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Localized Janus Kinase Inhibition Modulation as Standalone or Synergistic Therapy with Narrowband UVB Photo stimulation in Vitiligo Management: A Systematic Review and Meta-Analysis

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Abstract

Background: Vitiligo is a chronic autoimmune dermatosis characterized by progressive hypopigmentation, which affects approximately 0.2% to 2% of the global population. This condition can have significant psychosocial impacts, particularly in individuals with darker skin phenotypes. Recent studies have suggested that Janus kinase (JAK) inhibitors, especially topical ruxolitinib, could offer therapeutic potential in managing vitiligo.

Objective: To systematically review the therapeutic efficacy, safety profile, and potential synergistic effects of topical JAK inhibitors, particularly ruxolitinib, in the treatment of vitiligo.

Methods: A systematic review was conducted in accordance with the PRISMA guidelines. Data from six studies, encompassing 385 subjects, were synthesized. The primary outcome measure was the improvement in Vitiligo Area Scoring Index (VASI), and the methodological quality was assessed using the MINORS scale.

Results: Topical ruxolitinib demonstrated a statistically significant improvement in VASI scores (pooled estimate = 0.58; 95% CI: 0.44–0.73; p≤0.001). The synergistic effect of ruxolitinib combined with Narrow Band Ultraviolet (NB-UVB) phototherapy yielded a mean VASI score improvement of 37.6%. Furthermore, 30.4% of patients receiving 1.5% ruxolitinib cream achieved a 75% improvement in facial VASI (F-VASI) scores.

Conclusion: Topical JAK inhibitors, including ruxolitinib, show considerable efficacy in improving VASI scores and facilitating repigmentation in vitiligo patients. The combination of JAK inhibitors with NB-UVB therapy demonstrates enhanced therapeutic effects. These findings underscore the potential of JAK inhibitors as effective treatment modalities, although further research is needed to standardize treatment protocols and evaluate long-term impacts on patient quality of life.

Keywords: Vitiligo; Topical Janus Kinase Inhibitor; Vitiligo Area Scoring Index; Facial Vitiligo Area Scoring Index; Narrow Band Ultraviolet (NB-UVB)

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Introduction

Vitiligo is a chronic autoimmune disorder typified by the progressive loss of cutaneous pigmentation, resulting in the emergence of well-defined hypopigmented macules and patches. This condition affects approximately 0.2% to 2% of the global population and is frequently correlated with other autoimmune pathologies, including halo nevus and malignant melanoma [1]. Although vitiligo is not life-threatening, it imposes considerable psychological distress, particularly among individuals with darker skin phenotypes [2]. The visibility of vitiligo lesions often precipitates diminished self-esteem, social isolation, and stigmatization, profoundly affecting an individual's mental health [3]. Individuals afflicted with vitiligo frequently endure psychological distress that necessitates a comprehensive, multidisciplinary treatment paradigm. Such an approach should

holistically address both physical manifestations and psychological well-being, integrating counselling and support groups to assist individuals in navigating the emotional challenges associated with the condition. The incorporation of psychological support into treatment regimens is paramount for enhancing overall quality of life for those affected.

Recent advancements in the management of vitiligo have introduced promising therapeutic modalities, notably the application of Janus Kinase (JAK) inhibitors [4]. Originally developed for the treatment of inflammatory conditions such as rheumatoid arthritis, JAK inhibitors function by modulating the immune response that culminates in melanocyte destruction these are the cells responsible for skin pigmentation [5]. These inhibitors exert their pharmacological effects by inhibiting specific tyrosine kinases implicated in signal transduction pathways and the activation of autoimmune processes. While broad-spectrum JAK inhibitors have demonstrated clinical efficacy, they are not devoid of potential adverse effects. Notable side effects may include an increased susceptibility to opportunistic infections, cytopenias, dyslipidemia, and gastrointestinal complications. Thus, while these agents represent a significant advancement in the therapeutic landscape for vitiligo, meticulous consideration of their risk-benefit profile is essential in clinical practice [6].

