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In response to: “Reply to research letter”



To the Editor: We appreciate the interest of Rivera-Oyola et al¹ in our meta-estimate evaluating the risk of respiratory tract infections (RTIs) and symptoms in patients with psoriasis treated with biologics that inhibit the interleukin (IL) 17 pathway.² The authors make a cogent case for the importance of not cherry-picking data when evaluating drug safety by selecting a few examples in which perhaps patients treated with IL-17 inhibitors have a lower risk of RTIs compared with placebo. The examples they provided are precisely why one needs to look at all the data through an unbiased meta-estimate approach.

As we noted in our initial publication,² the results demonstrated a statistically significant 31% to 56% increased risk of RTI in patients treated with biologics targeting IL-17 compared with placebo. Sensitivity analyses varying the definition of RTI yielded similar findings. The interpretation of these results is that there is a potential safety signal for RTI associated with IL-17 inhibition. A safety signal is simply defined as a hypothesis between exposure to a drug and an adverse event that warrants further investigation.³ Taking the same analytical approach, we did not find a safety signal for RTI associated with IL-23 inhibitors.⁴

As we pointed out, in the IL-17 analysis, the risk of RTI in clinical trials is difficult to classify because the diagnosis is made clinically, without objective testing. Therefore, the etiology of these symptoms, be they viral, bacterial, fungal, or allergic, is unknown. In the IL-23 analysis, we also noted that the confidence intervals overlap, and therefore, we cannot conclude with certainty that there is a true difference in RTI risk between biologics that target IL-17 vs IL-23. Current data are insufficient to reliably distinguish the risk of becoming infected with severe acute respiratory syndrome coronavirus 2 and having worse outcomes from COVID-19 illness between our various biologic treatment options for psoriasis.

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Conflicts of interest: Dr Wan is supported in part by a grant from Pfizer. Dr Winthrop receives grants from Bristol-Myers Squibb and Pfizer and is a consultant for UCB, AbbVie, Lilly, Bristol-Myers Squibb, Pfizer, GlaxoSmithKline, and Roche. Dr Gelfand served as a consultant for Bristol-Myers Squibb, Boehringer Ingelheim, GlaxoSmithKline, Janssen Biologics, Novartis Corp, Regeneron, UCB (Data Safety and Monitoring Board), Sanofi, and Pfizer Inc, receiving honoraria; receives research grants (to the Trustees of the University of Pennsylvania) from AbbVie, Janssen, Novartis Corp, Sanofi, Celgene, Ortho Dermatologics, and Pfizer Inc; and has received payment for CME work related to psoriasis that was supported indirectly by Eli Lilly and Company and Ortho Dermatologics. Dr Gelfand is a copatent holder of resiquimod for treatment of cutaneous T-cell lymphoma and is a deputy editor for the *Journal of Investigative Dermatology*, receiving honoraria from the Society for Investigative Dermatology. Dr Shin has no conflicts of interest to declare.

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Reprints not available from the authors.

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