Comparative Efficacy of JAK Inhibitors Indicated for Severe Alopecia Areata: A Bayesian Network Meta-Analysis and Matching-Adjusted Indirect Comparison

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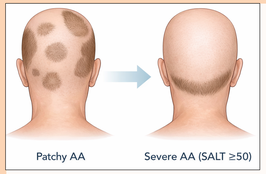
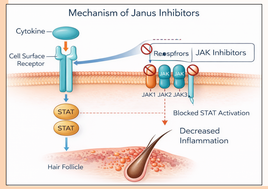
Background





Alopecia areata (AA) is an autoimmune, non-scarring hair loss disorder with an estimated lifetime prevalence of approximately 0.1 to 2%. Severe AA, defined as ≥50% scalp hair loss (Severity of Alopecia Tool [SALT] score ≥50), is associated with substantial psychosocial distress and impaired QoL. Systemic Janus kinase inhibitors (JAKIs) have transformed the therapeutic landscape of AA. However, despite regulatory approval of baricitinib, ritlecitinib, and deuruxolitinib, the absence of head-to-head randomized controlled trials and limitations of prior meta-analyses hinder evidence-based comparative treatment selection.

Objectives

To compare the short-term efficacy of FDA-and EMA-approved oral JAKIs for severe AA using advanced indirect comparison methods. Specifically, we evaluated **baricitinib, ritlecitinib**, and **deuruxolitinib** based on Week-24 SALT ≤10 and ≤20 response outcomes.

Study Design

PROSPERO registered systematic review (CRD420251116775), conducted according to PRISMA 2020 identified 7 RCTs (n=4560) of approved JAKIs for severe AA from PubMed, Embase, Cochrane CENTRAL, & Clinical-Trials.gov (to 7/2025). Week-24 efficacy (**SALT ≤10 & ≤20**) was compared using Bayesian network meta-analysis, multilevel network meta-regression (ML-NMR), & matching-adjusted indirect comparisons (MAIC). Surface under the cumulative ranking (SUCRA) ranked treatments.

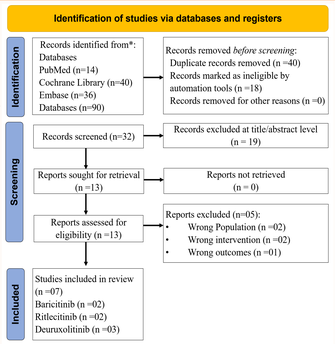


Figure 1: PRISMA flow diagram

Results

Across Bayesian network meta-analysis, multilevel network meta-regression, and matching-adjusted indirect comparison models, **deuruxolitinib 8 mg BID consistently demonstrated the highest efficacy** for achieving clinically meaningful hair regrowth at Week 24. Deuruxolitinib showed superior odds of achieving **SALT ≤10 and ≤20** compared with baricitinib (2 mg and 4 mg), while comparisons with ritlecitinib 50 mg were directionally favorable but not statistically significant. **SUCRA rankings consistently placed deuruxolitinib highest among approved oral JAK inhibitors**.

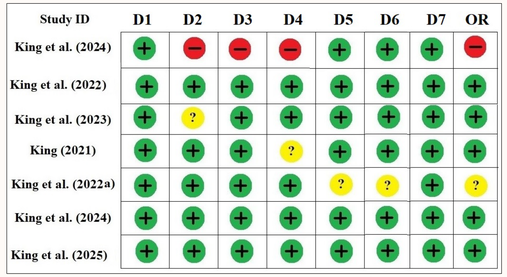


Figure 2. Risk of bias was assessed using the Cochrane RoB 2.0 Tool. Five studies were rated as low risk overall. BRAVE-AA1 was rated as "high risk" due to concerns related to reporting of allocation concealment, blinding, and outcome assessment