Ongoing investigations are concentrated on the refinement of selective Janus kinase (JAK) inhibitors, which aim to optimize therapeutic efficacy while concurrently mitigating adverse effects [7]. A notable therapeutic modality for vitiligo is narrowband ultraviolet B (NB-UVB) phototherapy, employing a specific wavelength of UVB light (~311 nm) to induce immunosuppression and stimulate melanocyte proliferation [8]. The initial efficacy of NB-UVB was elucidated by Westerhof et al [9] in 1997, establishing it as a widely accepted treatment paradigm for vitiligo. This systematic review endeavors to critically evaluate the efficacy and safety profile of topical JAK inhibitors, both as monotherapy and in conjunction with NB-UVB phototherapy, for individuals diagnosed with vitiligo. By synthesizing extant research, this review seeks to furnish valuable insights into optimal treatment strategies for managing vitiligo, ultimately enhancing clinical outcomes and ameliorating the quality of life for those affected by this condition. The integration of JAK inhibitors into therapeutic regimens is predicated on their mechanism of action, which involves modulation of intracellular signalling pathways governing immune responses that lead to melanocyte destruction. The concomitant application of NB-UVB phototherapy is hypothesized to enhance repigmentation through stimulation of melanocyte migration from hair follicles to depigmented areas, thereby facilitating a synergistic effect that may surpass the efficacy of either treatment modality administered in isolation.

Methodology

Focused research framework

Participants/Population (P): This investigation will encompass individuals aged 18 to 75 years diagnosed with vitiligo, including diverse phenotypic expressions such as non-segmental and refractory vitiligo, while explicitly excluding lesions localized to the perioral and periocular regions.

Intervention (I): The intervention will involve the administration of topical Janus kinase (JAK) inhibitors, specifically ruxolitinib at a concentration of 1.5% or tofacitinib at 2%, utilized either as monotherapy or in conjunction with narrowband ultraviolet B (NB-UVB) phototherapy.

Comparator(s)/Control (C): Control groups will consist of subjects receiving a vehicle devoid of active pharmaceutical ingredients (Standard of Care – SoC) or those undergoing no supplementary treatment.

Outcome (O): The primary endpoint will entail a rigorous analysis of overall improvement in vitiligo patients, quantitatively assessed through validated scales, including the Vitiligo Area Scoring Index (VASI), the Facial Vitiligo Area Scoring Index (F-VASI), and metrics established by the Vitiligo European Task Force. Secondary endpoints will encompass photographic evaluations, patient-reported satisfaction metrics, and additional standardized dermatological assessment tools.

Study design (S): The research design will incorporate pilot clinical studies, non-randomized open-label investigations, and randomized controlled trials categorized as phase 2 and phase 3 studies.

Eligibility

Inclusion criteria: The criteria for inclusion in this investigation are as follows: (i) Participants must be individuals aged between 18 and 75 years with a confirmed diagnosis of vitiligo; (ii) The therapeutic regimen must primarily involve the administration of Janus kinase (JAK) inhibitors, either as monotherapy or in conjunction with adjunctive modalities; (iii) Participants must be compared against a control cohort receiving narrowband ultraviolet B (NB-UVB) phototherapy, either as monotherapy or in combination with other interventions; (iv) The assessment of repigmentation must be included as a primary evaluative metric; and (v) All studies must be published exclusively in the English language.

Exclusion criteria: The exclusion criteria are delineated as follows: (i) Studies that do not specify the subtype of vitiligo under investigation; (ii) Research lacking a definitive intervention strategy concerning JAK inhibitors; (iii) Clinical trials that do not report primary outcome measures, such as the Vitiligo Area Scoring Index (VASI) or Facial Vitiligo Area Scoring Index (F-VASI); (iv) Studies devoid of validated instruments for evaluating treatment efficacy; (v) Research lacking empirical substantiation, including case reports, editorials, or reviews without original data; (vi) Trials failing to provide clear numerical results or statistical analyses; (vii) Studies involving fewer than five participants; (viii) Investigations focused exclusively on pediatric populations; and (ix) Clinical reports on vitiligo treatments that do not incorporate JAK inhibitors.

