Vitiligo affects an estimated 1% of the global population, with no clear etiology and a significant negative impact on quality of life and psychological functioning. An important treatment advance has expanded the treatment landscape for the disease, and researchers are currently exploring a range of additional promising treatment options for this patient population.

"Depending on the extent, stability, and location of vitiligo, treatment can range from topical creams and nutritional changes to phototherapy and systemic immunosuppressives, as well as surgical options for some types of vitiligo," Iltefat Hamzavi, MD, told Practical Dermatology. Dr. Hamzavi is a dermatologist at Hamzavi Dermatology and senior staff physician and researcher at Henry Ford Hospital in Detroit, MI.

Until recently, the typical treatment approach for vitiligo consisted of "topical immunosuppressants such as steroids alternating with calcineurin inhibitors to start, followed by narrow band UVB when necessary if the disease covered more than 5% of the body or was spreading," said John E. Harris, MD, PhD, in an interview with Practical Dermatology. Dr. Harris is professor and chair in the department of dermatology, founding director of the Vitiligo Clinic and Research Center, and founding director of the Autoimmune Therapeutics Institute at UMass Chan Medical School in Worcester, MA. "The topical immunosuppressants inhibit the autoimmune attack on melanocytes in the skin. Narrow band UVB also inhibits the immune attack, while also stimulating melanocytes to regrow."

RUXOLITINIB

In July 2022, topical ruxolitinib (Opzelura) was approved by the US Food and Drug Administration for the treatment of nonsegmental vitiligo in patients aged 12 years and older, making it the first approved pharmacologic therapy for repigmentation in vitiligo.

Vitiligo was first recognized in ancient Indian medical texts written 3,400 years ago, and it was treated with sunlight plus a medicinal plant with good effect. The use of sunlight, or nbUVB, hasn't really changed for thousands of years, so the new advancements are particularly exciting now."

Ruxolitinib was approved based on results of two phase 3 randomized double-blind trials (Topical Ruxolitinib Evaluation in Vitiligo Study 1 [TruE-V1] and 2 [TruE-V2]) demonstrating its safety and efficacy in this patient population. The trials included 330 and 344 participants, respectively, who were assigned to apply either ruxolitinib or placebo cream twice daily for 24 weeks; all subjects subsequently applied ruxolitinib for 28 additional weeks.

After the 24-week treatment period, facial Vitiligo Area Scoring Index (F-VASI) values decreased by at least 75% (primary endpoint) in 29.8% of patients in the ruxolitinib group compared to 7.4% of the placebo group in TruE-V1 (relative risk [RR], 4.0; 95% CI, 1.9-8.4; P <0.001), and in 30.9% and 11.4% of patients in TruE-V2, respectively (RR, 2.7; 95% CI, 1.5-4.9; P <0.001).

"Topical ruxolitinib is a Janus kinase (JAK) inhibitor and specifically interferes with IFNg signaling, a cytokine that drives the progression of vitiligo," said Dr. Harris, who served as an investigator in the trials. "I'm very excited that we have an FDA-approved option for patients. We use ruxolitinib frequently instead of the other creams because it seems to work better and doesn't have the same side effects as steroids."
DIVERSITY IN SKIN TONE

THE PROS AND CONS OF VARIOUS THERAPIES FOR VITILIGO
By Jordan Talia, MD

“I think all of these approaches have a role and a place in vitiligo treatment, and depending on each patient, the location of the lesions, severity, the cost, and insurance coverage, each therapy may have a role as a first-line agent,” according to Dr. Talia. “I think the topical JAK therapy is very promising.”

In many cases, combining therapies – such as phototherapy with topical medications or systemic immunosuppressants – will provide better efficacy than either approach alone. The use of ruxolitinib in combination with biologics, other JAK inhibitors, or immunosuppressants such as azathioprine or cyclosporine, is not recommended.

Topical corticosteroids
- **Pros:** Low-cost, effective medication; can be used in patients of all ages and during pregnancy
- **Cons:** Often requires intermittent breaks in treatment to avoid side effects such as telangiectasias, skin atrophy, and striae; not preferred in intertriginous, genital, face, or neck regions; if used in these areas, lower potency steroids would be preferred, which are less effective

Topical calcineurin inhibitors (tacrolimus, pimecrolimus)
- **Pros:** Beneficial for face (especially around eyelids), neck, intertriginous, and genital regions; can be used in children and adults, though this therapy is not approved for patients younger than 2 years of age
- **Cons:** These agents have not been specifically studied in pregnancy but have been deemed generally safe in pregnancy and breastfeeding, according to some published reports; may not be as beneficial as high-potency topical steroids for extra-facial lesions

Topical JAK inhibitor (ruxolitinib)
- **Pros:** Can be used on various areas of the body
- **Cons:** Only approved for patients aged 12 years of age and older; product labeling limits usage to up to 10% of the body surface area; safety during pregnancy has not been established and it is not known if ruxolitinib passes into breastmilk

nbUVB phototherapy (home-based or office-based)
- **Pros:** Beneficial for patients with involvement of more than 10% of the body surface area and widespread disease where topical applications may be impractical for less than 10% of the body surface area or when the patient is not responding to topical medications alone; options exist for focal lesions and more extensive body surface involvement; better compliance given home use option in some cases
- **Cons:** May be impractical for young age groups; requires three sessions per week, though two sessions can be acceptable; office phototherapy will depend on patient availability for scheduling

