NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the safety of NIO752 in people with progressive supranuclear palsy

Thank you!

Thank you to the participants who took part in the clinical trial for **progressive supranuclear palsy**. Every participant helped the researchers learn more about the trial drug **NIO752**.

Novartis sponsored this trial and believes it is important to share what was learned from the results of this trial with the participants and the public. We hope this helps the participants understand their important role in medical research.

Trial information

Trial number: CNIO752A02101

Novartis drug studied: NIO752

Sponsor: Novartis

If you were a participant and have any questions about the results, please talk to the doctor or staff at the trial site.

This summary only shows the results of a single clinical trial. Other clinical trials may have different results.

What was the main purpose of this trial?

The purpose of this trial was to learn about the safety of different doses of **NIO752** in people with progressive supranuclear palsy.

Progressive supranuclear palsy, also called **PSP**, is a rare disease that damages cells in the brain. People with PSP have problems with balance, eye movements, swallowing, and thinking.

Past research found that the damaged cells in the brain have too many tau proteins. **Tau proteins** are in healthy brain cells, but a buildup of these proteins can damage brain cells. Researchers do not know what causes PSP, but they think the buildup of tau proteins could play a role in PSP.

Currently, there is no treatment to delay or stop PSP from getting worse.

NIO752 is a trial drug designed to block cells from making tau proteins.

The trial's purpose was to answer this main question:

- What medical problems, also called adverse events, happened during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial. Adverse events **may** or **may not** be caused by treatments in the trial.

Why the researchers did this trial

This trial was the first time that **NIO752** was given to people. Therefore, the researchers tested different doses in different groups of participants to find a dose without safety concerns. The researchers also carefully checked all the medical problems that happened during the trial in case the doses needed to change. This is the first step in testing a trial drug in people.

How long was this trial?

The trial began in February 2021 and ended in October 2024.

Who was in this trial?

59 participants with PSP joined this trial – 31 men and 28 women. Participants' ages ranged from 51 to 75 years. Their average age was 66 years.

The number of participants by race is shown below.

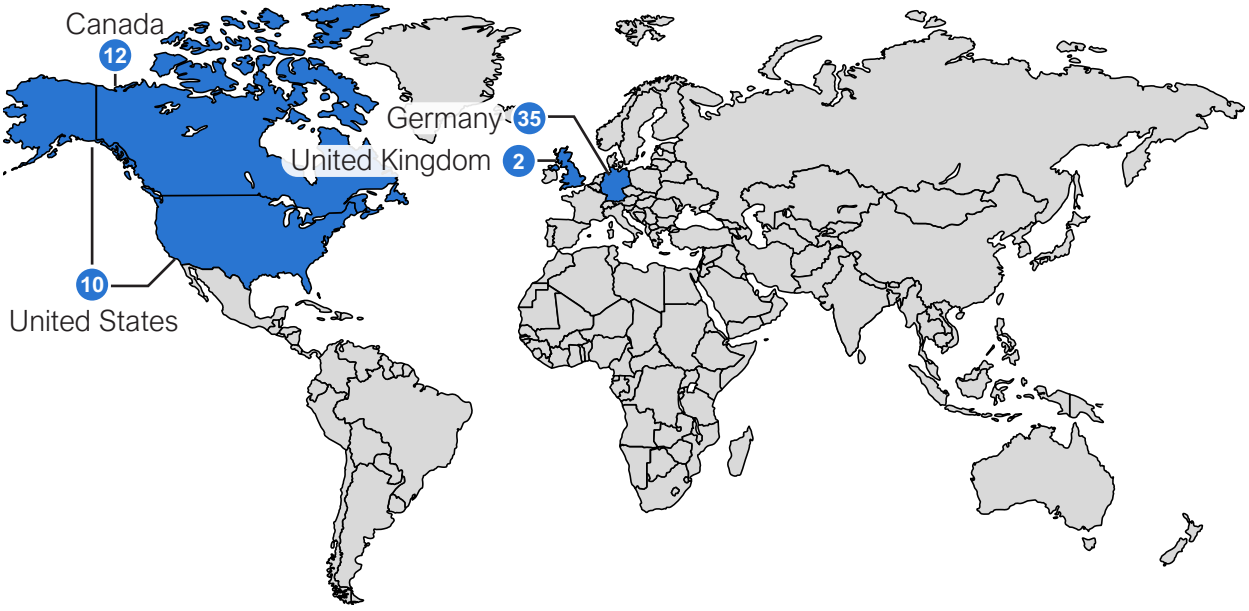
Race

1	Asian
1	Black or African American
57	White

The participants could take part in this trial if they:

- Had mild or moderate PSP for less than 5 years
- Could walk at least 5 steps with little help
- Had not attempted suicide or needed hospital care due to plans of suicide within the past year

59 participants from 4 countries received treatment. The map below shows the number of participants who took part in each country.