Search strategy

The current inquiry was meticulously conducted in strict adherence to the updated PRISMA 2020 guidelines [10]. A comprehensive exploration of primary databases was undertaken for articles published subsequent to June 2017, encompassing a diverse array of repositories such as PubMed/MEDLINE, Embase, PsycINFO, TRIP, the Cochrane Library, and the specialized register of the Cochrane Skin Group. The search strategy employed a rigorously formulated Boolean query: (vitiligo) AND (topical Janus kinase inhibitor OR JAK inhibitor OR ruxolitinib OR tofacitinib) AND (treatment OR therapy) AND (clinical trial OR study OR pilot) AND (VASI OR Vitiligo Area Scoring Index OR F-VASI OR Facial Vitiligo Area Scoring Index OR repigmentation) AND (topical application OR cream

OR NB-UVB OR ultraviolet B). This methodical approach ensured a thorough and exhaustive compilation of pertinent literature from inception to the present date. The article selection process adhered to a dual-phase methodology; initially, two independent reviewers (V.K. and D.S.) scrupulously scrutinized the titles and abstracts of all retrieved references in alignment with pre-established inclusion and exclusion criteria. Studies excluded at this juncture were those that failed to conform to the review's focal parameters. Subsequently, full-text articles of the remaining references underwent an exhaustive evaluation utilizing Mendeley Reference Manager by the reviewers. Discrepancies between reviewers were resolved through deliberative discourse aimed at achieving consensus; in instances where consensus proved elusive, a third reviewer (D.S.) was consulted to arbitrate the final inclusion decision. Furthermore, cross-referencing of citations from selected studies was performed to unearth supplementary relevant research. The resultant corpus of literature was collectively ratified by all reviewers engaged in this comprehensive process.

Study selection and data extraction

In the present investigation, the processes of study selection and data extraction were executed by two independent investigators who scrupulously screened the extant literature for inclusion, retrieved potentially relevant studies, and adjudicated eligibility based on meticulously predefined criteria. Any discrepancies in evaluative judgment were resolved through a consensus-driven methodology. Subsequently, these same investigators undertook the independent extraction of data from the selected studies, employing standardized data collection instruments, while a third investigator was appointed to ascertain the accuracy and integrity of the extracted data.

For each included study, a comprehensive array of descriptive parameters was systematically extracted, encompassing the year of publication, authorship, sample size, demographic characteristics of participants, methodological frameworks employed, treatment arms delineated, specific Janus kinase (JAK) inhibitors administered, duration of follow-up, observed clinical outcomes, and documented adverse reactions. In instances where supplementary information was deemed requisite for elucidation or completeness, correspondence was initiated with the corresponding authors via electronic mail. This rigorous approach ensures that the data extraction process is both exhaustive and reproducible, thereby enhancing the reliability and validity of the findings derived from this systematic review.

Summary of study characteristics that were included has been illustrated in Table 1.

Quality assessment and risk of bias assessment

In the present investigation, the evaluation of study quality and risk of bias was conducted by two independent reviewers employing specific quality assessment instruments, with oversight from a third author to ensure methodological rigor. Discrepancies in judgment were resolved through a consensus-driven mechanism. For the two randomized controlled trials (RCTs), the Cochrane RevMan 5 software (Version 5.4) [11] was utilized to systematically scrutinize critical domains, including random sequence generation, allocation concealment, participant and personnel blinding, outcome assessment blinding, management of incomplete outcome data, and selective reporting biases. Concurrently, for the four non-randomized studies, the Methodological Index for Non-Randomized Studies (MINORS) scale [12] was employed to assess biases related to confounding variables, participant selection methodology, intervention classification accuracy, deviations from intended interventions, handling of missing data, outcome measurement validity, and the selection of reported results. This dual-faceted approach ensures a comprehensive appraisal of methodological integrity across the included studies.

