First patient trials new treatment for rare inherited disease

August 12 2014

Jack Baird will be the UK's first patient to try a new treatment

Researchers at The University of Manchester and The Royal Manchester Children's Hospital have recruited the first child into a new study, which aims to evaluate the clinical effectiveness of a treatment developed in Manchester.

Funded by charity, The Society for Mucopolysaccharide Diseases (The MPS Society), the study could alter the lives of patients with Sanfilippo Disease – a fatal inherited condition which causes progressive dementia in children.

Jack Baird, who is four years old and from Sunderland, has the condition Sanfilippo Disease, also known as Mucopolysaccharidosis (MPS) III,

which affects around one in 85,000 people in the UK.

Sanfilippo Disease is a progressive, genetic and life-threatening disease for which there is currently no effective treatment. The syndrome is diagnosed in childhood, with sufferers experiencing deafness, hyperactivity and behavioural problems, progressive developmental delay, and seizures during the later stages of the condition. The condition is usually fatal in late childhood or early adulthood.

"Jack's condition means that he doesn't speak much, is very hyperactive and has to be sedated to go to sleep. Jack isn't very interested in toys, but he loves going to school, and out elsewhere. He enjoys going on the bus and going to Asda where everybody knows him.

"We found out about the clinical trial through The MPS Society, which was working with Dr Jones at The Royal Manchester Children's Hospital. We got involved initially in 2012, by helping to fundraise for the study. We know that the treatment is not going to save Jack, but if the drug works we will have more time to make more memories, and memories are priceless," explained Gemma Nelson, Jack's mum.

The study conducted by the National Institute for Health Research (NIHR) / Wellcome Trust Manchester Clinical Research Facility at The Royal Manchester Children's Hospital builds on initial research from The University of Manchester, which was funded by the MPS Society. It aims to establish whether high doses of the treatment Genistein Aglycone is effective in people with Sanfilippo Disease.

People with Sanfilippo Disease have too much of the substance heparan sulphate in their cells, particularly cells in the brain, because they lack the enzyme that usually breaks the heparan sulphate down. It is thought that Genistein Aglycone works by blocking the production of heparan sulphate and associated damage to the cells.

Genistein is a naturally occurring chemical found in soya beans. In the study the researchers will use a synthetic version, Genistein Aglycone, to maximise absorption through the gut.

Previous research in patients with Sanfilippo Disease has shown that low doses of Genistein reduce the heparan sulphate in the blood and urine, but are not sufficient to be effective in the brain1. However, research at The University of Manchester using higher doses of Genistein Alygone in the mouse model of Sanfilippo Disease has shown that this is effective in reducing neurodegeneration2,3.

Dr Brian Bigger, Chief Scientific Investigator for the study from The University of Manchester said: "It is fantastic to see a treatment we developed at The University of Manchester, in collaboration with clinicians, reach the point where we can test its effectiveness in patients. A US study published last year, demonstrated the safety of high doses of Genistein Alygone in patients with Sanfilippo Disease4.

"This new study is the first to test the effectiveness of the higher doses of Genistein, which are thought to be of the strength required to see an effect in the brain. We are looking forward to analysing the results of the trial and hope that the treatment will benefit patients."

Dr Simon Jones, Consultant in Paediatric Inherited Metabolic Disease at Saint Mary's Hospital, Manchester, who is leading the study explains: It's important for us to undertake research in rare diseases, like Sanfilippo Disease, so that we can provide these patients with the best possible care. During the later stages of the disease, patients experience seizures, become wheelchair bound and can have trouble swallowing.

"This new study is open to children aged 2–15 years old. Patients taking part in the study will receive either Genistein Aglycone or placebo (an inactive substance that looks like the treatment) with food, over a period

of 12 months.

After 12 months all children will receive Genistein Aglycone for a further 12 months", adds Dr Jones, who is also Honorary Senior Lecturer at The University of Manchester.

Over the course of the study, patients will attend up to nine clinic visits where they will have the level of heparan sulphate in the spinal fluid measured, as well as undergoing physical examinations and other assessments. It is anticipated that the study will take around three years to complete.

"Sanfilippo Disease is rare, affecting about 150 children in the UK. The MPS Society is proud of its collaboration with The University of Manchester and The Royal Manchester Children's Hospital, which will bring this important research to the clinic and the patient. The funds raised so far allow for 24 children to be on the Genistein clinical trial. We need to raise a further £120,000, so that another six children can be involved and I'd like to urge people interested in making a real difference to donate, however big or small, and get in touch with The MPS Society," adds Christine Lavery, Chief Executive of The MPS Society, the major funder of the study.

More information: References

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Provided by University of Manchester