United States and China, respectively (Table *2*). Across trials, study designs, dosing regimens, and assessment schedules were sufficiently comparable to support inclusion in a unified evidence network.

Author	Trial name	Registration	Country/region	Design	Wk	Agent‡	N
King et al.	BRAVE-AA2 Phase 3	NCT03899259	Argentina, Australia, Brazil, China, Israel, Japan, South Korea, Taiwan, USA (85 sites)	MC, R, DB, PC, PG	24	BARI 2/4 mg	546

2022 [36]	BRAVE-AA1 Phase 3	NCT03570749	Japan, Mexico, South Korea, USA (75 sites)	MC, R, DB, PC, PG	24	BARI 2/4 mg	654
Passeron et al. 2025 [28]	BRAVE-AA-PEDS Phase 3	NCT05723198	Argentina, Australia, Canada, France, Germany, Hungary, Japan, Poland, South Korea, Spain, Taiwan, USA (127 sites)	MC, R, DB, PC, PG	36*	BARI 2/4 mg	257
King et al. 2022 [29]	CTP-543 Phase 2	NCT03137381	USA (13 sites)	MC, R, DB, PC, PG	24	DEUR 8 mg	149
Tsianakas et al. 2026 [31]	THRIVE-AA2 Phase 3	NCT04797650	USA, Canada, France, Germany, Hungary, Poland, Spain (63 sites)	MC, R, DB, PC, PG	24	DEUR 8 mg	517
King et al. 2024 [30]	THRIVE-AA1 Phase 3	NCT04518995	Canada, France, Poland, South Korea, Spain, USA (72 sites)	MC, R, DB, PC, PG	24	DEUR 8 mg	706
Zhou et al. 2026 [34]	SHR0302 Phase 3	NCT05470413	China (31 sites)	MC, R, DB, PC, PG	24	IVAR 4/8 mg	330
King et al. 2023 [22]	ALLEGRO Phase 2b/3	NCT03732807	Argentina, Australia, Canada, Chile, China, Colombia, Czechia, Germany, Hungary, Japan, Mexico, Poland, Russia, South Korea, Taiwan, UK, USA (118 sites)	MC, R, DB, PC, PG	24	RIT 50 mg	718#
Mostaghimi et al. 2026 [18]	UP-AA1 Phase 3	NCT06012240	UP-AA1 and UP-AA2 Argentina, Australia, Belgium, Brazil, Bulgaria, Canada, Chile, China, Croatia, France, Germany, Greece, Hungary, Israel, Italy, Japan, New Zealand, Poland, Portugal, Puerto Rico, Slovakia, South Korea, Spain, Sweden, Taiwan, Turkiye, UK, USA (283 sites: UP-AA1 and UP-AA2)	MC, R, DB, PC, PG	24	UPA 15/30 mg	676
	UP-AA2 Phase 3	NCT06012240	See UP-AA1 (283 sites)	MC, R, DB, PC, PG	24	UPA 15/30 mg	723

TABLE 2: Characteristics of the included randomized, placebo-controlled trials

Sample size represents the total randomized population reported for each trial.

‡All treatments were given once a day, except for deuruxolitinib, which was given twice a day.

*BRAVE-AA-PEDS [28] was a 36-week study with extractable 24-week data.

#Ritlecitinib population (N=718) comprised 10 mg, 30 mg, 50 mg, 200/30 mg, and 200/50 mg, although only the 50 mg once a day without a loading dose was eventually approved.

BARI: baricitinib; DB: double-blind; DEUR: deuruxolitinib; IVAR: ivarmacitinib; MC: multicenter; N: sample size; NCT: National Clinical Trial registration number; PC: placebo-controlled; PG: parallel-group; R: randomized; RIT: ritlecitinib; UPA: upadacitinib

Baseline Participant Characteristics

The included populations comprised adults and adolescents with severe AA. Data for ritlecitinib [22] and upadacitinib [18] were derived from predominantly adult trials with smaller adolescent subgroups, whereas data for baricitinib [36], deuruxolitinib [29-31], and ivarmacitinib [34] were from studies in adults, except for one dedicated pediatric study of baricitinib [28]. Reported mean ages were generally between approximately

31.6 and 39.7 years in the predominantly adult trials, while participants in BRAVE-AA-PEDS had a mean age of 14.7 years. The upadacitinib studies enrolled participants aged 12-63 years. Among studies reporting sex distribution, females accounted for 49.4-68.6% of participants. The reported duration of AA varied across studies and treatment groups, ranging from approximately 2.9 to 13.1 years. Baseline disease severity was high, with mean SALT scores ranging from 78.6 to 93.0. Where reported, 33-63.8% of participants had baseline SALT scores of 95-100, while the prevalence of alopecia universalis ranged from 18% to 53.7%. Baseline demographic and disease characteristics were generally comparable between the intervention and placebo groups within individual trials (Table 3). The distributions of the principal potential effect modifiers were broadly comparable across treatment comparisons. However, some between-study variation was observed in age, geographic region, disease duration, baseline SALT score, and the prevalence of alopecia totalis or alopecia universalis. These differences were considered when evaluating the transitivity assumption and interpreting the network estimates. Overall, no systematic imbalances were identified that would preclude valid indirect comparisons.

Study	Treatment‡	N	Age (yr)	Female (%)	Disease duration (yr)	Baseline SALT score	SALT 95-100, n (%)	AU (%)
Mostaghimi et al. 2026 [18] UP-AA1	Placebo	135	12-63	NR	<8 years	NR	NR	NR
	Upadacitinib 15 mg QD	270	12-63	NR	<8 years	NR	NR	NR
	Upadacitinib 30 mg QD	271	12-63	NR	<8 years	NR	NR	NR
Mostaghimi et al. 2026 [18] UP-AA2	Placebo	135	12-63	NR	3.1±2.2	83.8±19.2	NR	NR
	Upadacitinib 15 mg QD	270	12-63	NR	3.1±2.2	83.8±19.2	NR	NR
	Upadacitinib 30 mg QD	271	12-63	NR	3.1±2.2	83.8±19.2	NR	NR
King et al. 2022 [29]	Placebo	43	37.8±13.50	65.9	NR	86.8±18.39	NR	NR
	Deuruxolitinib 8 mg	38	37.3±14.18	68.4	NR	89.1±16.41	NR	NR
King et al. 2022 [36] BRAVE-AA1	Placebo	189	37.4±12.9	57.7	12.6±11.2	84.7±17.8	51.3	39.2
	Baricitinib 2 mg	184	38.0±12.8	59.2	12.1±9.8	86.8±18.0	58.2	45.1
	Baricitinib 4 mg	281	36.3±13.3	58.7	11.8±11.1	85.3±18.2	52.7	45.2
King et al. 2022 [36] BRAVE-AA2	Placebo	156	37.1±12.4	62.8	11.8±10.2	85.0±17.8	52.3	42.3
	Baricitinib 2 mg	156	39.0±13.0	66	13.1±11.8	85.6±18.1	55.1	44.9
	Baricitinib 4 mg	234	38.0±12.7	61.5	11.9±11.1	84.8±18.1	50.9	47.4
King et al. 2023 [22] ALLEGRO-2b/3	Ritlecitinib 50 mg	124	32.4±13.4	55	8.7	90.3	NR	18
	Placebo	130	34.0±15.0	66	11	93	NR	26
King et al. 2024 [30] THRIVE-AA1	Placebo	140	38.5 (18-65)	63.6	3.3	88.1±15.10	55.7	NR
	Deuruxolitinib 8 mg	351	37.0 (18-65)	61.8	2.9	85.5±18.35	55.8	NR
Passeron et al. 2025 [28] BRAVE-AA-PEDS	Baricitinib 2/4 mg or placebo	257	14.7±1.7	49.4	6.4	89	63.8	53.7
Tsianakas et al. 2025 [31] THRIVE-AA2	Placebo	119	39.7±12.49	67.7	3.8±3.10	88.9±16.20	60.8	NR
	Deuruxolitinib 8 mg	233	38.4±12.30	68.6	3.8±2.76	88.1±17.40	61.1	NR
Zhou et al. 2026 [34]	Placebo	110	32.4±10.3	51.8	6.3±5.5	79.1±18.2	34.5	NR
	Ivarmacitinib 4 mg	109	31.7±8.9	53.2	5.4±5.7	78.6±18.3	33	NR
	Ivarmacitinib 8 mg	111	31.6±10.0	55.9	6.0±5.7	78.6±18.7	33.3	NR

TABLE 3: Baseline demographic and disease characteristics of the participants

‡All treatments were given once a day, except for deuruxolitinib, which was given twice a day; data are presented as mean (standard deviation), mean (range), range, n (%), or percentage, as reported in the original studies.

AU: alopecia universalis; N: sample size; NR: not reported; SALT: Severity of Alopecia Tool

Safety Outcomes

The incidence of any adverse event varied across the included treatments and studies, ranging from 50.8% to 85%. Adverse events were generally reported more frequently in the active-treatment groups than in their corresponding placebo groups, particularly with ritlecitinib, deuruxolitinib, ivarmacitinib, and the higher dose of upadacitinib. Serious adverse events were uncommon across the evaluated regimens, generally

occurring in 0-3.7% of participants. Serious infections were also infrequent, with reported incidences ranging from 0% to 1.8%. Discontinuation because of adverse events was uncommon and generally occurred in fewer than 3.1% of participants, except in the phase 2 deuruxolitinib study, in which discontinuation rates were 5.3% with deuruxolitinib and 6.8% with placebo.

Herpes infections were uncommon across most treatment groups. The highest overall incidence was reported with ritlecitinib 50 mg once daily at 3.8%. In the baricitinib trials, the reported incidence of herpes zoster ranged from 0.5% to 1.9%, while herpes simplex infections ranged from 0% to 5.2%. No deaths were reported in the studies providing mortality data. Overall, serious adverse events, serious infections, treatment discontinuations, herpes infections, and deaths were uncommon, although the completeness of safety reporting varied among the included trials (Table *4*). Safety findings should therefore be interpreted with appropriate caution given the differences in reporting detail across studies.

