Summary of Clinical Trial Results

A study to look at how a certain type of medicine (RO7248824) spread in the brain and spine after an injection, and how safe the study medicine was in healthy male participants

See the end of the summary for the full title of the study.

About this summary

This is a summary of the results of a clinical trial (called a 'study' in this document) – written for:

- members of the public and
- people who took part in the study.

This summary is based on information known at the time of writing.

The study started in March 2021 and finished in August 2022. This summary was written after the study had ended.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.
This means that you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment.

Contents of the summary

Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about how the study medicine reaches, is absorbed by, and moves throughout the brain and spine.

Key information about this study

- This study was done to look at how the study medicine spreads in the brain and spine after a single injection.
- In this study, people were given the study medicine only.
- This study included 24 people in the Netherlands.
- The main findings are listed in section 4 below ("What were the results of the study?")
- Overall, the study medicine was well-tolerated and most side effects were mild.
- None of the people taking part in the study had a serious side effect.

1. General information about this study

Why was this study done?

Angelman Syndrome (AS) is a rare genetic nerve disease that can prevent the brain from producing a specific protein that is vital for brain development. This can lead to developmental disabilities, nerve-related symptoms, and other medical problems. The study medicine, RO7248824, is designed to treat AS by helping to produce this protein.

Before a medicine can be given to patients, it's important to learn how the medicine moves throughout and is processed by the body. So, in this study, researchers wanted to learn more about how RO7248824 spreads in the brain and spine after it is injected into the spine.

Researchers can use scans, such as Positron Emission Tomography (PET) and Computed Tomography (CT) scans, to track how medicines move throughout the body. But it can be difficult to track how medicines move throughout the brain. In these and other cases, researchers sometimes attach a 'radiolabel' to a medicine. Radiolabels are radioactive substances that can be attached to a medicine to help track the medicine in the body. They are small radioactive doses, similar to ones used during X-ray scans. Because the researchers in this study wanted to track how RO7248824 moves throughout the brain, they attached a radiolabel so they could track RO7248824 with PET and CT scans.

What was the medicine being studied?

A medicine called 'RO7248824' was the focus of this study. RO7248824 works by helping to produce a specific protein that is vital for brain development.

What did researchers want to find out?

- Researchers did this study to look at how the study medicine spreads in the brain and spine after a single injection into the spine.
- They also wanted to find out how safe the medicine was – by checking how many people had side effects and seeing how serious they were, when receiving the medicine during this study (see section 5 "What were the side effects?").

The main question that researchers wanted to answer was:

1. How did the radiolabeled study medicine spread in the brain and spine?

What kind of study was this?

This study was a 'Phase 1' study, which means that this was one of the first studies in people for the study medicine. A small number of healthy people received the study medicine, and the researchers did medical tests on the people who took part to find out more about the study medicine.

This study was 'open-label'. This means that both the people taking part and the study doctors knew what study medicine people were receiving.

When and where did the study take place?

The study started in March 2021 and finished in August 2022. This summary was written after the study had ended.

The study took place at one centre in one country (the Netherlands).

2. Who took part in this study?

In this study, 24 healthy people took part.

People who took part in the study were between 25 and 51 years of age. All of the people were male.

People could take part in the study if they:

- Were males considered generally healthy and well.
- Had a body weight that was healthy to slightly overweight based on their body mass index, or BMI.

People could not take part in the study if they:

- Were not considered generally healthy or well.

3. What happened during the study?

During the study, the participants received 1 injection of 10 milligrams (mg) of radiolabeled RO7248824 into their spine. The researchers used different injection procedures to learn which procedure might be the most effective at spreading RO7248824 through the brain and spine. The 4 injection procedures were based on the below:

- The amount of spinal fluid sample taken.
- The amount of liquid mixed in with the 10 mg of radiolabeled RO7248824.
- The amount of a 'saline flush' used with the injection. Flushes can be used to replenish spinal fluid.

The table below shows these 4 procedures. The amounts were measured in milliliters (mL):

Number of participants	**Procedure**	**Spinal fluid sample amount**	**Liquid amount mixed in with radiolabeled RO7248824**	**Saline flush amount**
6 participants	A	5 mL	5 mL	5 mL
6 participants	B	0.5 mL	5 mL	0.5 mL
6 participants	C	15 mL	5 mL	15 mL
6 participants	D	0.5 mL	5 mL	0.5 mL

When the study finished, the people who took part were asked to go back to their study centre for another visit – to check their overall health. The image below shows more information about what happened in the study:

Up to 6 weeks before people received their study medicine

The people

- visited their study site 2 times.

The study doctors

- carried out tests to make sure the people were able to take part in the study.

While the people were receiving their study medicine

The people

- visited their study site up to 4 times over the course of about 2 weeks.
- during the first visit, they received 1 injection of radiolabeled RO7248824 through procedure A, B, C, or D.

The study doctors

- performed PET and CT scans to track the radiolabeled RO7248824 in the brain and spine.
- continued checking the people's health and taking blood and urine samples.

