Table II. Probandwise concordance rates and tetrachoric correlations for tanning addiction and heritability estimate for tanning addiction (controlling for age and sex)

Zygosity	Concordant pairs	Discordant pairs	Unaffected pairs	Probandwise CR (95% CI)	TCR (95% CI)
MZ	34	29	84	0.70 (0.60-0.80)	0.75 (0.56-0.86)
DZ	4	8	12	0.50 (0.20-0.80)	0.38 (0.30-0.45)

Heritability Estimate	Model	A, % (95% CI)	C, % (95% CI)	E, % (95% CI)	AIC
	ACE	75.4 (60.6-90.2)	0.0 (0.0-0.0)	24.6 (9.8-39.4)	401.16
	AE	**75.4 (60.6-90.2)**	—	**24.6 (9.8-39.4)**	**399.16**
	CE	—	70.7 (55.4-86.0)	29.3 (14.0-44.6)	401.43

A, Additive genetic effects (heritability); *AIC,* Akaike information criterion; *C,* common environmental effects; *CI,* confidence interval; *CR,* concordance rate; *DZ,* dizygotic; *E,* unique environmental effects; *MZ,* monozygotic; *TCR,* tetrachoric concordance rate.
Bold values indicate the model chosen for this study, based on lowest AIC.

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The risk of respiratory tract infections in patients with psoriasis treated with interleukin 23 pathway–inhibiting biologics: A meta-estimate of pivotal trials relevant to decision making during the COVID-19 pandemic

To the Editor: The COVID-19 pandemic caused by the severe acute respiratory syndrome virus (SARS-CoV-2) has led to uncertainty regarding the safety of immunosuppressive psoriasis therapy. We recently reported a meta-estimate that showed a 30% to 60% increase in the risk of respiratory tract infections (RTIs) in patients with psoriasis receiving interleukin (IL) 17 biologics compared to placebo.[1] Similar to IL-17, IL-23 is a key cytokine in the maintenance of T-helper 17 cells, which mediate protection against pathogens. Although not believed to be a central cytokine in the defense of viral infections, reduced levels of IL-23 may contribute to impairment of mucosal barrier immunity, resulting in an increased risk of respiratory infections.[2] Biologics that specifically target IL-23 have high efficacy for psoriasis and a favorable risk-benefit profile.[3] However, data on the use of IL-23 inhibitors and their impact on the incidence and outcomes of novel SARS-CoV-2 infection are limited. A study from

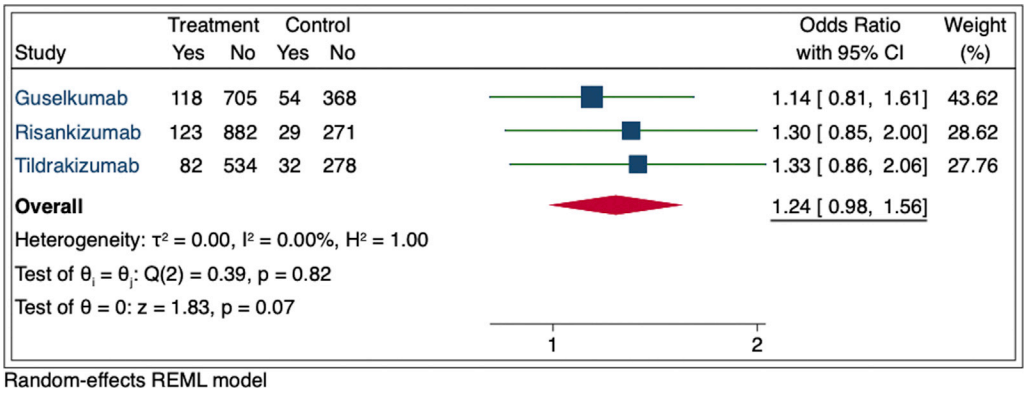

Fig 1. Meta-estimate of respiratory tract infections from prescribing information adverse events tables (includes "upper respiratory tract infections," "nasopharyngitis," "respiratory tract infection (viral, bacterial and unspecified)," "influenza," "sinusitis (including acute)," "pharyngitis (including viral)," "tonsillitis," and "rhinitis"). Doses used in this meta-estimate were guselkumab 100 mg, risankizumab 150 mg, and tildrakizumab 100 mg for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy. The size of the square corresponds to the relative weight assigned in the pooled analysis, and the horizontal lines indicate the 95% CI. The diamond denotes the overall effect size, and the lateral tips of the diamond indicate the associated CI. *CI,* Confidence interval; *REML,* restricted maximum likelihood.