Treatment	NMA OR (95% CrI)	Model 1 OR (95% CrI) (Base Case: sex, baseline SALT, episode duration, disease duration)	Model 2 OR (95% CrI) (Baseline SALT only)	Model 3 OR (95% CrI) (All covariates)
SALT ≤10				
Baricitinib 2 mg QD vs Ritlecitinib 50 mg QD	2.45 (0.49-21.98)	7.15 (1.25-60.02)	3.02 (0.57-22.32)	8.29 (1.41-72.62)
Baricitinib 2 mg QD vs Deuruxolitinib 8 mg BID	4.27 (2.66-7.02)	3.68 (2.25-6.02)	2.56 (1.52-4.30)	2.20 (1.28-3.78)
Baricitinib 4 mg QD vs Ritlecitinib 50 QD mg	0.91 (0.19-7.96)	1.93 (0.36-15.43)	1.11 (0.22-7.96)	2.12 (0.39-17.70)
Baricitinib 4 mg QD vs Deuruxolitinib 8 mg BID	2.53 (1.52-4.20)	2.21 (1.25-3.90)	1.30 (0.71-2.39)	0.77 (0.36-1.60)
Ritlecitinib 50 mg QD vs Deuruxolitinib 8 mg BID	1.18 (0.26-5.37)	0.86 (0.18-4.18)	1.01 (0.21-4.83)	0.77 (0.16-3.81)
SALT ≤20				
Baricitinib 2 mg QD vs Ritlecitinib 50 QD mg	5.53 (1.28-39.67)	5.84 (0.42-27.38)	3.34 (0.55-27.86)	2.41 (0.09-75.60)
Baricitinib 2 mg QD vs Deuruxolitinib 8 mg BID	5.71 (3.42-9.50)	5.00 (3.11-8.76)	3.40 (2.00-5.77)	2.96 (1.67-5.16)
Baricitinib 4 mg QD vs Ritlecitinib 50 QD mg	1.93 (0.47-14.04)	0.78 (0.11-6.66)	1.04 (0.18-9.07)	0.49 (0.02-1.50)
Baricitinib 4 mg QD vs Deuruxolitinib 8 mg BID	3.38 (1.94-5.78)	2.93 (1.66-5.17)	1.72 (0.94-3.16)	1.03 (0.49-2.17)
Ritlecitinib 50 mg QD vs Deuruxolitinib 8 mg BID	1.97 (0.46-8.52)	1.50 (0.32-6.93)	1.72 (0.37-7.87)	1.32 (0.27-6.35)

Table 1. Anchored ML-NMR on SALT ≤ 10 & ≤ 20 at Week 24. Odds ratio (OR) above 1 favor deuruxolitinib 8 mg BID.

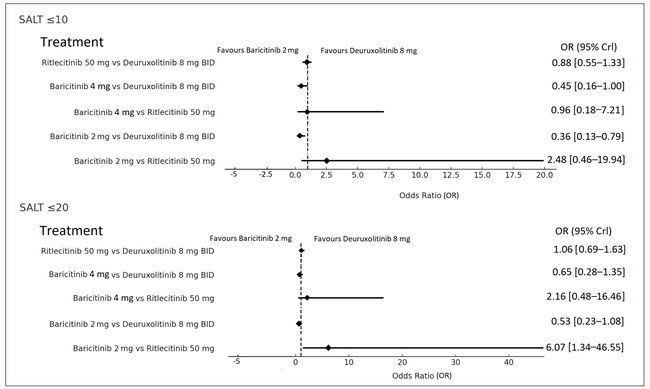


Figure 3. Forest plot comparing ritlecitinib 50 mg QD vs. deuruxolitinib 8 mg BID, baricitinib 4 mg QD vs. deuruxolitinib 8 mg BID, baricitinib 4 mg QD vs. ritlecitinib 50 mg QD, baricitinib 2 mg QD vs. deuruxolitinib 8 mg BID, baricitinib 2 mg QD vs. ritlecitinib 50 mg QD on SALT ≤ 10 & ≤ 20 are shown. Results to the right of the dashed line indicate evidence of a difference in favor of deuruxolitinib 8 mg BID.

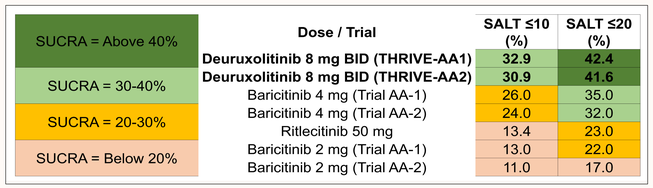


Figure 4. SUCRA-based ranking of approved oral JAKIs for severe AA at Week 24. The heatmap displays SUCRA values for achieving SALT ≤10 & SALT ≤20 responses. Dark green (>40%) indicates highest efficacy, light green (30–40%) moderate–high efficacy, yellow (20–30%) moderate efficacy, & orange (10–20%) lowest efficacy. Deuruxolitinib 8 mg BID consistently ranked highest across both outcomes.