After the final dose of medicine

The study doctors

- checked the people's health and took blood and urine samples within 6 weeks after their study medicine injection.

4. What were the results of the study?

How did the radiolabeled study medicine spread in the brain and spine?

To answer this question, the researchers used PET scans and CT scans to track the radiolabeled study medicine in the participants' brain and spine after the injection. Then, they compared the results among the participants. Doctors use PET scans and CT scans to see inside the body, which can also help them learn how medicine is moving throughout the body.

Overall, the researchers found that:

- The way the radiolabel was absorbed in the spine over time was similar among the participants.
- The highest amount of the radiolabel absorbed by the brain was on the day after treatment.
- The participants who received Procedure B and Procedure D had the highest average amount of the radiolabeled study medicine that reached their brain.
- The participants who received Procedure B had the highest average amount of the radiolabeled study medicine absorbed by the brain.
- The amount of the radiolabeled study medicine absorbed by the brain did not affect how the radiolabeled study medicine was distributed across the different brain regions.
- The saline flush negatively affected how much of the radiolabeled study medicine reached the brain.
- Overall, the physical activity did not meaningfully alter how much of the radiolabeled study medicine reached the brain.

This section only shows the key results from this study. You can find information about all other results on the websites at the end of this summary (see section 8 "Where can I find more information?").

5. What were the side effects?

Side effects (also known as 'adverse reactions') are unwanted medical problems (such as feeling dizzy) that happen during the study.

- They are described in this summary because the study doctor believes the side effects were related to the treatment in the study.
- Not all of the people in this study had all of the side effects.
- Side effects may be mild to very serious and can be different from person to person.
- It is important to be aware that the side effects reported here are from this single study. Therefore, the side effects shown here may be different from those seen in other studies.
- Serious and non-serious side effects are listed in the following sections.

Serious side effects

A side effect is considered 'serious' if it is life-threatening, needs hospital care, or causes lasting problems.

None of the people taking part in this study had a serious side effect or died during the study due to side effects that may have been related to the study medicine.

During the study, none of the people taking part decided to stop receiving the study medicine because of side effects that may have been related to the study medicine.

Non-serious side effects

During this study, all side effects that may have been related to the study medicine were mild, moderate, or severe. Around 33% of people (8 out of 24 people) receiving the study medicine had a side effect that was not considered serious that may have been related to the study medicine.

The side effects that happened during the study that may have been related to the study medicine are shown in the following table:

Side effects reported in this study	**People receiving RO7248824** (24 people total)
Headache	21% (5 out of 24)
Nausea	13% (3 out of 24)
Back pain	8% (2 out of 24)
Health complication from spinal injection	8% (2 out of 24)
Dizziness	4% (1 out of 24)
Eye sensitivity to light	4% (1 out of 24)
Fatigue	4% (1 out of 24)
Muscle pain	4% (1 out of 24)
Vomiting	4% (1 out of 24)

6. How has this study helped research?

The information presented here is from a single study of 24 healthy people. These results helped researchers learn more about how radiolabeled RO7248824 spreads in the brain and spine after a single injection into the spine.

- Overall, the study medicine was well-tolerated, and most side effects were mild.
- There were no serious side effects, no one stopped treatment due to side effects, and no one died due to study treatment.
- Around 33% of people (8 out of 24 people) who took part in the study had a side effect that was not considered serious.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

- **This means that you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment.**

7. Are there plans for other studies?

Studies with RO7248824 are still happening, and further studies are planned.

8. Where can I find more information?

You can find more information about this study on the websites listed below:

- https://clinicaltrials.gov/ct2/show/results/NCT04863794
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2019-003786-18
- https://forpatients.roche.com/en/trials/neurodevelopmental-disorder/angelman-syndrome/a-study-to-assess-distribution-of-ro7248824-in-the-cent-71322.html

Who can I contact if I have questions about this study?

If you have any further questions after reading this summary:

- Visit the ForPatients platform and fill out the contact form – https://forpatients.roche.com/en/trials/neurodevelopmental-disorder/angelman-syndrome/a-study-to-assess-distribution-of-ro7248824-in-the-cent-71322.html

- Contact a representative at your local Roche office.

If you took part in this study and have any questions about the results:

- Speak with the study doctor or staff at the study hospital or clinic.

If you have questions about your own treatment:

- Speak to the doctor in charge of your treatment.

Who organised and paid for this study?

This study was organised and paid for by F. Hoffmann-La Roche Ltd who have their headquarters in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study is: A non-randomized, open-label, adaptive, single center, positron emission tomography (PET) study to assess distribution of RO7248824 in the central nervous system following single intrathecal doses of [89Zr] labelled RO7248824 in healthy male participants.

- The protocol number for this study is: BP41660.
- The ClinicalTrials.gov identifier for this study is: NCT04863794.
- The EudraCT number for this study is: 2019-003786-18.