e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(4); 1666-1673

Original Research Article

Comparative Efficacy and Safety of Oral Tofacitinib Plus PUVASOL Versus Oral Betamethasone Plus PUVASOL in Adults with Vitiligo: A Randomized Controlled Trial

Supriya Behera[1], Debasisha Parida[2], Prasenjeet Mohanty[3]

[1]Senior Resident, Department of Dermatology, GMCH Phulbani, Orissa, India
[2]Assistant Professor, Department of General Medicine, IMS & SUM HOSPITAL- 3, Sitalapalli, Berhampur, Orissa, India
[3]Head of Department (HOD), Department of Dermatology, IMS & SUM HOSPITAL- 2, Phulnakhara, Bhubaneswar, Orissa, India

Received: 06-02-2026 / Revised: 16-03-2026 / Accepted: 10-04-2026
Corresponding Author: Dr. Supriya Behera
Conflict of interest: Nil

Abstract

Background: Rapidly progressive vitiligo often requires systemic therapy to arrest activity and induce repigmentation. Oral corticosteroid mini-pulse regimens are widely used, whereas oral Janus kinase inhibition is an emerging targeted strategy. Comparative data between these approaches in combination with psoralen-sunlight therapy remain limited.

Aim: To compare the efficacy and safety of oral tofacitinib plus PUVASOL versus oral betamethasone plus PUVASOL in adults with vitiligo.

Methods: This randomized controlled trial was conducted in the Department of Dermatology, SCB Medical College and Hospital, between August 2022 and December 2023. Forty patients were enrolled and 36 completed follow-ups. Participants were randomized 1:1 to oral tofacitinib 5 mg twice daily plus oral PUVASOL or oral betamethasone pulse therapy plus oral PUVASOL for 24 weeks. VASI was recorded at baseline, week 12, and week 24. Efficacy analyses included within-group and between-group comparisons, responder analysis, and repeated-measures mixed-effects modeling. Adverse events were recorded in both groups.

Results: Eighteen patients were analyzed in each arm. Both groups showed significant within-group VASI reduction at week 12 and week 24 (all $P < 0.001$). Mean absolute VASI reduction at week 24 was 3.12 ± 2.62 with betamethasone and 3.64 ± 2.70 with tofacitinib ($P = 0.535$). Mean percentage VASI reduction at week 24 was $30.63 \pm 14.23\%$ and $27.49 \pm 9.37\%$, respectively ($P = 0.566$). Betamethasone showed greater early percentage reduction at week 12 ($P = 0.045$), but this was not sustained. Mixed-effects analysis confirmed a significant time effect ($P < 0.001$) without a significant group × time interaction ($P = 0.716$). Adverse events were mild in both groups.

Conclusion: Both oral betamethasone plus PUVASOL and oral tofacitinib plus PUVASOL significantly improved vitiligo severity over 24 weeks. In this study, tofacitinib did not show superiority over betamethasone for short-term VASI improvement, although both regimens were well tolerated and clinically active.

Keywords: vitiligo; tofacitinib; betamethasone; PUVASOL; randomized controlled trial; VASI; JAK inhibitor.
DOI: 10.25258/ijcpr.18.4.263

Introduction

Vitiligo is a chronic acquired depigmenting disorder characterized by the selective destruction or functional loss of melanocytes, leading to well-demarcated hypopigmented to depigmented macules and patches. Although vitiligo is not life-threatening, its effect on appearance, self-image, social participation, and treatment-seeking behavior makes it a disease of substantial clinical and public health relevance [1-5]. A recent global burden analysis estimated a lifetime prevalence of approximately 0.36%, with higher estimates in adults than in children and substantial geographic variation, underscoring that vitiligo is neither rare nor trivial in routine dermatologic practice [1]. The disease may begin at any age, but a large proportion of cases arise before early adulthood, resulting in a prolonged disease course and cumulative psychosocial burden [2,4,5]. The current understanding of vitiligo pathogenesis supports a multifactorial model in which genetic susceptibility, oxidative stress, innate immune activation, and adaptive immune mechanisms converge to produce melanocyte loss [2,3]. Among these pathways, IFN-γ-driven cytotoxic CD8+ T-

cell responses have emerged as central drivers of nonsegmental vitiligo. This inflammatory cascade promotes chemokine-mediated recruitment and retention of autoreactive T cells, especially through CXCL9 and CXCL10 signaling, thereby perpetuating melanocyte damage [3,6]. These mechanistic insights are clinically relevant because they provide a biologic rationale for targeted treatment, particularly Janus kinase (JAK) inhibition, which can interrupt downstream IFN-γ signaling [3,6,7].