Outcome measurements

The Vitiligo Area Scoring Index (VASI) serves as a standardized and quantitative metric for the assessment of temporal variations in vitiligo lesions [13]. In this investigation, VASI was employed to evaluate both the extent and severity of vitiligo among participants, thereby facilitating the appraisal of therapeutic efficacy. The VASI methodology quantifies the involvement of vitiligo in terms of Body Surface Area (BSA) and the degree of depigmentation. Specifically, affected anatomical regions are compartmentalized into discrete sections, with the extent of vitiligo in each section quantified as a percentage. The severity of depigmentation is assessed utilizing a grading scale that spans from 0 to 10, where elevated scores correspond to an augmented severity of depigmentation.

Effect measures and synthesis method

A meta-analysis was performed employing STATA® SE 16.1 (Stata Corp. LLC, Texas, USA) [14] to facilitate direct comparative evaluations across the studies. Outcomes were delineated as percentage discrepancies accompanied by 95% confidence intervals (CIs), utilizing a fixed-effect model, with significance delineated at $p \leq 0.05$. The I^2 statistic and Cochran's Q-test were employed to ascertain heterogeneity among the studies. Furthermore, funnel plot analysis was conducted to elucidate potential publication bias.

Results

Search Results and data analysis

A flowchart of identification, inclusion and exclusion of studies is shown in Figure 1. Primary search yielded a total of 542 records, of which 156 duplicate records and 76 ineligible records were removed (Figure 1).

Post-applying the inclusion criteria and retrieval filter, 26 records were assessed for the inclusion criteria. A total of 20 records were eliminated due to the exclusion criteria, and a final 6 studies were included for this review.

Out of the included 6 studies, 4 studies are non-randomised controlled trials (n-RCTs) which evaluated the efficacy of ruxolitinib or tofacitinib in the treatment of vitiligo. Only those studies utilizing topical JAK inhibitor containing cream on vitiligo patches in human subjects have been included in this review.

Grading scale

Photographs of vitiligo patches were taken at all study visits to help monitor clinical progression. The most commonly used assessment parameter was the Vitiligo Area Scoring Index (VASI) [15]. The total body VASI is calculated using a formula that includes contributions from all body regions (possible range, 0 to 100).

$$VASI = \sum \text{All Body Sites}[\text{Hand Units}] \times [\text{Residual Depigmentation}]$$

One hand unit is used to assess the baseline proportion of vitiligo involvement in each body region. It consists of the palm and the volar surface of all the digits. One hand unit is roughly 1% of the entire body surface area.

The hands, upper extremities (excluding hands), trunk, lower

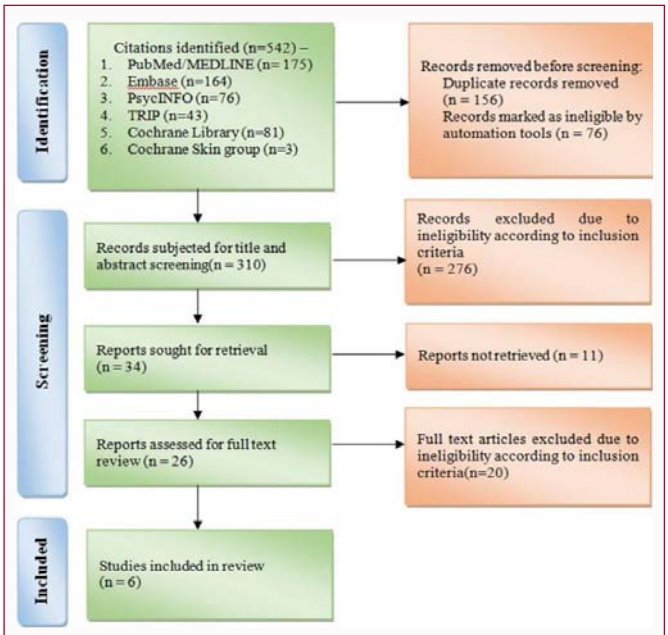

Figure 1: Flowchart describing article inclusion strategy.

extremities (except feet), and feet are the five distinct and mutually exclusive areas of the body. The lower extremities include the buttocks and inguinal areas, whereas the upper extremities comprise the axillary region.

