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Topical Ruxolitinib Therapy Decreases Rates of Depression and Anxiety: A Retrospective Analysis in Vitiligo Patients

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To the Editor,

Vitiligo, a chronic autoimmune condition characterized by loss of melanocytes and resultant skin depigmentation, is associated with reduced quality of life, and increased risks of psychiatric comorbidities such as depression and anxiety.[1-3] While current clinical assessments focus on improving objective markers of disease burden, such as percentage of Body Surface Area (BSA), little is known about the effect of vitiligo treatment on other patient outcomes like depression and anxiety.

Ruxolitinib, a topical Janus kinase (JAK) inhibitor, is a novel and effective therapy approved for repigmentation in non-segmental vitiligo.[3] Despite its growing use, its potential impact on depression and anxiety rates in treated patients has not yet been reported.

In this retrospective cohort study, we used the TriNetX Network to examine rates of depression and anxiety in vitiligo patients treated with ruxolitinib. The TriNetX Network allows examination of claims and electronic health record data for patients from 24 US healthcare organizations. This type of claims-level analysis offers, among its advantages, the ability to evaluate large numbers of patients, to associate different clinical states in each patient (via ICD codes), and to evaluate interventions via pharmacy claims data.

TABLE 1.

Risk of Depression and Anxiety Disorders in Patients with Vitiligo Treated with Ruxolitinib Compared to Those Not Treated with Ruxolitinib

Outcome	Cohort	Patients in Cohort	Patients with Outcome	Risk (%)	Risk Ratio	95% CI	*P*-Value
6-month time window							
Anxiety Disorder	JAKi + Vitiligo	4,166	38	0.90%	0.675	(0.449, 1.013)	0.056
	Control	4,289	58	1.40%			
Depression	JAKi + Vitiligo	4,291	27	0.60%	0.49	(0.310, 0.775)	0.002
	Control	4,284	55	1.30%			
1-year time window							
Anxiety Disorder	JAKi + Vitiligo	4,640	48	1.03%	0.66	(0.504, 0.865)	0.002
	Control	4,725	55	1.16%			
Depression	JAKi + Vitiligo	4,379	76	1.73%	0.553	(0.406, 0.752)	0
	Control	4,436	155	3.49%			
18-month time window							
Anxiety Disorder	JAKi + Vitiligo	4,166	84	2.00%	0.675	(0.543, 1.419)	0.59
	Control	4,289	131	3.10%			
Depression	JAKi + Vitiligo	4,291	62	1.40%	0.49	(0.332, 0.667)	0
	Control	4,284	112	2.60%			
2-year time window							
Anxiety Disorder	JAKi + Vitiligo	4,640	31	0.67%	0.876	(0.543, 1.419)	0.59
	Control	4,725	36	0.76%			
Depression	JAKi + Vitiligo	4,379	50	1.14%	0.478	(0.332, 0.667)	0
	Control	4,436	106	2.39%			

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Vitiligo patients treated with ruxolitinib were matched 1:1 to vitiligo patients not treated with ruxolitinib using a greedy nearest neighbor algorithm based on age, sex, and race/ethnicity. All patients with a history of depression (ICD-10: F32) or anxiety disorder (ICD-10: F41.9) prior to vitiligo diagnosis were excluded. Matching yielded two otherwise similar cohorts (all p-values for age, sex, race/ethnicity were greater than 0.05). Concurrent use of other treatments was allowed in both groups. Presence of new depression and anxiety diagnoses was measured at 6, 12, 18, and 24 months after patient enrollment.

Compared to matched controls, ruxolitinib-treated patients had a significantly lower rate of depression at all measured timepoints (range: 44.7 – 52.2%; Table 1). Anxiety disorder risk also trended lower in the Ruxolitinib group, but only reached statistical significance at the 18 month timepoint, suggesting a less consistent relationship compared to depression outcomes. Ruxolitinib inhibits JAK1 and JAK2, core enzymes in the JAK-STAT signaling pathway that regulate inflammatory and immune responses. In vitiligo, aberrant activation of this pathway leads to the recruitment of CXCR3+ CD8+ T cells, which selectively destroy melanocytes. Ruxolitinib disrupts this mechanism, thereby allowing repigmentation to occur.[1,2]

In conclusion, topical ruxolitinib is associated with a reduction in depression rates among vitiligo patients, with improvement observed across all time points evaluated (6, 12, 18, and 24 months). Anxiety risk showed a downward trend and reached significance only at 18 months posttreatment.These findings can assist physicians in considering ruxolitinib for vitiligo patients at risk for mood disorders such as depression and may also inform insurance coverage decisions and enhance patient compliance. Limitations include the study's retrospective design, reliance on ICD codes from electronic health records, and potential unmeasured confounding despite propensity score matching. Future research should prospectively assess the psychiatric effects of vitiligo treatments using validated mental health measures and investigate whether JAK inhibitors have direct neuroprotective or mood-stabilizing properties.

DISCLOSURES

The authors have no conflicts of interest to disclose.

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