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EFFICACY AND SAFETY OF ORAL JAK INHIBITOR AS CURRENT THERAPY OF VITILIGO: A SYSTEMATIC REVIEW

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ABSTRACT
Vitiligo is an autoimmune depigmenting disorder driven by IFN-γ–mediated, CD8+ T cell cytotoxicity against melanocytes via JAK-STAT signaling. While topical ruxolitinib (JAK1/2) is FDA-approved, the efficacy and safety of oral JAK inhibitors for vitiligo remain under investigation. This systematic review evaluates current evidence for oral JAK inhibitors (upadacitinib, abrocitinib, tofacitinib) in vitiligo, including their use with adjunctive therapies. Following a PRISMA-ScR approach, PubMed was searched (2019–2026) using MeSH terms ("JAK Inhibitor" AND "Vitiligo"). Eligible designs included case reports, case series, and randomized controlled trials. Studies are organized into table with each selected data. The data extracted are explained. Evidence consists predominantly of case reports/series and one randomized trial. Oral JAK1-selective agents (upadacitinib, abrocitinib) and JAK1/3 inhibitor tofacitinib frequently produced meaningful repigmentation, especially on facial sites, with response often enhanced by light-based adjuncts (NB-UVB or 308-nm excimer). Reported examples include ~60–90% facial repigmentation with upadacitinib or abrocitinib when combined with excimer or in patients with concomitant atopic dermatitis, and near-complete facial repigmentation with tofacitinib, particularly in sun-exposed areas or when paired with NB-UVB. Abrocitinib's higher JAK1 selectivity may preserve JAK2-mediated melanocyte survival signals, potentially explaining benefit in a case where vitiligo worsened on upadacitinib but improved after switching to abrocitinib. Safety across studies was generally acceptable, with mostly mild adverse events (e.g., acne, upper respiratory infections, fatigue, nasopharyngitis, weight gain, lipid elevations). Laboratory abnormalities were typically minimal. Oral JAK inhibitors show promising efficacy for vitiligo, particularly for facial lesions and when combined with phototherapy, with an overall favorable short- to mid-term safety profile. Adjunctive light therapy likely augments outcomes and may permit lower systemic doses.

Keywords: efficacy; JAK inhibitor; safety; vitiligo

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INTRODUCTION

Vitiligo is an autoimmune disease which resulting in destruction of melanocytes causing milky-white spots on the skin that may also include white hairs, or poliosis. Prevalence of vitiligo all around the world is estimated at 0.5% to 1%(Sewon Kang, Masayuki Amagai, Anna L. Bruckner, Alexander H. Enk, David J. Margolis, Amy J. McMichael, 2019). Vitiligo can happen at any age and affect equally males and females(Passeron et al., 2024). Even though vitiligo is seen as cosmetic problem, many patient devastated psychologically because they feel stigmatized and have low self-esteem with poor look on their skin color. Any part of the body may be involved in vitiligo. Face, acral, and genital is the most common initial sites(Craiglow & King, 2015). The pathogenesis of vitiligo involves CD8+ T cells that target melanocytes and destroy them which leaving areas without pigment production. T-cell mediated cytotoxicity is the key event in vitiligo, CD8+ T cells found infliltrate lesional epidermis where dying melanocytes were found next to it. IFN-y is cytokine that released by melanocyte-reactive autoimmune CD8+ T cells, induced production of CXCL9 and CXCL10 and other chemokines from keratinocytes. Secretion and level of IFN-y could

be useful for biomarkers of disease activity(Sewon Kang, Masayuki Amagai, Anna L. Bruckner, Alexander H. Enk, David J. Margolis, Amy J. McMichael, 2019).