Study	Treatment†	Any AE (%)	Serious AE (%)	Serious infection (%)	Discontinuation due to AE (%)	Herpes infection (%)	Death
Mostaghimi et al. 2026 [18] UP-AA1	Placebo	53.3	0.7	0.7	0	0	0
	Upadacitinib 15 mg	59.6	1.9	0	1.1	1.1	0
	Upadacitinib 30 mg	64.2	1.8	0.4	1.5	0.7	0
Mostaghimi et al. 2026 [18] UP-AA2	Placebo	60.7	0	0	0	0.7	0
	Upadacitinib 15 mg	65.5	1.4	0.7	0.7	0.3	0
	Upadacitinib 30 mg	69.9	2.8	1	1.4	1.4	0
King et al. 2022 [29]	Placebo	70.5	0	0	6.8	NR	0
	Deuruxolitinib 8 mg	81.6	0	0	5.3	NR	0
King et al. 2022 [36] BRAVE-AA1	Placebo	51.3	1.6	0	1.1	HZ: 0.5; HSV: 2.1	0
	Baricitinib 2 mg	50.8	2.2	0	1.6	HZ: 0.5; HSV: 0	0
	Baricitinib 4 mg	59.6	2.1	0	1.8	HZ: 0.7; HSV: 1.8	0
King et al. 2022 [36] BRAVE-AA2	Placebo	63	1.9	0	2.6	HZ: 0.6; HSV: 5.2	0
	Baricitinib 2 mg	68.4	2.6	1.3	2.6	HZ: 1.9; HSV: 3.9	0
	Baricitinib 4 mg	66.1	3.4	0.4	2.6	HZ: 1.3; HSV: 0.9	0
King et al. 2023 [22] ALLEGRO-2b/3	Ritlecitinib 50 mg	85	2	0	3	3.8	0
King et al. 2024 [30] THRIVE-AA1	Placebo	55.7	2.9	NR	1.4	0	0
	Deuruxolitinib 8 mg	65.1	1.1	NR	2.6	0.3	0
Passeron et al. 2025 [28] BRAVE-AA-PEDS	Placebo	53.4	3.4	NR	2.3	NR	NR
	Baricitinib 2 mg	60.2	NR	NR	NR	NR	NR
	Baricitinib 4 mg	70.6	NR	NR	NR	NR	NR
	Placebo	70	0	0	0.8	1.5	0

Tsianakas et al. 2025 [31] THRIVE-AA2	Deuruxolitinib 8 mg	80.5	1.2	0.4	3.1	2	0
	Deuruxolitinib 12 mg‡	81.4	16	0	2.3	2.3	0
Zhou et al. 2026 [34]	Placebo	75.5	0	0	0	0	0
	Ivarmacitinib 4 mg	77.1	3.7	0	1.8	0	0
	Ivarmacitinib 8 mg	84.7	2.7	1.8	0.9	0.9	0

TABLE 4: Safety outcomes reported across the included randomized controlled trials

†All treatments were given once a day, except for deuruxolitinib, which was given twice a day.

‡The deuruxolitinib 12 mg dose is included in this safety table for completeness. It was the subject of an FDA clinical hold on May 17, 2023, for "unfavorable benefit-risk" and never approved due to at least 14 nonfatal thrombotic events, including deep vein thrombosis, bilateral pulmonary embolism, cerebral venous thrombosis, thrombophlebitis, and transient ischemic attack [46]; values are percentages of participants experiencing each safety outcome unless otherwise indicated.

AE: adverse event; HSV: herpes simplex virus; HZ: herpes zoster; NR: not reported

BNMA

Network geometry: The BNMA of SALT ⩽20 and SALT ⩽10 responses at week 24 each included 10 studies, 26 treatment arms, and nine treatment nodes. Placebo was the principal comparator, although the amount of direct evidence varied among treatments (Figure *2*). The resulting networks provided sufficient connectivity to support indirect comparisons across all included treatments.

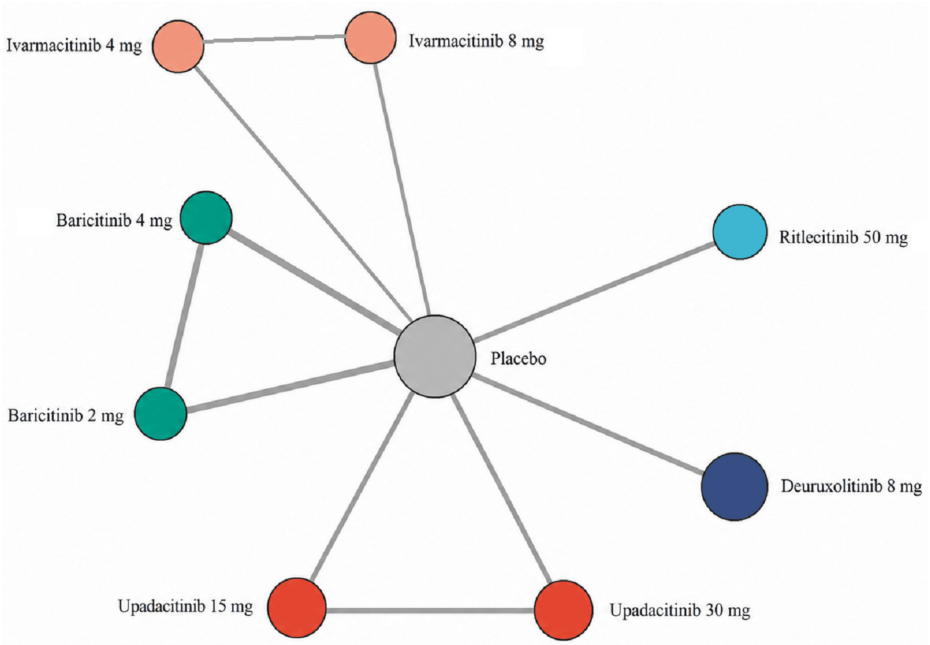

FIGURE 2: Network geometry of treatment comparisons included in the Bayesian network meta-analysis

Network plot showing the available direct comparisons among baricitinib, deuruxolitinib, ivarmacitinib, ritlecitinib, upadacitinib, and placebo. Nodes represent treatment interventions, and connecting lines indicate direct comparisons within the included randomized controlled trials. Node size reflects sample size, and line thickness reflects the amount of direct comparative evidence.

Sources: Mostaghimi et al., 2026, upadacitinib [18]; King et al., 2023, ritlecitinib [22]; Passeron et al., 2025, baricitinib [28]; King et al., 2022, deuruxolitinib [29]; King et al., 2024, deuruxolitinib [30]; Tsianakas et al., 2026, deuruxolitinib [31]; Zhou et al., 2026, ivarmacitinib [34]; and King et al., 2022, baricitinib [36]

Model convergence and fit: Convergence was satisfactory for both analyses. All potential scale reduction factors were approximately 1.00, with upper confidence limits ⩽1.01. Trace plots demonstrated adequate mixing and no persistent trends across the four Markov chains. For the SALT ⩽20 analysis, the random-effects model had a Dbar of 30.70 across 26 data points, corresponding to a residual deviance ratio of 1.18. The pD was 19.74, and the DIC was 50.44. Heterogeneity was low (I^2=12%), with a median between-study standard deviation (τ) of 0.17 (95% CrI 0.01-0.83; Figure *3*). For the SALT ⩽10 analysis, the Dbar was 31.59 across 26 data points, with a residual deviance ratio of 1.22, a pD of 16.42, and a DIC of 48.01. Heterogeneity was also low (I^2=21%), with a median τ of 0.14 (95% CrI 0.01-0.72; Figure *4*). Across both outcomes, model diagnostics supported adequate fit and stability of the posterior estimates.

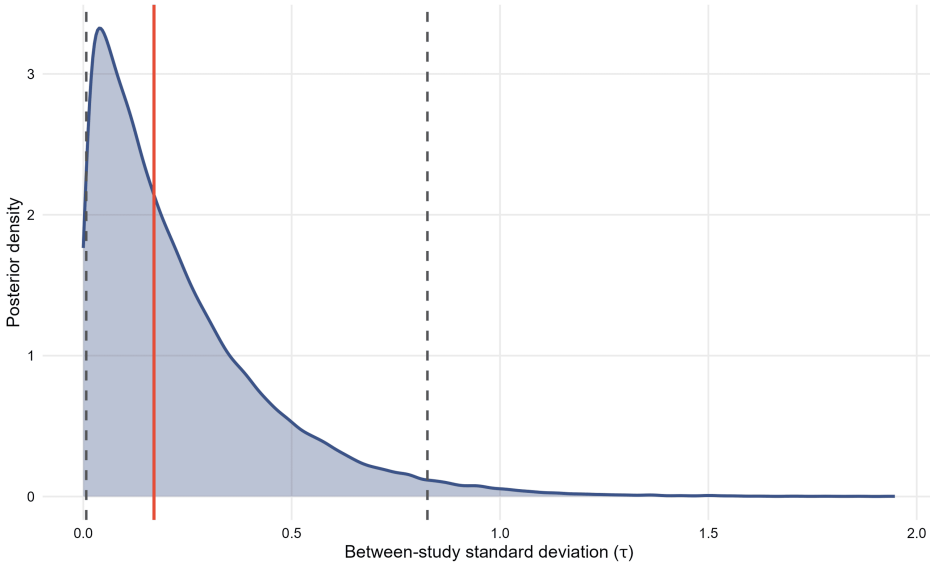

FIGURE 3: Posterior distribution of between-study heterogeneity for SALT ≤20 response

Posterior density distribution of the between-study standard deviation (τ) for the random-effects Bayesian network meta-analysis of SALT ≤20 response. The plot displays the posterior median and 95% credible interval (CrI) for τ together with the corresponding I^2 estimate (median τ=0.17 (95% CrI 0.01-0.83); I^2=12%).

Sources: upadacitinib [18], deuruxolitinib [29-31], ritlecitinib [22], baricitinib [28,36], and ivarmacitinib [34]

I^2: measure of statistical heterogeneity; SALT: Severity of Alopecia Tool; τ: between-study standard deviation

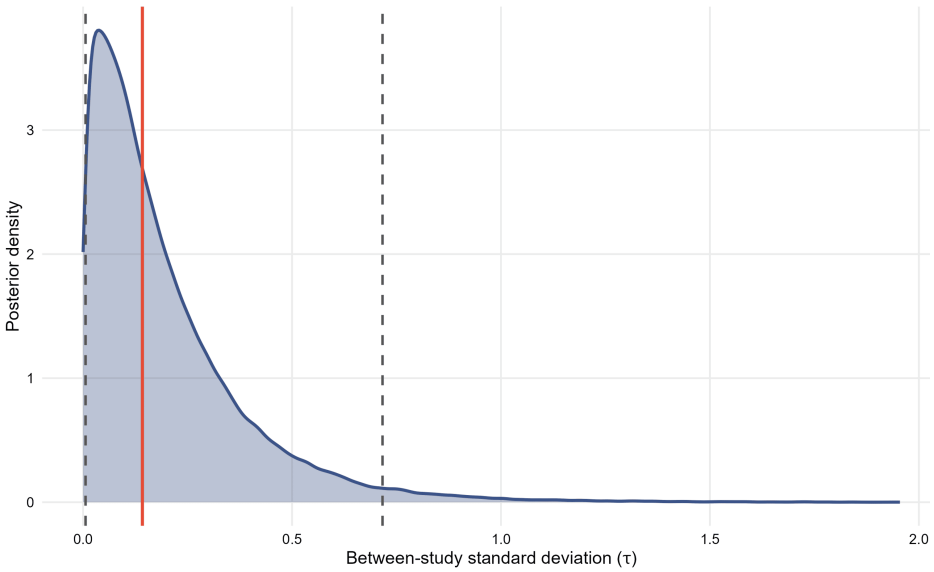

FIGURE 4: Posterior distribution of between-study heterogeneity for SALT ≤10 response

Posterior density distribution of the between-study standard deviation (τ) for the random-effects Bayesian network meta-analysis of SALT ≤10 response. The plot displays the posterior median and 95% credible interval (CrI) for τ together with the corresponding I^2 estimate (median τ=0.14 (95% CrI 0.01-0.72); I^2=21%).