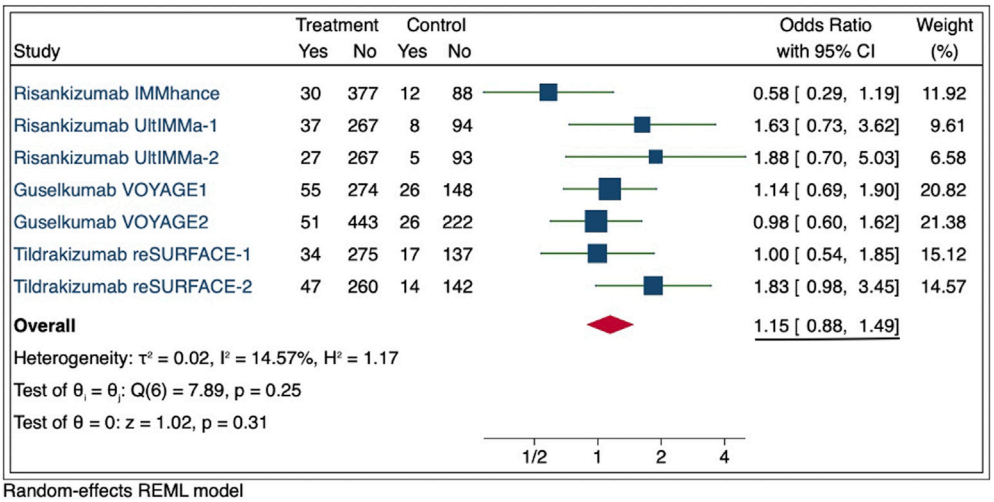

Fig 2. Meta-estimate of respiratory tract infections from clinicaltrials.gov in phase 3 randomized controlled trials that were submitted for US Food and Drug Administration approval (includes "upper respiratory tract infections," "viral upper respiratory tract infections," "influenza," "chylothorax," "sinusitis," "bronchitis," "tonsillitis," "nasopharyngitis," and "pneumonia"). Doses used in this meta-estimate were guselkumab 100 mg, risankizumab 150 mg, and tildrakizumab 100 mg for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy. The size of the square corresponds to the relative weight assigned in the pooled analysis, and the horizontal lines indicate the 95% confidence interval. The diamond denotes the overall effect size, and the lateral tips of the diamond indicate the associated CI. reSURFACE-2 adverse events were verified from the sponsor because clinicaltrials.gov adverse events were reported in the sum of the extended trial period. *CI,* Confidence interval; *REML,* restricted maximum likelihood.

northern Italy found that patients with psoriasis receiving biologics had a higher risk for becoming infected with SARS-CoV-2 and hospitalization for COVID-19 but saw no difference in mortality or use of a ventilator.[4] A case report observed improvement in COVID-19 illness after guselkumab injection.[5]

To evaluate the risk of RTIs associated with IL-23 biologic use, we analyzed data reported in US Food and Drug Administration–approved phase 3 placebo-controlled clinical trials for guselkumab, risankizumab, and tildrakizumab from US Food and Drug Administration prescribing information (PI) and clinicaltrials.gov. To ensure uniformity, terms were reviewed to include only those consistent with RTI. RTI events were divided by the total number of patients at risk in each study and compared to the placebo group by a meta-estimate. In the PI, we found an increased risk of RTI in the IL-23 groups compared to placebo, but this did not achieve statistical significance (odds ratio, 1.24; 95% confidence interval, 0.98-1.56; $P = .07$) (Fig 1). Because limited terms consistent with RTI were reported in the PI, we broadened our search to include additional RTI adverse events reported by the same trials in clinicaltrials.gov. Our risk assessment showed similar results, with attenuation in the association and no statistical significance (odds ratio, 1.15; 95% confidence interval, 0.88-1.49) (Fig 2). Sensitivity analyses were conducted, including additional adverse events reported in phase 2 trials included in the PI, which yielded similar findings.