Results

SALT ≤10					
COMPARATOR	Naive OR (95% CI)	Base Case OR (95% CI)	SALT at Baseline OR (95% CI)	AIC Selected OR (95% CI)	All Possible OR (95% CI)
Baricitinib 2 mg QD	2.69 (2.34-3.09) (p<0.0001)	2.41 (1.46-3.98) (p=0.0005)	2.97 (1.93-4.57) (p<0.0001)	2.47 (1.58-3.84) (p<0.0001)	2.53 (1.23-5.19) (p=0.0114)
Baricitinib 4 mg QD	1.19 (1.05-1.36) (p=0.0074)	1.16 (0.67-2.03) (p=0.5)	1.38 (0.89-2.13) (p=0.144)	1.20 (0.77-1.86) (p=0.411)	1.205 (0.52-2.74) (p=0.658)
Deuruxolitinib 8 mg BID	11.48 (4.36-30.23) (p<0.0001)	11.55 (4.25-31.52) (p<0.0001)	13.22 (4.63-38.85) (p<0.0001)	13.67 (4.66-41.06) (p<0.0001)	13.42 (4.61-40.57) (p<0.0001)
Ritlecitinib 50 mg QD	13.38 (5.70-34.67) (p<0.001)	13.34 (5.67-34.63) (p<0.001)	12.95 (5.43-34.27) (p<0.001)	13.09 (5.48-34.31) (p<0.001)	13.33 (5.66-34.70) (p<0.001)
SALT ≤20					
COMPARATOR	Naive OR (95% CI)	Base Case OR (95% CI)	SALT at Baseline OR (95% CI)	AIC Selected OR (95% CI)	All Possible OR (95% CI)
Baricitinib 2 mg QD	2.75 (2.43-3.12) (p<0.0001)	2.71 (1.67-4.39) (p<0.0001)	3.05 (2.03-4.57) (p<0.0001)	2.10 (1.34-3.29) (p=0.001)	2.49 (1.25-4.96) (p=0.009)
Baricitinib 4 mg QD	1.26 (1.12-1.42) (p=0.0001)	1.31 (0.78-2.18) (p=0.294)	1.45 (0.96-2.19) (p=0.07)	0.99 (0.64-1.54) (p=0.988)	1.16 (0.54-2.52) (p=0.692)
Deuruxolitinib 8 mg BID	57.25 (18.50-173.30) (p<0.0001)	60.48 (18.10-205.60) (p<0.0001)	69.64 (20.20-238.50) (p<0.0001)	72.06 (20.60-257.20) (p<0.0001)	71.55 (20.50-256.10) (p<0.0001)
Ritlecitinib 50 mg QD	18.64 (6.77-61.80) (p<0.001)	18.35 (6.64-60.94) (p<0.001)	17.54 (6.25-58.50) (p<0.001)	17.72 (6.30-58.84) (p<0.001)	18.27 (6.62-60.86) (p<0.001)

Table 2. MAIC results for baricitinib 2 mg QD vs ritlecitinib 50 mg QD, baricitinib 2 mg QD vs deuruxolitinib 8 mg BID, baricitinib 4 mg QD vs ritlecitinib 50 mg QD, baricitinib 4 mg vs deuruxolitinib 8 mg BID, ritlecitinib 50 mg vs deuruxolitinib 8 mg BID mg (SALT≤10 & SALT ≤20).

Conclusion

Across multiple indirect comparison frameworks, deuruxolitinib 8 mg BID demonstrated the highest probability of achieving clinically meaningful hair regrowth at Week 24 among approved oral JAKIs for severe AA. These findings provide comparative efficacy insights to support treatment selection in the absence of head-to-head RCTs.

References

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3. **Veroniki AA et al.** Update to the PRISMA guidelines for network meta-analyses and scoping reviews and development of guidelines for rapid reviews: A scoping review protocol. *JBI Evid Synth* 2025;23:517-26.