The Egyptian Journal of Hospital Medicine (January 2025) Vol. 98, Page 135-139

Clinical and Dermoscopic Evaluation of the Safety and Efficacy of Oral baricitinib (JAK Inhibitor) in Treatment of Localized Vitiligo Either Alone or with Topical Tacrolimus

Noura A. Elseessy*, Heba A. Abdel-Azeem
Department of Dermatology, Faculty of Medicine, Kafrelsheik University, Egypt
***Corresponding author:** Noura A. Elseessy, **Mobile:** (+20) 01000117186, **Email:** nouraelseessy@yahoo.com

ABSTRACT

Background: Baricitinib is used in dermatology as a novel molecular-targeted therapy and it is suggested to be effective against vitiligo. **Objective:** To evaluate efficacy and safety of oral baricitinib only and with topical tacrolimus in the treatment of localized stable vitiligo.

Patients and methods: 10 cases (> 18 years) with at least 2 separated vitiligo lesions were treated with oral baricitinib (4 mg / day) for a total of 24 weeks. In the same patient, topical tacrolimus 0.1% was applied twice every day to one of the lesions. The patients were recruited from the outpatient clinics of Dermatology Department, Kafrelsheik University Hospital between August 2023 and August 2024.

Results: The current study demonstrated that there was a significant repigmentation in all lesions but more improvement in lesions treated also by topical tacrolimus without any side effects. The percentage of improvement in the lesions treated by oral therapy only was about 77% and the percentage of improvement in the lesions treated by oral therapy and topical tacrolimus was about 82% with no significance (P=0.177). Only 2 patients (20%) were unsatisfied with lesions treated by oral therapy only with no significance (P=0.5).

Conclusions: Baricitinib is efficient and safe in treatment of adult localized vitiligo as monotherapy or in combination of topical tacrolimus.

Keywords: Vitiligo; Baricitinib; JAK inhibitors; Tacrolimus.

INTRODUCTION

Vitiligo is an idiopathic acquired multifactorial disease presented by milky white depigmented macules or patches in the skin and hair may be affected [1-2]. It affects about 0.5–2% of people [3]. Patients with vitiligo suffer mainly from negatively impacting quality of life [4]. Vitiligo has multifactorial pathogenesis as genetic, oxidative stress, metabolic or autoimmune disorder. Cell-mediated immunity has main role in destruction of melanocytes [5,6]. In vitiligo, the active CXCR3+ CD8+ T cells cause melanocyte apoptosis through interferon-gamma (INF-γ) and chemokines produced by keratinocytes that activated by the Janus kinase (JAK)/signal transducer and activator of transcription (STAT)-I signaling pathway. JAK inhibitors (JAKi) act on the JAK/STAT pathway and recently have gained approval as promising agents for the management of several autoimmune disorders. JAKi, which include ruxolitinib, baricitinib, and tofacitinib, are efficient for blocking the INF-γ and chemokine signaling axis in vitiligo pathogenesis [1, 5].

Baricitinib is the first generation of JAKi, which blocks the intracellular cytokine transmission across JAK-STATs, so it could be used in rheumatoid arthritis (RA) management. Also, many studies reported that baricitinib could be utilized to treat different dermatologic disorders, which include atopic dermatitis, psoriasis, vitiligo, and alopecia areata [6].

Calcineurin inhibitors (pimecrolimus and tacrolimus) and topical steroids are approved for treatment of vitiligo but calcineurin inhibitors are superiors in particular for long-term treatment as they don't cause any damage of the skin barrier [7].

This study aimed to evaluate safety and efficacy of only oral baricitinib or with topical tacrolimus in localized vitiligo management.

PATIENTS AND METHODS

This study included ten (10) patients recruited from the outpatient clinics of Dermatology Department, Kafrelsheik University Hospital between August 2023 and August 2024.

Nonsmoker patients, > 18 years old, with at least 2 separated vitiligo lesions, stable, and didn't not receive any treatment for vitiligo 6 months ago were included in this study.

Pregnancy, lactating women, any treatment within the last 6 months, any comorbidities including diabetes, collagen diseases, autoimmune diseases, cardiac diseases or coagulation defects, and history of allergy to any topical or systemic drug were excluded.

History taking, general examination, and routine laboratory investigations were done for all cases.

