Clinical Trial Information for Sanfilippo Syndrome Type C

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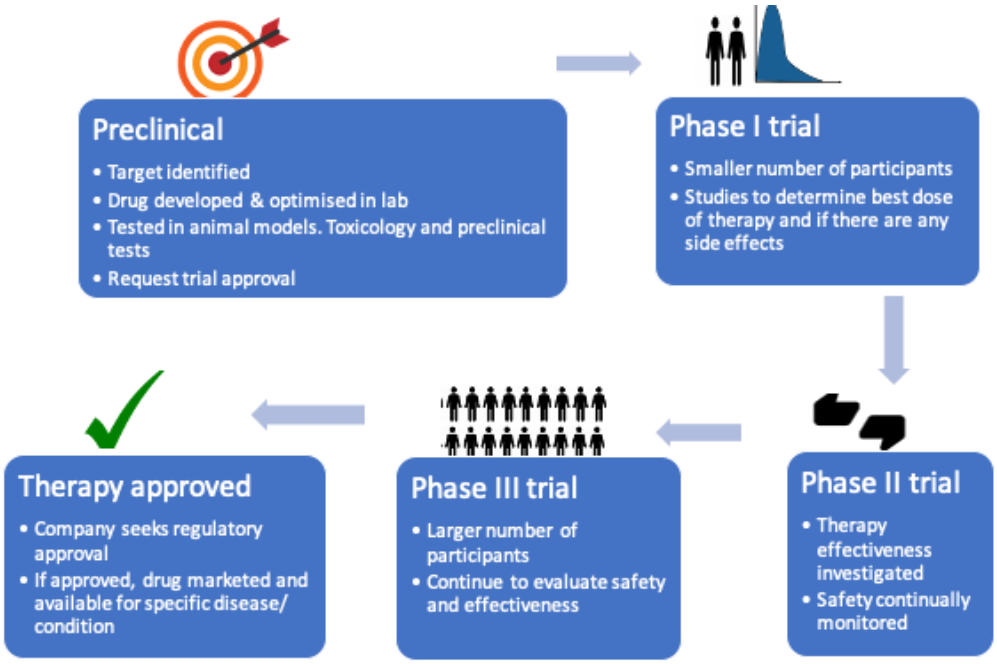
Sanfilippo Children's Foundation

Introduction

The aim of a clinical trial is to determine whether a potential treatment is safe and that it works. Clinical trials involving rare diseases may be run differently to a usual clinical trial, often due to the small number of people with the disease. The process may be shorter than a usual clinical trial, and different phases may be combined. The diagram below outlines some common steps seen in the drug development process:



There are criteria that must be fulfilled in order to be included in a clinical trial. Similarly, there can be criteria that may render someone unable to participate. These strict criteria are chosen by the company carrying out the trial, to protect the safety of the trial participants and to give the trial the best chance of proving that the therapy works.

A well-executed clinical trial that proves a therapy to be safe and effective offers the best chance at getting regulatory approval and allowing more patients to access it.

Participating in a clinical trial is not a guarantee of a treatment, as not all therapies are proven to be safe and effective; however, at this point in time, clinical trials offer the only hope of getting early access to potential Sanfilippo treatments.

This document contains information on clinical trials for Sanfilippo Syndrome Type C – a table with a brief overview, a more detailed description and a handy glossary at the end. If you have any questions about this document or would like more information about Sanfilippo and/or clinical trials, please contact the Foundation.

For more information contact the Research Manager at the Sanfilippo Children's Foundation: research@sanfilippo.org.au

Sanfilippo Syndrome Type C Clinical Trials

Company	Trial	Trial Location(s)	Type of Therapy	Mode of Application	Important Inclusion/ Exclusion Criteria (note: others may also apply)	Current Results/ Progress (that has been made public)	Trial status
Lundquist Institute for Biomedical Innovation	Anakinra drug trial (all types of Sanfilippo) Phase II/III.	USA	Anti-inflammatory drug (already approved for rheumatoid arthritis)	Injection of drug subcutaneously (under the skin) once a day	**Inclusion**: Ages 4+. All Sanfilippo Types. Attenuated patients accepted. **Exclusion**: Current participation in another clinical trial. Previous or current treatment with specific anti-inflammatory drugs. Severe liver or kidney disease/ impairment.	Update from 2021 WORLDSymosium: Recruitment and data analysis are ongoing, but initial results with 8 patients (either type A or B) are encouraging. Parent-reported measures of symptoms such as movement, fatigue, behaviour, pain or parental stress are indicating improvements. Further follow-up is required to confirm results.	Active, not recruiting

Please note: If your child does not meet the strict criteria for a Clinical Trial, it does not mean they will be unable to receive that treatment in the future (if the Clinical Trial is successful and the therapy is approved).