Sources: upadacitinib [18], deuruxolitinib [29-31], ritlecitinib [22], baricitinib [28,36], and ivarmacitinib [34]

I^2: measure of statistical heterogeneity; SALT: Severity of Alopecia Tool; τ: between-study standard deviation

Treatment Effects Versus Placebo

Primary analysis: SALT ⩽20 response: All active treatments significantly increased the odds of achieving SALT ⩽20 at week 24 compared with placebo, as their 95% CrIs excluded 1 (Figure 5). Upadacitinib 30 mg had the largest estimated effect (OR 36.50; 95% CrI 16.53-83.18), followed by upadacitinib 15 mg (OR 24.68; 95% CrI 11.27-56.16) and deuruxolitinib 8 mg twice daily (OR 17.96; 95% CrI 8.05-42.79). Ritlecitinib 50 mg once daily (OR 10.74; 95% CrI 3.80-34.94) and baricitinib 4 mg once daily (OR 10.23; 95% CrI 5.59-19.88) also demonstrated substantial efficacy. The corresponding estimates were OR 6.13 (95% CrI 2.31-15.42) for ivarmacitinib 8 mg, OR 4.82 (95% CrI 1.81-12.33) for ivarmacitinib 4 mg, and OR 3.67 (95% CrI 1.94-7.39) for baricitinib 2 mg. These findings indicate that all evaluated JAK inhibitors produced clinically meaningful improvements relative to placebo.

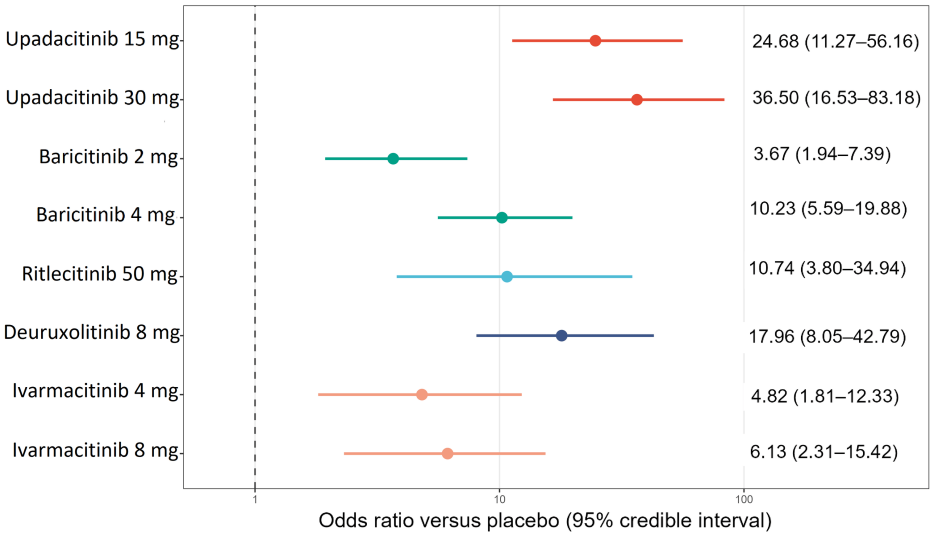

FIGURE 5: Forest plot of treatment efficacy versus placebo (SALT ≤20)

Odds ratios (ORs) and 95% credible intervals (CrIs) from the Bayesian random-effects network meta-analysis for SALT ≤20 response. Values >1 favor active treatment over placebo.

Sources: Mostaghimi et al., 2026, upadacitinib [18]; King et al., 2023, ritlecitinib [22]; Passeron et al., 2025, baricitinib [28]; King et al., 2022, deuruxolitinib [29]; King et al., 2024, deuruxolitinib [30]; Tsianakas et al., 2026, deuruxolitinib [31]; Zhou et al., 2026, ivarmacitinib [34]; and King et al., 2022, baricitinib [36]

SALT: Severity of Alopecia Tool

Secondary analysis: SALT ⩽10 response: Findings for SALT ⩽10 outcome were consistent with SALT ⩽20. All treatments significantly increased the odds of SALT ⩽10 response versus placebo (Figure 6). Upadacitinib 30 mg had the largest estimated effect (OR 69.03; 95% CrI 26.14-221.38), followed by upadacitinib 15 mg (OR 43.83; 95% CrI 16.57-141.77) and deuruxolitinib 8 mg twice daily (OR 39.80; 95% CrI 12.46-172.80). The estimates for the remaining treatments were as follows: baricitinib 4 mg, OR 12.45 (95% CrI 6.10-27.59); ritlecitinib 50 mg, OR 6.70 (95% CrI 2.43-21.59); ivarmacitinib 8 mg, OR 5.07 (95% CrI 1.94-13.56); baricitinib 2 mg, OR 4.62 (95% CrI 2.13-10.57); and ivarmacitinib 4 mg, OR 3.69 (95% CrI 1.38-9.95). Although the ORs were numerically larger for SALT ⩽10, they should not be interpreted as indicating a stronger absolute treatment response due to differences in event frequencies and placebo response rates.

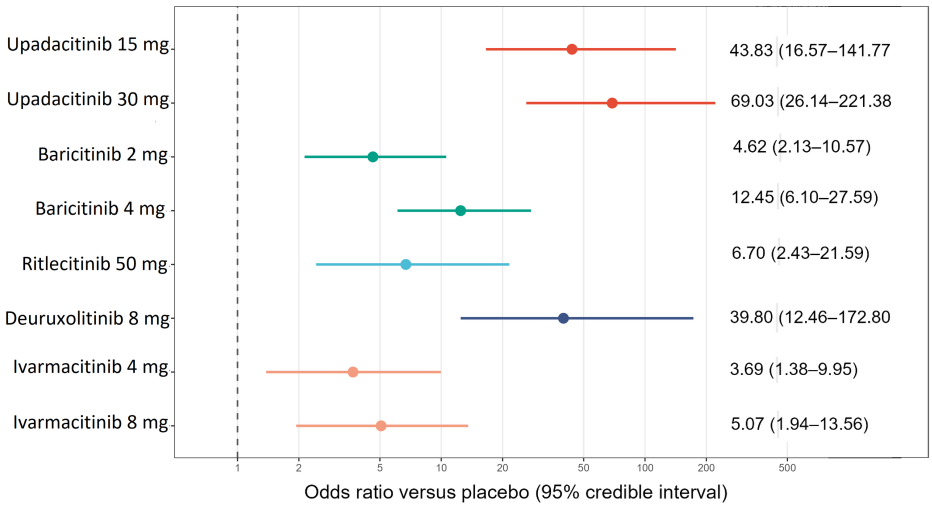

FIGURE 6: Forest plot of treatment efficacy versus placebo (SALT ≤10)

Odds ratios (ORs) and 95% credible intervals (CrIs) from the Bayesian random-effects network meta-analysis for SALT ≤10 response. Values >1 favor active treatment over placebo.

Sources: Mostaghimi et al., 2026, upadacitinib [18]; King et al., 2023, ritlecitinib [22]; Passeron et al., 2025, baricitinib [28]; King et al., 2022, deuruxolitinib [29]; King et al., 2024, deuruxolitinib [30]; Tsianakas et al., 2026, deuruxolitinib [31]; Zhou et al., 2026, ivarmacitinib [34]; and King et al., 2022, baricitinib [36]

SALT: Severity of Alopecia Tool

Observed placebo-adjusted response differences at week 24: The treatment effects were supported by the placebo-adjusted response differences. For SALT ⩽20 and SALT ⩽10, upadacitinib 30 mg produced the largest absolute improvement, followed by upadacitinib 15 mg and deuruxolitinib 8 mg (Figure 7, Figure 8, and Table 5).

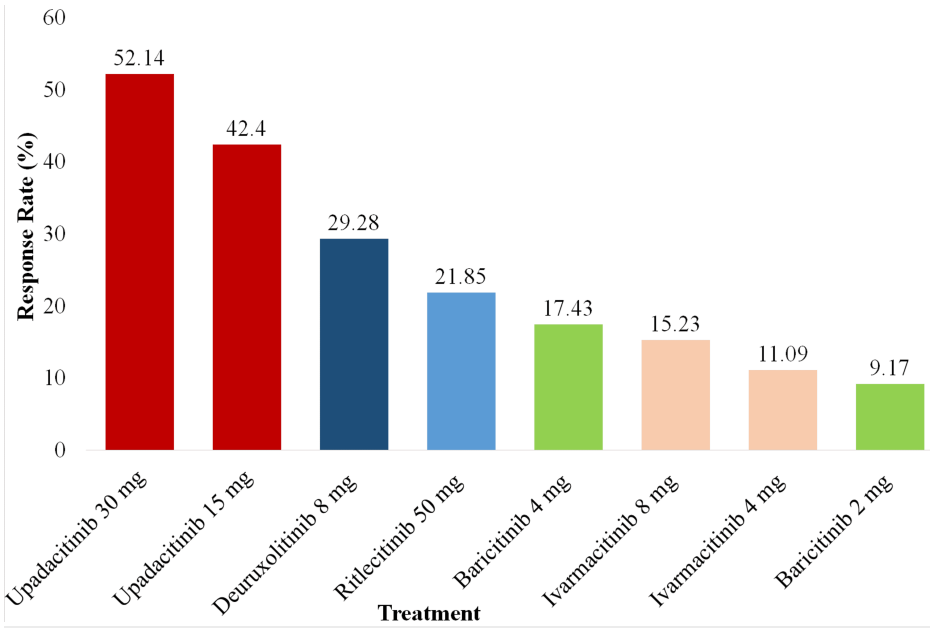

FIGURE 7: Estimated placebo-adjusted response rate (SALT ≤20)

Placebo-adjusted treatment-specific response rates for SALT ≤20 at week 24.