Wood's lamp examination was conducted, in case of doubt for confirmation of vitiligo.

Local examination was done for the vitiligo patches regarding; site, size, degree of depigmentation and Vitiligo Extent Tensity Index (VETI) score [8].

The VETI score is composed of five stages: stage zero: normal skin, Stage I: hypopigmentation (such as trichrome and homogeneous lighter pigmentation); Stage II: total depigmentation with black hair and with perifollicular pigmentation (PFP); Stage III: total depigmentation with black hair and without PFP; Stage IV: total depigmentation with a compound of white and black hair in the presence or absence of PFP; and Stage

Received: 02/09/2024
Accepted: 01/11/2024

V: total depigmentation together with considerable hair whitening.

Localized stable non-segmental vitiligo with no new lesions or enlargement of pre-existing lesions and negative Koebner phenomenon for at least 6 months were included.

Selected vitiligo lesions were more or less matching in size with surface area less than 20 cm^2.

All cases were treated by oral baricitinib (4 mg/day) for a total of 24 weeks. In the same patient, topical tacrolimus 0.1% was applied every 12 hours one of the lesions for 24 weeks. Accordingly, lesions were categorized in to 2 groups:

Group I: lesion left as such (monotherapy with oral baricitinib) as control.

Group II: lesion was treated by topical tacrolimus 0.1% was applied twice daily with oral baricitinib.

All lesions were evaluated clinically and dermoscopic before and after 6 months.

Standardized dermoscopic and digital-colored photographs were taken before and after the treatment with the same settings by digital camera of a mobile phone OPPO F7 (OPPO Company, CPH1821, China).

Patients were attended every 2 weeks during the treatment and every month for 6-month follow up after treatment and photographs were taken to determinate the recurrence. The degree of repigmentation was evaluated by two blinded physicians before and after the treatment (immediately after, three months and six months after the treatment) according to **Physician Global Assessment (PGA)** as follows: No change: (0%), Mild: (1 –25%), Moderate: (26–50%), Good: (51 –75%) and Excellent: (> 75%).

The degree of satisfaction of the patient:

Whether the patient was not satisfied, satisfied or markedly satisfied; and assessment was done immediately after, three months and six months after the treatment.

Dermoscopic evaluation:

Patients were evaluated before and after treatment by dermoscope (Elite II) to measure degree and pattern of repigmentation (marginal, perifollicular, diffuse, and combined).

Ethical approval:

The study was submitted for approval by the Scientific Research Ethics Committee of Kafrelsheik University (Code number: KFSIRB200-42, Date: 31-7-2023). All cases wrote informed consents before the beginning of the study. Patient's privacy was respected. All data were used only for scientific purposes. The study adhered to the Helsinki Declaration throughout its execution.

Statistical analysis

Data were analysed using IBM SPSS software, version 20.0. Qualitative data were presented as number and percent and compared by McNemar test. Quantitative data were presented as mean±SD, median, and range and were compared by paired T-test. The significance was set at $P \leq 0.05$.

RESULTS

The study included ten (10) patients with 2 separated vitiligo lesions or more since 2 to 8 years **(Table 1)**.

Table (1): Demographic data of the studied cases (n = 10)

Demographic data	No. (%)
Sex	
Male	7 (70%)
Female	3 (30%)
Age (years)	
Mean ± SD	28.7 ± 8.64
Median (Min – Max)	27.5 (19 – 43)
Duration of lesion (years)	
Mean ± SD.	4.30 ± 2.21
Median (Min – Max)	4 (2 – 8)

SD: Standard deviation, Min: Minimum, Max: Maximum

According to site of the lesions, they were distributed between arm, face, foot, hand, neck, and trunk without any significant difference. Before the treatment, all the lesions were stage 3 by VETI score. After the treatment by VETI score, in both groups 40% of the lesions became stage 0, 30% of them became stage 1 and 30% of them became stage 2 with no recurrence through 6 months of follow up **(Table 2)**.