Residual depigmentation might be represented as 0, 10%, 25%, 50%, 75%, 90%, or 100% of the original colour.

At 100% depigmentation, no pigment is present; at 90%, specks of pigment are present; at 75%, the depigmented area exceeds the pigmented area; at 50%, the depigmented and pigmented areas are equal; at 25%, the pigmented area exceeds the depigmented area; at 10%, only specks of depigmentation are present.

Factor wise comparison of the treatment modalities

JAK Inhibitors as monotherapy: In four of the studies reviewed, JAK inhibitors tofacitinib or ruxolitinib in varying degrees of concentration was applied as monotherapy. Two of these studies were RCTs, whereas two were n-RCTs. All the studies reported improvement in VASI scores, and a significant proportion of the participants experienced repigmentation.

Rothstein et al. [16], in their study evaluating topical ruxolitinib1.5%, reported a statistically significant mean percentage improvement in overall VASI score corresponding from 9.8 at baseline to 8.9 at end-point. The study also measured the Disease Extent in Vitiligo European Task Force scale using Body Surface Area (BSA), which underwent a mean percentage reduction of 11.2% ± 26.4% (P = 0.19).

Mobasher et al. [17] evaluated the effects of 2% tofacitinib in the treatment of refractory vitiligo. The assessment of outcome was done by calculating the mean percentage repigmentation of treated lesions by BSA in 16 patients. A total of 13 out of 16 patients experienced repigmentation with 4 patients experiencing >90% repigmentation [17].

Rosmarin et al. [18,19] studied the therapeutic potential of ruxolitinib cream in different degrees of concentration in a Phase 2 clinical trial for a period of 52 weeks in 157 patients. The study reported great improvement (more than 50%) in F-VASI scores of patients receiving 1.5% ruxolitinib twice daily.

On further conducting the Phase 3 clinical trial, Rosmarin et al. (2022) 18 investigated the therapeutic potential of 1.5% ruxolitinib cream in 674 patients for a period of 24 weeks. This was done via 2 study treatment arms- TRuE-V1 in North America and TRuE-V2in Europe. The study reported that at week 24, F-VASI of 75 was achieved in 29.8% of the patients in TRuE-V1 and in 30.9% of the patients in TRuE-V2 in the treatment groups.

JAK Inhibitors as combination therapy with NB-UVB phototherapy: Out of the six studies reviewed, two evaluated the effect of topical JAK inhibitors with NB-UVB phototherapy.

Joshipura et al. [20] reported a study evaluating topical ruxolitinib with optional NB-UVB. Five patients completed this study, out of which, 3 opted for combination therapy with NB-UVB phototherapy. At week 52 from baseline, a statistically significant improvement in mean overall VASI score of 37.6% was observed. 2 out of the 3 patients who were undergoing combination therapy responded with a mean VASI score of 16.7% ± 16.7.

McKesey et al. [21] conducted a pilot study to evaluate the efficacy of 2% tofacitinib given twice daily with NB-UVB phototherapy given thrice weekly over a period of 3 months. The mean facial VASI was reported to be 0.80 at baseline which improved to 0.23 post-follow-up.