Despite advances in pathobiology, treatment of vitiligo remains challenging. Standard management is guided by disease extent, site, activity, and pace of progression. Topical corticosteroids, topical calcineurin inhibitors, narrowband ultraviolet-B (NB-UVB), psoralen-based photochemotherapy, excimer-based modalities, and selected surgical procedures remain core therapeutic options in contemporary practice [6,8]. For rapidly progressive disease, clinicians frequently use systemic therapy to arrest activity before or alongside repigmentation-directed treatment. Oral mini-pulse corticosteroid regimens are commonly employed for this purpose because they can suppress inflammatory activity while avoiding some toxicities of daily systemic steroid exposure [6,9,10]. However, response rates vary, relapse may occur, and adverse effects such as weight gain, edema, and metabolic changes still limit prolonged use [9,10].

Phototherapy is another key pillar of treatment. The Vitiligo Area Scoring Index (VASI), introduced as a practical quantitative tool to measure disease extent and response, has helped standardize clinical assessment across trials and real-world studies [11]. Long-duration phototherapy improves repigmentation outcomes, with better responses generally observed on the face and neck and poorer outcomes at acral sites [12,13]. Historically, psoralen with ultraviolet A (PUVA) and sunlight-based psoralen activation (PUVASOL) have been widely used in resource-constrained settings because of accessibility and lower direct cost, even though controlled NB-UVB is currently preferred in many centers because of greater standardization and tolerability [6,12,13]. In many parts of India and similar settings, PUVASOL continues to be relevant because it remains practical, affordable, and feasible for outpatient management.

The development of JAK inhibitors has introduced a targeted therapeutic strategy for vitiligo. Systematic and mechanistic reviews have highlighted the importance of the JAK-STAT pathway in melanocyte-directed autoimmunity and identified JAK blockade as one of the most promising advances in the field [3,6,7]. However, the clinical evidence base for systemic JAK inhibition has evolved more slowly than enthusiasm for its mechanism. Early reports suggested that repigmentation with tofacitinib may require concomitant light exposure, implying that immunologic suppression alone may arrest disease activity but is insufficient for melanocyte regeneration without photostimulation [14]. This interaction between targeted immunomodulation and light therapy is especially relevant when designing combination regimens for active vitiligo.

Recent studies have added important but still incomplete evidence. A 2025 meta-analysis of randomized trials found that JAK inhibitors improved repigmentation outcomes over placebo and were generally well tolerated, although the available evidence remained limited and heterogenous [7]. A recent randomized controlled trial comparing oral tofacitinib with oral dexamethasone mini-pulse therapy in active nonsegmental vitiligo reported broadly similar ≥50% responder rates at 24 weeks, but greater overall reduction in disease extent by 36 weeks with tofacitinib [15]. Another randomized trial found that combination treatment with tofacitinib and NB-UVB produced better recovery than NB-UVB alone [16]. In a retrospective 2025 series, oral tofacitinib stabilized disease in more than half of patients after 3 months, with greater repigmentation after 6-9 months of therapy and no major safety signal [17]. Together, these studies support the promise of tofacitinib, but also indicate that treatment duration, co-administered light exposure, baseline disease activity, and disease subtype may strongly influence outcomes.

The psychosocial burden of vitiligo further strengthens the need for effective, safe, and practical systemic options. Large multinational data from the Global VALIANT study demonstrated substantial impairment in emotional well-being and quality of life, particularly in patients with greater body surface involvement, darker skin phototypes, and lesions on the face or hands [4]. Similar work has shown that increasing disease extent and visible lesion distribution are associated with greater quality-of-life impairment [5,18,19]. These observations are especially pertinent in progressive vitiligo, where halting spread is often a priority equal to or greater than immediate repigmentation.

Given these unmet needs, the present randomized controlled study was designed to compare two clinically relevant combination regimens in adults with vitiligo: oral tofacitinib plus oral PUVASOL versus oral betamethasone plus oral PUVASOL. The study hypothesis, based on prior mechanistic and emerging clinical evidence, was that tofacitinib combined with photochemotherapy would produce greater improvement in VASI while maintaining an acceptable safety profile. Because comparative data between systemic JAK inhibition and systemic corticosteroid pulse therapy remain limited,

especially in real-world South Asian practice settings where PUVASOL remains common, this study sought to provide direct head-to-head evidence on efficacy and tolerability over 24 weeks.

