Summary of Clinical Trial Results

A study in healthy people to look at how much RO7268489 reaches the brain and how long it stays there

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 August 2023 and finished in January 2024. 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 the medicine studied – 'RO7268489', and which doses to give people with multiple sclerosis (MS) in future studies.

Key information about this study

- This study was done to find out if a potential new medicine for MS attaches to a protein in the brain called 'monoacylglycerol lipase' (MAGL), and for how long.
- In this study, people were given the medicine being studied (called 'RO7268489') and a radioactive 'tracer' that is known to attach to MAGL for a short time. Researchers could work out how much RO7268489 was attached to MAGL by comparing the amount of tracer in the brain before and after RO7268489 was given.
    - This study included 8 people in 1 country.
- The main findings were that after being given RO7268489:
    - The highest levels of MAGL with RO7268489 attached were seen within 2 days of RO7268489 being given.
    - Between 46% and 72% of MAGL seen in the brain had RO7268489 attached to it.
    - After this, the amount of MAGL with RO7268489 attached slowly decreased over time. This was at the same rate as the amount of RO7268489 decreased over time in the blood.
    - There was no direct relationship between the amount of RO7268489 in the blood and the amount of MAGL in the brain with RO7268489 attached to it.
- No one taking RO7268489 had any serious unwanted effects.

1. General information about this study

Why was this study done?

Multiple sclerosis (MS) is a health condition in which the immune system, the body's natural defence that protects the body from harmful substances, attacks the protective covering of nerve fibres in the brain and spinal cord. This leads to communication problems between the brain and the rest of the body.

Inflammation leads to nerve damage and causes symptoms of MS, such as muscle weakness, pain, and difficulty with coordination, thinking, memory and reasoning.

People with MS have more inflammation signals in the fluid that surrounds and protects the brain and spinal cord, than people without MS.

Monoacylglycerol lipase, or 'MAGL' is a protein in the body that helps control inflammation and pain. MAGL increases the amount of signals and cells of the immune

system that cause inflammation, and reduces the amount of signals that help reduce pain.

Blocking the action of MAGL in people with MS may reduce inflammation and prevent further nerve damage by lowering levels of inflammation signals and activity of certain cells of the immune system. It may also help reduce pain symptoms by stopping the breakdown of 'pain-relief' signals in the brain.

This study was done to learn more about a potential new medicine that blocks the action of MAGL. It is being developed as an add-on treatment (to be taken with other medicines) for adults with MS.

What was the medicine being studied?

A medicine called 'RO7268489' was the focus of this study.

- RO7268489 is a MAGL 'inhibitor'. Inhibitors work by blocking or reducing the activity of specific proteins, such as MAGL.

- This may mean that RO7268489 could help reduce inflammation for people with MS, protect against further nerve damage and reduce pain.

What did researchers want to find out?

- Researchers did this study to see how RO7268489 worked. The study was carried out in healthy people (without MS); (see Section 4 "What were the results of the study?").

- They also wanted to find out how safe the medicine was – by checking how many people had unwanted effects and seeing how serious they were, when taking each of the medicines during this study (see section 5 "What were the unwanted effects?").

The main question that researchers wanted to answer was:

1. How much MAGL in the brain did RO7268489 attach to, when, and for how long?

What kind of study was this?

This study was a 'Phase 1' study, which means that this was one of the first studies for RO7268489. A small number of healthy people without MS, took RO7268489, and the researchers did medical tests on the people who took part to find out more about RO7268489.

This was an 'open label' study. This means that both the people taking part in the study and the study doctors knew it was the study medicine, RO7268489 that people were given.

When and where did the study take place?

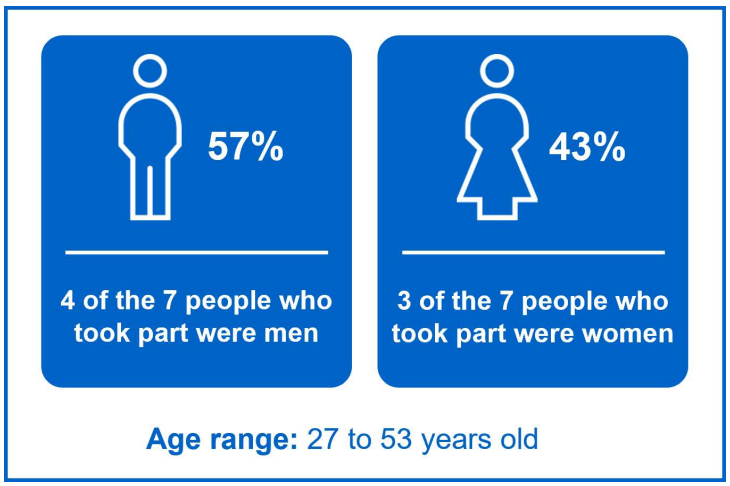
The study started in August 2023 and finished in January 2024. This summary was written after the study had ended.

The study took place at 1 study centre – in the United States, North America.

2. Who took part in this study?

In this study, 8 healthy people without MS took part. 1 person decided to leave the study before they were given RO7268489, so their results are not included in this summary.

More information on the people who took part is given below.



People could take part in the study if they:

- Were between 18 and 55 years old
- Were healthy following a detailed physical examination

People could not take part in the study if they:

- Were not able to have a thin, flexible tube inserted into their body to put fluids into or remove fluids from the body (arterial cannulation)
-

3. What happened during the study?

Positron emission tomography (PET) imaging is a scanning test used in medical practice and research to see where substances go in the body. A radioactive substance called a 'PET tracer' is detected by a PET scan.