JAK Inhibitors with other treatment modalities: Mobasher et al. [17] evaluated 2% tofacitinib given concomitant with topical steroids, topical calcineurin inhibitors, supplements (*e.g. Polypodium leucotomos* and *Ginkgo biloba*) or phototherapy. This study being

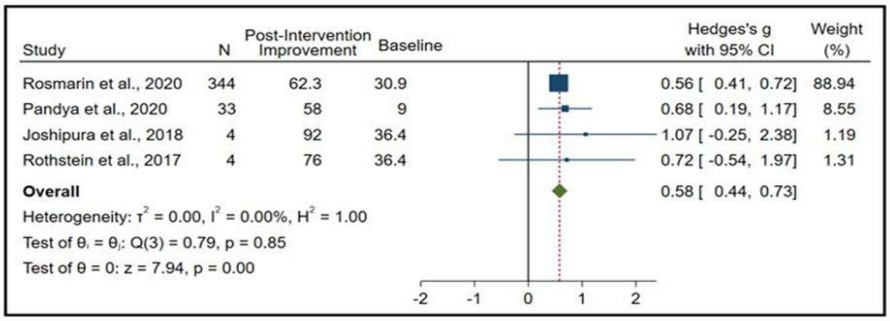

Figure 2: Forest plot evaluating the comparison of significant improvement in overall VASI after treatment with topical Janus kinase (JAK) inhibitors like Ruxolitinib; VASI: Vitiligo Area Scoring Index.

Table 1: MINORS assessment for non-randomized studies.

Study:	A clearly stated aim	Inclusion of consecutive patients	Prospective collection of data	Endpoints appropriate to the aim of the study	Unbiased assessment of the study endpoint	Follow-up period appropriate to the aim of the study	Loss to follow up less than 5%	Prospective calculation of the study size	An adequate control group	Contemporary groups	Baseline equivalence of groups	Adequate statistical analyses	Total score
Rothstein (2017)16	2	1	2	2	2	2	1	0	0	0	0	0	Dec-24
Mobasher (2020)17	1	1	0	1	1	0	1	0	0	1	1	1	Aug-24
Joshipura (2018)20	2	1	0	2	0	2	1	0	0	0	0	0	Aug-24
McKesey (2019)21	1	1	0	0	0	1	1	0	0	0	0	0	Apr-24

Study	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Rosmarin (2020)17	+	?	+	+	−	+	?
Rosmarin (2022)18	+	+	+	+	−	?	?

Table 2: Cochrane Risk of Bias for Randomised Studies ("-", "+", and "?" indicate high, low and unclear risk of bias respectively).

conducted in an uncontrolled setting did not allow the assessment of the concomitant treatments on the outcome. Therefore, the synergistic role of topical steroids, topical calcineurin inhibitors, supplements, etc. has not been established in literature.

Risk of bias

The risk of bias for the two randomized controlled trials (RCTs) assessed via the Cochrane RevMan 5 program (Version 5.4) has been summarised in Table 2.

The risk of bias for the four non-randomized studies assessed via the Methodological Index for Non-Randomized Studies (MINORS) scale has been summarised in table I. Total scores in the range of 19 to 24, 13 to16, 9 to12, 5 to 8 and 0 to 4 indicate very high, high, moderate, low and very low quality respectively.

Rosmarin et.al [18,19] had two clinical trials (RCTs) for the analysis; its risk of bias was undertaken using Cochrane risk of bias assessment tool (Table. 2).

Effect measures

The meta-analysis of four included studies (2 studies were excluded because of different outcome assessment parameter) with outcomes expressed as percentage difference found a significant difference in the improvement in overall VASI after treatment with topical Janus kinase (JAK) inhibitors like Ruxolitinib (Pooled estimate= 0.58; 95% CI:0.44 to 0.73; p=≤0.001) (Figure 2).

The treatment with ruxolitinib was associated with substantial repigmentation of vitiligo lesions. These suggest that ruxolitinib might be an effective treatment option for patients with vitiligo.

Publication bias

A funnel plot analysis detected no evidence of publication bias. In addition, Egger's regression test revealed no existence of publication bias (p<0.05) (Figure 3).