Materials and Methods

This randomized controlled trial was conducted in the Department of Dermatology, SCB Medical College and Hospital, from August 2022 to December 2023 after institutional ethical clearance and written informed consent. Adult patients aged 18 years or older with vitiligo were enrolled according to the thesis protocol. Eligible participants had progressive vitiligo of recent spread and body surface involvement below the universal vitiligo threshold. Patients with leukoderma due to other causes, universal vitiligo, pregnancy or lactation, photosensitivity, prior radiotherapy, current immunosuppressive therapy, history of skin cancer, or unwillingness to participate were excluded. The sample size was calculated for superiority, and the planned analysis population was 36 patients. According to the study flow chart, 40 patients were enrolled, 4 were lost to follow-up, and 36 completed the trial.

Participants were randomized in a 1:1 ratio using a computer-generated sequence to one of two intervention groups. Group A received oral tofacitinib 5 mg twice daily plus oral PUVASOL, and Group B received oral betamethasone pulse therapy calculated according to body weight plus oral PUVASOL. PUVASOL was administered with oral psoralen (8-methoxypsoralen, 5-methoxypsoralen, or trimethylpsoralen as available) three times weekly followed by sunlight exposure 1 to 3 hours later, as per the thesis treatment plan. Both treatment arms were continued for 24 weeks. Patients were assessed at baseline, week 12, and week 24.

Clinical details including age, sex, body mass index, family history, associated autoimmune disease, vitiligo type, disease duration, treatment allocation, and adverse effects were recorded in a predesigned proforma and master chart. Disease extent and response were quantified using the Vitiligo Area Scoring Index (VASI) [11]. The primary outcome was change in VASI at 12 and 24 weeks. Secondary outcomes included categorical response rates based on percentage reduction in VASI and treatment-emergent adverse events. The present manuscript was prepared from the uploaded thesis protocol and the final master chart. Data were cleaned and analyzed using Python. Continuous variables were summarized as mean ± standard deviation or median (interquartile range), and categorical variables as number (percentage). Between-group comparisons for continuous variables were performed using the Mann-Whitney U test because of the small sample size and non-normal distribution of several variables; categorical variables were compared using Fisher exact test or chi-square test as appropriate. Within-group changes in VASI from baseline to week 12 and week 24 were examined using the Wilcoxon signed-rank test. A linear mixed-effects model with random intercept for participant was used to evaluate repeated VASI measurements over time and to test the overall time effect and group × time interaction. Two-sided P values below 0.05 were considered statistically significant.

Results

Thirty-six patients completed the study and were analyzed, with 18 participants in each treatment group. The mean age of the cohort was 33.33 ± 10.75 years. Baseline demographic and clinical characteristics are summarized in Tables 1 and 2. The two groups were broadly comparable with respect to age, body mass index, disease duration, baseline VASI, family history of vitiligo, family history of other autoimmune disease, associated autoimmune disease, and vitiligo morphology (all $P > 0.05$). However, sex distribution differed significantly between groups, with male patients comprising 77.8% of the tofacitinib arm and 33.3% of the betamethasone arm ($P = 0.018$).

At baseline, mean VASI was 11.72 ± 11.49 in the betamethasone plus PUVASOL group and 14.19 ± 11.31 in the tofacitinib plus PUVASOL group. Both groups showed significant within-group reductions in VASI at week 12 and week 24 (all $P < 0.001$). By week 24, mean VASI decreased to 8.60 ± 9.23 in the betamethasone group and 10.56 ± 9.04 in the tofacitinib group. Mean absolute VASI reduction at week 24 was 3.12 ± 2.62 with betamethasone and 3.64 ± 2.70 with tofacitinib ($P = 0.535$). Mean percentage VASI reduction at week 24 was 30.63 ± 14.23% and 27.49 ± 9.37%, respectively ($P = 0.566$). At week 12, percentage VASI reduction was significantly greater with betamethasone than with tofacitinib (25.88 ± 12.05% vs 18.71 ± 5.80%, $P = 0.045$), but this early advantage was not sustained by week 24. Adjusted analysis using baseline VASI as a covariate did not show a significant group effect at week 12 ($P = 0.444$) or week 24 ($P = 0.991$).