Sources: [18,22,28-31,34,36]

SALT: Severity of Alopecia Tool

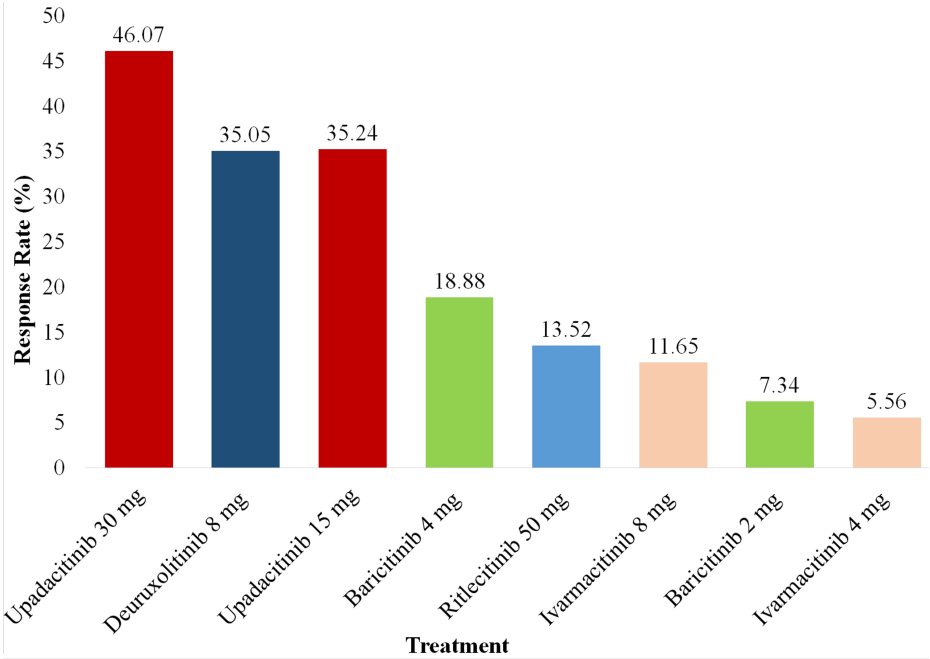

FIGURE 8: Estimated placebo-adjusted response rate (SALT ≤10)

Placebo-adjusted treatment-specific response rates for SALT ≤10 at week 24.

Sources: [18,22,28-31,34,36]

SALT: Severity of Alopecia Tool

Study	Name	Treatment‡	Outcome	Wk	Resp	Total	%
Mostaghimi et al. 2026 [18]	UP-AA1	UPA 15 mg	SALT ≤20	24	122	270	45.19
		UPA 30 mg		24	149	271	54.98
		PBO		24	2	135	1.48
		UPA 15 mg	SALT ≤10	24	95	270	35.19
		UPA 30 mg		24	124	271	45.76
		PBO		24	1	135	0.74
	UP-AA2	UPA 15 mg	SALT ≤20	24	129	289	44.64
		UPA 30 mg		24	157	289	54.33
		PBO		24	5	145	3.45
		UPA 15 mg	SALT ≤10	24	104	289	35.99
		UPA 30 mg		24	136	289	47.06
		PBO		24	0	145	0.00
King et al. 2022 [29]	NR	DEUR 8 mg	SALT ≤20	24	10	38	26.32
		PBO		24	3	43	6.98
	BRAVE-AA1	BARI 2 mg	SALT ≤20	24	21	184	11.40
		BARI 4 mg		24	75	281	26.70
		PBO		24	9	189	4.80
		BARI 2 mg		24	14	156	7.6

King et al. 2022 [36]		BARI 4 mg	SALT ≤10	24	51	234	18.1
		PBO		24	5	156	2.6
	BRAVE-AA2	BARI 2 mg	SALT ≤20	24	17	184	10.90
		BARI 4 mg		24	66	281	28.20
		PBO		24	2	189	1.30
		BARI 2 mg	SALT ≤10	24	12	156	7.70
		BARI 4 mg		24	44	234	18.80
		PBO		24	1	156	0.64
King et al. 2023 [22]	ALLEGRO-2b/3	RIT 50 mg	SALT ≤20	24	29	124	23.39
		PBO		24	2	130	1.54
		RIT 50 mg	SALT ≤10	24	17	124	13.71
		PBO		24	2	130	1.54
King et al. 2024 [30]	THRIVE-AA1	DEUR 8 mg	SALT ≤20	24	94	318	29.56
		PBO		24	1	128	0.78
		DEUR 8 mg	SALT ≤10	24	73	351	20.80
		PBO		24	0	140	0.00
Passeron et al. 2025 [28]	BRAVE-AA-PEDS	BARI 2 mg	SALT ≤20	24	14	84	16.67
		BARI 4 mg		24	27	85	31.76
		PBO		24	3	88	3.41
		BARI 2 mg	SALT ≤10	24	9	84	10.71
		BARI 4 mg		24	18	85	21.18
		PBO		24	0	88	0.00
Tsianakas et al. 2025 [31]	THRIVE-AA2	DEUR 8 mg	SALT ≤20	24	77	233	33.05
		PBO		24	1	119	0.84
		DEUR 8 mg	SALT ≤10	24	58	233	24.89
		PBO		24	0	119	0.00
Zhou et al. 2026 [34]	NR	IVAR 4 mg	SALT ≤20	24	38	109	34.90
		IVAR 8 mg		24	45	111	40.60
		PBO		24	10	110	9.00
		IVAR 4 mg	SALT ≤10	24	24	109	22.00
		IVAR 8 mg		24	31	111	27.90
		PBO		24	7	110	6.20

TABLE 5: Study-level efficacy data for SALT ≤20 and SALT ≤10 at week 24

‡All treatments were given once a day, except for deuruxolitinib, which was given twice a day.

Percentage was calculated as the number of responders divided by the corresponding total population×100. For Zhou et al. [34], responder counts were derived from the reported percentages and sample sizes and may therefore be non-integer because of rounding.

BARI: baricitinib; DEUR: deuruxolitinib; IVAR: ivarmacitinib; NR: not reported; PBO: placebo; Resp: responders; RIT: ritlecitinib; SALT: Severity of Alopecia Tool; SUCRA: surface under the cumulative ranking curve; UPA: upadacitinib; Wk: weeks

Comparisons Between Active Treatments

Primary analysis: SALT ⩽20 response: The league table demonstrated that upadacitinib 30 mg was significantly more effective than baricitinib 2 mg, baricitinib 4 mg, ivarmacitinib 4 mg, and ivarmacitinib 8 mg (Table 6). However, no statistically credible difference was observed between upadacitinib 30 mg and upadacitinib 15 mg (OR 1.48; 95% CrI 0.87-2.48), ritlecitinib, or deuruxolitinib. Upadacitinib 15 mg was significantly more effective than baricitinib 2 mg, ivarmacitinib 4 mg, and ivarmacitinib 8 mg. Its comparisons with baricitinib 4 mg, ritlecitinib, and deuruxolitinib remained inconclusive. Baricitinib 4 mg was more effective than baricitinib 2 mg (OR 2.79; 95% CrI 1.67-4.62). Deuruxolitinib was also more effective than baricitinib 2 mg (OR 4.91; 95% CrI 1.65-14.28). Ivarmacitinib 4 mg was less effective than deuruxolitinib (OR 0.27; 95% CrI 0.07-0.91). Most other active-treatment comparisons had wide CrIs crossing 1. Overall, the comparative analyses indicated clear dose-response patterns within several JAK inhibitor classes but limited precision for many cross-class comparisons.

Row treatment	UPA 15 mg	UPA 30 mg	BARI 2 mg	BARI 4 mg	RIT 50 mg	DEUR 8 mg	IVAR 4 mg	IVAR 8 mg
Placebo	24.68 (11.27-56.16)	36.50 (16.53-83.18)	3.67 (1.94-7.39)	10.23 (5.59-19.88)	10.74 (3.80-34.94)	17.96 (8.05-42.79)	4.82 (1.81-12.33)	6.13 (2.31-15.42)
UPA 15 mg	-	1.48 (0.87-2.48)	**0.15 (0.05-0.43)**	0.41 (0.15-1.17)	0.44 (0.12-1.80)	0.73 (0.23-2.30)	**0.19 (0.06-0.66)**	**0.25 (0.07-0.83)**
UPA 30 mg	-	-	**0.10 (0.04-0.29)**	**0.28 (0.10-0.80)**	0.30 (0.08-1.23)	0.50 (0.16-1.57)	**0.13 (0.04-0.45)**	**0.17 (0.05-0.57)**
BARI 2 mg	-	-	-	**2.79 (1.67-4.62)**	2.94 (0.83-11.14)	**4.91 (1.65-14.28)**	1.31 (0.39-3.98)	1.67 (0.50-5.08)
BARI 4 mg	-	-	-	-	1.05 (0.31-3.96)	1.76 (0.61-4.99)	0.47 (0.14-1.41)	0.60 (0.18-1.79)
RIT 50 mg	-	-	-	-	-	1.68 (0.41-6.27)	0.44 (0.10-1.79)	0.56 (0.12-2.27)
DEUR 8 mg	-	-	-	-	-	-	**0.27 (0.07-0.91)**	0.34 (0.09-1.16)
IVAR 4 mg	-	-	-	-	-	-	-	1.27 (0.55-2.95)

TABLE 6: League table of comparative treatment efficacy for SALT ≤20 response at week 24

League table presenting pairwise odds ratios (ORs) with 95% credible intervals (CrIs) from the Bayesian network meta-analysis for SALT ≤20 response. Each cell represents the column treatment relative to the row treatment; OR >1 favors the column treatment, whereas OR <1 favors the row treatment. Bold values indicate 95% CrIs that exclude 1.

Sources: [18,22,28-31,34,36]

BARI: baricitinib; DEUR: deuruxolitinib; IVAR: ivarmacitinib; RIT: ritlecitinib; SALT: Severity of Alopecia Tool; UPA: upadacitinib

Secondary analysis: SALT ⩽10 response: For SALT ⩽10, upadacitinib 30 mg was significantly more effective than baricitinib 2 mg, baricitinib 4 mg, ritlecitinib, ivarmacitinib 4 mg, and ivarmacitinib 8 mg. Its comparison with upadacitinib 15 mg approached but did not reach statistical credibility (OR 1.57; 95% CrI 0.99-2.47), while the comparison with deuruxolitinib remained inconclusive. Upadacitinib 15 mg was significantly more effective than baricitinib 2 mg, baricitinib 4 mg, ritlecitinib 50 mg, ivarmacitinib 4 mg, and ivarmacitinib 8 mg. No credible difference was observed between upadacitinib 15 mg and deuruxolitinib 8 mg. Baricitinib 4 mg was more effective than baricitinib 2 mg (OR 2.69; 95% CrI 1.62-4.57). Deuruxolitinib 8 mg was more effective than baricitinib 2 mg (OR 8.63; 95% CrI 2.04-45.08) and ritlecitinib 50 mg (OR 5.95; 95% CrI 1.15-35.22). Most other comparisons between active treatments were inconclusive (Table 7). Overall, the active-treatment comparisons were broadly consistent between the primary and secondary outcomes, with upadacitinib 30 mg generally producing the largest efficacy estimates. These findings reinforced the dose-response pattern observed in the SALT ⩽20 analysis.

