Unlocking the Potential of Baricitinib for Vitiligo

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Vitiligo, the most common skin pigmentation disorder, has affected patients for thousands of years.[1] The psychological and social impacts on patients include sleep and sexual disorders, low self-esteem, low quality of life, anxiety, and depression when compared to those without vitiligo.[2,3] There have been substantial therapeutic advancements in the treatment of vitiligo, with the recent approval of ruxolitinib cream 1.5% by the US Food and Drug Administration (FDA) in 2022 and by the European Medicines Agency in 2023.[4] Ruxolitinib is the first topical Janus kinase (JAK) inhibitor approved by the FDA for the treatment of nonsegmental vitiligo in patients 12 years and older, ushering in the era of JAK inhibitors for patients affected by vitiligo. The efficacy and safety of ruxolitinib was supported by 2 randomized clinical trials.[4] It also is FDA approved for the intermittent and short-term treatment of mild to moderate atopic dermatitis in nonimmunocompromised patients 12 years and older whose disease is not adequately controlled with other topical medications.[5]

Vitiligo is characterized by an important inflammatory component, with the JAK/STAT (signal transducer and activator of transcription) pathway playing a crucial role in transmitting signals of inflammatory cytokines. In particular, IFN-γ and chemokines CXCL9 and CXCL10 are major contributors to the development of vitiligo, acting through the JAK/STAT pathway in local keratinocytes. Inhibiting JAK activity helps mitigate the effects of IFN-γ and downstream chemokines.[6]

Currently, baricitinib is not FDA approved for the treatment of vitiligo; it is FDA approved for moderate to severe active rheumatoid arthritis, severe alopecia areata, and in specific cases for COVID-19.[7] Mumford et al[8] first reported the use of oral baricitinib for the treatment of nonsegmental vitiligo. This patient experienced poor improvement using the oral JAK inhibitor tofacitinib for 5 months but achieved near-complete repigmentation after switching to baricitinib for 8 months (4 mg daily).[8] Furthermore, a recent study found that in vitro baricitinib could increase tyrosinase activity and melanin content as well as stimulate the expression of genes related to tyrosinase in damaged melanocytes.[9]

A recent study by Li et al[10] has shown satisfactory repigmentation and good tolerance in 2 cases of vitiligo treated with oral baricitinib in combination with narrowband UVB (NB-UVB) phototherapy. These findings are supported by a prior study of oral tofacitinib and NB-UVB phototherapy in 10 cases; the JAK inhibitor treatment demonstrated enhanced effectiveness when combined with light exposure.[11]

Large-scale randomized clinical trials are needed to evaluate the efficacy and safety of oral baricitinib for vitiligo treatment. Currently, a clinical trial is underway (recruiting phase) to compare the efficacy and safety of combining baricitinib and excimer lamp phototherapy vs phototherapy alone.[12] The results of this trial can provide valuable information about whether baricitinib is promising as part of the therapeutic arsenal for vitiligo treatment in the future. A recently completed multicenter, randomized, double-blind clinical trial assessed the efficacy and tolerability of oral baricitinib in combination with NB-UVB phototherapy for the treatment of vitiligo. The trial included 49 patients and may provide valuable insights for the potential future application of baricitinib in the treatment of vitiligo.[13] If the results of these clinical trials are favorable, approval of the first orally administered JAK inhibitor for repigmentation treatment in patients with vitiligo could follow, which would be a major breakthrough.

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The off-label use of baricitinib—alone or in combination with phototherapy—appears to be promising in studies with a small sample size (an important limitation). The results of clinical trials will help us elucidate the efficacy and safety of baricitinib for vitiligo treatment, which could be a subject of debate. Recently, the FDA issued a warning due to findings showing that the use of tofacitinib has been associated with an increased risk of serious heart-related events, such heart attack, stroke, cancer, blood clots, and death.[14] In response, the FDA issued warnings for 2 other JAK inhibitors—baricitinib and upadacitinib. Unlike tofacitinib, baricitinib and upadacitinib have not been studied in large safety clinical trials, and as a result, their risks have not been adequately evaluated. However, due to the shared mechanisms of action of these drugs, the FDA believes that these medications may pose similar risks as those observed in the tofacitinib safety trial.[14]

Disadvantages of JAK inhibitors include the high cost, immune-related side effects, potential cardiovascular adverse effects, and limited availability worldwide. If current and future clinical trials obtain objective evidence with a large sample size that yields positive outcomes with tolerable or acceptable side effects, and if the drug is affordable for hospitals and patients, the use of oral or topical baricitinib will be embraced and may be approved for vitiligo.

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