Responder analysis is shown in Table 4. At week 24, 61.1% of the betamethasone group and 55.6% of the tofacitinib group achieved at least 25% VASI reduction ($P = 1.000$). VASI50 was achieved by 3 patients (16.7%) in the betamethasone arm and by no patient in the tofacitinib arm ($P = 0.229$). No participant in either group achieved a very high response threshold consistent with VASI75 or VASI90 during the 24-week study period. Repeated-measures mixed-effects modeling showed a significant overall reduction in VASI

over time (P < 0.001) but no significant treatment group × time interaction (P = 0.716), indicating that both groups improved over time without evidence of differential trajectory. Adverse events were mild and no serious adverse events were documented. Any adverse event occurred in 27.8% of the betamethasone group and 16.7% of the tofacitinib group (P = 0.691). In the betamethasone arm, the most frequent adverse effects were weight gain and pedal edema. In the tofacitinib arm, the recorded adverse effects were elevated triglycerides and elevated total cholesterol. Figures 1 and 2 illustrate the temporal decline in VASI and the distribution of individual week-24 responses in both groups.

Table 1: Baseline demographic characteristics of the study population

Characteristic	Betamethasone + PUVASOL (n=18)	Tofacitinib + PUVASOL (n=18)	Overall (n=36)	P value
Participants analyzed, n	18	18	36	—
Age, years	34.06 ± 10.40	32.61 ± 11.30	33.33 ± 10.73	0.624
Male sex, n (%)	6 (33.3)	14 (77.8)	20 (55.6)	0.018
Female sex, n (%)	12 (66.7)	4 (22.2)	16 (44.4)	—
BMI, kg/m²	23.71 ± 1.61	23.12 ± 1.48	23.42 ± 1.55	0.217
Disease duration, years	1.00 (0.75-2.75)	1.00 (0.50-1.88)	1.00 (0.50-2.00)	0.512
Baseline VASI	11.72 ± 11.49	14.19 ± 11.31	12.96 ± 11.30	0.391

Data are presented as mean ± SD, median (IQR), or n (%). P values compare betamethasone versus tofacitinib groups.

Table 2: Baseline disease profile, family history, autoimmune associations, and vitiligo morphology

Characteristic	Betamethasone + PUVASOL (n=18)	Tofacitinib + PUVASOL (n=18)	Overall (n=36)	P value
First-degree relative with vitiligo, n (%)	1 (5.6)	2 (11.1)	3 (8.3)	1.000
Associated autoimmune disease present, n (%)	0 (0.0)	2 (11.1)	2 (5.6)	0.486
Family history of other autoimmune disease, n (%)	2 (11.1)	7 (38.9)	9 (25.0)	0.121
Vitiligo type: Focal	6 (33.3)	5 (27.8)	11 (30.6)	0.549
Segmental	1 (5.6)	5 (27.8)	6 (16.7)	—
Acral	2 (11.1)	1 (5.6)	3 (8.3)	—
Acrofacial	4 (22.2)	2 (11.1)	6 (16.7)	—
Mixed	2 (11.1)	3 (16.7)	5 (13.9)	—
Generalized	2 (11.1)	2 (11.1)	4 (11.1)	—
Facial	1 (5.6)	0 (0.0)	1 (2.8)	—

Associated autoimmune disease and vitiligo morphology were compared descriptively; morphology P value represents overall distribution.

Table 3: Comparative efficacy outcomes at week 12 and week 24

Outcome	Betamethasone + PUVASOL (n=18)	Tofacitinib + PUVASOL (n=18)	Overall (n=36)	P value
Baseline VASI	11.72 ± 11.49	14.19 ± 11.31	12.96 ± 11.30	0.391
Week 12 VASI	9.25 ± 9.97	11.60 ± 9.31	10.43 ± 9.58	0.211
Week 24 VASI	8.60 ± 9.23	10.56 ± 9.04	9.58 ± 9.06	0.253
Absolute VASI reduction at week 12	2.47 ± 1.95	2.59 ± 2.21	2.53 ± 2.05	1.000
Absolute VASI reduction at week 24	3.12 ± 2.62	3.64 ± 2.70	3.38 ± 2.64	0.535
Percent VASI reduction at week 12	25.88 ± 12.05	18.71 ± 5.80	22.30 ± 10.00	0.045
Percent VASI reduction at week 24	30.63 ± 14.23	27.49 ± 9.37	29.06 ± 11.98	0.566
Within-group P value (baseline vs week 12)	<0.001	<0.001	—	—
Within-group P value (baseline vs week 24)	<0.001	<0.001	—	—
Mixed-effects overall time effect	—	—	—	<0.001
Mixed-effects group × time interaction	—	—	—	0.716