By the dermoscopy examination, 50% of the lesions repigmented by diffuse pattern, 40% marginal and 10% by perifollicular **(Table 2 and Figure 1).**

Table (2): Comparison between oral treatment only and oral treatment plus topical tacrolimus according to different parameters (n = 10)

	Oral treatment only	Orat treatment + Topical tacrolimus
Site		
Arm	2 (20%)	1 (10%)
Face	3 (30%)	0 (0%)
Foot	1 (10%)	1 (10%)
Hand	3 (30%)	4 (40%)
Neck	1 (10%)	1 (10%)
Trunk	0 (0%)	3 (30%)
VETI score		
Before (Stage 3)	10 (100%)	10 (100%)
After		
Stage 0	4 (40%)	4 (40%)
Stage 1	3 (30%)	3 (30%)
Stage 2	3 (30%)	3 (30%)
Recurrence	0 (0%)	0 (0%)
Pattern of repigmentation		
Diffused	5 (50%)	5 (50%)
Marginal	4 (40%)	4 (40%)
Perifollicular	1 (10%)	1 (10%)

The percentage of improvement in the lesions treated by oral therapy only or by oral therapy and topical tacrolimus was not significantly different. Only 2 patients (20%) were unsatisfied with lesions treated by oral therapy only with no significant difference **(Table 3). Figure 2** and **Figure 3** show the clinical improvement of some cases.

Table (3): Comparison between oral treatment only and oral treatment plus topical tacrolimus according to percentage of repigmentation and patient satisfaction

	Oral treatment only	Oral treatment + Topical tacrolimus	Test of Sig.	p
Percentage of regimentation Mean ± SD. Median (Min. – Max.)	 77 ± 15.7 70 (50 – 90)	 82 ± 7.89 80 (70 – 90)	 t= 1.464	 0.177
Patient satisfaction Unsatisfaction Satisfaction	 2 (20%) 8 (80%)	 0 (0%) 10 (100%)	 McN	 0.500

