Case Report/Case Series

# Tofacitinib Citrate for the Treatment of Vitiligo
## A Pathogenesis-Directed Therapy

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**IMPORTANCE** Vitiligo is a common condition that is often emotionally devastating for patients. At present, no reliably effective treatments are available.

**OBSERVATIONS** Recent advances in the understanding of the pathogenesis of vitiligo suggest that Janus kinase inhibitors may be a therapeutic option. We report a case of generalized vitiligo for which treatment with tofacitinib citrate, an oral Janus kinase 1/3 inhibitor, resulted in significant repigmentation.

**CONCLUSIONS AND RELEVANCE** The results suggest that tofacitinib and other Janus kinase inhibitors may be effective in the treatment of vitiligo. Additional studies will be needed to confirm their efficacy and to explore their safety.

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Vitiligo is a condition that often causes significant psychological distress for patients. Treatment options are limited and often inadequate. Recent progress in the scientific understanding of vitiligo suggests that Janus kinase (JAK) inhibitors may be an effective therapy. We report a case of vitiligo treated with the JAK 1/3 inhibitor tofacitinib citrate.

## Report of a Case

A woman in her 50s presented for evaluation and management of vitiligo, which had been widespread and progressive for approximately the past 1 year. Increasing involvement of the face and hands was causing the patient significant concern. She had used triamcinolone ointment, 0.1% (owing to the need for a large amount of topical medication in the setting of generalized involvement), and tacrolimus ointment, 0.1%, without effect. Treatment with narrowband UV-B phototherapy had recently been initiated; however, after 3 treatments, the patient continued to note progression of the vitiligo and therefore sought a second opinion regarding treatment. She was otherwise healthy and denied a family history of vitiligo or other autoimmune conditions. Complete review of systems was negative. Physical examination revealed innumerable white macules and patches involving the forehead (**Figure 1**A), trunk, and extremities (**Figure 2**A) involving approximately 10% of body surface area, which highlighted with Wood's lamp.

The possibility of continuing phototherapy was discussed, including the typically months-long duration of treatment that is required to achieve repigmentation, which is usually incomplete.[1] Given the progressive, generalized nature of the vitiligo, the limited and often inadequate treatment options, and the patient's associated concern, we decided to pursue a therapeutic trial of an agent that, based on recent advances in the understanding of vitiligo,[2] might yield faster and more complete repigmentation.

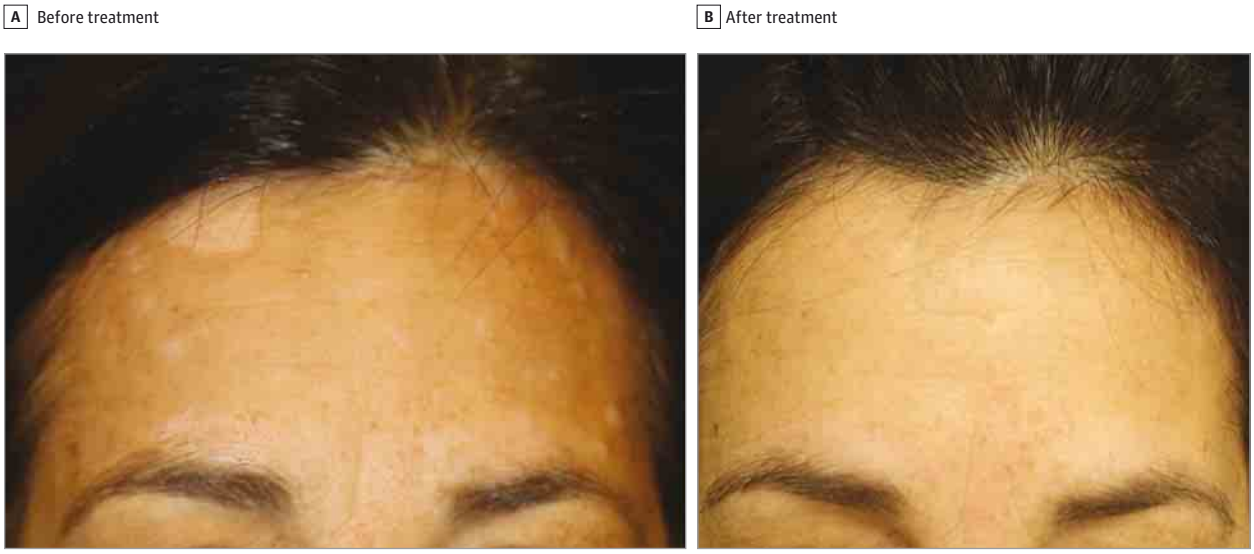
Treatment with oral tofacitinib citrate (Xeljanz) was initiated at a dosage of 5 mg every other day. After 3 weeks, the dosage was increased to 5 mg/d (half the approved dosage for rheumatoid arthritis, which is 5 mg twice daily). After 2 months of therapy, partial repigmentation of the face and upper extremities was evident. After 5 months, repigmentation of the forehead (Figure 1B) and hands (Figure 2B) was nearly complete, and the remaining involved areas demonstrated partial repigmentation. Approximately 5% of the total body surface area remained depigmented. The patient tolerated tofacitinib without adverse effects, and results of laboratory monitoring revealed no abnormalities in complete blood cell count, serum creatinine, hepatic function, or lipids during the course of treatment.

