

ForPatients

by Roche

Huntington Disease (HD)

A clinical trial to compare different doses of tominersen with a placebo in people with prodromal (very early subtle signs) and early manifest Huntington's disease

GENERATION HD2. A Study to Evaluate the Safety, Biomarkers, and Efficacy of Tominersen Compared With Placebo in Participants With Prodromal and Early Manifest Huntington's Disease.

Trial Status
Active, not recruiting

Trial Runs In
15 Countries

Trial Identifier
NCT05686551 Other
2022-001991-32
2023-503928-10-00 BN42489

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

A Phase II, Randomized, Double-blind, Placebo-controlled, Dose-finding Study to Evaluate the Safety, Biomarkers, and Efficacy of Tominersen in Individuals With Prodromal and Early Manifest Huntington's Disease

Trial Summary:

This study will evaluate the safety, biomarkers, and efficacy of tominersen compared with placebo in participants with prodromal and early manifest Huntington's Disease (HD).

Hoffmann-La Roche
Sponsor

Phase 2
Phase

NCT05686551 Other 2022-001991-32 2023-503928-10-00 BN42489
Trial Identifiers

Eligibility Criteria:

Gender
All

Age
#25 Years & # 50 Years

Healthy Volunteers
No

1. Why is the GENERATION HD2 clinical trial needed?

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Huntington's disease (HD) is a rare, inherited (genetic) disease that affects a person's moving, thinking and behaviour. It is a progressive disease, which means that it gets worse over time, and there is currently no way to prevent, slow or stop disease progression. Subtle changes in thinking, mood and behaviour are very early symptoms of HD (known as 'prodromal' HD). Jerky, involuntary movements of the body can make walking and eating difficult (known as 'early manifest HD'). A change (mutation) in a single huntingtin gene (HTT) causes HD. People who carry this gene make a toxic (mutant) version of the huntingtin protein called mHTT. mHTT builds up in the brain, which, over time, causes damage to nerves and HD symptoms.

Tominersen is an experimental drug, which means that health authorities have not approved it for the treatment of HD. The GENERATION HD2 clinical trial aims to compare the effects, good or bad, of tominersen against placebo to find a dose that may benefit people with prodromal or early manifest HD.

2. How does the GENERATION HD2 clinical trial work?

This clinical trial enrolled people with a health condition called HD. People with prodromal or early manifest HD could take part. The trial will be done in two periods. In the initial period, participants were given tominersen OR a placebo every 4 months for at least 16 months, which continued until all the participants completed 16 months of treatment. The treatment was administered by lumbar puncture, in which a needle is inserted into the lower back to deliver the medication into the cerebrospinal fluid surrounding the brain and spinal cord. This is a common medical procedure (known as 'intrathecal injection') which takes about 15–20 minutes. The clinical trial doctor met the participants (and their study companion for some visits) every 4 months, to check how the participant responds to the treatment and to see if they have any side effects (unwanted effects of a drug or medical treatment). After completion of the initial part of the study, if the development of tominersen continues, participants will have the option to receive tominersen in an extension phase of the trial for approximately 2 years.

3. What are the main endpoints of the GENERATION HD2 clinical trial?

The main clinical trial endpoints (the main results measured in the trial to see if the drug has worked) for the initial period, are:

- The number and seriousness of any side effects
- Changes in laboratory results from the cerebrospinal fluid, including the amount of white blood cells and protein
- Changes in results from the brain magnetic resonance imaging (MRI) scan
- Changes in function (for example, the ability to move, think and perform daily activities)

The main clinical trial endpoint for the extension period is to check the number and seriousness of any side effects.

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The other clinical trial endpoints for the initial period include changes in the amount of an indicator of nerve damage in cerebrospinal fluid and the effects of tominersen on the immune system. The other clinical trial endpoints for the extension period include the effects of tominersen on the immune system.