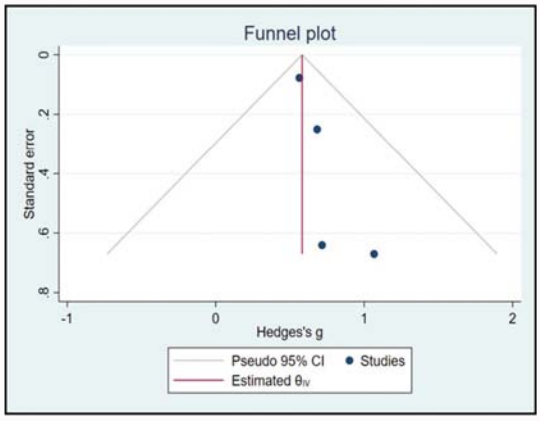

Figure 3: Funnel plot analysis with 95% CI: Confidence Interval.

Discussion

Vitiligo constitutes a multifaceted autoimmune pathology characterized by the progressive ablation of cutaneous pigmentation resultant from the targeted annihilation of melanocytes. This disorder not only undermines the aesthetic integrity of the integumentary system but also engenders profound psychological sequelae for affected individuals. Recent advancements have precipitated an escalating interest in the formulation of efficacious therapeutic interventions, particularly accentuating Janus kinase (JAK) inhibitors, such as tofacitinib and ruxolitinib. These pharmacotherapeutic agents have emerged as promising candidates for the management of vitiligo due to their capacity to modulate dysregulated immune responses and facilitate the repigmentation process through intricate immunological mechanisms.

Efficacy of JAK inhibitors

Recent inquiries have elucidated that monotherapy with topical Janus kinase (JAK) inhibitors can precipitate significant amelioration in the manifestations of vitiligo. Investigations by Rothstein et al. [16], Mobasher et al. [17], and Rosmarin et al. [18,19] have consistently revealed substantial enhancements in the Vitiligo Area Severity Index (VASI) scores among subjects administered these pharmacological

agents. Ruxolitinib cream, in particular, has emerged as a seminal therapeutic modality, being the inaugural FDA-sanctioned topical JAK inhibitor for vitiligo. Data from Phase 2 and Phase 3 clinical trials underscore its therapeutic efficacy, especially in achieving F-VASI75 scores indicative of considerable repigmentation. However, it is essential to scrutinize the subtleties inherent in these findings. A notable correlation exists between disease duration and the extent of repigmentation; while prolonged disease duration may statistically associate with diminished repigmentation outcomes, it is paramount to recognize that correlation does not imply causation. This suggests that chronic vitiligo may present challenges in attaining optimal therapeutic results, yet does not necessarily indicate that the duration of the condition directly obstructs the repigmentation process.

Variability in treatment outcomes

Notwithstanding the auspicious outcomes linked to Janus kinase (JAK) inhibitors, the heterogeneity in treatment duration and concentration across disparate studies engenders pertinent inquiries regarding the consistency and generalizability of these findings. This variability underscores an exigent necessity for standardized protocols in forthcoming clinical trials to facilitate the precise assessment and comparative analysis of treatment efficacy across diverse patient cohorts.

Combination therapies

The potential for synergistically amalgamating Janus kinase (JAK) inhibitors with narrowband ultraviolet B (NB-UVB) phototherapy delineates a compelling avenue for enhancing therapeutic efficacy in vitiligo management. Empirical data from studies by Joshipura et al. [20] and McKesey et al. [21] suggest that this combinatorial regimen may yield substantial enhancements in Vitiligo Area Severity Index (VASI) scores, indicating a synergistic effect that amplifies repigmentation beyond monotherapeutic outcomes. Additionally, the incorporation of JAK inhibitors with adjunctive modalities-such as topical corticosteroids, calcineurin inhibitors, and dietary supplements-may further optimize clinical results. Nevertheless, as emphasized by Mobasher et al. [17], there exists an exigent need for more exhaustive investigations to elucidate the complex synergistic interactions of these concomitant therapies. Rigorous clinical trials are essential to critically assess both the efficacy and safety profiles of such integrative approaches, thereby ensuring a comprehensive understanding of their therapeutic potential in vitiligo management.

