Update September 2018

I am pleased to give you an update on the progress of the TREATWOLFAM clinical trial.

Since my last update, the pharmacy department at Guy's and Thomas's hospital has been working hard to get us the medicine to use in the clinical trial. They have had to show that the medicine will be stable and still effective if kept in the clinical trial containers. They perfected the measuring methods during June and July, and have now shown the medicine is stable for at least 12 months. This means that finally, we can move the trial on. Our clinical trials unit has been finalising the contracts, and the pharmacy are about to start making the placebo medicine, planning to deliver both medicines to our UK sites during October.

At the same time, we have approached our funder, the Medical Research Council, for more funds to support the additional experiments needed to show the medicine is stable. The Council have kindly agreed to do this.

Our trials unit, led by Darren Barton, Sabrina Cronier, and Shazia Ahmed have gone through the study protocol with a fine toothcomb and made sure it is consistent and deliverable across all the sites. They have taken out some unnecessary interventions to make the study easier to deliver. This has now gone back to the regulatory authorities for approval, which we expect in the next 2 weeks.

Shazia has been busy developing the case report forms, which collect standardised information on the outcomes of the trial. These have now gone to the computer programmers who code all the information; these are now almost all ready to go.

We have been working closely with the hospital teams at University Hospitals Birmingham, and Birmingham Women's and Children's Hospital. Dr Renuka Dias has kept in close touch with developments at the children's hospital even though on maternity leave; and Josie Goodby our study coordinator has worked hard to get the children's site up and running. Lynne Savage, the adult neurology research nurse, has been working with Dr Ben Wright, lead at the University Hospitals Birmingham site, to look at the practicalities of delivering the study for young adults.

Dr Patrick Yu Wai Man has been advising on how we measure the main outcome, effects on vision; and our local ophthalmologists Susan Mollan, John Ainsworth and Archana Kulkarni have been advising what can be delivered practically, with our research optometrist Bavnesh Sond.

From the imaging side, Dr Heather Rose is our radiology research associate, and has worked with Prof Andrew Peet and Dr Martin Wilson to develop a manual for the imaging aspects. This is to standardise the brain imaging outcome, so that we can compare the same measurements in each centre. There has been a lot of discussion about how to keep all the data anonymised, and respect participants' confidentiality. At the same time, we would like to share anonymised images with international

collaborators such as Prof Tamara Hershey in Washington University, USA, and she has been working with us to make this possible.

Our international partners have been active; I had a telephone conference with Prof Wojciech Mlynarski's team on Friday, to finalise the investigations they will undertake, and the finances and they are very keen to take part. We have also been in recent contact with Gema Esteban in Almeria, and Sabrina has been working with the French teams.

The remaining barriers to starting the trial are completion of the pharmacy manual, and the laboratory manual. Now that the amended protocol has been submitted to the regulatory authorities, we are working on these 2 manuals and hope to complete these this coming week (to end Sept).

Our plan is to have a site initiation visit for the Children's Hospital site in mid-October; with a plan to recruit children after that. We will most likely post out study information to families and invite participants to attend the children's hospital to complete any baseline investigations, before being randomised to the study medicine or placebo medicine. We would like to start with opening the children's hospital site first, iron out any problems, then open the adult hospital site. We will most likely open the international sites early in the New Year.

Thank you so much for your patience, and I hope you can see from the above that there are a lot of people working together to open this clinical study safely, and have everything thoroughly prepared so that the trial delivers a clear result.

I look forward to meeting many of you again at the family meeting coming up in October

With best wishes

Tim Barrett