Row treatment	UPA 15 mg	UPA 30 mg	BARI 2 mg	BARI 4 mg	RIT 50 mg	DEUR 8 mg	IVAR 4 mg	IVAR 8 mg
Placebo	43.83 (16.57-141.77)	69.03 (26.14-221.38)	4.62 (2.13-10.57)	12.45 (6.10-27.59)	6.70 (2.43-21.59)	39.80 (12.46-172.80)	3.69 (1.38-9.95)	5.07 (1.94-13.56)
UPA 15 mg	-	1.57 (0.99-2.47)	**0.10 (0.03-0.37)**	**0.28 (0.07-0.98)**	**0.15 (0.03-0.69)**	0.90 (0.18-5.19)	**0.08 (0.02-0.34)**	**0.11 (0.03-0.46)**
UPA 30 mg	-	-	**0.07 (0.02-0.24)**	**0.18 (0.05-0.63)**	**0.10 (0.02-0.44)**	0.57 (0.12-3.31)	**0.05 (0.01-0.22)**	**0.07 (0.02-0.29)**
BARI 2 mg	-	-	-	**2.69 (1.62-4.57)**	1.46 (0.39-5.75)	**8.63 (2.04-45.08)**	0.80 (0.22-2.79)	1.10 (0.30-3.77)
BARI 4 mg	-	-	-	-	0.54 (0.15-2.11)	3.21 (0.78-16.44)	0.29 (0.08-1.01)	0.41 (0.12-1.36)
RIT 50 mg	-	-	-	-	-	**5.95 (1.15-35.22)**	0.55 (0.12-2.27)	0.75 (0.17-3.07)
DEUR 8 mg	-	-	-	-	-	-	**0.09 (0.02-0.43)**	**0.13 (0.02-0.58)**
IVAR 4 mg	-	-	-	-	-	-	-	1.38 (0.61-3.11)

TABLE 7: League table of comparative treatment efficacy for SALT ≤10 response at week 24

League table presenting pairwise odds ratios (ORs) with 95% credible intervals (CrIs) from the Bayesian network meta-analysis for SALT ≤10 response. Each cell represents the column treatment relative to the row treatment; OR >1 favors the column treatment, whereas OR <1 favors the row treatment. Bold values indicate 95% CrIs that exclude 1.

Sources: [18,22,28-31,34,36]

BARI: baricitinib; DEUR: deuruxolitinib; IVAR: ivarmacitinib; RIT: ritlecitinib; SALT: Severity of Alopecia Tool; UPA: upadacitinib

Treatment-Ranking Probabilities

Primary analysis: SALT ⩽20 response: Upadacitinib 30 mg had the highest probability of being the most effective treatment for SALT ⩽20 response, with an 82.7% probability of ranking first. Deuruxolitinib had a 9.5% probability of ranking first, followed by upadacitinib 15 mg at 3.7% and ritlecitinib at 3.4%. Upadacitinib 15 mg most frequently occupied the second rank, with a probability of 62.1%, whereas placebo had a 99.3% probability of ranking last (SALT ⩽20, Table *8*; SALT ⩽10, Table *9*). The SUCRA rankings also favored upadacitinib 30 mg, followed by upadacitinib 15 mg and deuruxolitinib 8 mg twice daily. Ritlecitinib 50 mg and baricitinib 4 mg occupied intermediate positions, while ivarmacitinib 8 mg, ivarmacitinib 4 mg, and baricitinib 2 mg ranked lower. Placebo occupied the lowest position in the treatment hierarchy (Figure *9*). Rank probabilities and SUCRA values were consistent with the relative treatment effects estimated in the network meta-analysis.

Treatment	Rank 1	Rank 2	Rank 3	Rank 4	Rank 5	Rank 6	Rank 7	Rank 8	Rank 9
Placebo	-	-	-	-	-	-	-	0.5%	99.3%
UPA 15 mg	3.7%	62.1%	25.8%	6.4%	1.4%	-	-	-	-
UPA 30 mg	82.7%	13.9%	2.6%	0.6%	-	-	-	-	-
BARI 2 mg	-	-	-	-	1.9%	13.7%	20.2%	63.9%	-
BARI 4 mg	-	1.5%	8.8%	35.3%	40%	9.6%	4.3%	-	-
RIT 50 mg	3.4%	5.1%	14.3%	29.5%	27.2%	10.4%	7.9%	2.2%	-
DEUR 8 mg	9.5%	16.7%	46.1%	19.2%	6.4%	1.4%	0.5%	-	-
IVAR 4 mg	-	-	0.6%	2.1%	6.2%	20.7%	44%	25.8%	-
IVAR 8 mg	-	-	1.8%	6.7%	16.6%	43.8%	22.9%	7.4%	-

TABLE 8: Treatment-ranking probabilities for SALT ≤20 response at week 24

Posterior probabilities of each treatment occupying each efficacy rank for SALT ≤20 response based on the Bayesian network meta-analysis. Rank 1 represents the most effective treatment and Rank 9 the least effective, with each cell indicating the probability that a treatment occupies the corresponding rank. For example, UPA 30 mg had an 82.7% probability of ranking first and a 13.9% probability of ranking second. Cells with "-" correspond to probabilities not displayed numerically in the source figure.

Sources: upadacitinib [18], deuruxolitinib [29-31], ritlecitinib [22], baricitinib [28,36], and ivarmacitinib [34]

BARI: baricitinib; DEUR: deuruxolitinib; IVAR: ivarmacitinib; RIT: ritlecitinib; SALT: Severity of Alopecia Tool; UPA: upadacitinib

Treatment	Rank 1	Rank 2	Rank 3	Rank 4	Rank 5	Rank 6	Rank 7	Rank 8	Rank 9
Placebo	-	-	-	-	-	-	-	0.9%	99%
UPA 15 mg	1.7%	53.7%	42%	2.3%	-	-	-	-	-
UPA 30 mg	72.5%	25.9%	1.4%	-	-	-	-	-	-
BARI 2 mg	-	-	-	-	17.3%	30.1%	23.9%	28.4%	-
BARI 4 mg	-	0.7%	6%	70.8%	18.4%	3%	0.9%	-	-
RIT 50 mg	-	-	1.5%	15.3%	37.7%	19.8%	14.2%	11.2%	-
DEUR 8 mg	25.5%	19.3%	48.8%	5.4%	0.8%	-	-	-	-
IVAR 4 mg	-	-	-	1%	5.1%	14.9%	28.9%	49.3%	0.7%
IVAR 8 mg	-	-	-	4.8%	20.4%	32%	32%	10.3%	-

TABLE 9: Treatment-ranking probabilities for SALT ≤10 response at week 24

Posterior probabilities of each treatment occupying each efficacy rank for SALT ≤10 response based on the Bayesian network meta-analysis. Rank 1 represents the most effective treatment and Rank 9 the least effective, with each cell indicating the probability that a treatment occupies the corresponding rank. For example, UPA 30 mg had a 72.5% probability of ranking first and a 25.9% probability of ranking second. Cells with "-" correspond to probabilities not displayed numerically in the source figure.

Sources: upadacitinib [18], deuruxolitinib [29-31], ritlecitinib [22], baricitinib [28,36], and ivarmacitinib [34]

BARI: baricitinib; DEUR: deuruxolitinib; IVAR: ivarmacitinib; RIT: ritlecitinib; SALT: Severity of Alopecia Tool; UPA: upadacitinib

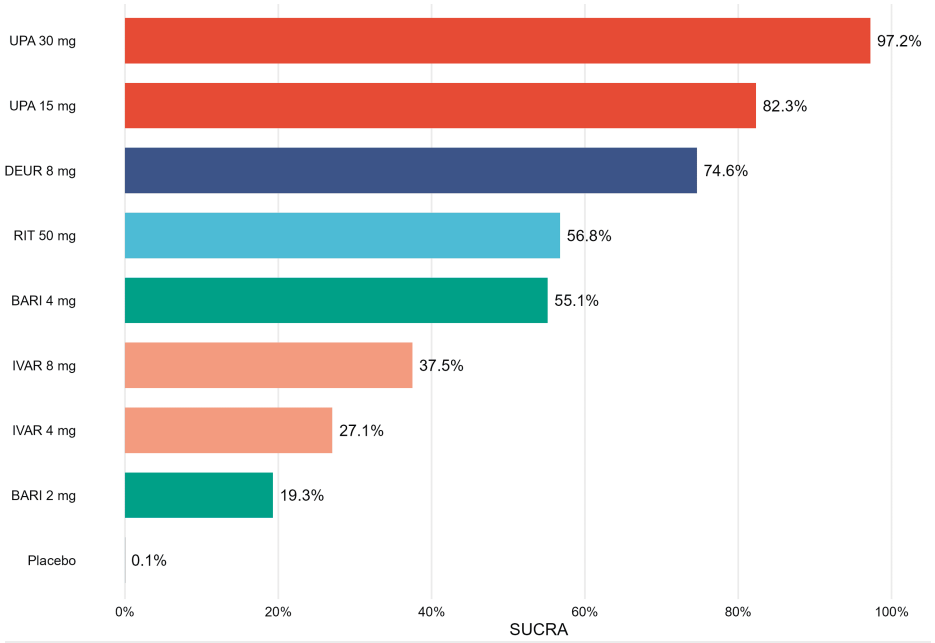

FIGURE 9: SUCRA rankings of treatments for SALT ≤20 responses

Treatment rankings according to the SUCRA for SALT ≤20 responses. Higher SUCRA values indicate a greater probability of a treatment being among the most effective interventions.

Sources: upadacitinib [18], deuruxolitinib [29-31], ritlecitinib [22], baricitinib [28,36], and ivarmacitinib [34]

SUCRA: surface under the cumulative ranking curve; BARI: baricitinib; DEUR: deuruxolitinib; IVAR: ivarmacitinib; RIT: ritlecitinib; SALT: Severity of Alopecia Tool; UPA: upadacitinib

Secondary analysis: SALT ⩽10 response: For SALT ⩽10, upadacitinib 30 mg also had the highest probability of ranking first at 72.5%, followed by deuruxolitinib at 25.5% and upadacitinib 15 mg at 1.7%. Placebo had a 99% probability of ranking last. The SUCRA rankings similarly placed upadacitinib 30 mg highest, followed by deuruxolitinib 8 mg twice daily and upadacitinib 15 mg. Baricitinib 4 mg occupied the next position, followed by ritlecitinib 50 mg, ivarmacitinib 8 mg, baricitinib 2 mg, and ivarmacitinib 4 mg. Placebo was ranked lowest (Figure *10*). Overall, upadacitinib 30 mg consistently occupied the highest position for both SALT ⩽20 and SALT ⩽10 responses. However, SUCRA rankings should be interpreted alongside the magnitude and precision of the relative treatment effects and not as definitive evidence of superiority. The ranking results for SALT ⩽10 closely mirrored those for SALT ⩽20, indicating stability of the treatment hierarchy across efficacy thresholds.