SD: Standard deviation, t: Paired t-test, McN: McNemar test

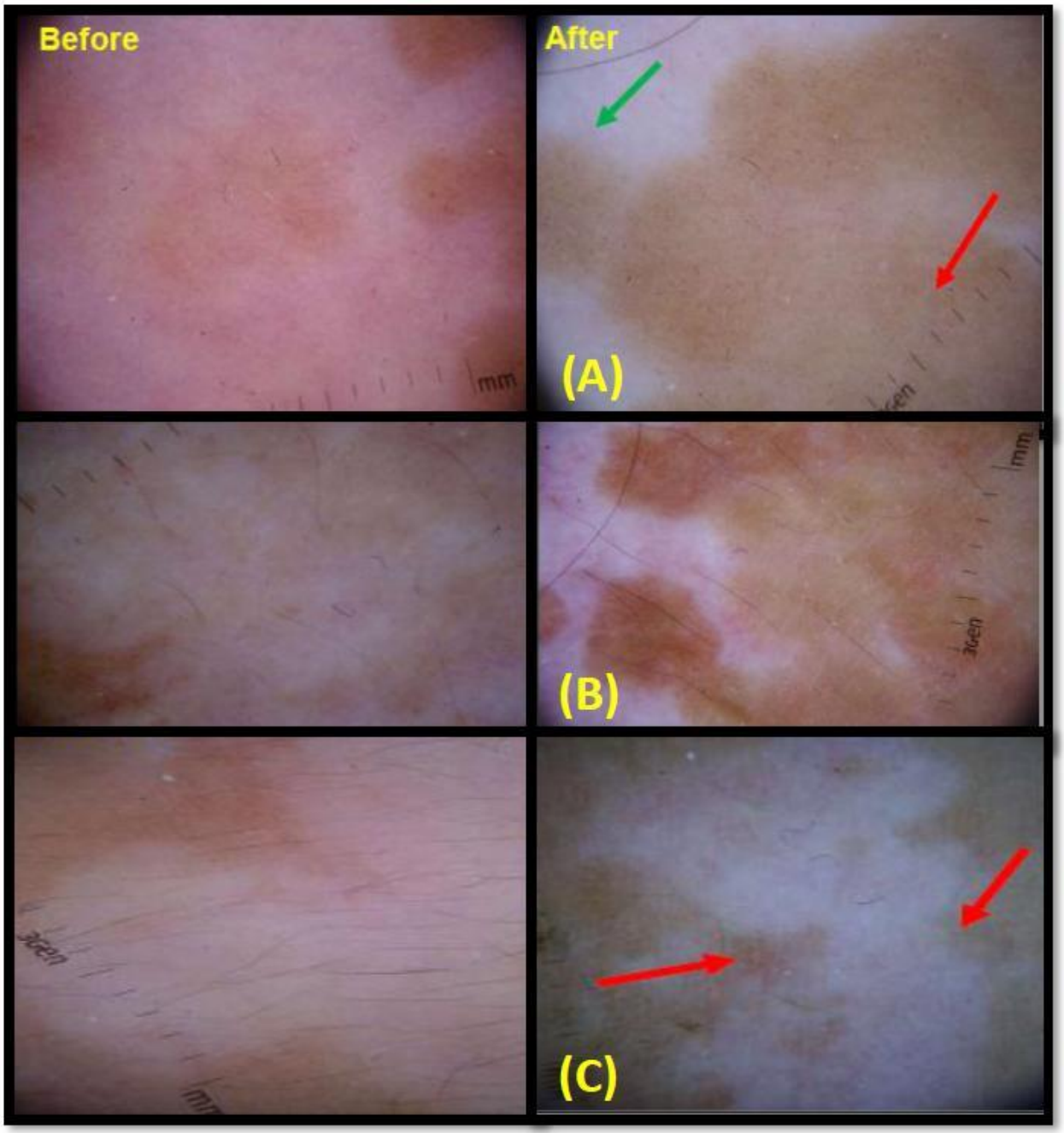

Figure (1): Patterns of pigmentation before and after the treatment by dermoscopy, (A): diffuse repigmentation, (B): perifollicular, repigmentation (c): marginal repigmentation.

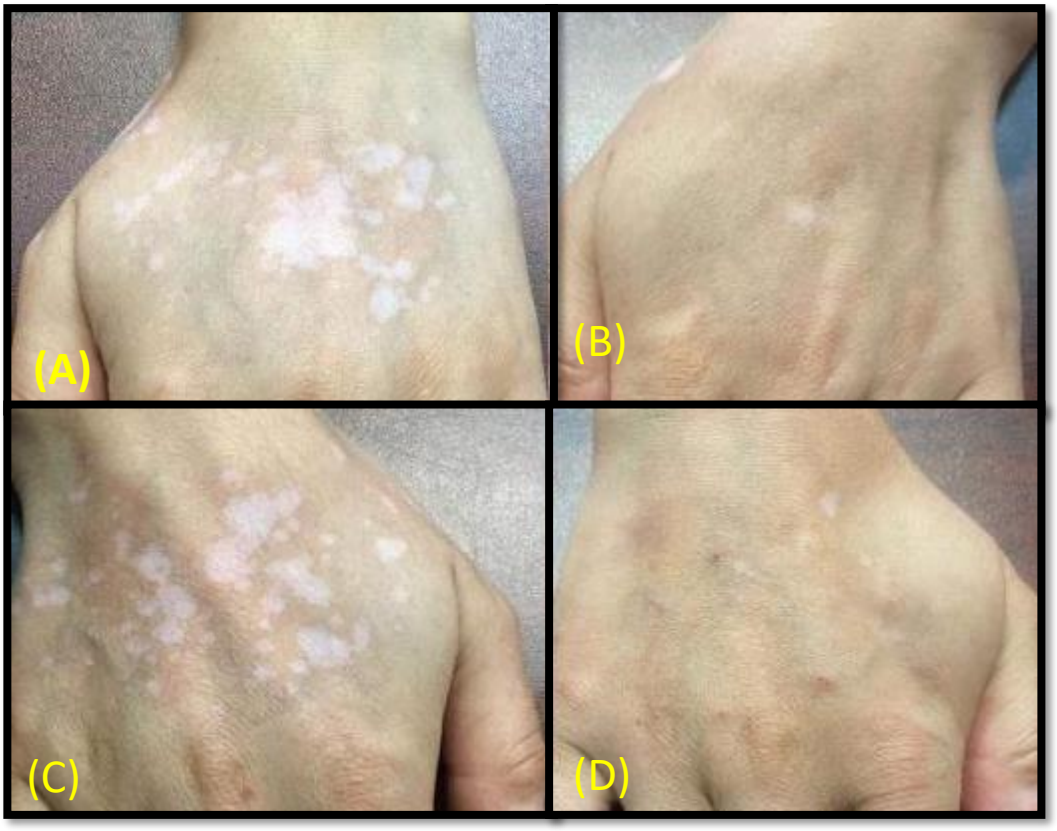

Figure (2): (A): Right hand of female patient aged 32 years old with vitiligo before the treatment, (B): Right hand of the same patient after 3 months of oral therapy only with excellent improvement, (C): Left hand of the same patient with vitiligo before the treatment, (D): Left hand of the same patient after 3 months of oral therapy and dermapen with tacrolimus with excellent improvement.