What treatments did the participants receive?

The treatments in this trial were:

NIO752 – given as an intrathecal (IT) injection a total of 4 times. An **IT injection** is given through a thin needle placed in the lower back and into the fluid around the spinal cord.

This trial looked at different doses of **NIO752**.

Placebo – given as an IT injection a total of 4 times. It looks like the trial drug but does not have any drug in it. Using a placebo helps researchers better understand the effect of a trial drug.

Participants could continue taking certain medicines for PSP during the trial.

Researchers used a computer to randomly assign participants to receive one of the treatments listed above.

The participants, researchers, and trial staff did not know what treatment the participants were receiving. Some trials are done this way because knowing what treatment the participants receive can affect the results of the trial. Doing a trial this way helps to make sure that the results are looked at with fairness across all treatments.

What happened during this trial?

Before treatment

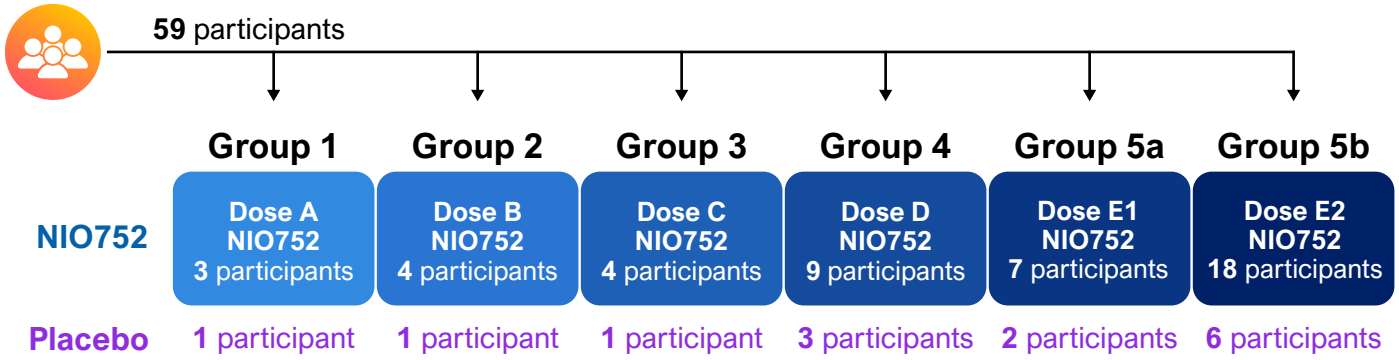
About 6 weeks

The trial staff checked to make sure the participants could be in this trial.

During treatment

Up to about 9 months

The graphic below shows how many participants in each group were assigned each treatment. It was planned for each participant to receive either **NIO752** or **placebo** a total of 4 times.



First, 2 participants received Dose A of **NIO752** or **placebo** in Group 1. The researchers checked for any safety concerns for at least 2 days before giving **NIO752** or **placebo** to the next participant. After everyone in Group 1 received **NIO752** or **placebo**, researchers checked for any safety concerns before giving a different dose of **NIO752** to 2 participants in the next group. This continued until participants in Groups 5a and 5b received their dose of **NIO752**.

After treatment

Up to about 9 months

Trial staff checked participants for any medical problems until up to about 9 months after participants' first dose of trial treatment.

Trial staff checked the participants' general health throughout the trial.

What were the main results of this trial?

What medical problems, also called adverse events, happened during this trial?

Trial doctors keep track of all medical problems, also called **adverse events**, that happen in trials. They track adverse events even if they think the adverse events are not related to the trial treatments.

Many trials are needed to know if a drug or treatment causes an adverse event.

This section is a summary of the adverse events that happened from the start of treatment until about one year after the first dose of trial treatment.