JAK (Janus-Kinase) is protein which assist transduce and activate signal of cytokine-mediated pathway. IFN-y activated this pathway and is involved in many immune-related disorders, including vitiligo. JAK inhibition work in 2 ways depending on which type of pathways is blocked(Utama et al., 2024). Type I receptor bind several interleukins, colony-stimulating factors, and hormones. Type II receptors bind pro inflammatory interferons and cytokines. JAK inhibitor work by blocking receptor of JAK and preventing phosporylation and activation of inflammatory signal(Damsky & King, 2017). Current JAK inhibitor which approved by FDA for vitiligo is topical ruxolitinib. Ruxolitinib works by inhibiting JAK 1/2. Other JAK inhibitor which taken orally for vitiligo are still on ongoing studies. This review asses the efficacy and safety of ongoing studies of oral JAK inhibitor for vitiligo(Samuel et al., 2023). Determine the effectiveness and safety of oral JAK inhibitors for the management of vitiligo, which include to analyze the effectiveness of oral JAK inhibitors in the management of vitiligo. To analyze the side effects and safety factors of oral JAK inhibitors in the management of vitiligo. To compare the use of adjunctive therapies with oral JAK inhibitors in patients with vitiligo. To identify factors influencing the effectiveness and safety of JAK inhibitors in patients with vitiligo.

METHOD

Study design and objectives

This study is a systematic review accordance with the PRISMA-ScR framework. Eligible studies are case reports, case series, and randomized control trial that discussed about oral JAK inhibitor for vitiligo. 21 studies are gathered and 5 of them is excluded because did not meet the disease and treatment requirement for this studies.

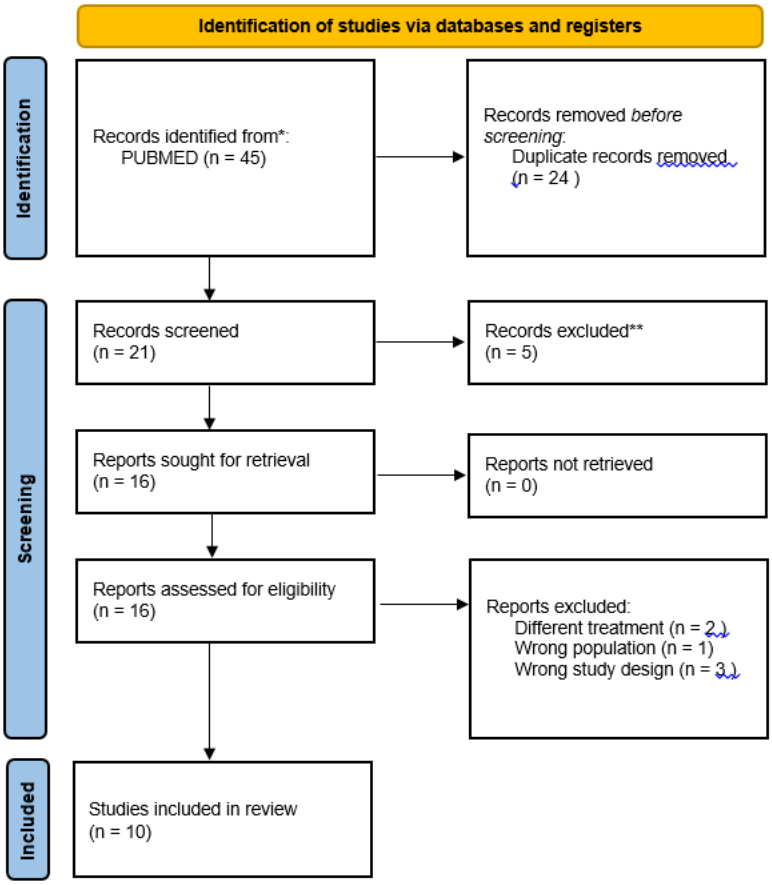

Figure 1 PRISMA flow chart of systematic review

Search strategy and data extraction

Authors searched through PUBMED database independently from 2019 to 2026, using search query from MeSH terms :("Jak Inhibitor") AND ("Vitiligo"). Gathered studies are analyzed and excluded from duplication. After that the studies are assesed wheter it meets the inclusion criteria. The quality of evidence and risk of bias in all included studies was assessed using the GRADE criteria.