Limitations

Despite the promising findings, several limitations are inherent within the included studies. The foremost limitation pertains to the inclusion criteria; a predominant proportion of the studies were non-randomized controlled trials (n-RCTs), which may introduce biases and circumscribe the generalizability of the results. This limitation often arises from the stringent parameters characteristic of n-RCTs [22].

The second limitation involves the heterogeneity in study design, treatment duration, and outcome metrics, which obfuscates direct comparisons among studies. The inconsistency in measurement parameters engenders a scenario where conclusive interpretations deviate from the original hypothesis, culminating in information bias.

A further constraint of this review is the paucity of studies; only six investigations were incorporated, resulting in an insufficient evidentiary foundation to substantiate the review's objectives. Scientific treatment modalities encompassing JAK inhibitors or NB-UVB phototherapy necessitate robust empirical validation through adequately powered studies to facilitate their integration into routine clinical practice.

Future inquiries should prioritize large-scale, randomized controlled trials with standardized protocols to elucidate optimal dosing regimens, treatment durations, and the overall efficacy of JAK inhibitors in the management of vitiligo.

Conclusion

In conclusion, the systematic review accentuates the promising therapeutic efficacy of Janus kinase (JAK) inhibitors, specifically ruxolitinib and tofacitinib, in the management of vitiligo. Both monotherapeutic and combinatorial strategies involving narrowband ultraviolet B (NB-UVB) phototherapy manifest substantial potential in facilitating repigmentation and enhancing Vitiligo Area Severity Index (VASI) scores among affected cohorts. The data corroborate that JAK inhibitors can precipitate significant enhancements in cutaneous pigmentation, particularly in facial vitiligo, where response rates are markedly elevated. However, it is paramount to recognize the exigent necessity for further scholarly inquiry to address prevailing lacunae regarding the long-term efficacy and safety profiles of JAK inhibitors. Ongoing clinical trials will be instrumental in refining therapeutic protocols and optimizing patient outcomes within the ambit of vitiligo management. As our comprehension of these pharmacological interventions evolves, they may herald a notable advancement in the therapeutic repertoire available for individuals afflicted by this condition. Ultimately, the incorporation of JAK inhibitors into clinical praxis harbours substantial promise for ameliorating the quality of life for patients with vitiligo; nevertheless, meticulous consideration of their long-term ramifications is imperative. Continued investigation will ultimately furnish clinicians with the requisite insights to make judicious decisions that align with best practices for efficaciously managing vitiligo.

Summary

This systematic review and meta-analysis rigorously scrutinizes the therapeutic efficacy and safety of topical Janus kinase (JAK) inhibitors, with a predominant emphasis on ruxolitinib, in the management of vitiligo, either as monotherapy or in conjunction with narrowband UVB (NB-UVB) phototherapy. The analysis synthesizes data from six studies encompassing 385 participants, revealing a statistically significant enhancement in the repigmentation of vitiligo lesions, assessed via the Vitiligo Area Scoring Index (VASI).

Monotherapy utilizing JAK inhibitors manifested substantial reductions in VASI scores, while the incorporation of adjunctive NB-UVB phototherapy further amplified repigmentation outcomes, particularly within facial vitiligo presentations. These findings accentuate the therapeutic promise of JAK inhibitors in the treatment paradigm for vitiligo. Nonetheless, there remains an imperative for further investigative endeavors to delineate long-term efficacy and to refine treatment protocols effectively.

Conflict of Interest

The authors state no conflict of interests

Ethics Statement

No ethical approval was required as this is a review article with no original research data.

Proprietary Interest Statement

None of the authors have a financial interest in any of the products, devices, or drugs mentioned in this article.

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