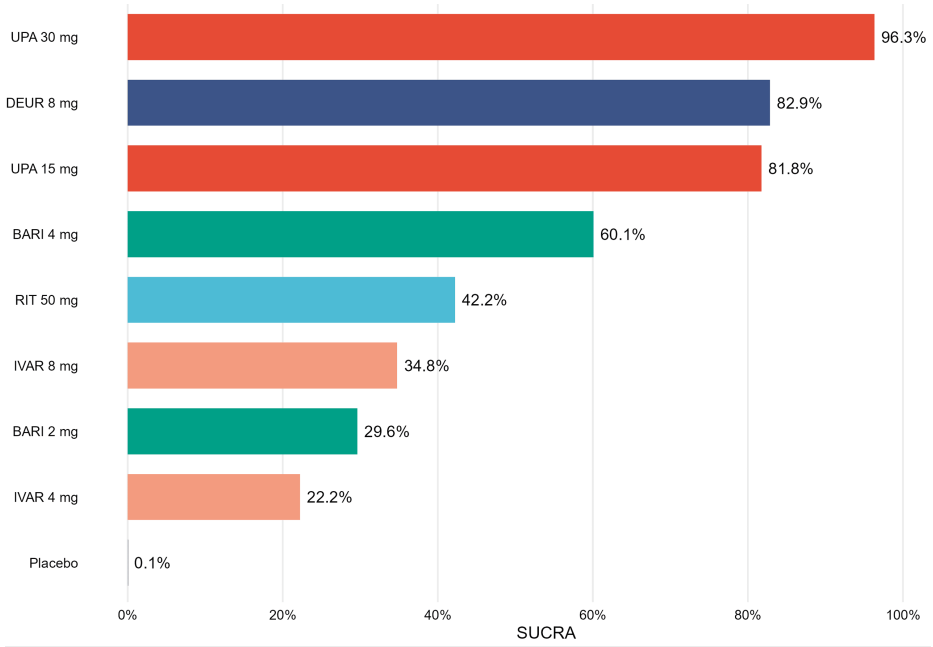

FIGURE 10: SUCRA rankings of treatments for SALT ≤10 responses

Treatment rankings according to the SUCRA for SALT ≤10 responses. Higher SUCRA values indicate a greater probability of a treatment being among the most effective interventions.

Sources: upadacitinib [18], deuruxolitinib [29-31], ritlecitinib [22], baricitinib [28,36], and ivarmacitinib [34]

SUCRA: surface under the cumulative ranking curve; BARI: baricitinib; DEUR: deuruxolitinib; IVAR: ivarmacitinib; RIT: ritlecitinib; SALT: Severity of Alopecia Tool; UPA: upadacitinib

Residual Deviance and Leverage Assessment

For SALT ⩽20, two placebo arms had residual deviance contributions greater than 2: BRAVE-AA2 [36] (2/189 responders; residual deviance 2.41) and King et al. [29] (3/43 responders; residual deviance 2.24). For SALT ⩽10, four zero-event placebo arms had residual deviance contributions greater than 2: UP-AA Study 2 [18], BRAVE-AA-PEDS [28], Tsianakas et al. [31], and THRIVE-AA1 [30]. Nevertheless, the leverage plots did not identify any studies with a clearly disproportionate influence on the overall findings (SALT ⩽20, Figure *11*; SALT ⩽10, Figure *12*). These assessments indicated that no single study exerted undue influence on the network estimates.

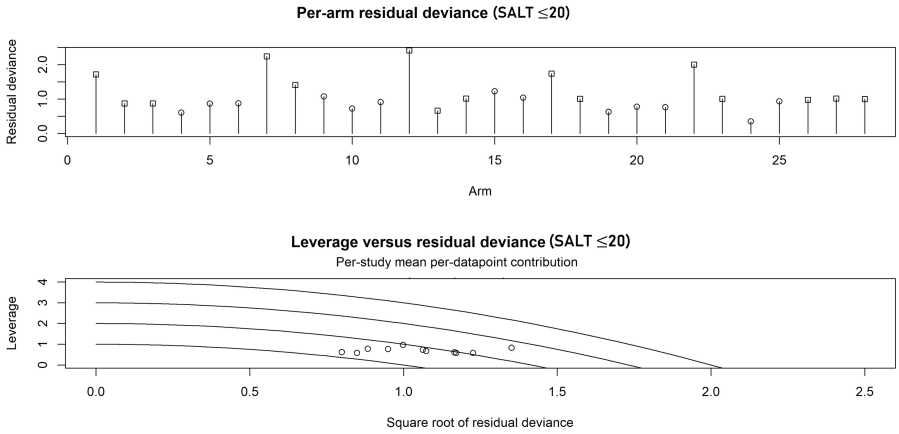

FIGURE 11: Residual deviance and leverage diagnostics for the Bayesian network meta-analysis of SALT ≤20 response

Model-fit diagnostic plots showing per-arm residual deviance and study-level leverage versus residual deviance for SALT ≤20 response. These plots were used to identify observations or studies with potentially poor model fit or disproportionate influence.

Sources: upadacitinib [18], deuruxolitinib [29-31], ritlecitinib [22], baricitinib [28,36], and ivarmacitinib [34]

SALT: Severity of Alopecia Tool

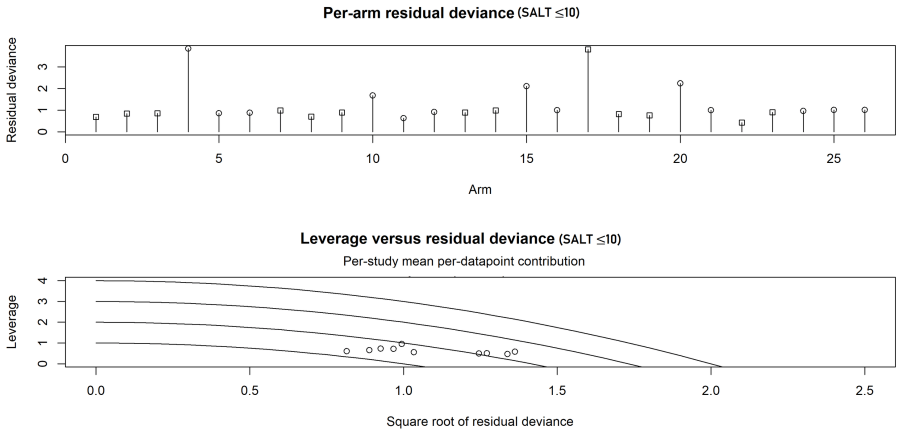

FIGURE 12: Residual deviance and leverage diagnostics for the Bayesian network meta-analysis of SALT ≤10 response

Model-fit diagnostic plots showing per-arm residual deviance and study-level leverage versus residual deviance for SALT ≤10 response. These plots were used to identify observations or studies with potentially poor model fit or disproportionate influence.

Sources: upadacitinib [18], deuruxolitinib [29-31], ritlecitinib [22], baricitinib [28,36], and ivarmacitinib [34]

SALT: Severity of Alopecia Tool

Sensitivity Analyses

Fixed-effects and random-effects models generated similar treatment estimates, with substantially overlapping CrIs for both outcomes. For SALT ⩽20, the fixed-effects and random-effects models had DIC values of 49.08 and 50.44, respectively (Figure *13*). For SALT ⩽10, the corresponding DIC values were 46.44 and 48.01 (Figure *14*). The small DIC differences did not indicate a clinically meaningful improvement in model fit with either specification. For SALT ⩽10, an additional sensitivity analysis using a wider treatment-effect prior produced the same direction of effects and did not alter the principal conclusions, although

estimates for some sparsely informed treatments increased and became less precise. Overall, the sensitivity analyses supported the robustness of the primary findings. These results indicated that the main conclusions were stable across alternative model assumptions and prior specifications.

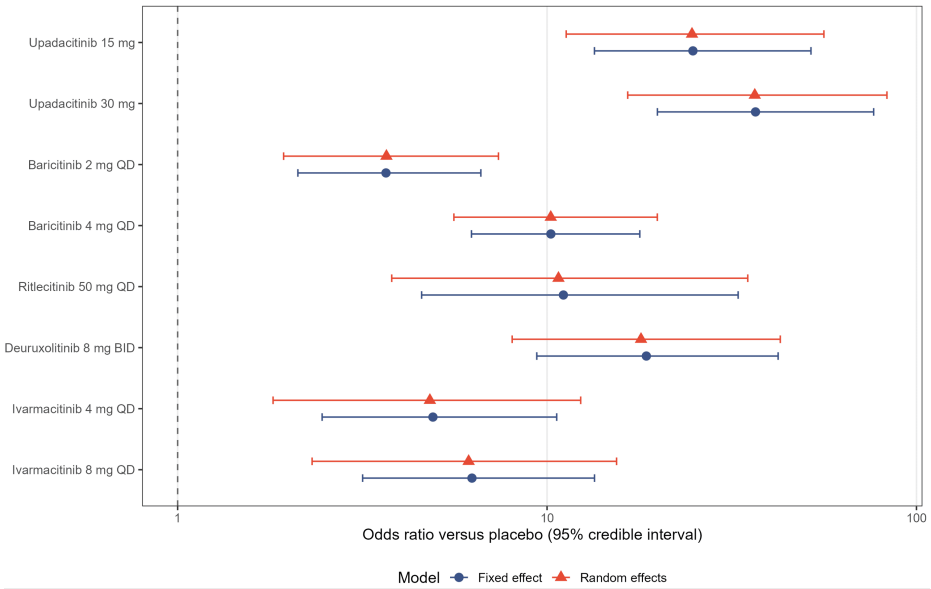

FIGURE 13: Sensitivity analysis comparing random-effects and fixed-effects Bayesian network meta-analysis models for SALT ≤20 response

Forest plots comparing treatment-effect estimates from random-effects and fixed-effects Bayesian network meta-analysis models for SALT ≤20 response. Effect estimates are expressed as odds ratios (ORs) versus placebo with 95% credible intervals (CrIs).

