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Assessing the Risk of Apremilast Use for Psoriasis During the COVID-19 Pandemic

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As the COVID-19 pandemic persists globally, physicians continue to assess the safety and benefit of immunomodulatory medications, in order to reduce the risk of infection or worsened disease outcomes in patients. While there is emerging evidence that targeted immunosuppression may be helpful in cases of severe COVID-19 infection with cytokine storm, this effect cannot be generalized to all immunomodulatory medications.1 Though there is limited real-life data of SARS-CoV-2 infection in patients receiving apremilast for psoriasis, we can use clinical trials data to approximate the medication's potential risk based on its infection rate when compared to placebo.

Apremilast, a phosphodiesterase-4 (PDE-4) inhibitor, is an oral small molecule inhibitor approved for patients with psoriatic arthritis and/or moderate-to-severe plaque psoriasis. PDE-4 inhibition with apremilast has been experimentally shown to inhibit Th1/Th17 immune responses in patients, causing statistically significant decreases in TNF-α, IL-8, IL-6, and eventually IL-17 after longer periods of treatment (40 weeks).2 While cytokines are necessary for a competent immune response, severe cases of COVID-19 infection are often characterized by increased levels of proinflammatory cytokines, with serum levels of IL-6 and IL-10 positively correlating with disease severity and organ failure.3 This study will discuss current knowledge regarding the risk of infection with apremilast use, with an emphasis on its safety profile during the COVID-19 pandemic.

METHODS

A simple comparative analysis of the results from ESTEEM I/II was performed.

In two placebo-controlled phase III trials (ESTEEM I/II), 1,255 adults with moderate-to-severe psoriasis were randomized (2:1) to receive apremilast 30 mg twice daily (BID) or placebo for 16 weeks.4 At week 16, placebo-treated patients were switched to apremilast. Dosing with apremilast was maintained for all patients from weeks 16–32. Treatment from weeks 32–52 was based on the original treatment assignment and the PASI response at week 32. At the end of the 16-week placebo-controlled period, upper respiratory tract infections (URTIs) occurred in 6.5% of placebo-treated patients compared to 8.4% of apremilast-treated patients. Nasopharyngitis occurred in 6.9% of placebo-treated patients and 7.3% of apremilast-treated patients. From weeks 16–52, rates of URTI and nasopharyngitis increased to 16.9% and 15%, respectively. Unfortunately, no placebo-control group was included in the second and third period of trials (weeks 16–52) for inclusion in our analysis.

RESULTS

Based on data from the first 16 weeks of both trials, apremilast has no apparent increased risk of infection compared to placebo (Table 1).The findings from this study are consistent with a recent case report of a patient with erythrodermic psoriasis who received apremilast during hospitalization for COVID-19 and experienced a mild, uncomplicated infection despite having multiple risk factors for poor outcome (obesity, cancer, and chemotherapy use).[5] This study's analysis is limited by the absence of a placebo control group in the second and third periods of both trials. Additionally, the trials did not specify whether the URTIs were caused by viral or bacterial pathogens. Nonetheless, we believe this study suggests apremilast does not increase the risk of URTI or nasopharyngitis compared to placebo and may be safe to continue during the COVID-19 pandemic, although further research and continued patient-observation are recommended.

TABLE 1.

Rate of Infections in Apremilast for Psoriasis Compared to Placebo*

Upper Respiratory Tract infections		Nasopharyngitis	
Apremilast n (%)	Placebo n (%)	Apremilast n (%)	Placebo n (%)
70 (8.4)	27 (6.5)	61 (7.3)	29 (6.9)

*This data is a combined average of two phase III trials. Only placebo-controlled periods from the trials were included in the analysis.[4]

DISCLOSURES

Dr. Wu is or has been an investigator, consultant, or speaker for AbbVie, Almirall, Amgen, Arcutis, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dermavant, Dermira, Dr. Reddy's Laboratories, Eli Lilly, Janssen, LEO Pharma, Novartis, Regeneron, Sanofi Genzyme, Sun Pharmaceutical, UCB, Valeant Pharmaceuticals North America LLC. The other authors have no conflicts.

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