Between-group P values for continuous outcomes were obtained using Mann-Whitney U test. Within-group P values were obtained using Wilcoxon signed-rank test. Mixed-effects model used repeated VASI values at baseline, week 12, and week 24.

Table 4: Responder analysis and adverse events

Outcome	Betamethasone + PUVASOL (n=18)	Tofacitinib + PUVASOL (n=18)	Overall (n=36)	P value
≥25% VASI reduction at week 12, n (%)	8 (44.4)	3 (16.7)	11 (30.6)	0.146
≥50% VASI reduction at week 12, n (%)	1 (5.6)	0 (0.0)	1 (2.8)	1.000
≥25% VASI reduction at week 24, n (%)	11 (61.1)	10 (55.6)	21 (58.3)	1.000
≥50% VASI reduction at week 24, n (%)	3 (16.7)	0 (0.0)	3 (8.3)	0.229
Week 24 response category: <25%	7 (38.9)	8 (44.4)	15 (41.7)	0.193
25%-49.9%	8 (44.4)	10 (55.6)	18 (50.0)	—
≥50%	3 (16.7)	0 (0.0)	3 (8.3)	—
Any adverse event, n (%)	5 (27.8)	3 (16.7)	8 (22.2)	0.691
Weight gain, n (%)	4 (22.2)	0 (0.0)	4 (11.1)	—
Pedal edema, n (%)	2 (11.1)	0 (0.0)	2 (5.6)	—
Elevated triglycerides, n (%)	0 (0.0)	2 (11.1)	2 (5.6)	—
Elevated total cholesterol, n (%)	0 (0.0)	1 (5.6)	1 (2.8)	—

Responder rates are based on percentage VASI reduction from baseline. Safety categories are descriptive.

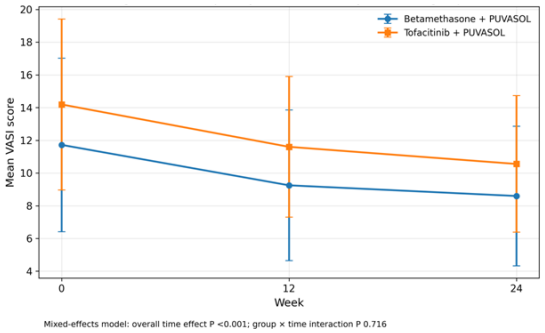

Figure 1: Mean VASI trajectory over 24 weeks in the two treatment groups. Error bars indicate 95% confidence intervals

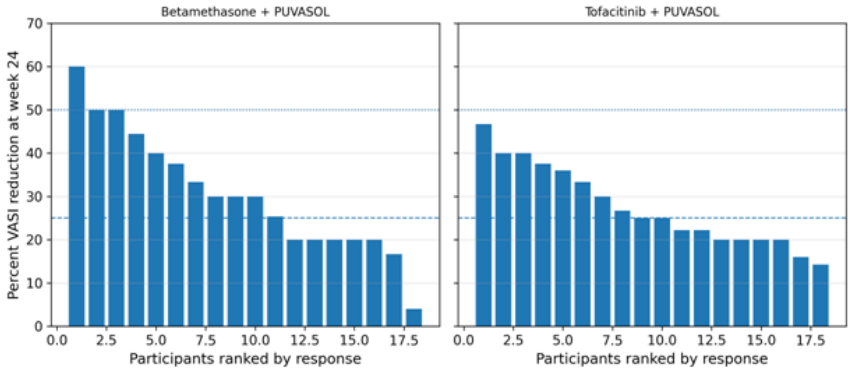

Figure 2: Waterfall plot showing individual percentage VASI reduction at week 24 in each treatment group

Discussion

Both treatment regimens in this randomized study produced significant within-group improvement in disease extent over 24 weeks, confirming that combination systemic therapy plus psoralen-based photochemotherapy can reduce vitiligo burden in active disease. However, the principal finding was that oral tofacitinib plus PUVASOL did not demonstrate superiority over oral betamethasone plus PUVASOL in the primary efficacy analysis. Absolute VASI reduction was similar at week 12 and week 24, and the mixed-effects model showed a strong overall time effect but no significant group-by-time interaction. The only statistically significant between-group difference was a greater mean percentage VASI reduction at week 12 in the betamethasone arm, a difference that disappeared by week 24. These data suggest that both regimens were active, but neither produced a decisive 24-week advantage in this cohort.

