

Tim Barrett update for Spring TreatWolfram newsletter

Dear friends and colleagues,

I hope everyone is keeping OK. I have 3 items to update you on.

Firstly, the TREATWOLFRAM trial is continuing to progress well. We had an independent Data Monitoring Committee meeting in January. This is chaired by Professor Karen Morrison, an honorary consultant in adult neurology, who previously led the highly specialised service for adults with Wolfram syndrome. The Data Monitoring Committee reviewed the unblinded data. I am pleased to say that they had no safety concerns, and were happy for the trial to continue to completion. Following this meeting, our Trial Steering Committee met, chaired by Professor Marc Peschanski, Director of INSERM, a large research institute outside Paris. We discussed the trial progress so far, and plans for acting on the results at the end of the trial. The last participant will complete the trial at the end of October 2024. We will then have 2-3 months to collect any outstanding data from study sites. The Clinical Trials Unit will then 'lock' the database and all trial related data is passed onto our statistician to analyse. We expect to find out whether the treatment is effective or not, by the end of March 2025. As soon as I am told the results, I have to write a report to our funder, the UK Medical Research Council; and I will of course share through Wolfram Syndrome UK. Our trials unit team, Amy Lamb, Lewis James Victoria Homer and Darren Barton, are working hard to make sure all the information that participants have kindly supplied, will be ready to be analysed when the trial ends in October 2024.

Secondly, I wanted to give some extra information about our investigational medicine, Sodium Valproate. Valproate is a medicine that has been used since the 1960s for the treatment of epilepsy. Many hundreds of thousands of patients have been treated worldwide, and it is a very effective treatment for this condition. We selected it for our TREATWolfram trial as we had strong laboratory data to suggest it will slow down disease progression; and as it is known as a 'neuro-protector', keeping brain cells healthy.

Sodium valproate has been in the news recently because tragically, it can damage unborn babies if given in pregnancy. More than 20,000 babies have been damaged in this way in the UK alone over the last 50 years.

There has been a national patient safety alert from the UK Medicines Regulator (MHRA) to remind patients and the public about the safety precautions we all need to follow for people taking sodium valproate:

**A.** Valproate must not be started in new patients (male or female) younger than 55 years, unless two specialists independently consider and document that there is no other effective or tolerated treatment, or there are compelling reasons that the reproductive risks do not apply.

**B.** At their next annual specialist review, women of childbearing potential and girls should be reviewed using a revised valproate Risk Acknowledgement Form, which will include the need for a second specialist signature if the patient is to continue with valproate and subsequent annual reviews with one specialist unless the patient's situation changes.

There is helpful information on this UK Government website:

<https://www.gov.uk/drug-device-alerts/national-patient-safety-alert-valproate-organisations-to-prepare-for-new-regulatory-measures-for-oversight-of-prescribing-to-new-patients-and-existing-female-patients-natpsa-slash-2023-slash-013-slash-mhra>

During the TREATWolfram clinical trial, we have been following the country-specific pregnancy prevention programmes, for every female participant who is of childbearing age. As the trial closed to recruitment some time ago, we have not started anybody on sodium valproate since these guidelines were introduced.

Going forwards to the end of the clinical trial: if the trial is successful and sodium valproate is shown to be effective in slowing progression in Wolfram syndrome, then we will make it available to everyone with Wolfram who wants the medicine. We will, however, strictly follow the national patient safety alert advice so that it is not given to females while they are trying to conceive or while they are pregnant.

Please do get in touch with me or with other members of the clinical trials team if you have questions about this medicine or about its safety.

Thirdly, I am incredibly grateful to Shiffa Ahmed for sharing her story, and Tracy Lynch, for helping me and others write an article about the TREATWolfram trial that was featured in The Guardian Newspaper for Rare Disease Day yesterday. You can find the article at the following link:

<http://tinyurl.com/2hez7sud>

All our study team owes a big thank you to Wolfram syndrome UK for their generous support, and for bringing the Wolfram community of families, researchers and health care professionals together. I wish you all a peaceful Easter and here's hoping for some better weather!

Sincerely