Protocol Summary

of Clinical Trial

The protocol of a clinical study is a document that explains why and how a study will be carried out.

A first-in-human study of S233107 in participants with spinocerebellar ataxia type 3

Full scientific title: *A Phase 1b/2a first-in-human, multicentre, randomized, double-blind, placebo-controlled study of multiple ascending dose (Part1) followed by an open-label extension (Part 2) to assess the safety, tolerability, and pharmacokinetics of intrathecally administered S233107 in participants with spinocerebellar ataxia type 3 (EU Study Number: 2025-525111-17-00)*

1 Why is this study needed?

This study is needed to find a specific treatment for a type of degenerative disease called spinocerebellar ataxia type 3 (SCA3). Symptoms of ataxia are unsteady walking, balance, and speech problems.

SCA3 is caused by changes in a gene called ATXN3. These changes lead to a faulty protein called Ataxin-3, which disrupts how brain cells work.

The study drug, S233107, is designed to reduce the amount of the faulty version of the Ataxin-3 protein made by the body. Researchers believe that S233107 may help to treat patients with SCA3. This study is important because it could lead to a treatment that prevents the disease from worsening in patients with SCA3.

2 What are we mainly looking for?

What is the main goal of the study?

The main goal of the study is to find out if S233107 is safe and how well participants with SCA3 tolerate receiving multiple increasing doses of it.

What are the main study endpoints?

A study endpoint is the criteria used to decide whether a study goal is reached or not. The main endpoints of this study are:

- The number of unwanted medical events that occur during the study and how serious they are.
- The number of abnormal findings in heart test (ECGs), blood and spinal fluid tests, as well as in vital signs (such as blood pressure and heart rate), body weight, and suicide risk assessments.

3 What about the other goals of the study?

What are the other goals of this study?

The other goal of this study is to understand how the body processes S233107. Scientists call this pharmacokinetics (PK).

What are the other study endpoints?

The other study endpoints are PK measurements, including the levels of S233107 in the spinal fluid and blood at different times.

4 Who is participating in the study?

Approximately, 62 participants are expected in the study.

To take part, participants have to:

- Have a confirmed diagnosis of SCA3 through genetic test.
- Be an adult aged 18 to 65 years.
- Be able to walk on their own without any support.

Participants cannot take part if they have other types of brain disorders, major reduced kidney function, or a history or presence of significant suicide risk.

5 How is the study carried out?

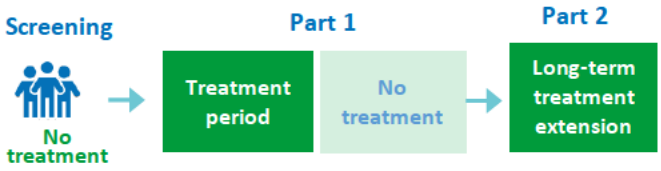
The study has two parts: Part 1 and Part 2.
Part 1 is "double-blind", which means that neither the participants nor the research doctors know which treatment is taken. This is to avoid any influence on the results. Part 2 is "open-label", which means that both the participants and the research doctors know which treatment is taken.

There will be a screening period before Part 1. During this time, the doctors will check if the participants meet all requirements to take part in the study.

Part 1: Small groups of participants will receive different doses of S233107 or placebo. A placebo looks like S233107 but does not contain any real medicine. The first group receives the lowest dose, then each new group receives a higher dose. This part is called "randomised", meaning the participants are put into a group that receives either S233107 or a placebo by chance.

Part 2: Participants who complete Part 1 will receive S233107 until the end of the study. There is no placebo in this part. Participants will continue to have regular check-ups for any unwanted medical events.

The study design is presented in the image below:



6 What are the treatments and tests used in the study?

Participants will receive S233107 or placebo. S233107 or placebo will be given as an injection into the spinal fluid through a needle in the lower back (lumbar puncture).

The participants will visit the study doctor regularly. During the visits, the doctor will collect information about the participants' health. Participants will give blood, urine, spinal fluid samples, and undergo exams to see how the brain, spine, nerves and body are working (neurological and physical exams). They will have tests to record heart electrical activity and imaging tests of the brain. Participants will also have to wear a device at the wrist and ankle to measure different aspects of how a person walks and maintains balance.

7 What are the possible benefits and risks?

The participant's disease may or may not improve with the study drug. Participants will receive close medical follow-up. The results of this study will help the researchers learn more about the study drugs. Studies such as this one could lead in the future to a treatment that prevents the disease from worsening for people with similar medical conditions.

The study is designed to be safe, with strict safety rules and regular check-ups. Some discomfort may be felt during the lumbar puncture and the planned tests (blood sampling, imaging and recording of heart electrical activity). As with all medicines, S233107 treatment may cause side effects. Every care will be taken to avoid and treat side effects if they occur.

This is the first time S233107 is being given to humans, there may be risks that we do not yet know about. The study doctors will tell the participants about the known and possible risks and side effects of S233107.

Before enrolling in the study, participants will be provided with an informed consent document, and they will have the opportunity to ask questions and discuss any concerns with their healthcare provider. The informed consent document will explain all the known benefits, risks, and side effects. This is a document that provides people with the information they need to decide if they want to join the study.