Upadacitinib Leads in Efficacy: Bayesian Network Meta-Analysis of Four JAK Inhibitors for Moderate-to-Severe Atopic Dermatitis

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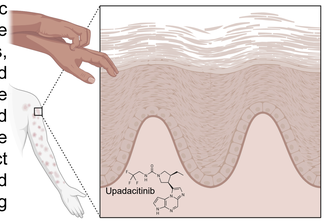
Background

Atopic dermatitis (AD) is a chronic inflammatory skin disease associated with severe pruritus, sleep disturbance, and impaired quality of life. Oral Janus kinase inhibitors (JAKis) provide rapid symptom control, but multiple agents are available and direct head-to-head randomized controlled trials (RCTs) comparing their efficacy are lacking.



Objectives

This study aimed to compare and rank the short-term efficacy of oral JAKis when dose as monotherapy for moderate-to-severe AD using a Bayesian network meta-analysis (BNMA).

Study Design

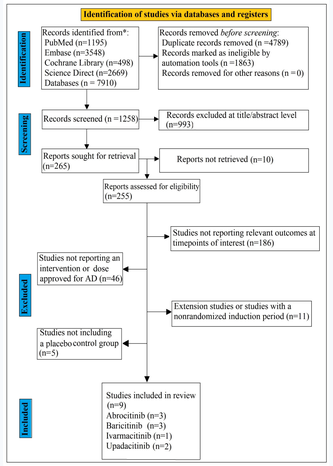


Figure 1. PRISMA Flow Diagram

A PRISMA compliant, prospectively registered systematic review was executed (PROSPERO CRD420251116775). 9 double-blind, placebo-controlled RCTs in patients with moderate-to-severe AD were analyzed (N=4,261). Treatments included upadacitinib (15 mg, 30 mg), abrocitinib (100 mg, 200 mg), baricitinib (2 mg, 4 mg), and ivarmacitinib (4 mg, 8 mg). Primary outcomes were Eczema Area and Severity Index (EASI-75), Investigator's Global Assessment (IGA-AD 0/1), and ≥4-point reduction in itch numeric rating scale (Itch NRS) at 12 or 16 wk. Bayesian hierarchical network meta-analysis was used to estimate OR and rank treatments using Surface under the cumulative ranking (SUCRA) probabilities.

Results

Nine RCTS (N=4,261) formed a fully connected treatment network for comparative efficacy analysis. Upadacitinib 30 mg consistently demonstrated the highest efficacy and achieved the greatest odds of EASI-75 response, IGA-AD 0/1, and a ≥4-point improvement in itch NRS vs. placebo and other oral JAKis.

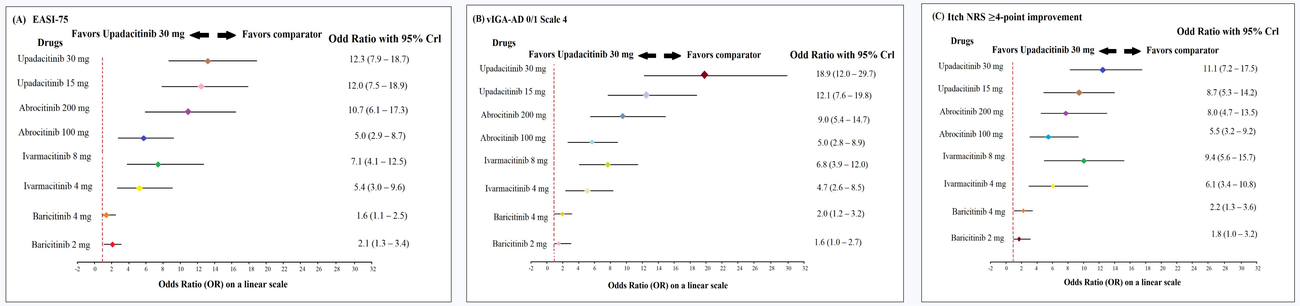


Figure 2. BNMA Forest Plots for Primary Efficacy Outcomes (Pooled ORs with 95% credible intervals [CrI]): (**A) EASI-75; (B) IGA-AD 0/1; and (C) Itch NRS ≥4-point improvement (**12-16 wk)**.** Relative to placebo, for all endpoints, the order of efficacy was upadacitinib 30 mg, upadacitinib 15 mg & abrocitinib 200 mg.