Sources: upadacitinib [18], deuruxolitinib [29-31], ritlecitinib [22], baricitinib [28,36], and ivarmacitinib [34]

SALT: Severity of Alopecia Tool

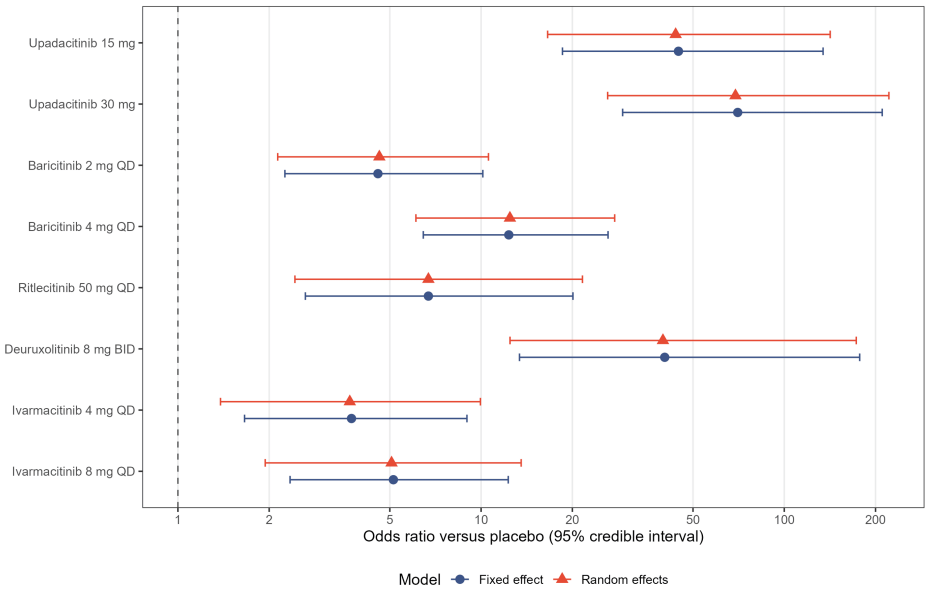

FIGURE 14: Sensitivity analysis comparing random-effects and fixed-effects Bayesian network meta-analysis models for SALT ≤10 response

Forest plots comparing treatment-effect estimates from random-effects and fixed-effects Bayesian network meta-analysis models for SALT ≤10 response. Effect estimates are expressed as odds ratios (ORs) versus placebo with 95% credible intervals (CrIs).

Sources: upadacitinib [18], deuruxolitinib [29-31], ritlecitinib [22], baricitinib [28,36], and ivarmacitinib [34]

SALT: Severity of Alopecia Tool

Assessment of Inconsistency

Node-splitting analyses did not identify any eligible comparisons for either outcome because no treatment contrast had sufficient independent direct and indirect evidence. Therefore, local inconsistency could not be formally evaluated. This reflects the structure of the available evidence network and should not be interpreted as confirmation that inconsistency was absent. The absence of node-splitting contrasts highlights the reliance on consistency models for inference but does not imply that the network was free of potential inconsistency.

Risk of Bias

For week 24 SALT ⩽20 (primary outcome), six of 10 trial results were judged to be at low risk of bias, and four raised some concerns (Figure *15*). Missing outcome data contributed to all four judgments of some concerns for ritlecitinib (ALLEGRO Phase 2b/3 [22]), deuruxolitinib (CTP-543 Phase 2 [29]), and deuruxolitinib (THRIVE-AA1 Phase 3 [30] and THRIVE-AA2 Phase 3 [31]). Deuruxolitinib (CTP-543 Phase 2[29]) also raised concerns regarding the randomization process. For week 24 SALT ⩽10, four of nine trial results were judged to be at low risk of bias, and five raised some concerns. Missing outcome data contributed to the judgments of some concerns for ritlecitinib (ALLEGRO Phase 2b/3 [22]), baricitinib (BRAVE-AA1 Phase 3 and BRAVE-AA2 [36]), deuruxolitinib (THRIVE-AA2 Phase 3 [31]), and upadacitinib (UP-AA1 Phase 3 [18] and UP-AA2 Phase 3 [18]). No trial result was judged to be at high risk of bias for either outcome.

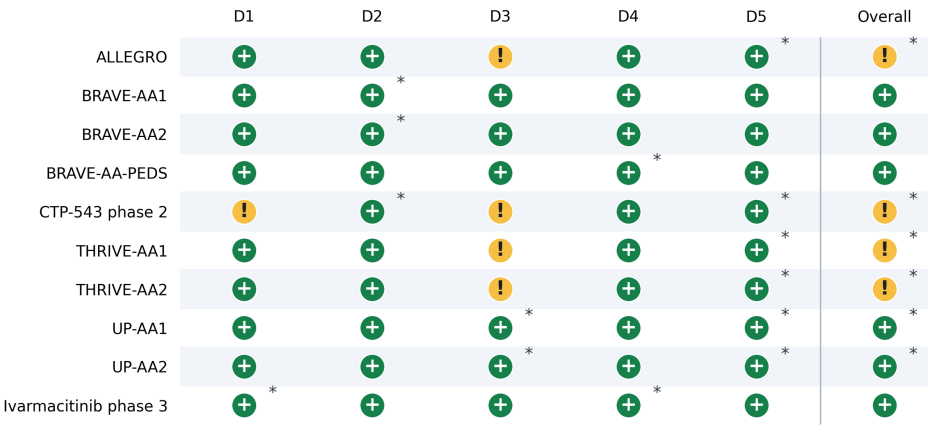

FIGURE 15: Risk-of-bias assessment of the included randomized controlled trials

Risk of bias was assessed using the Cochrane Risk of Bias 2 (RoB 2) tool for week 24 SALT ≤20 outcomes across five domains: D1, bias arising from the randomization process; D2, bias due to deviations from intended interventions; D3, bias due to missing outcome data; D4, bias in measurement of the outcome; and D5, bias in selection of the reported result. Domain-specific and overall judgments were classified as low risk (green, +), some concerns (yellow, !), or high risk (red, −). Asterisks indicate provisional judgments. Rows with multiple doses summarize dose-versus-placebo comparisons.

Sources: ALLEGRO-2b/3 (ritlecitinib, King et al. 2023 [22]); BRAVE-AA1 and BRAVE-AA2 (baricitinib, King et al. 2022 [36]); BRAVE-AA-PEDS (baricitinib, Passeron et al. 2025 [28]); CTP-543 phase 2 (deuruxolitinib, King et al. 2022 [29]); THRIVE-AA1 (deuruxolitinib, King et al. 2024 [30]); THRIVE-AA2 (deuruxolitinib, Tsianakas et al. 2025 [31]), UP-AA1 and UP-AA2 (upadacitinib, Mostaghimi et al. 2026 [18]); and ivarmacitinib phase 3 (Zhou et al. 2026 [34])

SALT: Severity of Alopecia Tool

Discussion

JAK inhibitors represent a major advance in the therapeutic management of AA, a long-neglected and underserved condition, offering targeted immunomodulation with unprecedented efficacy [6-8,20]. They are now widely considered first-line treatment for severe AA, and their global clinical development has catalyzed a new era in clinical trial design and outcomes assessment. Despite these advances, an unmet medical need persists for more efficacious and safer agents, as AA is a chronic condition requiring long-term maintenance therapy to sustain treatment success. Although JAK inhibitors provide robust efficacy compared with previous therapies, all approved agents carry boxed warnings in the United States or equivalent regulatory safety statements in major regulatory markets, including increased risks of serious infections, mortality, malignancy, major adverse cardiovascular events, and thrombosis.

In pivotal studies, approximately half of the participants receiving baricitinib, ritlecitinib, deuruxolitinib, and ivarmacitinib fail to achieve the therapeutic SALT target score of ⩽20 after 24, 48, or 52 weeks of uninterrupted therapy [9-11,13,19-25,27-37]. Furthermore, among patients who experience meaningful hair regrowth, discontinuation of JAK inhibitors often leads to loss of benefit over time, and some responders fail to recapture their response upon retreatment [35,37].

Until mechanistically differentiated and potentially safer alternatives, such as rezpegaldesleukin, a first-in-class interleukin-2 receptor agonist anticipated to carry no boxed warnings or require ongoing laboratory monitoring [62,63], become available for the management of severe AA, strategic intraclass JAK inhibitor rotation will remain an important approach for patients who do not achieve or sustain adequate responses. Suboptimal efficacy or tolerability will therefore likely require switching among available oral JAK inhibitors to take advantage of interindividual or intraclass differences, while future agents with nonoverlapping mechanisms may eventually provide additional options [39-45]. For these reasons, identifying the JAK inhibitor with the greatest likelihood of achieving meaningful scalp hair regrowth at treatment initiation is of paramount importance.

In this BNMA of 10 RCTs enrolling 5,276 participants, all five evaluated JAK inhibitors significantly improved the likelihood of achieving SALT ⩽20 and SALT ⩽10 at week 24 compared with placebo. Upadacitinib 30 mg once daily produced the largest relative and placebo-adjusted effects for both outcomes and had the highest probability of ranking first. Upadacitinib 15 mg and deuruxolitinib 8 mg twice daily also occupied consistently high positions, whereas ritlecitinib 50 mg once daily and baricitinib 4 mg demonstrated intermediate efficacy, and ivarmacitinib 8 mg, ivarmacitinib 4 mg, and baricitinib 2 mg

generally ranked lower. Although the ranking probabilities favored upadacitinib, the hierarchy was less definitive than these probabilities alone might suggest, because CrIs for many active-treatment comparisons were wide and crossed the null, particularly for treatments informed by a single trial. The most reliable conclusion is therefore that all assessed regimens were efficacious relative to placebo, while evidence supporting superiority between individual active treatments remains more limited.

It is also notable that deuruxolitinib is the only twice-daily regimen among the evaluated JAK inhibitors. In chronic conditions, adherence is generally higher with once-daily dosing [64-69], and prior attempts to convert deuruxolitinib to a once-daily schedule by doubling the dose were not successful [70], as the altered regimen produced inferior efficacy and a less favorable safety profile in the RCT. The 8-mg twice-daily schedule (n=29) led to substantially greater scalp hair regrowth than the 16-mg once-daily schedule (n=28). A SALT reduction of at least 90% by week 24 was achieved by 20.7% of patients receiving 8 mg twice daily compared with only 3.6% of those receiving 16 mg once daily. Treatment-emergent adverse events were also more common with the once-daily regimen, occurring in 77% of patients versus 57% with twice-daily dosing.

Direct week 24 responder rates aligned with the placebo-adjusted differences in absolute response. For the primary endpoint (SALT ⩽20), the placebo-adjusted response rate for upadacitinib 30 mg showed the greatest improvement and significantly outperformed deuruxolitinib, baricitinib, ritlecitinib, and ivarmacitinib. Taken together, these response patterns indicate that upadacitinib provided the most robust clinical benefit, followed by deuruxolitinib, whereas baricitinib, ivarmacitinib, and ritlecitinib yielded more moderate and generally comparable outcomes. The overall distribution of effects illustrates meaningful therapeutic variation among approved and emerging JAK inhibitors for severe AA and reinforces the value of comparative evidence when direct head-to-head trials are unavailable. The descriptive findings demonstrated close agreement with the model-based estimates, lending additional support to the relative ranking of therapies. These findings challenge the long-standing assumption that all orally administered JAK inhibitors for severe AA achieve essentially comparable efficacy and suggest that upadacitinib may occupy a distinct therapeutic tier within the class, with the potential to reduce the need for successive switching in many patients.

