Conjunctivitis Risk with Dupilumab Versus Upadacitinib in Atopic Dermatitis: A Propensity-Matched Cohort Study

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INTRODUCTION

Biologic-associated conjunctivitis represents a clinically meaningful adverse effect in patients with atopic dermatitis (AD), with implications for treatment selection and patient quality of life.[1] Dupilumab (DUPI), an IL-4 receptor alpha antagonist widely used for moderate-to-severe AD, has demonstrated an increased incidence of conjunctivitis in clinical trials and real-world settings.[2] In contrast, upadacitinib (UPA), a selective JAK-1 inhibitor, has not shown a similar signal in trials, prompting interest in comparative safety.[3]

MATERIALS AND METHODS

In this retrospective cohort study using the TriNetX Global Collaborative Network (TriNetX, Cambridge, Massachusetts, USA), adult patients with AD initiating DUPI or UPA were identified. Following 1:1 propensity score matching on demographic variables (age, sex, race, and ethnicity), 1,369 patients were included in each treatment group. Conjunctivitis risk was assessed using both odds ratios and time-to-event analyses. Median follow-up duration was longer in the DUPI cohort (664 days) compared to the UPA cohort (310 days).

RESULTS

DUPI use was associated with a significantly increased likelihood of conjunctivitis compared to UPA (odds ratio: 2.71; 95% CI: 1.65–4.45; p<0.001). Time-to-event analysis supported this finding, demonstrating a 70% higher hazard of conjunctivitis among DUPI-treated patients (hazard ratio: 1.70; 95% CI: 1.26–2.29; p=0.001). These findings suggest a consistent elevation in both cumulative and longitudinal risk.

Mechanistically, the increased risk observed with DUPI may be related to IL-4/IL-13 pathway inhibition, which has been associated with reduced conjunctival goblet cell density, impaired mucin production, and tear film instability.[4] In contrast, JAK-1 inhibition with UPA modulates inflammatory signaling through multiple cytokine pathways

without direct IL-4 receptor alpha blockade, which may preserve epithelial homeostasis and avoid these downstream ocular effects.

CONCLUSION

Overall, these real-world data support a differential ocular safety profile between DUPI and UPA. UPA may represent a reasonable therapeutic alternative in patients at higher risk for conjunctivitis or those who develop ocular adverse events while receiving DUPI. Further prospective studies are warranted to validate these findings and clarify underlying mechanisms.

References

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