In summary, we did not observe a statistically significant signal for RTI in patients with psoriasis treated with IL-23 biologics. Although we did observe a statistically significant increased risk of RTI using the same analysis approach with IL-17 biologics, we note that the confidence intervals overlap with our current analysis, and therefore, we cannot conclude with certainty that there is a true difference in RTI risk between biologics that target IL-17 versus IL-23. There were greater than 900 more patients treated with IL-17 biologics, and therefore, sample size may explain the different statistical results. Because of the highly variable course of COVID-19 and the potential differences between COVID-19 and other pathogens, large studies with appropriate epidemiologic methods are still needed to determine if IL-17/23–targeted biologics meaningfully alter the risk of COVID-19 in patients with psoriasis.

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Sensitivity of Fite-Faraco versus auramine-rhodamine in mycobacterial infection

To the Editor: Culture, in conjunction with reflexive molecular testing, remains the criterion standard for mycobacterial diagnosis and species identification.[1] However, most require 6 to 8 weeks of incubation to rule out infection,[1] and negative culture results do not rule out mycobacterial infection.[2] For this reason, many clinicians also send a specimen to anatomic pathology for analysis. Auramine-rhodamine (AR) fluorescence (Fig 1) is the preferred stain in many countries where tuberculosis or leprosy remain endemic,[3] but Fite-Faraco (FF) (Fig 2) is more commonly used in the United States.[2,4] We sought to compare the sensitivity of the stains for the detection of acid-fast bacilli (AFB).

After approval by the local institutional review board, all AR^+ blocks diagnosed between 2000 and 2020 were retrieved. Fresh sections were stained with FF and reviewed by a single pathologist. Fifty-three AR^+ cases (26 male, 27 female) (Table I) were stained with FF, of which 28 showed positive results (52.8%). Positive culture results were reported in 30 of 40 (75.0%) patients, with 30 of 31 (96.7%) corresponding molecular test results positive (Table I). Polymerase chain reaction (PCR) study results were positive in only 7 of 17 (41.2%) specimens.

We previously showed that AR can detect AFB in PCR^+/FF^- cases of leprosy.[4] Our current findings suggest the superiority of AR over FF in detecting mycobacteria beyond leprosy[3,4] and tuberculosis.[1] Even with the availability of culture and molecular testing, 17% of cases relied on histology alone for AFB detection.

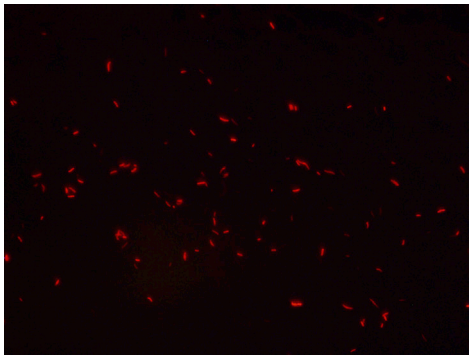

Fig 1. AR fluorescence staining of mycobacteria. Fluorescing bacilli (red) stained with AR. (original magnification: ×400). AR exhibits a strong red-orange mycobacterial fluorescence against a black background. *AR,* Auramine-rhodamine.

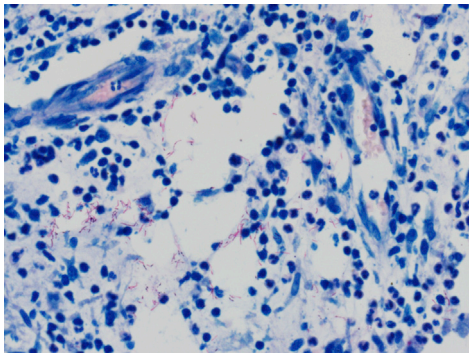

Fig 2. FF staining of mycobacteria. Mycobacteria (red) stained with FF. (Original magnification: ×600). FF stains acid-fast bacilli pink-red on a blue background. *FF,* Fite-Faraco.

Ziehl-Neelsen and Kinyoun stain have also displayed inferiority to AR in some settings,[1,3] yet AR is not widely used in the United States. A survey of 363 US pathologists reported that 68.2% use no more than 1 AFB stain in indeterminate cases and that only 14.2% use AR.[5] AR is not only more sensitive but also decreases slide evaluation time, thereby reducing observer fatigue.[3] On average, traditional AFB stains require 9.5 minutes per slide.[5] The stark color contrast of AR against the dark background facilitates visualization of mycobacteria.[4]

Limitations of the study include the retrospective design and that samples were limited to AR^+ cases. Despite these limitations, our findings suggest that AR should be used as a first-line stain in addition to AFB culture and molecular techniques.

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