An **adverse event** is:

- Any **sign or symptom** that the participants have during a trial
- Considered **serious** when it is life-threatening, causes lasting problems, the participant needs hospital care, or results in death

Adverse events **may** or **may not** be caused by treatments in the trial.

Almost all the participants (58 of 59) had adverse events. 22 participants had serious adverse events. 2 participants left the trial due to an adverse event. 2 participants died. The researchers concluded there were some safety concerns at certain doses of **NIO752** in this trial.

How many participants had adverse events?

	Group 1 Dose A NIO752 3 participants	Group 2 Dose B NIO752 4 participants	Group 3 Dose C NIO752 4 participants	Group 4 Dose D NIO752 9 participants	Group 5a Dose E1 NIO752 7 participants	Group 5b Dose E2 NIO752 18 participants	Groups 1-5b Placebo 14 participants
Had **any adverse event,** including serious and other	3 of 3 100%	4 of 4 100%	3 of 4 75%	9 of 9 100%	7 of 7 100%	18 of 18 100%	14 of 14 100%
Had at least 1 **serious adverse event**	1 of 3 33%	0 of 4 0%	1 of 4 25%	5 of 9 56%	3 of 7 43%	5 of 18 28%	7 of 14 50%
Had at least 1 **other adverse event**	3 of 3 100%	4 of 4 100%	3 of 4 75%	9 of 9 100%	7 of 7 100%	18 of 18 100%	14 of 14 100%
Left the trial due to an adverse event	0 of 3 0%	0 of 4 0%	0 of 4 0%	0 of 9 0%	1 of 7 14%	1 of 18 6%	0 of 14 0%
Died	0 of 3 0%	0 of 4 0%	0 of 4 0%	0 of 9 0%	1 of 7 14%	0 of 18 0%	1 of 14 7%

What serious adverse events did the participants have?

22 participants had serious adverse events.

The table below shows the most common serious adverse events that happened in **2 or more** participants. Additional serious adverse events happened in fewer participants.

	Group 1 Dose A NIO752 3 participants	Group 2 Dose B NIO752 4 participants	Group 3 Dose C NIO752 4 participants	Group 4 Dose D NIO752 9 participants	Group 5a Dose E1 NIO752 7 participants	Group 5b Dose E2 NIO752 18 participants	Groups 1-5b Placebo 14 participants
Part of the intestine bulges into the groin Inguinal hernia	1 of 3 33%	0 of 4 0%	0 of 4 0%	0 of 9 0%	0 of 7 0%	0 of 18 0%	1 of 14 7%
Lung infection from breathing food or liquid into the lungs Pneumonia aspiration	0 of 3 0%	0 of 4 0%	0 of 4 0%	0 of 9 0%	0 of 7 0%	0 of 18 0%	2 of 14 14%
Broken rib Rib fracture	0 of 3 0%	0 of 4 0%	0 of 4 0%	1 of 9 11%	1 of 7 14%	0 of 18 0%	0 of 14 0%
A change in how the brain works, which may affect thinking, memory, mood, and balance Encephalopathy	0 of 3 0%	0 of 4 0%	0 of 4 0%	1 of 9 11%	1 of 7 14%	0 of 18 0%	0 of 14 0%
Medical aid in dying Assisted suicide	0 of 3 0%	0 of 4 0%	0 of 4 0%	0 of 9 0%	1 of 7 14%	0 of 18 0%	1 of 14 7%

What other adverse events did the participants have?

58 participants had other adverse events.

The table below shows the other adverse events that happened in **11 or more** participants. Additional adverse events happened in fewer participants.

	Group 1 Dose A NIO752 3 participants	Group 2 Dose B NIO752 4 participants	Group 3 Dose C NIO752 4 participants	Group 4 Dose D NIO752 9 participants	Group 5a Dose E1 NIO752 7 participants	Group 5b Dose E2 NIO752 18 participants	Groups 1-5b Placebo 14 participants
Fall	2 of 3 67%	1 of 4 25%	2 of 4 50%	4 of 9 44%	6 of 7 86%	4 of 18 22%	7 of 14 50%
Cut on the skin Skin laceration	1 of 3 33%	2 of 4 50%	1 of 4 25%	4 of 9 44%	0 of 7 0%	5 of 18 28%	1 of 14 7%
Back pain	3 of 3 100%	1 of 4 25%	1 of 4 25%	1 of 9 11%	3 of 7 43%	0 of 18 0%	3 of 14 21%
Scratch on the skin Skin abrasion	0 of 3 0%	1 of 4 25%	0 of 4 0%	4 of 9 44%	1 of 7 14%	3 of 18 17%	2 of 14 14%

What other safety measures did researchers look at?