During the study, people were given:

- RO7268489, as a capsule (to be swallowed).
- A PET tracer that is known to attach to MAGL for a short time, as a drip into a vein (infusion) immediately before each PET scan.

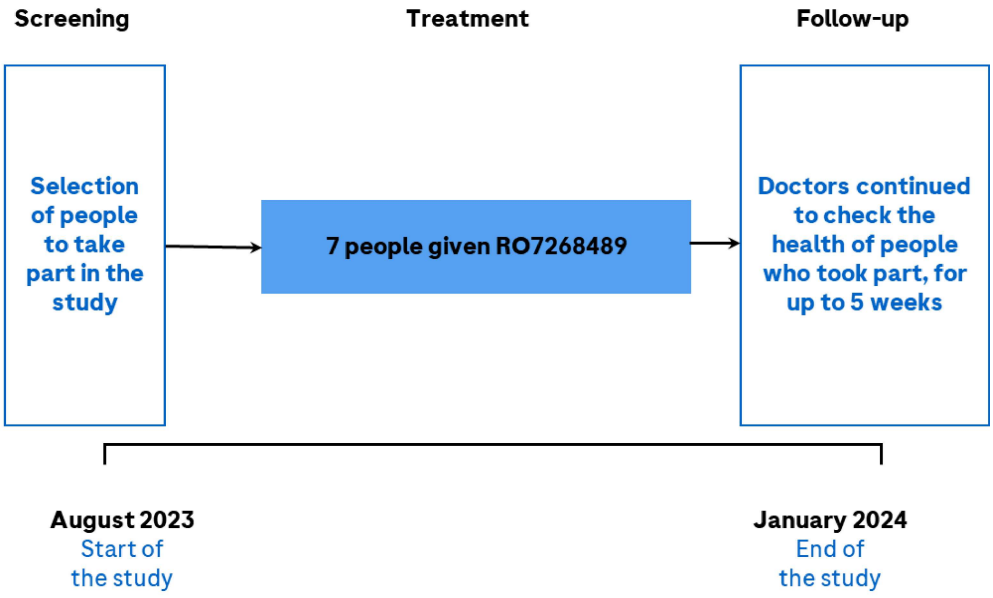
Participants had up to 3 PET scans of the brain.

First, the PET scan was done before RO7268489 was given, to see how much of the PET tracer attached to MAGL in the brain.

Then, participants were given RO7268489.

Researchers could work out how much MAGL had RO7268489 attached to it by looking at the amount of PET tracer in the brain in the first scan (before RO7268489 was given), and comparing it to the amount detected in later scans (after RO7268489 was given). If RO7268489 worked as expected and attached to MAGL in the brain, the PET tracer would not be able to attach to MAGL, and lower amounts of the tracer would be detected in the second and third scans.

When the study finished, the people who took part were asked to go back to the study centre for more visits – to check their overall health. Look below to see more information about what happened in the study.



4. What were the results of the study?

Question 1: How much MAGL in the brain did RO7268489 attach to, when, and for how long?

Researchers looked at how much of the PET tracer attached to MAGL in the brain after taking a single dose of RO7268489. This helped them understand how much RO7268489 was already attached to MAGL (and was stopping the PET tracer from attaching instead).

- The highest levels of MAGL with RO7268489 attached to it were seen within 2 days of RO7268489 being given.
- Between 46% and 72% of MAGL in the brain had RO7268489 attached to it within the first 2 days.
- After this, the amount of MAGL with RO7268489 attached to it slowly decreased over time. This was at the same rate as the amount of RO7268489 decreased over time in the blood.

Another piece of information that researchers collected was the amount of RO7268489 in the body, to see how this was related to the amount that attached to MAGL in the brain.

- There was no relationship between the amount of RO7268489 in the body and the amount of RO7268489 that had attached to MAGL in 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).

5. What were the unwanted effects?

Unwanted effects are medical problems (such as feeling dizzy) that happen during the study.

- Unwanted effects may be mild to very serious and can be different from person to person.
- It is important to be aware that the unwanted effects reported here are from this single study. Therefore, the unwanted effects shown here may be different from those seen in other studies.
- Serious and common unwanted effects are listed in the following sections.

Serious unwanted effects

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

During this study, no one had any serious unwanted effects or died.

Most common unwanted effects

During this study, no one had an unwanted effect that was considered not serious.

Other unwanted effects

You can find information about other unwanted effects (not shown in the sections above) on the websites listed at the end of this summary – see Section 8.

6. How has this study helped research?

The information presented here is from a single study of 7 people without MS. These results helped researchers learn more about RO7268489 and which doses to give people with MS in future studies.

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 RO7268489 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://forpatients.roche.com/en/trials/healthy-volunteers/a-single-center--non-randomized--open-label--parallel-group--ada.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/healthy-volunteers/a-single-center--non-randomized--open-label--parallel-group--ada.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 single-center, non-randomized, open-label, parallel group, adaptive, phase I positron emission tomography (PET) study to assess the brain occupancy of brain monoacylglycerol lipase (MAGL) enzyme of RO7268489 using [^{18}F]mni-1188 following single oral doses in healthy participants".

- The protocol number for this study is: BP44712.