Current Clinical Trials and Clinical Trial Plans for Sanfilippo Type C

Updated April 2021

Gene therapy clinical trials

Gene therapy for Sanfilippo type C

In November 2018 Phoenix Nest Inc. acquired rights to the Sanfilippo type C gene therapy developed by Dr. Brian Bigger at the University of Manchester. This approach involves gene therapy using an AAV vector to deliver a healthy copy of the gene that is faulty in Sanfilippo type C - HGSNAT. A clinical trial is currently being planned, but more pre-clinical tests are necessary so it may be a while before the trial starts.

Other targets

Researchers are working to find other drugs that may reduce the progression of Sanfilippo and improve quality of life, these include:

- Substrate reduction therapies to reduce the amount of heparin sulphate that is produced by the body so that there is less to build up
- Chaperones that help the faulty enzymes fold correctly and do their job of breaking down heparin sulphate
- Drugs that increase a process called “autophagy” that clears unnecessary or dysfunctional components from cells, allowing them to function better
- Drugs to target certain parts of the immune system that are thought to contribute to the cognitive decline seen in children with Sanfilippo
- Treatments targeting the symptoms of the disease such as behavioural problems, sleeping issues or lung function, which aim to improve the quality of life of children with Sanfilippo and their families.

There are two trials in this category, either started or being planned:

- Anakinra, a drug that suppresses inflammation, is in clinical trial at the Lundquist Institute (formerly LA Biomed) in the USA. It is thought that Anakinra could target the inflammation in the brain which is common across all types of Sanfilippo. A phase II/III trial is currently underway, which was developed in collaboration with, and funded by,

Cure Sanfilippo Foundation and other community stakeholders. It aims to assess whether Anakinra can improve the behavioural and other physical symptoms of Sanfilippo. Recruitment and data analysis are still ongoing, but so far the trial has treated 8 patients with either Sanfilippo type A or B. It is showing encouraging signs with most parents reporting improvements in one or more symptoms, such as movement, fatigue, behaviour, pain or parental stress. Longer follow-up and more detailed statistical analysis of the data is still required to determine if the treatment is having a significant effect on symptoms. This drug is approved for the treatment of rheumatoid arthritis (RA). There is a very wide inclusion criteria for this trial – all ages, types and attenuated patients are able to participate (please note that the trial is active but not currently recruiting). More information about this trial can be found on its clinicaltrials.gov page.

- A clinical trial of Trehalose, a small sugar, is being planned by Seelos Therapeutics and Team Sanfilippo in the USA and Europe. Trehalose is to be given intravenously (through the vein). It is able to enter the central nervous system (the brain and spinal cord), stabilise proteins, and promote autophagy, a process to dispose of aggregated proteins and other cellular waste. Clinical trial design currently being negotiated with the FDA and EU.

For more information contact the Research Manager at the Sanfilippo Children's Foundation: research@sanfilippo.org.au

Glossary

Adeno-associated virus (AAV)

An adeno-associated virus is a specific virus that is able to infect humans, but not currently known to cause disease. Because of these features, researchers want to use this virus as a delivery vehicle, in order to deliver therapies into cells. There are many different variants of AAV that occur (both naturally and engineered) such as AAV9 and AAVrh10, and some can cross the blood-brain barrier.

Attenuated form

An attenuated form of Sanfilippo is one that is less severe and/or slower to progress than a severe Sanfilippo form. Whether an individual has a severe or attenuated form of Sanfilippo largely depends on the type of genetic change that the individual has.

Blood-brain barrier

The blood-brain barrier (BBB) is a very thin layer of cells that separates the blood from the central nervous system (CNS). It is highly selective, meaning that only specific things are able to exit the bloodstream and enter the CNS. This helps to protect the brain from harmful bacteria and viruses, but it can hinder the effectiveness of therapies that must cross the BBB to work in the brain.

CNS (Central nervous system)

The CNS is comprised of the brain and the spinal cord.

Clinical Trial

Clinical trials are research studies that test a specific therapy in humans, with the aim of confirming whether a therapy is safe and effective to be used in a specific population.

Gene Therapy

Gene Therapy involves the delivery of a healthy copy of a gene into the body. The four subtypes of Sanfilippo correspond to four different genes. For MPS IIIC, the gene involved is called *HGSNAT*.

Heparan sulfate

Heparan sulfate is a complex, long, linear sugar molecule found in the body. It is an important molecule that is made by the body, but also must be broken down after use. In Sanfilippo Syndrome, one of the four enzymes involved in degrading heparan sulfate is faulty.

Intravenous injection

An intravenous injection is an injection directly into the vein. Common sites include the elbow, wrist, or back of the hand.

Phases of clinical trial

Clinical trial Phases are different stages or steps with different goals and experimental set ups. Traditionally, there are four stages: I, II, III and IV. The increasing numbers represent a more advanced stage of the clinical trial.

Subcutaneous injection

A subcutaneous injection is an injection directly under the skin, between the skin and muscle.

Substrate reduction therapy (SRT)

Substrate reduction therapy aims to reduce the amount of substrate involved in a disease state, in order to improve symptoms. In the case of Sanfilippo, SRT involves therapies that aim to decrease the amount of heparan sulfate, which normally builds up to toxic levels inside the body.