A Gene Therapy Clinical Trial Option
for Children With

Tay-Sachs Disease or Sandhoff Disease

As a caregiver of a child diagnosed with GM2 gangliosidosis (Tay-Sachs disease or Sandhoff disease), you may be looking for treatment options for your child. Having your child take part in a clinical trial is a big decision. We are here to help you carefully consider whether this gene therapy clinical trial is a good option for your child.

Queen's University

Gene therapy for Tay-Sachs disease and Sandhoff disease

Researchers are conducting a clinical trial to learn if a gene therapy called TSHA-101 can help treat children with Tay-Sachs disease or Sandhoff disease. Tay-Sachs disease and Sandhoff disease are caused by 2 genes that do not work properly. This gene therapy trial aims to deliver new, working copies of both of these genes in an investigational treatment called TSHA-101.

This clinical trial aims to test the safety of TSHA-101 and its effectiveness at improving survival and symptoms of Tay-Sachs disease and Sandhoff disease. This will be the first time that TSHA-101 is studied in humans. Every qualified child enrolled in the clinical trial will receive the gene therapy (a one-time treatment of TSHA-101) and will be monitored regularly for up to 5 years to check the effect on their health and symptoms.

Who can participate in the clinical trial?

The clinical trial will enroll children who:

- Are aged 12 months or younger
- Have been diagnosed with Tay-Sachs disease or Sandhoff disease

The clinical trial team will do assessments and discuss other factors with you to ensure the trial is appropriate for your child.

Making an informed choice for your child

Participating in a clinical trial may be a good opportunity for some families, but everyone's situation is different. We encourage you to ask your healthcare team questions about participating in this clinical trial and talk it over with trusted family and friends. Having all the information you need will help you feel confident in your decision.

The clinical trial team is available to answer your questions and talk about concerns you may have with TSHA-101 and the clinical trial. A description of this clinical trial will also be available on www.clinicaltrials.gov.

Learn more

If you are interested in learning more about this clinical trial and if it would be a good option for your child, you can contact the research team at info@TSD-SDGTXtrial.com

What is involved in the clinical trial?

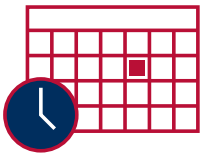
Screening

To see if your child qualifies for the clinical trial, the clinical trial team will ask questions and do a series of assessments, including laboratory tests and exams of your child's health and function. These assessments will take place over the course of up to 30 days.

Gene therapy procedure

If your child qualifies, he or she will receive 1 dose of TSHA-101. The procedure involves an injection into the spinal fluid, known as intrathecal delivery, while your child is sedated. After the injection, your child will stay in the hospital for monitoring.

Follow-up assessments



After receiving TSHA-101, your child will have regular follow-up visits at the clinical trial site to assess his or her health and symptoms.

FIRST 3 MONTHS	MONTHS 3-12	YEAR 2	YEARS 3-5
every week or every 2 weeks	every 3 months	every 6 months	1 visit to clinical trial site per year and 1 phone visit per year

Frequently asked questions

Q. How could the same gene therapy work for both Tay-Sachs disease and Sandhoff disease?

A. Although Tay-Sachs disease and Sandhoff disease are different forms of GM2 gangliosidosis, both are caused when an enzyme called Hex A doesn't work properly. Hex A is an enzyme that breaks down GM2, a type of fat found in the brain. In Tay-Sachs disease and Sandhoff disease, the Hex A enzyme doesn't break down the GM2 fat properly, and GM2 starts to build up. Too much GM2 destroys brain cells, which leads to Tay-Sachs disease and Sandhoff disease.

Hex A

Genes contain instructions for the body to make proteins, and enzymes are a type of protein. Tay-Sachs disease and Sandhoff disease are both caused by changes, or mutations, in the genes that make the Hex A enzyme. Hex A is made of 2 subunits, or building blocks, alpha and beta. Changes in the alpha subunit cause Tay-Sachs disease, and changes in the beta subunit cause Sandhoff disease. TSHA-101 is designed to deliver new, working copies of the genes that create both subunits so that Hex A can be made correctly.

Q. What is TSHA-101?

A. TSHA-101 is a liquid that contains new, working copies of the genes for Hex A. The new, working genes are delivered to cells through a package called a vector. TSHA-101 uses a specially modified virus called adeno-associated virus 9, or AAV9, as a vector. TSHA-101 is given as an injection into the spinal fluid, which is then carried to the brain so that the new genes can go into the cells that need them.

Q. What are the potential risks and benefits of participating in this clinical trial?

A. Every qualified child enrolled in the trial will receive TSHA-101. Children who participate in the clinical trial may experience side effects. However, because this will be the first time that TSHA-101 will be studied in humans, the potential side effects in humans are unknown. The benefits of TSHA-101 in humans are also currently unknown. Previous studies in a laboratory and in mice that have a condition like Sandhoff disease suggest that TSHA-101 may slow or stop the progression of Tay-Sachs disease and Sandhoff disease.

Frequently asked questions (continued)

Q. Who is conducting this clinical trial?

A. The clinical trial is sponsored and conducted by Queen's University in Ontario, Canada. The trial received financial support from the Canadian Glycomics Network (GlycoNet) and from Taysha Gene Therapies, Inc., a patient-centric gene therapy company focused on monogenic diseases of the central nervous system.

Q. Where will this clinical trial take place? Will I have to pay for travel?

A. Clinical trial visits will be conducted in person at Kingston Health Sciences Center at Queen's University in Kingston, Ontario, Canada. The caregiver of a participating child must agree to reside within 30 kilometers (approximately 19 miles) of the study site during the 1-month screening period and until at least 3 months after treatment, for a total of 4 months. **Non-Canadian families will be required to obtain travel medical insurance coverage for the duration of their stay in Kingston, Ontario, Canada. Parents/guardians of a study participant will receive reimbursement for eligible and appropriate expenses incurred while in Kingston, Ontario, Canada for clinical trial site visits:**

- Driving/mileage
- Tolls/parking
- Flights
- Accommodations
- Rental cars
- Public transportation/taxi
- Meals/food
- Travel medical insurance

Notes