## Discussion

Tofacitinib is a JAK 1/3 inhibitor that was approved by the US Food and Drug Administration in 2012 for the treatment of moderate to severe rheumatoid arthritis. Within dermatology, oral and topical formulations of tofacitinib have been demonstrated to be safe and effective for the treatment of plaque psoriasis,[3-7] and we have recently described the success of oral tofacitinib in treating alopecia universalis.[8] Clinical trials evaluating tofacitinib treatment of several disorders are presently under way.

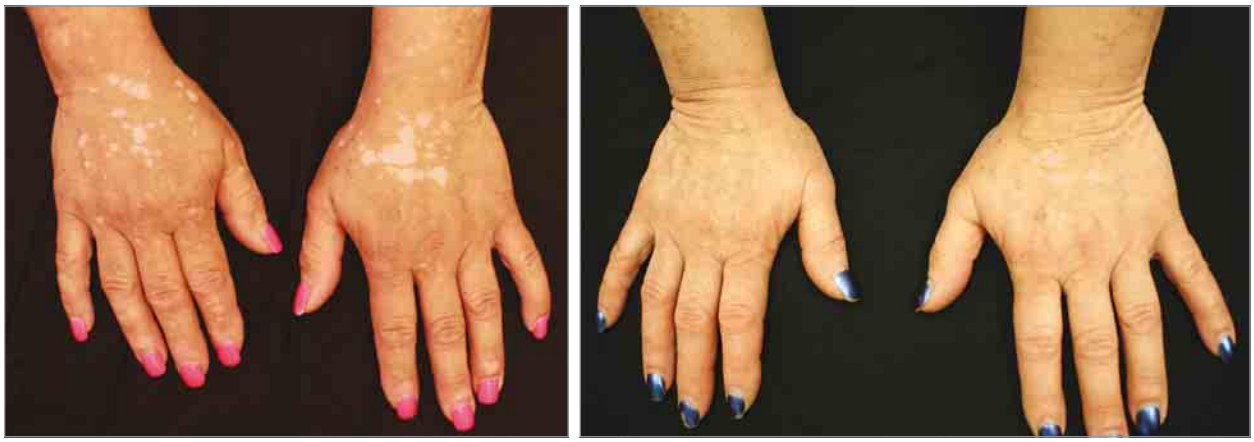
Alopecia areata and vitiligo share genetic risk factors and can co-occur within families and individual patients, suggesting a

Figure 1. Forehead of the Patient Before and After Treatment With Tofacitinib Citrate




A, At baseline, numerous white macules and patches are evident. B, After 5 months of treatment, repigmentation is nearly complete.