The absence of superiority for tofacitinib deserves careful interpretation. Active vitiligo is driven by inflammatory pathways that may be attenuated by either corticosteroid pulse therapy or JAK inhibition, while concomitant photochemotherapy provides a melanocyte-stimulating signal that can

facilitate repigmentation [3,6,14]. The present study therefore compared two biologically plausible combination strategies rather than an active drug against an inert control. In addition, the small sample size and moderate baseline heterogeneity likely reduced the ability to detect clinically meaningful differences. Although baseline age, BMI, duration, and VASI were comparable, the tofacitinib arm had a significant male predominance and numerically higher baseline VASI, factors that may have influenced averaged percentage change in a small open-label trial.

The response pattern in our study differs somewhat from the expectation set by recent literature. Dev et al. compared oral tofacitinib with oral dexamethasone mini-pulse therapy in active nonsegmental vitiligo and found similar ≥50% responder rates at 24 weeks but greater overall reduction in disease extent by 36 weeks with tofacitinib [15].

In contrast, our week-24 data showed no advantage for tofacitinib, and only the betamethasone arm achieved any VASI50 responders. One explanation may be treatment duration. Tofacitinib may require longer treatment to translate immunologic suppression into visible repigmentation, especially when light exposure is variable and less standardized than cabin-based NB-UVB [14,15,17]. Our results therefore suggest that a tofacitinib advantage, if present, may not be fully expressed within 24 weeks in all clinical settings.

The form of light exposure used in this trial is highly relevant. Evidence from mechanistic and clinical studies indicates that light is often necessary for optimal repigmentation during JAK inhibitor therapy [14]. Randomized data from Guo et al. showed that tofacitinib combined with NB-UVB outperformed NB-UVB alone, reinforcing the concept that targeted immunomodulation and controlled phototherapy act synergistically [16]. Our study paired tofacitinib with oral PUVASOL rather than NB-UVB. Unlike monochromatic cabin-based phototherapy, sunlight-based activation is inherently variable because it depends on weather, timing, adherence, and local ultraviolet intensity. This variability may have blunted the incremental benefit of tofacitinib and partly explains why the tofacitinib arm did not outperform the steroid arm.

Our findings are more consistent with the view that corticosteroid mini-pulse therapy remains an effective stabilizing option in progressive vitiligo. Systematic review data suggest that oral mini-pulse regimens can arrest disease activity in a substantial proportion of patients, with weight gain being the most frequent adverse effect [9]. Clinical studies have similarly shown that pulse corticosteroids are useful for rapidly progressive vitiligo, especially when the immediate therapeutic goal is disease arrest rather than maximal repigmentation [10,20]. In the present study, betamethasone plus PUVASOL produced significant VASI reduction, higher early percent improvement, and 16.7% VASI50 response at week 24, albeit with steroid-related adverse events such as weight gain and pedal edema. These findings reinforce that corticosteroid pulse therapy remains a meaningful comparator in unstable disease. The safety profile observed in this cohort was acceptable in both groups. No serious adverse events were identified. Steroid-associated effects were mainly weight gain and pedal edema, whereas the tofacitinib group showed lipid abnormalities without major clinical sequelae. This pattern is broadly consistent with reports that oral tofacitinib can be tolerated in vitiligo with mostly mild adverse events [7,17].

Nevertheless, a reassuring 24-week safety signal should not be overinterpreted as proof of long-term safety. JAK inhibitors still require vigilance for laboratory abnormalities and infection risk, while corticosteroids remain limited by cumulative metabolic and endocrine toxicity [6,7]. Given that both regimens produced statistically comparable absolute and percentage VASI reduction at week 24 ($P = 0.535$ and $P = 0.566$, respectively), with no significant group-by-time interaction on mixed-effects modelling ($P = 0.716$), tofacitinib may be considered a preferable long-term option in patients who require prolonged or repeated systemic therapy. Its adverse-event profile — predominantly mild lipid changes — is less burdensome than the cumulative metabolic and endocrine morbidity associated with corticosteroid pulse therapy, including weight gain and pedal edema observed in the betamethasone arm of this trial. Clinicians may therefore consider tofacitinib plus PUVASOL as an efficacy-equivalent but potentially safer systemic alternative, particularly in patients at higher risk for steroid-related complications.

