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Risankizumab Associated With Lower Incident Depression and Sleep Disorders in Psoriasis: A TriNetX Study

Victoria Garfinkel BSA,* Hermon Feron BA,* Kaveh Nezafati MD

Department of Dermatology, UT Southwestern Medical Center, Dallas, TX

*Co-first authors

To the Editor,

Psoriasis (PsO) is a chronic inflammatory disease associated with significant psychiatric comorbidity.[1] Emerging evidence suggests that inflammatory pathways in PsO may contribute to neuroinflammation and mood symptoms, raising the possibility that biologic therapies could differentially influence mental health outcomes.[2] However, direct longitudinal comparisons between biologic classes remain limited. Using real-world data from the TriNetX database, we compared incident depression, anxiety, and sleep disorders among PsO patients treated with risankizumab versus adalimumab at 12-,18-, and 24-month follow-up. Cohorts included PsO patients (≥2 ICD-10 L40 codes) with exposure to risankizumab or adalimumab, excluding comparator biologic use and other labeled indications to better reflect psoriasis-specific use.

Across all follow-up intervals, risankizumab was associated with lower incident depression compared with adalimumab, with separation evident by 12 months and sustained through 24 months (12 month: RR, 0.741; 95% CI, 0.608-0.904; 18 months: RR, 0.714; 95% CI, 0.608–0.839; 24 months: RR, 0.701; 95% CI, 0.609–0.808; all $P \leq 0.003$) (Table 1; Figure 1). Sleep disorders similarly favored risankizumab beginning at 18 months (RR, 0.869; 95% CI, 0.764–0.988; $P=0.032$) and persisted at 24 months (RR 0.817, 95% CI, 0.728–0.918; $P=0.001$), while the 12-month comparison was not significant. Anxiety outcomes did not differ at 12 or 18 months but favored risankizumab at 24 months (24 months: RR, 0.871; 95% CI, 0.765–0.99; $P=0.038$).

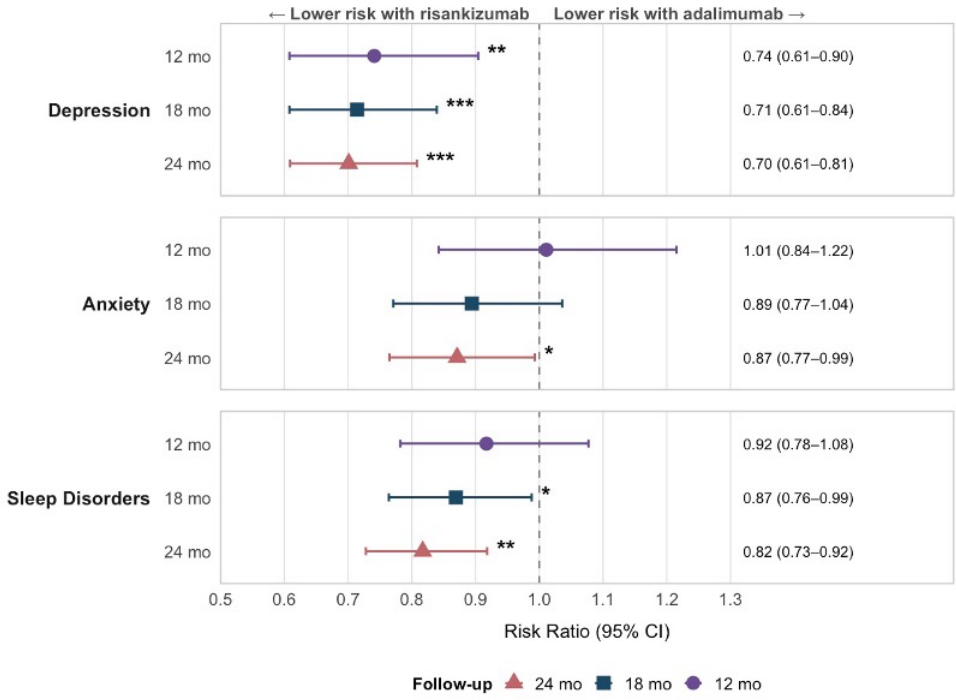
TABLE 1.

Risk of Incident Depression, Anxiety, and Sleep Disorders at 12, 18, and 24 Months Risankizumab vs Adalimumab

Outcome	Time Point	Risankizumab n / Total (%)	Adalimumab n / Total (%)	Risk Ratio (95% CI)	RR *P*-Value
Depression	12mo	163 / 10,031 (1.6%)	233 / 10,628 (2.2%)	0.741 (0.608, 0.904)	0.003
	18mo	242 / 10, 597 (2.3%)	360 / 11,258 (3.2%)	0.714 (0.608, 0.839)	0.000
	24mo	307 / 10,597 (2.9%)	465 / 11,258 (4.1%)	0.701 (0.609, 0.808)	0.000
Anxiety	12mo	215 / 9,872 (2.2%)	233 / 10,820 (2.2%)	1.011 (0.842, 1.215)	0.904
	18mo	311 / 10,420 (3.0%)	381 / 11,412 (3.3%)	0.894 (0.771, 1.036)	0.136
	24mo	389 / 10,420 (3.7%)	489 / 11,412 (4.3%)	0.871 (0.765, 0.993)	0.038
Sleep Disorders	12mo	268 / 9,530 (2.8%)	319 / 10,406 (3.1%)	0.917 (0.782, 1.077)	0.290
	18mo	400 / 10,090 (4.0%)	500 / 10,961 (4.6%)	0.869 (0.764, 0.988)	0.032
	24mo	474 / 10,090 (4.7%)	630 / 10,961 (5.7%)	0.817 (0.728, 0.918)	0.001

Incident outcomes were assessed after a 90-day post index wash-in. Depression was defined by ICD-10 F32.x, anxiety by F41.9, and sleep disorders by G47. Risk ratios (RRs) compare risankizumab vs adalimumab; $P<0.05$ was considered statistically significant.

FIGURE 1. Incident depression, anxiety, and sleep disorders in psoriasis: risankizumab versus adalimumab.



Forest plot of RRs with 95% confidence intervals comparing incident diagnoses at 12, 18, and 24 months after index biologic exposure (outcomes assessed 90 days post-index) RR < 1 indicates lower risk with risankizumab. *P<.05; **P<.01; ***P<.001.

Our findings build on prior evidence that biologic therapy can improve mental health outcomes in psoriasis.[3] In our analysis, risankizumab was associated with earlier and sustained reductions in incident depression, with later separation for sleep disorders and anxiety, suggesting a time-dependent benefit across symptom domains. Potential explanations include differential immunologic effects of IL-23 versus TNF-α inhibition, with IL-23 blockade downregulating Th17/IL-17 signaling implicated in neuroinflammatory mechanisms relevant to mood symptoms.[1,4] Limitations include the retrospective nature, reliance on diagnosis codes, and limited data on psoriasis severity, adherence, and concomitant psychiatric treatments in TriNetX. Nonetheless, these real-world findings suggest risankizumab is associated with more favorable longitudinal mental health outcomes than adalimumab through 24 months, warranting prospective confirmation with validated psychiatric and sleep measures.

DISCLOSURES

The authors have no conflicts of interest to disclose.

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AUTHOR CORRESPONDENCE

Hermon Feron BA
E-mail:..... Hermon.Feron@utsouthwestern.edu