4. Who can take part in this clinical trial?

People took part in the initial period of the trial if they fit certain criteria, including if they:

- Are aged 25 to 50 years (at the start of the trial)
- Have a CAP score (a research calculation based on age and the number of times the mutated section within the HD gene repeats itself – known as the CAG number) of 400 to 500
- Have been diagnosed with early manifest HD or are carriers of the abnormal huntingtin gene who are starting to show very early, subtle signs of HD (known as prodromal HD). This may only be clear during a detailed examination by a physician
- Can tolerate giving blood, having lumbar punctures and MRIs
- Have a person who can act as a 'study companion' throughout the trial

People could not to take part in the initial period of the trial if they:

- Are receiving or have had certain treatments before, including those for HD that may affect HTT levels
- Have a history of gene therapy, cell transplantation, or brain surgery
- Have certain other medical conditions, including a build-up of fluid in the brain (hydrocephalus), chronic migraines, certain mental health issues or certain infections, or are pregnant or breastfeeding, or are planning to become pregnant during or soon after the clinical trial

People could take part in the optional extension period of the trial, if available, if they meet certain criteria including, if they completed the initial treatment period and remain in the safety follow-up period until the extension period starts.

5. What treatment will participants be given in the clinical trial?

During the initial period, participants were split into 3 groups randomly (by chance) and given:

- **Group 1:** 60 milligrams (mg) of tominersen, given as an injection by lumbar puncture (intrathecal injection) once every 4 months for 16 months **OR**
- **Group 2:** 100 mg of tominersen, given as an intrathecal injection once every 4 months for 16 months **OR**
- **Group 3:** an equal amount of placebo, given as an intrathecal injection once every 4 months for 16 months

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Participants had an equal chance of being placed in any group. This is a 'placebo-controlled' clinical trial, which means that one of the groups will be given a substance with no active ingredients (also known as a 'placebo'); it looks like the drug being tested but does not contain any real medicine. This initial period of this trial was a double-blinded period, which means that neither the participant nor the clinical trial doctor can choose or know the group the participant is in until the trial is over. This approach helps to prevent bias.

After completing the double-blinded treatment period, and if the results from the main double-blind period confirms that tominersen development continues, participants will have the option to continue into the optional extension part of the trial, called the "open-label extension (OLE) period. "Open-label" means everyone involved, including the participant and the clinical trial doctor, will know that the participant will be given tominersen. In the open-label period, all participants will receive tominersen, given as an intrathecal injection once every 4 months for approximately 2 years.

6. Are there any risks or benefits in taking part in this clinical trial?

The safety or effectiveness of the experimental treatment may not be fully known at the time of the trial. Most trials involve some risks to the participant. However, it may not be greater than the risks related to routine medical care or the natural progression of the health condition. People who would like to participate will be told about any risks and benefits of taking part in the clinical trial, as well as any additional procedures, tests, or assessments they will be asked to undergo. All of these will be described in an informed consent document (a document that provides people with the information they need to decide to volunteer for the clinical trial).

Risks associated with the clinical trial drug Participants may have side effects from the drug used in this clinical trial. Side effects can be mild to severe, even life-threatening, and vary from person to person. Participants will be closely monitored during the clinical trial; safety assessments will be performed regularly.

People considering enrolling in the trial will be told about the known side effects of tominersen and possible side effects based on human and laboratory studies or knowledge of similar drugs. They will also be informed of any known side effects of having an intrathecal injection.

Potential benefits associated with the clinical trial

Participants' health may or may not improve from participation in the clinical trial. Still, the information collected may help other people with similar medical conditions in the future.

Inclusion Criteria:

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- HD gene expansion mutation carrier status with a cytosine-adenine-guanine-age product (CAP) score of 400-500 inclusive

Either:

- Prodromal HD (defined as Diagnostic Confidence Level (DCL) 2 to 3, Independence Scale (IS) #70, and TFC #8); or
- Early manifest HD (defined as DCL 4, IS #70, and TFC #8);
- Total body weight > 40 kilograms (kg) and a body mass index (BMI) within the range of 18-32 kilograms per meter square (kg/m²)
- Study companion

Exclusion Criteria:

- Current or previous use of an antisense oligonucleotide (ASO) (including small interfering ribonucleic acid [RNA]) or any huntingtin gene/protein (HTT) lowering therapy (including tominersen)
- Anti-platelet or anticoagulant therapy within 14 days prior to screening or anticipated use during the study, including, but not limited to, aspirin (unless # 81 milligrams per day [mg/day]), clopidogrel, dipyridamole, warfarin, dabigatran, rivaroxaban, apixaban, and heparin
- History of gene therapy, cell transplantation, or brain surgery
- Hydrocephalus
- Pregnancy or breastfeeding, or intention of becoming pregnant during the study or within 5 months after the final dose of study drug
- History of attempted suicide or suicidal ideation with plan (i.e., active suicidal ideation) that required hospital visit and/or change in level of care within 12 months prior to screening