Although all evaluated JAK inhibitors demonstrated clinically meaningful benefit, the magnitude and consistency of responses observed with upadacitinib suggest that it may offer a higher likelihood of achieving substantial scalp hair regrowth in many patients. These observations are consistent with current understanding of AA pathobiology and the central involvement of JAK-STAT signaling [8,71-73]. Interferon gamma and related inflammatory cytokines promote immune-mediated follicular injury, and targeted suppression of JAK-dependent pathways is believed to help reestablish follicular immune privilege and support regrowth.

Dermatologists have accumulated several years of clinical experience with baricitinib and ritlecitinib for severe AA across major regulatory markets, following their commercialization in the United States in 2022 and 2023, respectively. Clinical experience with deuruxolitinib and ivarmacitinib remains limited, as these agents were commercialized only in the United States and China in 2025, with deuruxolitinib subsequently authorized in the United Kingdom in 2026. Upadacitinib was authorized in the European Union for severe AA in July 2026 and remains under active review by the United States FDA for this indication. Recent data increasingly point to substantial benefit associated with selective JAK1 inhibition using upadacitinib in both adolescents and adults [15,18]. Our treatment hierarchy differs partly from earlier network meta-analyses, in which deuruxolitinib often appeared among the most effective oral JAK inhibitors [48]. This difference is plausibly explained by the inclusion of the two recent upadacitinib phase 3 trials [18], the incorporation of newly available adolescent baricitinib data [28], and restriction to clinically relevant week 24 SALT thresholds and approved doses. Within this expanded evidence base, upadacitinib 30 mg demonstrated the highest probability of ranking first for both SALT ⩽20 and SALT ⩽10.

The relative efficacy estimates observed in the present analysis are broadly consistent with previously published network meta-analyses. In particular, the numerical similarity between ritlecitinib 50 mg once daily and baricitinib 4 mg once daily for SALT ⩽20 should not be considered unexpected. In a Bayesian indirect comparison of these regimens at week 24, Aceituno et al. found no statistically credible difference between ritlecitinib 50 mg and baricitinib 4 mg for either SALT ⩽20 (OR 2.16; 95% CrI 0.48-16.46) or SALT ⩽10 (OR 0.96; 95% CrI 0.18-7.21); adjustment for potential effect modifiers using multilevel network meta-regression did not materially alter these findings [47]. Similarly, Gupta et al. reported no significant efficacy differences among deuruxolitinib 8 mg twice daily, ritlecitinib 50 mg once daily, and baricitinib 4 mg once daily [48], while Yan et al. [74] found relatively similar efficacy rankings for baricitinib 4 mg and ritlecitinib 50 mg, with their relative ordering varying according to the SALT endpoint evaluated. These observations align closely with the present analysis, in which ritlecitinib 50 mg and baricitinib 4 mg produced nearly identical placebo-referenced effects for SALT ⩽20 (OR 10.74 and 10.23, respectively), with a numerically larger effect for baricitinib 4 mg for the more stringent SALT ⩽10 endpoint (OR 12.45 versus 6.70). Importantly, the wide CrIs around indirect comparisons indicate that these findings should be interpreted as an absence of a statistically credible difference rather than evidence of therapeutic equivalence. Deuruxolitinib 8 mg twice daily, by contrast, consistently occupied a higher efficacy position than ritlecitinib 50 mg and baricitinib 4 mg in the present analysis, particularly for SALT ⩽10, although the uncertainty

surrounding the indirect comparisons precludes definitive conclusions regarding superiority.

The concordant ordering across both SALT⩽20 and SALT⩽10 thresholds reinforces the robustness of the efficacy hierarchy. SALT ⩽20 is a widely used benchmark representing at least 80% scalp coverage and is generally considered clinically meaningful in patients with severe disease, whereas SALT ⩽10 captures a more demanding level of near-complete scalp regrowth. The persistence of the leading treatment estimates across both thresholds suggests that the findings were not dependent on a single response definition. Importantly, the numerically larger ORs for SALT ⩽10 should not be interpreted as a greater absolute benefit, because ORs are influenced by baseline risk and the stringent endpoint produced fewer events in placebo groups. The placebo-adjusted response differences provide a more clinically intuitive interpretation: improvements were largest with upadacitinib 30 mg, upadacitinib 15 mg, and deuruxolitinib, but the size of benefit varied between the two SALT thresholds.

A dose-response pattern was evident for agents evaluated at more than one dose. Baricitinib 4 mg was credibly more effective than 2 mg for both outcomes, supporting the dose-response relationship observed in the BRAVE-AA trials and subsequent longer-term analyses [11,19,21,36]. Upadacitinib 30 mg generated larger point estimates than 15 mg, although the between-dose comparisons did not reach statistical credibility. Ivarmacitinib 8 mg also ranked above 4 mg, but the uncertainty around both estimates precluded a firm conclusion regarding a dose-response effect. Incremental benefit must be weighed against adverse events, age, comorbidities, and concomitant medications. Additional considerations include laboratory abnormalities, reproductive factors, and regulatory guidance.

Safety is particularly important for JAK inhibitors because risks may be modified by age and baseline cardiovascular, thromboembolic, malignant, or infectious risk. The descriptive safety findings were generally reassuring over the 24-week controlled periods. Serious adverse events, serious infections, treatment discontinuations, herpes infections, and deaths were uncommon, although adverse events were often numerically more frequent with active treatment than with placebo. These results are consistent with the short-term safety profiles reported in the individual trials. However, safety findings should be interpreted cautiously, as rare adverse events are inherently challenging to evaluate with precision, even when derived from sizable and well-designed studies. The present study did not undertake a comparative safety network meta-analysis, and definitions and completeness of safety reporting varied across trials.

This analysis has several strengths. It incorporated recent RCTs across five oral JAK inhibitors approved for severe AA in one or more major regulatory markets, evaluated both a clinically established response threshold and a more stringent endpoint at a common 24-week time point, and reported relative effects together with placebo-adjusted response differences and treatment-ranking probabilities. The Bayesian framework enabled the simultaneous comparison of multiple interventions, and convergence diagnostics, residual deviance and leverage assessments, and sensitivity analyses supported the stability of the model. Heterogeneity was low for both outcomes, and the close concordance between fixed-effect and random-effects estimates further reinforces the robustness of the principal conclusions.

Several limitations must also be acknowledged. First, the network was predominantly star-shaped around placebo, and no contrast contained sufficient independent direct and indirect evidence for node splitting. Consequently, local inconsistency could not be tested, and most active-treatment comparisons were indirect. Second, several nodes were informed by only one trial, producing wide CrIs and unstable ranking probabilities. Third, transitivity may have been affected by between-trial differences in age, geographic setting, duration of present episode and AA, baseline SALT score, prevalence of alopecia totalis or universalis, prior treatment exposure, and eligibility criteria. Adolescents and adults were combined, although treatment effects and background risk may differ by age. The ivarmacitinib evidence originated exclusively from China, which may limit generalizability, while the single ritlecitinib phase 2b/3 study and the upadacitinib program enrolled both adolescents and adults. Fourth, zero events in several placebo arms contributed to residual deviance outliers for SALT ⩽10, although no study showed clearly disproportionate leverage and sensitivity analyses did not materially alter the conclusions. Fifth, the analysis was limited to week 24 and therefore may not capture differences in the durability of response, relapse risk, or adverse events that could arise after 24 weeks, factors of particular relevance given the chronic and relapsing nature of AA. Sixth, we did not have access to individual patient data and therefore relied on aggregate data, which limits adjustment for individual-level effect modifiers and reduces the precision of indirect comparisons. Seventh, the risk-of-bias assessment identified some concerns for several trial results, primarily related to missing outcome data, although no result was judged to be at high risk of bias. These concerns may partly reflect limitations in the information available in published reports rather than established deficiencies in trial conduct; nevertheless, the potential influence of missing outcome data on the treatment estimates cannot be excluded. Finally, treatment rankings did not incorporate patient-reported outcomes, eyebrow or eyelash regrowth, health-related quality of life, cost, treatment access, or patient preferences, all of which are important in clinical decision-making.

In clinical practice, these results support oral JAK inhibitors as an effective therapeutic intervention for patients with severe AA who are appropriate candidates for systemic therapy. Upadacitinib 30 mg, in particular, along with upadacitinib 15 mg and deuruxolitinib 8 mg twice daily, produced the largest efficacy estimates in the current evidence base, but the absence of direct comparative trials prevents a definitive

declaration of the best agent. Treatment should therefore be individualized according to age, disease phenotype and duration, previous therapy, comorbidities, safety profile, approved indication and dose, monitoring requirements, availability, and patient preference. Well-powered head-to-head trials, harmonized reporting of safety and patient-reported outcomes, age-stratified analyses, and longer follow-up are needed to determine whether the apparent efficacy differences translate into durable comparative benefit. Overall, the evidence indicates a class-wide benefit of oral JAK inhibitors at week 24, with a probable efficacy gradient that remains to be confirmed through direct comparative evidence.

Conclusions

This systematic review and BNMA demonstrated that all evaluated oral JAK inhibitor regimens significantly increased the likelihood of achieving SALT ⩽20 and SALT ⩽10 at week 24 compared with placebo. Upadacitinib 30 mg once daily produced the largest relative and placebo-adjusted efficacy estimates and had the highest probability of ranking first for both outcomes, followed by upadacitinib 15 mg once daily and deuruxolitinib 8 mg twice daily. Although all active treatments were efficacious, the magnitude and consistency of responses observed with upadacitinib suggest that individual JAK inhibitors may not achieve comparable levels of benefit and that upadacitinib may represent a higher-performing tier within the class. However, many comparisons between active treatments remained inconclusive because of wide CrIs, reliance on indirect evidence, and the limited number of trials informing several treatment nodes. Short-term serious adverse events and serious infections were uncommon, but the available evidence was insufficient for a comparative safety analysis or for evaluating rare or long-term harms. Treatment selection should therefore consider regulatory approval, age, comorbidities, safety profile, monitoring requirements, availability, and patient preferences rather than efficacy rankings alone. Well-powered head-to-head trials with longer follow-up and standardized efficacy and safety reporting are needed to establish the comparative benefits and risks of individual oral JAK inhibitors.

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.

Concept and design: Arya Babul, Devina Mehta, Yssra Soliman, Anand Rajpara

Acquisition, analysis, or interpretation of data: Arya Babul

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Disclosures

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** Drs. Devina Mehta and Yssra Soliman are practicing dermatologists at Thomas Dermatology in Las Vegas. Dr. Soliman is also a Clinical Assistant Professor in the Department of Internal Medicine at the Kirk Kerkorian School of Medicine at the University of Nevada, Las Vegas. Dr. Anand Rajpara is a practicing dermatologist and Professor of Dermatology at the University of Missouri Kansas City School of Medicine and the Founding Chair of the Department of Dermatology at University Health in Kansas City.

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