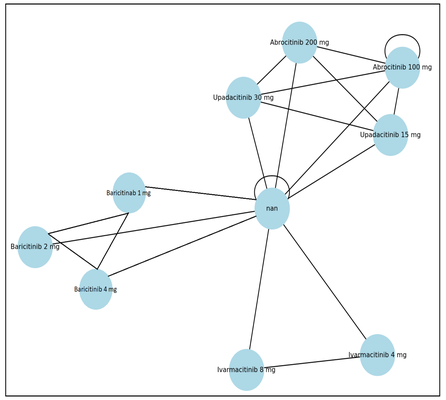


Figure 3. Network Geometry of Included Interventions. Plot illustrating evidence structure among RCTs. Each node represents an intervention (drug & dose); node size reflects sample size. Line thickness reflects number of RCTs; lines represent direct therapy comparisons.

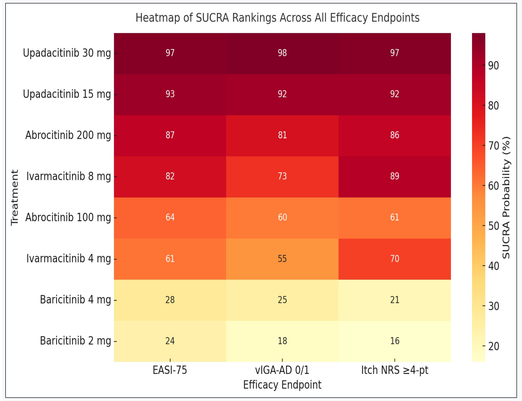


Figure 4. Heatmap of SUCRA Rankings Across All Efficacy Endpoints. SUCRA heatmap summarizing probability of each treatment being the most effective across all efficacy endpoints. (EASI-75, IGA-AD 0/1, and Itch NRS ≥4-point improvement). Upadacitinib 30 mg consistently ranked highest, followed by upadacitinib 15 mg and abrocitinib 200 mg.

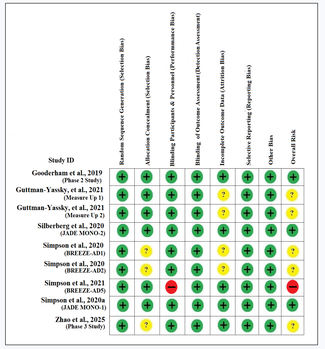


Figure 5. Risk of Bias (RoB) Assessment of Included Studies. Summary of RoB evaluation using the Cochrane Risk of Bias Tool (RoB 2) for all included RCTs. Most studies demonstrated low risk across all domains, with minor concerns related to reported allocation concealment and blinding in a few trials

Results

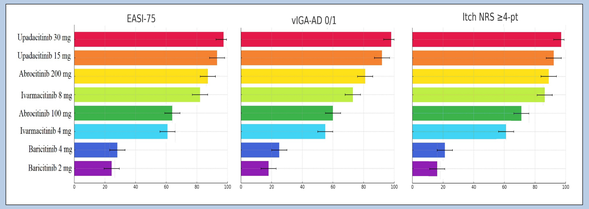


Figure 6. SUCRA-based ranking for EASI-75, vIGA-AD 0/1, and ≥4-point improvement in itch NRS, derived from BNMA. Higher values indicate greater probability of being the most effective treatment

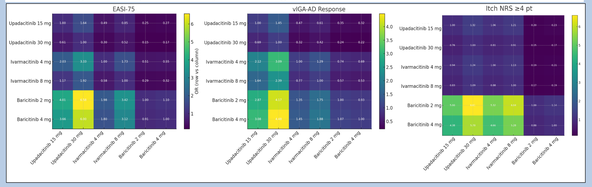


Figure 7. Ranking heatmaps for comparative efficacy across three primary outcomes after removal of 12-week abrocitinib trials. (A) EASI-75, (B) vIGA-AD response, and (C) Itch NRS ≥4-point improvement.

Conclusion

This Bayesian network meta-analysis demonstrates that upadacitinib 30 mg provides the greatest short-term efficacy among oral JAK inhibitors for moderate-to-severe atopic dermatitis, with consistent superiority in skin clearance and itch reduction. These findings establish a clear efficacy hierarchy and support preferential consideration of upadacitinib when oral JAK inhibitor therapy is indicated.

References

1. RINVOQ (upadacitinib), US FDA Label (Prescribing Information). https://tinyurl.com/d7k9eu9v. Accessed 23 December 2025.
2. CIBINQO (abrocitinib), US FDA Label (Prescribing Information). https://tinyurl.com/353x4umy. Accessed 23 December 2025.
3. **Zhao et al.** Ivarmacitinib for Moderate to Severe Atopic Dermatitis in Adults and Adolescents: A Phase 3 Randomized Clinical Trial. JAMA Dermatol. 2025;161(7):688-697.