A Long but Worthwhile Wait for Vitiligo Treatments

The drug development landscape for vitiligo is sparse despite its social impact on individuals irrespective of race, ethnicity, or gender. Sometimes dubbed a "cosmetic condition," years of research suggest vitiligo is an autoimmune disorder that could be triggered by an event (e.g., sunburn, illness, stress) or linked to specific genes. Approximately 25–50% of people diagnosed with vitiligo have a relative with the condition.[1] Individuals with this disorder may be more predisposed to having other autoimmune disorders as well, such as Addison's disease, psoriasis, rheumatoid arthritis, systemic lupus erythematosus, thyroid disease, and type 1 diabetes. The cause for vitiligo is unknown.

Vitiligo is a chronic disorder in which the skin loses its pigment cells (melanocytes), resulting in a "milky-white color," according to the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) of the National Institutes of Health (NIH).[2] These cells produce melanin; when they die or no longer make melanin, patches of white slowly grow on the skin in irregular shapes. Vitiligo is classified into two types:

1. **Nonsegmental (or generalised), the most common type of vitiligo.** This type is characterised by white patches that appear symmetrically on both sides of the body (i.e., on both hands, on both knees). Nonsegmental vitiligo can develop rapidly, resulting in loss of pigment over a large area.
2. **Segmental vitiligo.** This form of vitiligo is less common and occurs when white patches appear only on one segment or side of the body. Segmental vitiligo usually begins at an early age, progressing for approximately 1–2 years and typically stopping.

Worldwide, 70 million people are diagnosed with vitiligo, according to the Global Vitiligo Foundation.[3] In 2020, vitiligo prevalence (diagnosed and undiagnosed) in the US was estimated at approximately 0.76% (1.9 million) to 1.11% (2.8 million individuals), and approximately 40% of vitiligo cases in adults may be undiagnosed.[4]

There are no available treatments that are approved by the US Food and Drug Administration (FDA) for repigmentation of vitiligo lesions. Monobenzone, an FDA-approved therapy for patients with vitiligo, is no longer on the market and was indicated for final depigmentation. Patients seek treatment for vitiligo to slow or stop disease progression, encourage melanocyte regrowth, and restore colour to the affected skin area. Treatments include corticosteroids, calcineurin inhibitors, vitamin D analogs, phototherapy, and surgical procedures, such as skin or blister grafting.

Bringing Vitiligo to Light

A year has passed since the FDA engaged patients in a full-day discussion about their perspectives on vitiligo – its effects on their overall health and well-being, their experiences using treatments, and challenges to accessing medical treatments. In March 2021, the agency held a public workshop as part of its patient-focused drug development (PFDD) initiative to ask patients about living with vitiligo.

In December 2021, the FDA published *The Voice of the Patient*, a publication resulting from the March 2021 workshop that summarised the discussions at the meeting.[5] Some patients noted experiencing "severe emotional distress," social isolation and stigma, and impacts on relationships and identity due to their vitiligo. They also highlighted a need for further research into the causes of vitiligo and treating the "underlying pathology." Meeting participants and individuals who submitted comments to the FDA docket agreed that the "ideal treatment effect" would be permanently regaining pigment and stopping the spread of additional depigmentation.

Drug Development for Vitiligo

In the US, a few products are nearing the end stages of research into treating vitiligo. Three Janus kinase (JAK) inhibitors have reached phases 2 or 3 of clinical development, and one monoclonal antibody is in phase 2. The end goal with these treatments is to stop depigmentation and provide repigmentation that is lasting.

Ruxolitinib

Incyte Corporation has developed ruxolitinib, a JAK1 inhibitor approved by the FDA in September 2021 under the trade name Opzelura for an atopic dermatitis indication. In December 2021, the FDA accepted a supplemental new drug application (sNDA) for ruxolitinib cream for the treatment of individuals aged ≥12 years with vitiligo and granted it priority review with a Prescription Drug User Fee Act (PDUFA) target action date of April 18, 2022.[6] If the FDA approves the sNDA, ruxolitinib could be the first US-marketed treatment for vitiligo that helps to restore pigmentation.

Incyte is evaluating the safety and efficacy of ruxolitinib cream in a phase 3 clinical program (TRuE-V) in >600 subjects aged ≥12 years with nonsegmental vitiligo. In 2 studies, the primary endpoint is the proportion of patients achieving ≥75% improvement from baseline in the facial Vitiligo Area Scoring Index (F-VASI75) at week 24. Results announced at the 30th European Academy of Dermatology and Venereology (EADV) Congress noted that 29.9% of patients who used ruxolitinib cream achieved 75% improvement from baseline in the F-VASI75.

INCB054707

Incyte is also evaluating the safety and efficacy of INCB054707, another JAK1 inhibitor in the company's pipeline, in a randomised, double-blind, placebo-controlled, dose-ranging phase 2 study followed by an extension period in >160 subjects with vitiligo. The primary endpoint is the percentage change in total VASI (T-VASI) at week 24. The estimated study completion date is January 2023.

Upadacitinib

Marketed in the US as Rinvoq, upadacitinib is a JAK1 inhibitor from AbbVie Inc indicated to treat rheumatoid arthritis, active psoriatic arthritis, and atopic dermatitis. The agent is under evaluation for the treatment of nonsegmental vitiligo in a multicenter, randomised, double-blind, placebo-controlled dose-ranging phase 2 study in >150 subjects with vitiligo. Participants will be placed in two of five treatment arms, and the primary endpoint is the percent change from baseline in F-VASI at 24 weeks. The estimated study completion date is December 2023.

AMG-714

The NIH's National Institute of Allergy and Infectious Diseases (NIAID), along with collaborators, including Amgen Inc, is evaluating AMG-714, a human IgG1-kappa anti-interleukin-15 (IL-15) monoclonal antibody, for the treatment of vitiligo in a double-blind, placebo-controlled, multicenter, proof-of-concept phase 2a study (REVEAL). The primary endpoint is the proportion of participants achieving facial VASI ≥35 (F-VASI35) at week 24. The study is estimated to complete in March 2023.

Filling an Unmet Need

For many people, white patches begin to appear before the age of 20, but vitiligo can develop early in childhood. While it is not life threatening and does not affect general functioning, it can have psychological effects. The skin discoloration can contribute to low self-esteem or poor quality of life and can increase the risk for sunburn. Almost half (46%) of respondents in the Vitiligo and Life Impact Among International Communities (VALIANT) study considered daily administration of their vitiligo burdensome to their lives.[7] The next few years could address this treatment void and lead to future breakthroughs in understanding the origin of vitiligo.

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Jaime Polychrones

Jaime Polychrones is a Senior Content Writer for the Cortellis suite of life science intelligence solutions at Clarivate. Her previous roles include writing and editing for books, online magazines, educational coursework, government proposals, and government regulatory publications. Her primary assignments at Clarivate include reporting on FDA drug/device advisory committee meetings and drug approvals.

Email: jaime.polychrones@clarivate.com