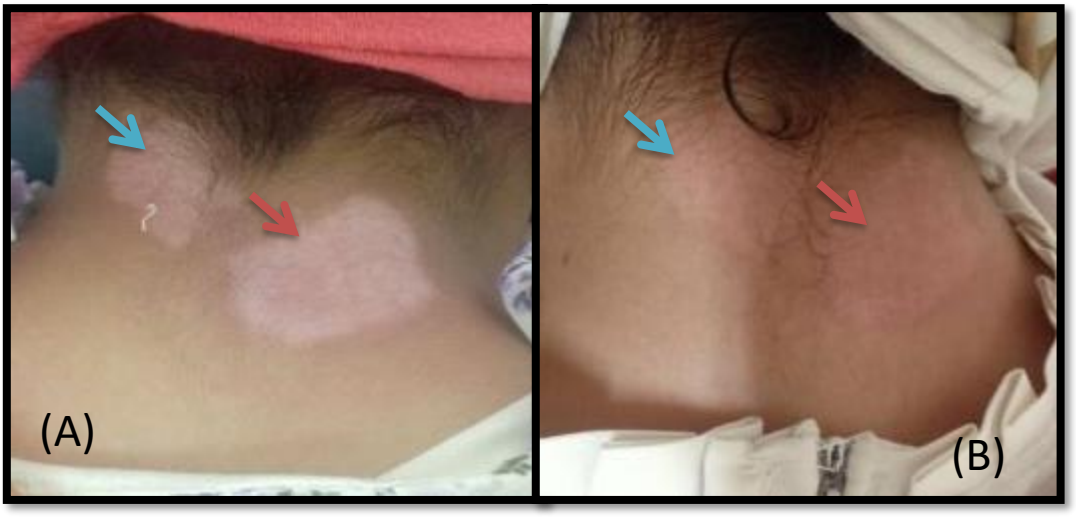

Figure 3: (A): Female patient aged 19 years old with 2 localised lesions of vitiligo at the back of the neck, (B): the same patient with excellent improvement in both lesions as the lesion indicated by blue arrow was treated by oral therapy only and the other indicated by red arrow was treated by oral therapy and dermapen with tacrolimus.

DISCUSSION

Vitiligo is an acquired autoimmune skin disease causing progressive damage of melanocytes [9].

The study included ten (10) patients with 2 separated vitiligo lesions or more since 2 to 8 years. They were 7 males and 3 females, aged from 19 to 43 years. All patients were treated with oral baricitinib (4 mg/day) for a total of 24 weeks. In the same patient, topical tacrolimus 0.1% was applied twice daily to one of the lesions. Accordingly, lesions were categorized into 2 groups with no significant difference between both groups.

According to site of the lesions, they were distributed between arm, face, foot, hand, neck, and trunk without any significant difference. Before the treatment, all the lesions were stage 3 by VETI score. After the treatment by VETI score, in both groups, 40% of the lesions became stage 0, 30% of them became stage 1 and 30% of them became stage 2 with no recurrence through 6 months of follow up. By the dermoscopy examination, 50% of the lesions repigmented by diffuse pattern, 40% marginal and 10% by perifollicular.

Frisoli *et al.* [10] and **Li *et al.*** [11] recorded that improvement rates and treatment efficacy have been variable. Much research has discovered that IFN-γ and related chemokine (CXCL 9, 10) are the main players of vitiligo pathogenesis and they are mediated by JAK/(STAT) pathway in keratinocytes.

Relke *et al.* [12] said that JAK members are (JAK_1, JAK_2, JAK_3) and (tyrosine kinase 2). JAKi could stop this pathway through blocking the action of IFN-γ and chemokines. Baricitinib is a recent blocker for $JAK_{1,2}$ and was approved for RA management.