Figure 2. Hands of the Patient Before and After Treatment With Tofacitinib Citrate




A, At baseline, numerous white macules and patches are evident. B, After 5 months of treatment, repigmentation is nearly complete.

common pathogenesis.[9] As such, it is not surprising that a medication that has been shown to be effective in treating alopecia areata[8] may also be effective in treating vitiligo. Moreover, recent advances in the scientific understanding of vitiligo support the use of JAK inhibitors for this condition. Interferon-gamma-induced expression of C-X-C motif chemokine 10 (CXCL10) in keratinocytes is an important mediator of depigmentation in vitiligo.[2] Antibody neutralization of interferon gamma or CXCL10 reverses depigmentation.[10] We propose that because interferon gamma signal transduction occurs through JAK 1/2,[11] the use of the JAK 1/3 inhibitor tofacitinib effectively leads to blockade of interferon gamma signaling and downstream CXCL10 expression, thus giving rise to repigmentation in vitiligo.

To our knowledge, this report is the first to demonstrate effective pathogenesis-based therapy for a patient with vitiligo. The fairly rapid response and the repigmentation of the hands, which are often resistant to therapy, are noteworthy. Further investigation of the efficacy and safety of tofacitinib in the treatment of patients with vitiligo, including those for whom the condition has been more long-standing, will be important. Although uncommon, serious adverse effects, including malignant disease, have been reported in patients taking tofacitinib; therefore, investigation of the efficacy of a topical formulation for the treatment of localized vitiligo would be useful.

This case exemplifies the ways by which advances in basic science can guide treatment decisions and ultimately benefit patients. As we better understand the pathomechanisms of different diseases, targeted therapy becomes possible, and existing medications can be repurposed and/or new medications created for diseases with limited, if any, treatment options.

ARTICLE INFORMATION

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NOTABLE NOTES

## Let Food Be Thy Medicine

Rashi Minocha, MBBS

Hippocrates is a historical figure often thought of as the "Father of Medicine." He is quoted as saying, "Let food be thy medicine and thy medicine be thy food." His wise words are not forgotten as modern medicine increasingly delves into the simplicity of food derivatives to conquer dermatological disease.

Since time immemorial, vitamin deficiency has been linked to various dermatoses.[1] A connection has been established between vitamin A deficiency and a follicular hyperkeratosis known as phrynoderma and papular acneiform eruptions. Deprivation in vitamin $B_2$ (riboflavin), commonly found in various plant and animal tissues, has been associated an oro-ocular genital syndrome, presenting as a scaly, seborrheoic dermatitis like eruption around the nose, eyes, ears, and genital areas.[2]

Vitamin $B_3$, or nicotinamide, is a derivative of niacin commonly found in a wide variety of animal- and plant-based foods, such as meat, seafood, vegetables, and legumes. Vitamin $B_3$ deficiency, also known as pellagra, is a rarity in the modern world; however, it has been shown to cause a "sunburn"-type dermatitis with erythema and hyperpigmentation on sites exposed to sunlight. Skin hyperpigmentation has also been associated with vitamin $B_{12}$ deficiency. Vitamin C deficiency, also known as scurvy, has been long linked with follicular hyperkeratosis and skin pigmentation.[1]

Folic acid, commonly found in green leafy vegetables, meat, and milk, causes grayish brown pigmentation in light-exposed areas of the skin during deficiency. Acrodermatitis enteropathica, a disorder of zinc metabolism, has been shown to cause vesicobullous eruption of the hands, feet, and perioorificial areas.

The increasing exploration of the link between diet and skin metabolism has led to the development of revolutionary therapies, such as vitamin A–derived oral retinoids, which have shown great promise in the treatment of acne, psoriasis, and the prevention of skin carcinogenesis. Also, oral supplementation of nicotinamide has been very well tolerated and has proven to be useful in the treatment of autoimmune bullous disorders, acne, and the reduction in the incidence of actinic keratoses.[3]

It is of great significance that affordable therapies, developed from food sources, are now being used to promote cutaneous homeostasis and disease prevention. In our modern time, food is of great abundance. Yet the enhancement and processing of food and a trend toward more calorie dense, but less nutrient-rich food could mean we are more malnourished than ever before. In recent times, have the words of Hippocrates been more greatly emphasized? Can food be our medicine? Could it be as simple as that?

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