RESULT

Table 1.
Summary of oral JAK inhibitor in the treatment of vitiligo

Author (Year)	Study type and risk of bias (GRADE)	Study population	Age (years) (mean/ range)	Treatment	Adjunctive Treatment	Duration (months)	Area affected	Efficacy for vitiligo	Safety
Wang Z, Wang M, Sun Y(Wang et al., 2025). (2025)	Case report (HIGH)	1	37	Oral Upadacitinib Oral Abrocitinib	308-nm excimer laser	7	Facial	~90% repigmmentation with abrocitinib	Not reported
Wang Z, Sun Y(Wang & Sun, 2025). (2025)	Case report (HIGH)	1	22	Oral Tofacitinib citrate sustained-release	308 nm excimer laser therapy, fractional laser, and topical tacrolimus 0.1% ointment.	13	Facial	~70% repigmentation	Not reported
Jin S, Wang S, Jin S, Tang C, Wang P(Report, 2025). (2025)	Case report (HIGH)	1	49	Oral Tofacitinib	Hydroxychloroquine	12	Head, face, forearm	~75% improvement. Depigmented area shows signs of perifollicular repigmentation	No adverse effect
Xu Z, Xing X, Xuan Y, Xiang LF, Zhang C. (2023)	Case report (HIGH)	1	40	Oral Tofacitinib	NB-UVB phototherapy	24	Facial and neck	~90% repigmentation achieved during 1 year therapy. Repigmentation pattern was mainly follicular	No adverse effect No laboratory abnormalities
Pan T, Mu Y, Shi X, Chen L(Pan et al., 2023). (2023)	Case report (HIGH)	1	16	Oral Upadacitinib	Crisaborole	4	Face, neck, chest and extremities	~90% repigmentation of the face and neck. ~60% repigmentation of the chest and only little of the extremity	Worsened acne within 3 months of therapy No laboratory abnormalities
Komnitski M, Komnitski A, Komnitski Junior A, Silva de Castro CC(Komnitski et al., 2020). (2019)	Case report (HIGH)	1	40	Oral Tofacitinib	Not reported	8	Face, neck, elbow, hands, and feet	Complete repigmentation of the forehead and perilabial. Partial repigmentation of neck	Not reported
Kim SR, Heaton H, Liu LY, King	Case report (HIGH)	2	(#1) 30s (#2)	Oral Tofacitinib	(#1) NB-UVB phototherap	3-6	(#1) 75% of face, patches	(#1) Complete repigmentat	No adverse effect No laboratory

Author (Year)	Study type and risk of bias (GRADE)	Study population	Age (years) (mean/ range)	Treatment	Adjunctive Treatment	Duration (months)	Area affected	Efficacy for vitiligo	Safety
BA(Low-dose, 2018).(2018)			50s		y 400-500 mJ (#2) NB-UVB phototherapy 360-500 mJ)		on neck, chest, forearms, hands and shins (#2) 90% of face, patches on torso and arms	ion of the face and 75% repigmentation of other parts (#2) 75% repigmentation of the face and no repigmentation at other parts	abnormalities
Craiglow BG, King BA(Craiglow & King, 2015). (2015)	Case report (HIGH)	1	50	Oral Tofacitinib	Not reported	5	~10% BSA, Forehead, trunk, and extremities	Near complete repigmentation of forehead and hands after 5 months. ~5% BSA remain depigmented	No adverse effect No laboratory abnormalities
Liu LY, Strassner JP, Refat MA, Harris JE, King BA(Liu et al., 2017). (2017)	Case series (HIGH)	10	4-33	Oral Tofacitinib	Not reported	9.9	Generalized and primary acral	Decrease of ~5.4% BSA involvement of 5 from 10 patients. Whereas other 5 did not had any repigmentation	Upper respiratory infection reported in 2 patients. Weight gain and arthralgia Mild elevation of lipid levels
Rosmarin et al(Passeron et al., 2024). (2020)	RCT (LOW)	185	18-65	Oral Upadacitinib	Not reported	13	Non-segmental vitiligo	Improvement of F-VASI from baseline by 53.7% in UPA 6, 60.7% in UPA 11, and 69.8% in UPA 22	COVID-19, headache, acne, fatigue, nasopharyngitis, cough, urinary tract infection, anxiety, nausea, vomitting, URTI, weight increase, insomnia

