ImmunoTargets and Therapy

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LETTER

Dupilumab Treatment is Not Associated with Increased Risk of Overall Skin Infections [Letter]

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Dear editor

The article by Labib et al[1] provides a valuable review of prurigo nodularis (PN). Dupilumab, recently approved by the U. S. Food and Drug Administration as the only systemic therapy for the treatment of PN, is mentioned among novel immunotherapies under investigation. Dupilumab safety is reviewed based on clinical trial data for atopic dermatitis (AD). However, the article cites skin infections as adverse reactions more commonly associated with dupilumab relative to placebo, a point that we believe warrants clarification.

Eichenfield et al[2] analyzed pooled data from 7 randomized, placebo-controlled trials in adults with AD and found that the exposure-adjusted proportion of patients with treatment-emergent non-herpetic adjudicated skin infections was significantly lower with dupilumab than with placebo (14.5% vs 26.6%, $p < 0.001$). In the same study, the incidence of herpetic infections was non-significantly higher with dupilumab (12.7% vs 10.4%, $p = 0.24$), while eczema herpeticum and herpes zoster were significantly less frequent with dupilumab versus placebo (1.1% vs 3.6%, $p = 0.004$). Similarly, in a pooled analysis of 2 randomized, placebo-controlled trials in children aged 6–17 years with AD, Paller et al[3] reported significantly lower exposure-adjusted proportions of patients with total and non-herpetic skin infections in the dupilumab group versus placebo (respectively, 35.9% vs 67.0%, $p = 0.001$ and 27.8% vs 56.9%, $p = 0.004$), while herpes viral infections did not differ significantly (total herpes infections, 8.9% vs 14.7%, $p = 0.262$; eczema herpeticum, 0.8% vs 1.6%, $p = 0.628$; herpes zoster, 0.8% vs 0, $p = 1.0$). Additionally, Blauvelt et al[4] analyzed treatment-emergent infections over 4 years of dupilumab treatment in an AD open-label study and found that the cumulative number of patients with serious or severe infections, non-herpetic or herpetic infections, and total skin infections, decreased yearly with continued treatment.

In PN, subsequent to the publication of Labib et al,[1] results from Phase 3 randomized LIBERTY-PN PRIME and PRIME2 trials showed, similarly to AD trials, that non-herpetic skin infections occurred less frequently in patients treated with dupilumab versus placebo (2.7% vs 9.3% in PRIME, and 5.2% vs 6.1% in PRIME2); herpetic skin infections did not occur in PRIME and were more frequent with dupilumab in PRIME2 (5.2% vs 0).[5]

AD patients are highly susceptible to non-herpetic skin infections, usually with Gram-positive bacteria, and dupilumab was shown to decrease abundance of *Staphylococcus aureus* in both AD lesional and non-lesional skin,[6] results further supported by comprehensive evidence from clinical trials and post-marketing studies. Herpes infections are a known adverse drug reaction in both AD and PN and included in the U.S. prescribing information.[7]

In conclusion, evidence from AD and PN trials demonstrates that dupilumab treatment does not increase the risk of skin infections overall, and is associated with fewer non-herpetic skin infections compared with placebo.

Received: 15 May 2023
Accepted: 20 May 2023
Published: 25 May 2023

Acknowledgments

Research sponsored by Sanofi and Regeneron Pharmaceuticals Inc. Medical writing/editorial assistance was provided by Iulia Oprea, MD, PhD, of Excerpta Medica, and was funded by Sanofi and Regeneron Pharmaceuticals Inc., according to the Good Publication Practice guideline.

Disclosure

Simmi Wiggins is a Sanofi employee and may hold stock and/or stock options in the company; Noah A. Levit was a Regeneron Pharmaceuticals Inc. employee and shareholder at the time this letter was written and reports compensation as non-promotional speaker from Sanofi, outside the submitted work.

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https://doi.org/10.2147/ITT.S421440