Another explanation for the modest overall response rates in both groups may be the clinical heterogeneity of the study population. Our cohort included focal, segmental, acral, acrofacial, mixed, and generalized patterns. Lesion distribution and subtype strongly influence repigmentation outcomes, with facial lesions generally responding better and acral lesions responding poorly [12,13]. Segmental vitiligo also differs biologically and therapeutically from nonsegmental disease [2]. Inclusion of mixed morphologic patterns likely reduced homogeneity and may have lowered average response in both arms.

The study also provides a pragmatic message for resource-limited settings. In many centers where regular NB-UVB access is limited, oral PUVASOL remains feasible because of affordability and

accessibility. Our data suggest that both oral betamethasone and oral tofacitinib can be paired with this approach with measurable short-term benefit. Yet the lack of clear superiority for tofacitinib implies that cost, monitoring requirements, and access should be weighed carefully before replacing established pulse corticosteroid protocols in routine practice. This study has several limitations: small sample size, open-label design, short follow-up, baseline sex imbalance, and limited patient-reported outcome data. Sunlight-based psoralen activation is also difficult to standardize, which may have increased exposure variability. Nonetheless, the study has important strengths, including randomized allocation, quantitative VASI-based assessment, direct head-to-head comparison of two clinically relevant systemic regimens, and data derived from a real-world tertiary care setting where PUVASOL remains highly relevant. In summary, oral tofacitinib plus PUVASOL was effective in reducing vitiligo burden over 24 weeks, but in this cohort it was not superior to oral betamethasone plus PUVASOL. Both regimens appear to be viable options for active vitiligo, with different adverse-event profiles and potentially different practical roles. Larger, blinded studies with longer follow-up, subtype-stratified analyses, controlled phototherapy exposure, and patient-reported outcomes are needed to clarify whether systemic JAK inhibition confers a delayed or subgroup-specific advantage over corticosteroid pulse therapy.

Conclusion

In adults with vitiligo treated for 24 weeks, both oral betamethasone plus PUVASOL and oral tofacitinib plus PUVASOL produced significant improvement in VASI and had acceptable short-term safety. Oral tofacitinib did not demonstrate superiority over betamethasone for short-term overall VASI improvement in this cohort.

Betamethasone showed a greater early percentage response, whereas both regimens had comparable 24-week outcomes. Larger and longer trials using standardized phototherapy are required to define the optimal place of systemic JAK inhibition in progressive vitiligo.

