

Dear Friends and colleagues,

I would like to give you an update as to progress with our clinical trial of a treatment for Wolfram syndrome.

We had the final confirmation of funding from the UK Medical Research Council on December 16th 2016, so were able to start work on the study protocol early in the New Year. We were fortunate to have Ms Rebecca Storey appointed as Senior Trials Coordinator in January. She has lots of experience in running clinical trials, and is based in the Clinical Trials Unit, University of Birmingham. She hopes to attend the family conference in October, so I hope some of you will meet her.

We then appointed local lead investigators for the UK: this will be Dr Renuka Dias for the children's hospital clinic, and Dr Ben Wright for the Queen Elizabeth Hospital adult clinic. Also in January, Tracy kindly met with me at my parents' house near Gatwick Airport, where we discussed what the clinical trial would look like, and what to include in the participant information sheets. The main point was that families would prefer participants to have an increased chance of receiving the study medicine rather than the placebo. I took this back to our trial statistician Kristian Brock, who has been able to include this request. Participants will now have a 2:1 chance of being given the study medicine rather than the placebo. Kristian Brock is an expert in statistics and trial design, and will also try to attend the family conference.

In February we started discussions with Guy's and Thomas's Pharmacy manufacturing unit to prepare the medicine and placebo. We also prepared the ethics application form, and had a telephone conference with our international partners in Spain, France and Poland.

In March I went to our local Young Persons' Advisory Group. This is a group of 11-23 year olds, who kindly volunteer to read study information and critically appraise it so that it is readable and easily understood. I took them the participant information sheets I had prepared, and I am sorry to say they looked them over very critically! They pointed out that the layout could be improved; that there was some repetition; and that a glossary of medical terms would help. I am very grateful to them and the information sheets are now shorter and clearer to read.

In April I attended the European Medicines Agency in London with Julie Warner, from Boyd Consultants, who provide regulatory advice. They agreed that we must check if the treatment slows the rate of deterioration of vision; however they would like a second outcome measure that is important for families. We are now working with experts on patient reported outcome measures, and would like to propose some ideas to you – things to measure which are important for a treatment to improve.

I also visited the French Wolfram association in Paris, just before Easter, and attempted to present the clinical trial in French. The audience was very polite and tolerated my schoolboy French! In May I gave a similar presentation to Spanish families in Almeria, hosted by Dr Gema Esteban, our Spanish collaborator. There is a lot of enthusiasm to take part, and there were many questions. Some of these related to randomisation, and I had to explain that the European Medicines Agency insist that some people receive the medicine and some the placebo. This is in order to provide the strongest evidence that our medicine works.

We are now hoping to sign the contract with the pharmacy manufacturers; submit the ethics application package in September; and recruit the first participants in the UK at the end of November. The timescale has been extended as we have to show that the medicine is stable outside the manufacturer's packaging, when we put it in airtight plastic containers. This stability testing started last week, and takes 3 months.

Later this month, we have a local investigator meeting, where we will sort out the practical aspects of what tests we will be asking participants to have. I would like to write another update at the beginning of July when I can feed back on this meeting.

Please don't hesitate to get in contact if I can help at all with any questions. Meantime, thank you all for your kind interest and support!

Sincerely

Prof Tim Barrett