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Assessing the risk of dupilumab use for atopic dermatitis during the COVID-19 pandemic

To the Editor: In the midst of the COVID-19 pandemic, physicians are using what is known of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus to establish practice guidelines for dermatologic conditions, particularly in regard to the use of immunosuppressive medications.[1] The effect of immunosuppressive medications on the clinical course of coronavirus disease 2019 (COVID-19) infection is currently unclear.

There is some evidence to support the use of targeted immunosuppressive medications against cytokine storm; however, there is concern that patients treated with biologic medications may have worse outcomes.[1] Although knowledge regarding the risk of biologic use during the COVID-19 pandemic is extremely limited, we can use data from previous trials to extrapolate a medication's potential risk based on its infection rate when compared with placebo.

Dupilumab, an interleukin (IL) 4-α receptor antagonist that inhibits IL-4 and IL-13 signaling, is a treatment for patients aged ≥12 years with moderate to severe atopic dermatitis (AD). IL-4 is critical in mediating type 2 T-helper cell polarization and regulating humoral immunity.[2] Given that IL-4 and IL-13 are significant in orchestrating and maintaining adaptive immunity, we sought to identify and address the risks associated with dupilumab use during the COVID-19 pandemic.

Infection rates with dupilumab were investigated in 3 randomized, placebo-controlled phase III clinical trials:

In three randomiazed, placebo-controlled phase III clinical trials (Study of Dupilumab Monotherapy Administered to Adult Patients With Moderate-to-Severe Atopic Dermatitis [SOLO] 1, SOLO 2, and Study to Assess the Efficacy and Long-term Safety of Dupilumab (REGN668/SAR231893) in Adult Participants With Moderate-to-Severe Atopic Dermatitis [CHRONOS]). Adults with moderate to severe AD received dupilumab (300 mg) weekly (QW), dupilumab 300 mg every 2 weeks (Q2W), or placebo. By week 16, "infection or infestations," as classified by Medical Dictionary for Regulatory Activities, developed in 35% of the patients receiving dupilumab Q2W and in 34% of those receiving dupilumab QW compared with 28% of patients receiving placebo in SOLO 1 and in 28%, 29%, and 32% of patients, respectively, in SOLO 2. In CHRONOS, where all 3 groups were allowed the use of concomitant topical corticosteroids, with or without topical calcineurin inhibitors, infection or infestations developed in 57% of the patients receiving dupilumab Q2W and in 53% of those receiving dupilumab QW, compared with 58% of patients receiving placebo. Nasopharyngitis was the most commonly reported infection among all treatment groups (Table I).[3] Furthermore, the conclusion in all 3 trials was that the rate of infection was not increased in dupilumab-treated patients compared with placebo.[4]

This study's analysis was limited to the data from the original dupilumab trials, because the authors did not specify whether infections were bacterial or viral. However, these findings support the notion that healthy patients with AD, without risk factors, using dupilumab during the COVID-19 pandemic should not be predisposed to infection, upper respiratory tract infection, or nasopharyngitis (Table I). Clinicians considering discontinuing dupilumab in high-risk patients should be aware that discontinuation of biologic medications has been shown to result in decreased response to treatment and the development of antidrug antibodies.[5] The American Academy of Dermatology currently recommends that patients with active COVID-19 infection should discontinue any systemic treatment under the guidance of a dermatologist. Furthermore, patients without high-risk comorbidities or signs/symptoms of active COVID-19 infection can continue or initiate dupilumab treatment based on the safety data from phase III clinical trials.

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Table I. Rate of infections in dupilumab for atopic dermatitis compared with placebo*

Infections, overall, No. (%)		URTI, No. (%)		Nasopharyngitis, No. (%)	
Dupilumab	Placebo	Dupilumab	Placebo	Dupilumab	Placebo
516 (41)	321 (41)	87 (6)	42 (5)	172 (13)	100 (13)

URTI, Upper respiratory tract infection.
*These data are a combined average of three phase III trials. The dupilumab group is a combined average of two treatment schedules (once per week or once per two weeks).

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