In our study, the percentage of improvement in the lesions treated by oral therapy only was about 77% and the percentage of improvement in the lesions treated by oral therapy and topical tacrolimus was about 82% with no significance (P=0.177). Only 2 patients (20%) were unsatisfied with lesions treated by oral therapy only with no significant difference (P=0.5).

Mumford *et al.* [13] in 2020 were the first that reported repigmentation in vitiligo lesions after administration of oral baricitinib for 8 months. **Dong *et al.*** [5] in 2022 found that baricitinib could improve tyrosinase activity and increase melanin amount causing repigmentation of vitiligo.

Topical medications (mostly steroid and calcineurin inhibitors) and phototherapy are the first-line treatments of vitiligo. The efficacy of the local calcineurin inhibitors is similar as the potent topical corticosteroid; however, they have not any steroid side effects as appearance of telangiectasia, increase the hair, and atrophy of skin [14].

Ebrahim *et al.* [15] recorded that repigmentation rate was >75% in 29.2% of his study cases treated by tacrolimus as monotherapy (p= 0.02).

CONCLUSION

Baricitinib is effective and safe in treatment as a monotherapy or in combination of topical tacrolimus of adult localized stable vitiligo.

Conflict of interest: None.
Financial disclosures: None.

REFERENCES

1. **Ezzedine K, Eleftheriadou V, Whitton M *et al.* (2015):** Vitiligo. Lancet, 386(9988):74–84.
2. **Qi F, Liu F, Gao L (2021):** Janus kinase inhibitors in the treatment of vitiligo: A review. Front Immunol., 12:790125. doi: 10.3389/fimmu.2021.790125.
3. **Bergqvist C, Ezzedine K (2020):** Vitiligo: A review. Dermatology, 236(6):571– 92.
4. **Kussainova A, Kassym L, Akhmetova A *et al.* (2020):** Vitiligo and anxiety: A systematic review and meta-analysis. PloS One, 15(11):e0241445. doi: 10.1371/journal.pone.0241445.
5. **Dong J, Huang X, Ma L *et al.* (2022):** Baricitinib is effective in treating progressing vitiligo in vivo and in vitro. Dose Response, 20 (2):15593258221105370. doi: 10.1177/15593258221105370.
6. **Kubelis-Lopez D, Zapata-Salazar N, Said-Fernandez S *et al.* (2021):** Updates and new medical treatments for vitiligo (Review). Exp Ther Med., 22(2):797. doi: 10.3892/etm.2021.10229.
7. **Ferrucci S, Angileri L, Marzano A *et al.* (2022):** Topical tacrolimus during systemic therapy for severe atopic dermatitis in the clinical practice. European Review for Medical and Pharmacological Sciences, 26: 2518-2523.
8. **Feily A (2014):** Vitiligo Extent Tensity Index (VETI) score: a new definition, assessment and treatment evaluation criteria in vitiligo. Dermatol Pract Concept., 4(4):81-84.
9. **Rahimi H, Zeinali R, Tehranchinia Z (2021):** Photodynamic therapy of vitiligo: a pilot study. Photodiagnosis Photodyn Ther., 36:102439. doi: 10.1016/j.pdpdt.2021.102439.
10. **Frisoli M, Essien K, Harris J (2020):** Vitiligo: mechanisms of pathogenesis and treatment. Annu Rev Immunol., 38:621–648.
11. **Li X, Sun Y, Du J *et al.* (2023):** Excellent repigmentation of generalized vitiligo with oral baricitinib combined with NB-UVB phototherapy. Clin Cosmet Investig Dermatol., 16:635-638.
12. **Relke N, Gooderham M (2019):** The use of Janus kinase inhibitors in vitiligo: a review of the literature. Review J Cutan Med Surg., 23(3):298–306.
13. **Mumford B, Gibson A, Chong A (2020):** Repigmentation of vitiligo with oral baricitinib. Australas J Dermatol., 61(4):374–376.
14. **Zhou F, Chen S, Jin W *et al.* (2022):** Comparison of the efficacy and safety of 308-nm excimer laser as monotherapy and combination therapy with topical tacrolimus in the treatment of periocular vitiligo. Dermatologic Therapy, 35(7):e15556. doi: 10.1111/dth.15556.
15. **Ebrahim H, Elkot R, Albalate W (2021):** Combined microneedling with tacrolimus vs tacrolimus monotherapy for vitiligo treatment. J Dermatolog Treat., 32(8):999-1004.