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Ravicti as therapy for bestrophinopathies: a double-blind crossover randomized controlled trial (BETTER Trial)

The BETTER trial was sponsored by Manchester University NHS Foundation Trust and funded by the Medical Research Council (MRC).

All participants were recruited at Manchester University NHS Foundation Trust. The first participant was screened for the trial in August 2024 and the final participant completed the trial in July 2025.

Patients between the ages of 18 and 65 with a genetic diagnosis of Autosomal Recessive Bestrophinopathy (ARB) or Best Vitelliform Macular Dystrophy (BVMD) were eligible to take part. A total of 10 participants were recruited.

ARB and BVMD can lead to irreversible sight loss and there is presently no proven treatment for this group of conditions. Ravicti (glycerol phenylbutyrate) is a liquid medication widely used to treat urea cycle disorders. Further studies have suggested that the medication has potential to help improve the function of the bestrophin 1 protein in individuals with the two most common types of bestrophinopathy.

This trial tested whether the medication Ravicti® (an odourless, tasteless liquid taken by mouth), can help improve the function of the bestrophin 1 protein in individuals with the two most common types of bestrophinopathy (ARB and BVMD)

As these conditions are rare, the study was designed as a 'cross-over' trial, where participants were either randomised to receive either the placebo ('dummy medicine') in the first weeks of the trial, followed by the active test medicine (Ravicti), or vice versa.

Participants attended six trial visits for assessments including safety blood tests, drug diary checks, eye tests, electrophysiology and eye imaging.

The medicine was well tolerated by participants with mild side effects reported. All participants managed to complete the course of treatment and follow up assessments.

The study did not show that Ravicti led to a statistically significant improvement in retinal pigment epithelium function, as measured by the electro-oculogram (EOG), or in retinal imaging findings compared with placebo.

Although this trial did not demonstrate a benefit, it is an important contribution to research in this area. Clinical trials help us understand which treatments are and are not effective, and this knowledge is essential for guiding future research and the development of new therapies for Bestrophin 1-related retinal diseases.