Oral steroids (dexamethasone, prednisone, prednisolone, methylprednisolone)
- **Pros:** Can be beneficial for rapidly progressive and extensive disease to halt progression of vitiligo
- **Cons:** Numerous possible side effects, including weight gain, hypertension, increased blood glucose, changes to bone metabolism, bone loss, and many others; not very beneficial for repigmentation; often recommended to be used in combination with nbUVB phototherapy

The most common side effects observed in patients treated with ruxolitinib were application-site acne (6.3% in TruE-V1 and 6.6% in TruE-V2), application-site pruritus (5.4% and 5.3%), and nasopharyngitis (5.4% and 6.1%).

OTHER OPTIONS

Regarding additional approaches to vitiligo treatment, Jordan Talia, MD, assistant professor of dermatology, director of Complex Medical Dermatology, and director of the Skin of Color Center at the Icahn School of Medicine at Mount Sinai in New York, cited in-office excimer laser as an effective option that can also be combined with other therapies for greater repigmentation; while this approach has a comparable or possibly higher efficacy than nbUVB, the cost is higher and may not be covered by insurance. In addition, this strategy is impractical for use on large areas of skin, and it must be used three times per week for the fastest results, he told *Practical Dermatology*. (See The Pros and Cons of Various Therapies for Vitiligo).

Treatment with other systemic immunosuppressants such as cyclosporine, methotrexate, or azathioprine can be considered for progressive recalcitrant vitiligo. “Of note, there have not been extensive studies demonstrating efficacy in vitiligo, and these therapies can have notable side effects that require careful selection of appropriate patients, as well as side effects that require lab monitoring,” Dr. Talia cautioned.
Patients with small amounts of disease that is not spreading may be candidates for surgical treatment, which “consists of moving melanocytes from one part of the body to the vitiligo spots,” Dr. Harris explained. “Also, for very widespread disease, some patients opt to use a depigmenting cream to worsen their disease and become completely depigmented, or one color.” This represents a major decision for patients, especially those with darker skin tones, given the drastic change in appearance that can result from this option, he said.

QUALITY OF LIFE AND OTHER CONSIDERATIONS
Along with the dermatologic effects of vitiligo, the disease can have a substantial impact on quality of life (Qol.), and a significant number of patients are diagnosed with anxiety or depression, Dr. Talia noted. In skin of color patients, vitiligo can have a starker contrast and may lead to greater Qol. impairment and social stigma compared to White patients.

“Mental health effects are present for all populations but even greater for skin of color patients,” Dr. Hamzavi said. “Offering support groups and camouflage options becomes even more important for these individuals.”

Dr. Talia highlighted the following additional considerations for clinicians treating patients with vitiligo:

- In general, if a patient is using a medication other than topical steroids or light therapy during pregnancy, and there is a paucity of data regarding safety during pregnancy, consult with the patient’s OB-GYN prior to use.
- Topical corticosteroids and topical calcineurin inhibitors can be used in patients with a body surface involvement greater than 10%, though nbUVB phototherapy can be a very beneficial option at home or in office.

- It is recommended to check TSH and anti-TPO antibodies in vitiligo patients as a routine screening.
- Increased sensitivity has been noted in depigmented skin in vitiligo patients, and sunscreen is essential.

Looking forward, Dr. Harris emphasized the importance of continued research to develop novel and safer therapies for the treatment of vitiligo.

“It’s an exciting time for new treatments for vitiligo with many currently in clinical trials [going on], including for systemic JAK inhibitors that could be useful for widespread or very actively spreading disease, and biologics that may have longer-lasting effects and may be safer,” he said. “Vitiligo was first recognized in ancient Indian medical texts written 3,400 years ago, and it was treated with sunlight plus a medicinal plant with good effect. The use of sunlight, or nbUVB, hasn’t really changed for thousands of years, so the new advancements are particularly exciting now.”

Dr. Hamzavi serves as a consultant to Abbvie, Pfizer, Incyte, UCB, Boehringer Ingelheim, Sonoma, Union Therapeutics, Novartis, Jansen, Avita, Galderma, Vimela, Almirall, and Sonoma; investigator for Lencica, Pfizer, Incyte, Avita, Loreal/Laroche Posay, and ITN; and board member and past president of the Hidradenitis Suppurativa Foundation and the Global Vitiligo Foundation.

Dr. Harris founded Villaris Therapeutics that developed a biologic drug, auremolab, to treat vitiligo. Incyte, the company that developed Opzelura, acquired Villaris and will soon begin trials to test auremolab. Dr. Harris serves as a consultant to Incyte to help further advance this potential treatment.

Dr. Talia stated that he has no relevant disclosures.