References

1. Akl J, Lee S, Ju HJ, Parisi R, Kim JY, Jeon JJ, et al. Estimating the burden of vitiligo: a systematic review and modelling study. Lancet Public Health. 2024;9(6):e386-e396. doi:10.1016/S2468-2667(24)00026-4.
2. Ezzedine K, Eleftheriadou V, Whitton M, van Geel N. Vitiligo. Lancet. 2015;386(9988):74-84. doi:10.1016/S0140-6736(14)60763-7.
3. Frisoli ML, Essien K, Harris JE. Vitiligo: Mechanisms of Pathogenesis and Treatment. Annu Rev Immunol. 2020; 38:621-648. doi:10.1146/annurev-immunol-100919-023531.
4. Bibeau K, Ezzedine K, Harris JE, van Geel N, Grimes P, Parsad D, et al. Mental Health and Psychosocial Quality-of-Life Burden Among Patients with Vitiligo: Findings From the Global VALIANT Study. JAMA Dermatol. 2023;159(10):1124-1128. doi:10.1001/jamadermatol.2023.2787.
5. Silverberg JI, Silverberg NB. Association between vitiligo extent and distribution and quality-of-life impairment. JAMA Dermatol. 2013;149(2):159-164. doi:10.1001/jamadermatol.2013.927.
6. Cunningham KN, Rosmarin D. Vitiligo Treatments: Review of Current Therapeutic Modalities and JAK Inhibitors. Am J Clin Dermatol. 2023;24(2):165-186. doi:10.1007/s40257-022-00752-6.
7. Huang F, et al. Efficacy and Safety of Janus Kinase Inhibitors in Patients with Vitiligo: A Systematic Review and Meta-Analysis. Clin Pharmacol Ther. 2025;117(3):659-669. doi:10.1002/cpt.3538.
8. van Geel N, Speeckaert R, Taïeb A, Ezzedine K, Lim HW, Pandya AG, et al. Worldwide expert recommendations for the diagnosis and management of vitiligo: Position statement from the International Vitiligo Task Force Part 1: towards a new management algorithm. J Eur Acad Dermatol Venereol. 2023;37(11):2173-2184. doi:10.1111/jdv.19451.
9. Chavez-Alvarez S, Herz-Ruelas ME, Raygoza-Cortez AK, et al. Oral mini-pulse therapy in vitiligo: a systematic review. Int J Dermatol. 2021;60(7):868-876. doi:10.1111/ijd.15464.
10. Kanwar AJ, Mahajan R, Parsad D. Low-dose oral mini-pulse dexamethasone therapy in progressive unstable vitiligo. J Cutan Med Surg. 2013;17(4):259-268. doi:10.2310/7750.2013.12053.
11. Hamzavi I, Jain H, McLean D, Shapiro J, Zeng H, Lui H. Parametric modeling of narrowband UV-B phototherapy for vitiligo using a novel quantitative tool: the Vitiligo Area Scoring Index. Arch Dermatol. 2004;140(6):677-683. doi:10.1001/archderm.140.6.677.
12. Bae JM, Jung HM, Hong BY, Lee JH, Choi WJ, Lee JH, et al. Phototherapy for Vitiligo: A Systematic Review and Meta-analysis. JAMA Dermatol. 2017;153(7):666-674. doi:10.1001/jamadermatol.2017.0002.
13. Bhatnagar A, Kanwar AJ, Parsad D, De D. Psoralen and ultraviolet A and narrow-band ultraviolet B in inducing stability in vitiligo, assessed by vitiligo disease activity score: an open prospective comparative study. J Eur Acad Dermatol Venereol. 2007;21(10):1381-1385. doi:10.1111/j.1468-3083.2007.02283. x.

14. Liu LY, Strassner JP, Refat MA, Harris JE, King BA. Repigmentation in vitiligo using the Janus kinase inhibitor tofacitinib may require concomitant light exposure. J Am Acad Dermatol. 2017;77(4):675-682.e1. doi: 10.1016/j.jaad.2017.05.043.
15. Dev A, Vinay K, Bishnoi A, Kumaran MS, Mehta H, Parsad D. Oral tofacitinib in comparison with dexamethasone oral mini-pulse therapy for the treatment of active nonsegmental vitiligo: A randomized controlled trial. J Am Acad Dermatol. 2025;93(4):937-945. doi: 10.1016/j.jaad.2025.06.006.
16. Guo X, Zhang D, Chen G, et al. The efficacy of narrowband ultraviolet B phototherapy combination with tofacitinib in the treatment of vitiligo: a randomized controlled trial. J Dermatolog Treat. 2025;36(1):2479567. doi:10.1080/09546634.2025.2479567.
17. Hu W, Cao C, Zheng Y, Lei J, Yu K, Sheng A, et al. A retrospective analysis of the efficacy and safety of oral tofacitinib in active vitiligo treatment. Arch Dermatol Res. 2025;317(1):645. doi:10.1007/s00403-025-04151-9.
18. Rios-Duarte JA, Sanchez-Zapata MJ, Silverberg JI. Association of vitiligo with multiple cutaneous and extra-cutaneous autoimmune diseases: a nationwide cross-sectional study. Arch Dermatol Res. 2023;315(9):2597-2603. doi:10.1007/s00403-023-02661-y.
19. Ezzedine K, Eleftheriadou V, Jones H, Bibeau K, Kuo FI, Sturm D, et al. Psychosocial Effects of Vitiligo: A Systematic Literature Review. Am J Clin Dermatol. 2021;22(6):757-774. doi:10.1007/s40257-021-00631-6.
20. Pasricha JS, Khaitan BK. Oral mini-pulse therapy with betamethasone in vitiligo patients having extensive or fast-spreading disease. Int J Dermatol. 1993;32(10):753-757. doi:10.1111/j.1365-4362. 1993.tb02754.x.