DISCUSSION

Vitiligo lession are asymptomatic, white, nonscaly macules and patches. It can happen at any age with half of patients presenting before the age 20 years and a third before the age of 12 years. Current management of vitiligo that involving JAK inhibitor is topical ruxolitinib. Ruxolitinib is a selective JAK 1/2 inhibitor and it is approved by FDA to treat vitiligo(Samuel et al., 2023; Sewon Kang, Masayuki Amagai, Anna L. Bruckner, Alexander H. Enk, David J. Margolis, Amy J. McMichael, 2019).

Oral Upadacitinib and Abrocitinib

Upadacitinib is a second generation of selective oral JAK1 inhibitor. It is distinct from any other first generation JAK inhibitor. Oral upadacitinib currently have good repigmentation respond in vitiligo. With 15 mg daily for one months, there were no new white patches appeared and repigmentation begin(Wang et al., 2025). After four months there were nearly 90% repigmentationof face and neck, 60% of chest. Within this case the patient also had concurrent condition that is atopic dermatitis. Both condition vitiligo and atopic dermatitis share almost similar inflamatory pathway, thus upadacitinib as JAK1 inhibitor can be a preferred treatment option when

two disease co-exist(Zhang & Zeng, 2025). A randomized control trial studies performed with 185 patients divided to recieve upadacitinib and placebo-controlled dose. Upadacitinib show a significant improvement in Facial-Vitiligo Area Scoring index (F-VASI) within week 24. By week 52, upadacitinib showing improvement in F-VASI 50 and F-VASI 75 reduction for -53.7% to -69.8%(Passeron et al., 2024).

One case show worsened case of atopic dermatitis and vitiligo treatetd with upadacitinib. Initial tofacitinib were given 11mg/day but led to minimal improvement, then upadacitinib were given 15mg/day, after two months, atopic dermatitis resolved completely but the facial vitiligo worsened. There are newly enlarged white patches. After two additional months there were no good progression despite combination of 308-nm excimer laser. Abrocitinib then started 100mg/day with continued laser therapy, three months later it has ~90% repigmentation of facial patches(Wang et al., 2025). Upadacitinib is selective to JAK1 but also have moderate inhibition of JAK2. JAK1 have role to mediate IFN-y cascades and upregulation of CXCL10 which progres in melanocyte-reactive autoimmune. Where JAK2 also have role for melanocyte survival(Pan et al., 2023). Abrocitinib is more selective to JAK1 than upadacitinib therefore less inhibition of JAK2. In that way inflammatory pathway can be blocked while preserving melanocyte-protective pathways(Ciechanowicz et al., 2018).

Oral Tofacitinib

Tofacitinib is JAK1/3 inhibitor that was approved by FDA in 2012 for the treatment of rheumatoid arthritis. Oral tofacitinib citrate reported used in vitiligo case, initial dose at 5mg every other day and after three weeks the dosage was increased to 5mg/day. Partial repigmentation of the face and upper extremity achieved in two months. At five months the repigmentation nearly complete on forehead and hands, other remaining involved area demonstrated partial repigmentation(Komnitski et al., 2020). Other case studies reported 5mg twice daily of tofacitinib in primarily facial vitiligo showed complete repigmentation after 6 months. In other same case, a patient with comorbid rheumatoid arthritis and vitiligo recieved tofacitinib 5mg twice daily. Complete repigmentation of the forehead and perilabial, partial repigmentation of neck(Cma et al., 2020). Vitiligo can occur with other autoimmune disease, one studies reported occurance of vitiligo on the skin lession with discoid lupus erythematosus, treatment begin with oral tofacitinib 5mg twice a day for 12 months. Showing ~75% improvement, depigmented area shows signs of perifollicular repigmentation(Report, 2025).

