Conquering sunlight sensitivity

Dersimelagon’s promise in photodermatoses

Two rare genetic dermatological conditions, erythropoietic protoporphyria and X-linked protoporphyria, bring about excruciating pain and skin damage upon exposure to sunlight. In groundbreaking research, a new medication called dersimelagon is addressing these conditions. Led by Dr. Kirstine Belongie and her expert team at Mitsubishi Tanabe Pharma America, a clinical trial was conducted to evaluate dersimelagon’s impact on the onset time and severity of symptoms triggered by sunlight exposure in affected patients. Promising results have emerged, suggesting dersimelagon’s potential as an effective treatment option, offering hope for improved symptom management and overall quality of life for those affected with these debilitating skin conditions.

Photodermatoses encompass a spectrum of skin disorders characterised by abnormal reactions to sunlight exposure, often manifesting as rashes, redness, blistering, or pain. Effective treatments for these conditions are scarce, but the pioneering work of Dr. Kirstine Belongie and colleagues at Mitsubishi Tanabe Pharma America offers hope. Their research targets erythropoietic protoporphyria and X-linked protoporphyria, two debilitating conditions marked by excruciating phototoxic attacks following exposure to visible light. Introducing dersimelagon, a novel orally administered drug aimed at providing relief to these patients, Belongie, Senior Director and Head, Immunology & Inflammation, Medical Sciences at Mitsubishi Tanabe Pharma America, conducted a randomised, placebo-controlled, phase 2 trial. Belongie’s study investigated the efficacy and safety of dersimelagon concerning the time to onset and severity of symptoms associated with sunlight exposure in patients with these protoporphyrias. Her groundbreaking research signifies a significant advancement in addressing the unmet medical needs of those affected by these challenging conditions, offering promise for improved symptom management and enhanced quality of life.

**UNDERSTANDING THE CONDITION**

Erythropoietic protoporphyria (EPP) and X-linked protoporphyria (XLP) are exceptionally rare genetic disorders, affecting an estimated one in 75,000 to one in 200,000 white persons. These conditions come from inherited genes that affect how the body makes heme, an important part of haemoglobin. As a result, there’s an unusual buildup of metal-free protoporphyrin, which is a precursor to heme, leading to the typical symptoms of these disorders. People dealing with EPP and XLP experience severe skin reactions when exposed to sunlight because of the increased levels of protoporphyrin. The resulting excruciating pain and discomfort significantly diminish patients’ quality of life, necessitating urgent intervention for effective treatment modalities.

Symptoms can differ from person to person. About a quarter of EPP patients feel symptoms within ten minutes of being in the sun, and around 60% feel them within 30 minutes. Existing therapies have failed to provide relief from the intense pain and accompanying symptoms following prolonged sun exposure, often necessitating a recovery period of two to seven days. Treatment protocols typically include sunlight avoidance strategies such as protective clothing, opaque sunscreen application, and indoor confinement during peak sunlight hours to mitigate phototoxic reactions. While current approaches focus on symptom management rather than genetic correction, novel therapeutic avenues like dersimelagon offer promise for individuals grappling with these debilitating conditions.

Afamelanotide is presently the sole approved treatment in the United States, the European Union, and Australia for enhancing sunlight tolerance in adults diagnosed with erythropoietic protoporphyria. This treatment involves subcutaneous administration every two months and has been extensively studied in clinical trials, demonstrating both efficacy and safety. However, there is currently no available medication for children, and as it requires administration by a healthcare professional via subcutaneous implant, there remains a need for an effective oral treatment option for individuals with erythropoietic protoporphyria or X-linked protoporphyria.

**Investigating Dersimelagon**

Dersimelagon is a new drug, designed to treat EPP and XLP. This medication is taken orally and works by boosting levels of skin pigment (eumelanin).
Behind the Research
Dr Kirstine Belongie

Detail
Bio
Dr Kirstine Belongie is Senior Director and Head of Immunology & Inflammation, Medical Science at Mitsubishi Tanabe Pharma America.

Funding
MTPA

Personal Response
How do you plan to further evaluate the effectiveness of dersimelagon in larger-scale studies or in clinical settings?

We just started a new global phase 3 clinical trial that will include up to 150 patients with EPP or XLP to validate dersimelagon’s efficacy and safety. Around 40 clinical trial sites are being activated now and we are looking for new EPP and XLP patients globally. Information on this can be found on clinicaltrials.gov or through the United Porphyria Association (UPA) patient advocacy group.

References

PROMISING RESULTS
The trial results yielded promising outcomes, with dersimelagon demonstrating a significant increase in the duration of symptom-free sunlight exposure compared to placebo. Patients receiving dersimelagon experienced a substantial delay in the onset of prodromal symptoms, indicating a tangible improvement in their tolerance to sunlight exposure. Quality of life assessments also showed positive trends, further underscoring the potential of dersimelagon as a game-changing treatment option.

The trial, comprising 102 participants, stands as one of the largest conducted for these rare diseases. These findings offer hope to patients and clinicians grappling with the challenges of managing erythropoietic protoporphyria and X-linked protoporphyria. The promising results of this phase 2 trial lay the foundation for further research into dersimelagon’s mechanism of action and its potential as a therapeutic agent for photodermatoses.

SAFETY AND FUTURE DIRECTIONS
Alongside its efficacy, dersimelagon showed an acceptable safety profile, with most adverse events being mild to moderate in severity. The findings pave the way for future research endeavours, emphasising the need for larger-scale trials to validate dersimelagon’s efficacy across diverse patient populations. This phase 2 trial lays the groundwork for further exploration of dersimelagon’s therapeutic potential, with ongoing efforts aimed at elucidating its mechanism of action and optimising treatment strategies for patients with these rare and challenging conditions. The safety data generated from this trial will inform future clinical development efforts, guiding researchers and clinicians in their quest to bring dersimelagon to market as a safe and effective treatment option.