

Brain disease treatment shows promising signs

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Early results for a potentially revolutionary brain disease therapy given under compassionate use to a two-year-old has shown promise, a University of Manchester scientist will tell an international conference on Wednesday (13 May).

Professor Brian Bigger will tell the American Society of Gene & Cell Therapy that the safety and feasibility of the investigational gene [therapy](#) for the rare and life limiting Sanfilippo disease type A is now becoming more clear, as a formal clinical trial gets underway.

The trial is funded by Orchard Therapeutics, who hold the license and commercial rights to the Sanfilippo disease type A program.

The investigational gene therapy, which involves harvesting patient's [blood stem cells](#), was delivered by Professor Rob Wynn under a special license at The Royal Manchester Children's Hospital (RMCH) in 2019.

The therapy and trial follow over a decade of development and preclinical work by Prof Bigger at The University, together with clinical collaborators

Prof Wynn, Prof Ed Wraith and Dr. Simon Jones at Manchester University NHS Foundation Trust (MFT) and Prof Adrian Thrasher at Great Ormond Street Hospital (GOSH).

A type of virus known as a lentiviral vector is used to deliver the patient's missing 'SGSH' gene to the blood stem cells in the laboratory.

The manufactured gene-modified stem cell product is transplanted back into the patient.

The stem cells then regenerate the immune system providing the patient with the working—and potentially permanent—copy of the gene.

Sanfilippo disease type A—or MPSIIIA—causes a progressive loss of developmental skills in young children.

They suffer deafness, hyperactivity and behavioral problems, progressive developmental delay, and seizures during the later stages of the condition.

The condition is usually fatal in late childhood or early adulthood.

Professor Bigger said: "These results are promising and provide some hope for these children whose condition was previously thought to be incurable. The trial is the critical next stage, but it's true to say we are excited.

"Sanfilippo Disease is an appalling disease which causes misery to these children- so the prospect of a treatment is tantalizing—especially when it was thought for years that no treatment would be possible."

The preliminary results of the patient treated under compassionate use and followed now for over a year post-treatment has shown rapid engraftment of the gene modified cells and greater than 25-fold of median normal SGSH enzyme levels achieved in

the blood. At 6 months post-treatment, CSF levels of SGSH enzyme were at the upper end of normal range.

Provided by University of Manchester

Sufficient replacement of the enzyme by blood cells in regions such as the brain, could result in prevention of the disease course, but it is still too early to know if this has happened in this case.

Sanfilippo [disease](#), is caused by defects in the SGSH gene, which is needed to break down complex sugars in the body. A lack of this enzyme leads to a build-up of these sugars in the body and this mainly affects normal brain function in these children.

In the phase I/II trial, the gene therapy transplant will be given to between three and five children, aged under two years with a severe MPSIIIA type.

The first patient was recruited to this trial in early January 2020, with their blood stem [cells](#) harvested and modified prior to transplanting the gene therapy product back into the patient in May 2020.

The safety of this investigational gene therapy, the level of SGSH enzyme and changes in patient behavior and quality of life, alongside other measures, will be continually assessed over the next three years.

The medical team include Paediatric Haematologist Professor Robert Wynn and Dr. Simon Jones from RMCH, who have experience of bone marrow transplantation for children with metabolic enzyme deficiencies.

Professor Wynn said: "RMCH has a long-standing expertise in [cell therapy](#) of metabolic diseases, and the original ideas and early attempts to use gene therapies in these diseases were three decades ago.

"This advance builds on that clinical experience and those ideas. We hope and expect that this gene therapy approach will make our treatments safer, more effective and, course, most importantly will lead to better lives for our patients."

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