A case series reported 10 patients, 8 with generalized vitiligo and 2 with acral vitiligo with body surface area ranging from 1% to 100% underwent treatment with tofacitinib 5-10 mg daily or twice daily for average 9.9 months. Five out of ten patient had decreased 5.4% BSA involvement, whereas the other five did not had any repigmentation. The five patients who had repigmentation, it only occur in sun-exposed area(Liu et al., 2017). Repigmentation require both suppression of the inflamation and stimulation of the melanocyte with light (UV) exposure. In other studies, it reported that tofacitinib alone as monotherapy is effective for vitiligo but it may require long-term medication use(Schatloff & Valenzuela, 2024).

Adjunctive Treatment

NB-UVB phototherapy

Melanocyte is important in the making of the skin color. In vitiligo, melanocytes are destroyed by our own immune system. Therefore there are no melanine produced. JAK inhibitor alone without any other adjuvant therapy was ineffective. Photoactivation is required for melanocyte regeneration. NB-UVB required less or smaller dose when combined with JAK inhibitor. In order to get satisfactory result, two mechanism must happen 1.) suppression of the immune system that destroyed melanocytes 2.) stimulation of melanocyte by exposure to sunlight or through NB-UVB(Liu et al., 2017).

Crisaborole

Crisaborole is a nonsteroidal topical PDE4 inhibitor. It was approved by FDA back in 2016 for the treatment of atopic dermatitis. Inhibition of PDE4 reduces the degradation of cyclic adenosine monophosphate (cAMP). Accumulation of cAMP intracellularly could prevent the activation of pro-inflamamatory T-helper 1 and 17 lymphocytes and increases the anti-inflamatory mediator. In 2020, Zaky et at demonstrated that PDE4 enzyme level were significantly higher in tissue and serum samples of 20 patients with vitiligo compared with healthy controls(Tam et al., 2021).

309-nm excimer laser

Stimulating melanocytes not only could be achieved by NB-UVB phototherapy. 308-nm excimer laser works by inducing T-cell apoptosis and stimulating melanocyte stem cell. Excimer laser emits a 308 nm wavelength that provide targeted UVB. It is used in vitiligo with less than 10% BSA. Excimer laser reported to have few adverse reactions compared to conventional NB-UVB(Schatloff & Valenzuela, 2024).

Safety

JAK inhibitor achieved their anti-inflammatory effect by suppressing cytokine production involved in Th1, Th2, Th17, and Th22 immune pathways(Damsky & King, 2017). In the studies mentioned in this review, only small number of patients had adverse effect. The variety of the adverse effect include acne, upper respiratory infection, weight gain, arthralgia, mild elevation of lipid levels. In larger studies, frequently reported adverse effect are COVID-19, headache, acne, fatigue, nasopharyngitis, cough, urinary tract infection, anxiety, nausea, vomitting, URTI, weight increased, and insomnia. Other less frequent adverse effect reported are herpes zoster, herpes simplex, anaemia, hepatic disorder. In general, treatment for vitiligo using oral JAK inhibitors appears safe(Passeron et al., 2024). Laboratory changes were minimal and mostly no abnormalities, only minor changes in lipid metabolism identified

CONCLUSION

Recent studies show that oral JAK inhibitors is promising to be used in vitiligo treatment, when combined with other adjuvant therapy such as NB-UVB, excimer laser, and other topical agents it showed great response in repigmentation. Combination with adjuvant therapy also reduces adverse effects of JAK inhibitors because the dose needed will be lower. Other adverse effects reported were also minimal and considered to be safe. However, there is a need for further long-term and larger studies to establish specific treatment protocols, combination, and safety issues.

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