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LETTER TO THE EDITOR

Author's Reply: Interpreting Treatment Rankings of Oral JAK Inhibitors in Atopic Dermatitis

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Dear Editor,

We thank Yılmaz, Koker Özer, and Topal for their thoughtful comments regarding our Bayesian network meta-analysis (BNMA) comparing the short-term efficacy of oral Janus kinase (JAK) inhibitors in moderate-to-severe atopic dermatitis (AD) [1]. We agree that treatment rankings, including the surface under the cumulative ranking curve (SUCRA), should not be interpreted in isolation or equated automatically with clinically meaningful superiority.

Our conclusions were based on the totality of evidence rather than SUCRA values alone. Upadacitinib 30 mg consistently ranked highest across three clinically relevant outcomes i.e., the Eczema Area and Severity Index (EASI)-75, Investigator's Global Assessment for Atopic Dermatitis (IGA-AD) 0/1, and a ≥4-point improvement in the Itch Numerical Rating Scale (Itch NRS) and this pattern was supported by placebo-referenced effect estimates, ranking probabilities, sensitivity analyses, and meta-regression models. The stability of this finding across outcomes and alternative model specifications supported our conclusion that upadacitinib 30 mg was the most consistently efficacious regimen under the conditions evaluated. Nevertheless, SUCRA represents a probabilistic summary of treatment rankings and does not independently establish the magnitude or clinical importance of differences between treatments [2].

We also agree that the similar placebo-referenced estimates for EASI-75 with upadacitinib 30 mg and 15 mg, whose odds ratios are 12.3 and 12.0 respectively, illustrate the importance of considering effect sizes and their uncertainty alongside rank ordering. These estimates should not be interpreted as demonstrating a substantial difference between the two doses for this individual outcome. However, the evidence supporting the overall ranking was not restricted to EASI-75: upadacitinib 30 mg showed greater numerical separation from the 15-mg dose for IGA-AD 0/1 and Itch NRS response. Accordingly, our inference concerned the consistency of short-term efficacy across all evaluated endpoints rather than a claim that every pairwise contrast demonstrated a clinically important difference. Direct responder rates from replicate placebo-controlled registration clinical trials provide additional clarity [3]. Upadacitinib 30 mg produced numerically higher placebo-adjusted responder rates than upadacitinib 15 mg across all evaluated outcomes, including EASI-75, EASI-90, EASI-100, Itch NRS and IGA-AD 0/1 in monotherapy trials (AD-1 and AD-2).

The term "superior" in our report was intended to describe the comparative short-term efficacy hierarchy generated by the BNMA, not to establish universal therapeutic superiority or recommend upadacitinib 30 mg for every patient. We explicitly characterized the resulting efficacy preference as provisional and acknowledged the absence of direct head-to-head trials comparing different oral JAK inhibitors, variation in assessment timepoints, reliance on indirect placebo-controlled comparisons, and exclusion of long-term safety and tolerability outcomes [1]. We further noted that 15 mg is the recommended starting dose of upadacitinib, with escalation to 30 mg considered only in appropriate patients with an inadequate response.

Clinical treatment selection necessarily extends beyond short-term efficacy. Safety, age, comorbidities, baseline scores, prior treatment response, disease severity, concomitant therapies, patient preferences, regulatory labeling, and the certainty of comparative evidence must all be considered. Formal certainty

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assessments, such as CINeMA, may further strengthen the interpretation of future network meta-analyses [4]. Direct head-to-head trials and longer-term comparative studies are the gold-standard for determining whether the observed probabilistic rankings translate into clinically meaningful differences in effectiveness and benefit–risk balance.

We therefore confirm that our findings should be interpreted as demonstrating that upadacitinib 30 mg had the highest and most consistent probability of short-term efficacy among the evaluated regimens, rather than as definitive evidence of an overall therapeutic preference independent of uncertainty, safety, and individual patient considerations.

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The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

1. A. Babul, D. Mehta, Y. Soliman, M. Hussain, and N. Babul, "Upadacitinib Leads in Efficacy: A Bayesian Network Meta-Analysis of Four JAK Inhibitors in Moderate-To-Severe Atopic Dermatitis," *International Journal of Dermatology* 65, no. 7 (2026): 1395–1409, https://doi.org/10.1111/ijd.70228.

2. G. Salanti, A. E. Ades, and J. P. A. Ioannidis, "Graphical Methods and Numerical Summaries for Presenting Results From Multiple-Treatment Meta-Analysis: An Overview and Tutorial," *Journal of Clinical Epidemiology* 64, no. 2 (2011): 163–171, https://doi.org/10.1016/j.jclinepi.2010.03.016.

3. Upadacitinib (RINVOQ), US Prescribing Information, 10/10/2025 (SUPPL-28), NDA 211675, "Abbvie," (n.d.), https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/218347Orig1s008,211675Orig1s034lbl.pdf.

4. A. Nikolakopoulou, J. P. T. Higgins, T. Papakonstantinou, et al., "CINeMA: An Approach for Assessing Confidence in the Results of a Network Meta-Analysis," *PLoS Medicine* 17, no. 4 (2020): e1003082, https://doi.org/10.1371/journal.pmed.1003082.

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