Researchers also checked participants for:

- Unwanted changes in their thoughts, including thoughts of suicide. This was because medicines used to treat PSP, PSP itself, and other diseases can sometimes cause these unwanted changes.
- Signs of inflammation in **cerebrospinal fluid**, also called **CSF**. CSF is the liquid that surrounds the brain and spinal cord. This was because medicines given as an IT injection can sometimes cause inflammation in CSF.

Compared to participants who received **placebo**, those who received **NIO752** had:

- About the same amount of unwanted changes in their thoughts, including thoughts of suicide about 1 year after starting treatment
- Higher levels of certain signs of inflammation in CSF, such as white blood cells, about 1 year after starting treatment

To measure these, the trial staff:

- Asked each participant to answer questions about thoughts of suicide. They looked for changes in these measures after the participants started receiving **NIO752**. They compared their results to those who received **placebo**.
- Collected up to 7 samples of each participant's CSF using a lumbar puncture, also called a **spinal tap**. During a spinal tap, trial staff inserted a needle in the lower back to collect a small amount of CSF. They checked the CSF for signs of inflammation, such as changes in the cells or proteins in the sample.

What were the other results of this trial?

How much and how fast did NIO752 get into participants' CSF and blood?

Overall, the researchers found that:

- The level of **NIO752** in CSF changed as the dose changed
- A low level of **NIO752** stayed in CSF between doses

They also found that:

- The level of **NIO752** in blood changed as the dose changed
- **NIO752** reached its peak level in blood around 3 hours after participants received it
- Most **NIO752** left blood in about 1 day

To learn this, the trial staff took many CSF and blood samples from each participant during the trial. This allowed the researchers to learn how much **NIO752** was in the participants' CSF and blood over time.

Researchers can use these results to decide how often and how much **NIO752** should be given in future trials.

What was learned from this trial?

Researchers learned about the safety of different doses of **NIO752** in people with progressive supranuclear palsy, also called PSP.

The researchers concluded that:

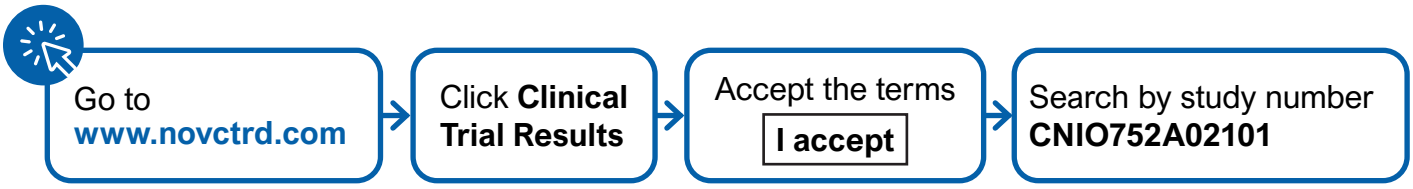
- There were some safety concerns at certain doses of **NIO752** in this trial
- Participants who received **NIO752** had about the same amount of unwanted changes in their thoughts, including thoughts of suicide about 1 year after starting treatment, compared to those who received **placebo**
- Participants who received **NIO752** also had higher signs of CSF inflammation compared to those who received **placebo**
- Overall, the level of **NIO752** in CSF and blood changed as the dose changed

When this summary was written, the sponsor had plans for future trials of **NIO752** in people with health conditions related to the tau protein.

Where can I learn more about this trial?

More information about the results and adverse events in this trial can be found in the scientific summary of the results available on the Novartis Clinical Trial Results website **www.novctrd.com**

Follow these steps to find the scientific summary:



For more information about this trial, go to this website:

- **clinicaltrials.gov** – search using the number **NCT04539041**

Other trials of **NIO752** may appear on the public website above. When there, search for **NIO752**.

Full clinical trial title: A Randomized, Participant, Investigator and Sponsor Blinded, Placebo-Controlled Study to Evaluate the Safety, Tolerability and Pharmacokinetics of Multiple Ascending Doses of Intrathecally Administered NIO752 in Participants with Progressive Supranuclear Palsy

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