

## **TREATWOLFRAM international clinical trial of sodium valproate in Wolfram syndrome: interim results**

First results from the TREATWOLFRAM trial, sponsored by the University of Birmingham, find sodium valproate treatment does not slow vision loss in Wolfram syndrome.

A clinical trial, named TREATWOLFRAM, aimed to test if a medicine, sodium valproate, could slow the progression of vision loss. The trial involved 63 children and adults, who took part from Birmingham UK, Paris and Montpellier in France, Almeria in Spain, and Lodz in Poland. Patients were randomised to either sodium valproate treatment or placebo (dummy) treatment. Neither the patients or the researchers knew which patients were taking the sodium valproate or the placebo.

The trial started in January 2019, and ended in November 2024. It was delivered by the Cancer Research Clinical Trials Unit, University of Birmingham. Patients were followed up for 36 months, with regular tests of vision, brain scans and many other measures. All the trial information has now been collected and the first results have been analysed.

The vision gradually worsened in all patients, as expected. The trial found the overall progression was the same in those treated with sodium valproate, as those treated with placebo. This means that sodium valproate treatment does not slow vision loss in Wolfram syndrome. The study was large enough for the researchers to have confidence in the results.

The first data on MRI brainstem volumes showed an overall gradual decrease in all patients, slightly more in those taking sodium valproate. At present the researchers have not found any benefit or harm to participants, and there were no unexpected safety issues found.

These early findings do not show the results that the Wolfram syndrome community would have hoped for. However, the researchers still have to analyse many other outcomes from this trial, and this will be done over the next 6 weeks.

The trial has provided an important data set, with careful measurements of this disease and its progression in the largest group of affected people from 4 countries. This will aid in designing future treatment studies, as the information may help reduce the need for a placebo group, and shorten the time taken to do these studies.

The research team advise that any TREATWOLFRAM trial participants, from any country, who are still taking sodium valproate should talk to their doctor for advice about how to stop the medicine, since no benefit for vision loss has been shown. We await the complete trial analysis to find out if there is any benefit of sodium valproate on other aspects of the condition.

Wolfram syndrome is a rare genetic disease causing childhood onset diabetes, progressive vision loss, and other symptoms that increase with age. There is no cure, or treatment to slow the disease progression.

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