Summary of Clinical Trial Results

A study to look at how RO7268489 was processed through the body when taken in different ways - and how safe this medicine was in healthy people

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 July 2023 and finished in February 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

1. General information about this study
2. Who took part in this study?
3. What happened during the study?
4. What were the results of the study?
5. What were the unwanted effects?
6. How has this study helped research?
7. Are there plans for other studies?
8. Where can I find more information?

Glossary

- MS = multiple sclerosis

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'.

Key information about this study

- This study was done to find out how a potential new medicine for multiple sclerosis (MS) gets to different parts of the body, and how the body changes and gets rid of it.
- The study compared these factors when:
    - A second dose was taken 1 or 3 weeks after the first dose, both without food (Part 1)
    - Either dose was taken with or without food (Part 2).
- In this study, people were given the medicine being studied (called 'RO7268489'), as a liquid (to be swallowed).
- This study included 24 people in 1 country.
- The main findings were:
    - Part 1: the amount of RO7268489 detected in blood after a second dose was:
        - Higher than after the first dose whether it was given 1 or 3 weeks earlier
        - Highest when there was only 1 week between doses, compared with 3 weeks
        - This suggests that RO7268489 stays attached to its target in the body for some time.
    - Part 2:
        - It took longer for RO7268489 to reach its highest level in the blood when taken with food
        - The total amount of RO7268489 in the body and the amount of time it stayed in the body were about the same, whether taken with or without food.
    - Parts 1 and 2: There was between 5 and 10 times more RO7268489 in the blood than in fluid that surrounds the brain and spinal cord ('cerebrospinal fluid', or 'CSF') during the study. This was true whether it was taken with or without food.
    - No one had serious unwanted effects that were related to taking RO7268489.

1. General information about this study

Why was this study done?

Multiple sclerosis (MS) is a health condition in which the body's natural defence (immune system) 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 break down signals in the brain that control inflammation and pain. MAGL increases the amount of signals and cells of the immune system that cause inflammation, and reduces the 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 the activity of immune cells. 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 to protect against further nerve damage, and reduce pain.

What did researchers want to find out?

- Researchers did this study to see what happened to RO7268489 in the body (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 medicine in these different ways during this study (see Section 5 'What were the unwanted effects?').

The main questions that researchers wanted to answer were:

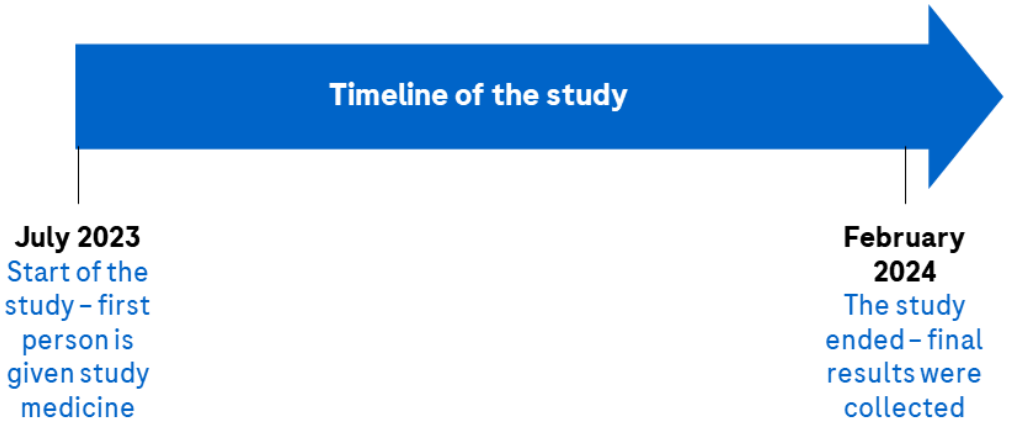
1. What happened to RO7268489 in the body when a second dose was taken 1 or 3 weeks after the first dose?
2. What happens to RO7268489 in the body when it is taken with or without food?

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.

When and where did the study take place?

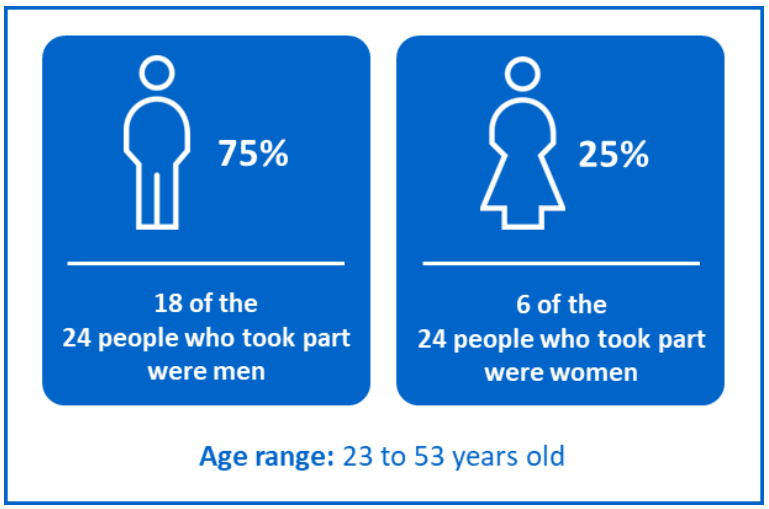
The study started in July 2023 and finished in February 2024. This summary was written after the study had ended.



The study took place at 1 study centre – in the Netherlands.

2. Who took part in this study?

In this study, 24 healthy people (without MS) took part. More information on the people who took part is given below.



People could take part in the study if they:

- Were between 18 and 54 years old
- Were healthy following a detailed physical examination

People could not take part in the study if they:

- Had a history of any serious illness or disorder, including cancer in the past 5 years

3. What happened during the study?

Everyone in the study was given:

- RO7268489 (the medicine being studied) – 2 equal doses, as a liquid (to be swallowed). The second dose was taken 1 or 3 weeks after the first dose.

The study was in 2 parts. People joined 1 part of the study only. RO7268489 was taken in different ways in each part of the study.

Researchers wanted to understand how long it takes for RO7268489 to be taken up into the blood, how much reaches the blood, and how long it takes for RO7268489 to be modified, distributed, and removed from the body when it was taken in different ways.

This helps them understand how long RO7268489 stays in the body and how much is available for use over time, to work out the best way for people to take it.

Part 1:

Part 1 of the study looked at what happened to RO7268489 in the body when taken twice with a 1 or 3-week treatment-free period in between doses.

People in this part of the study took both doses without food – 10 hours after their last meal.

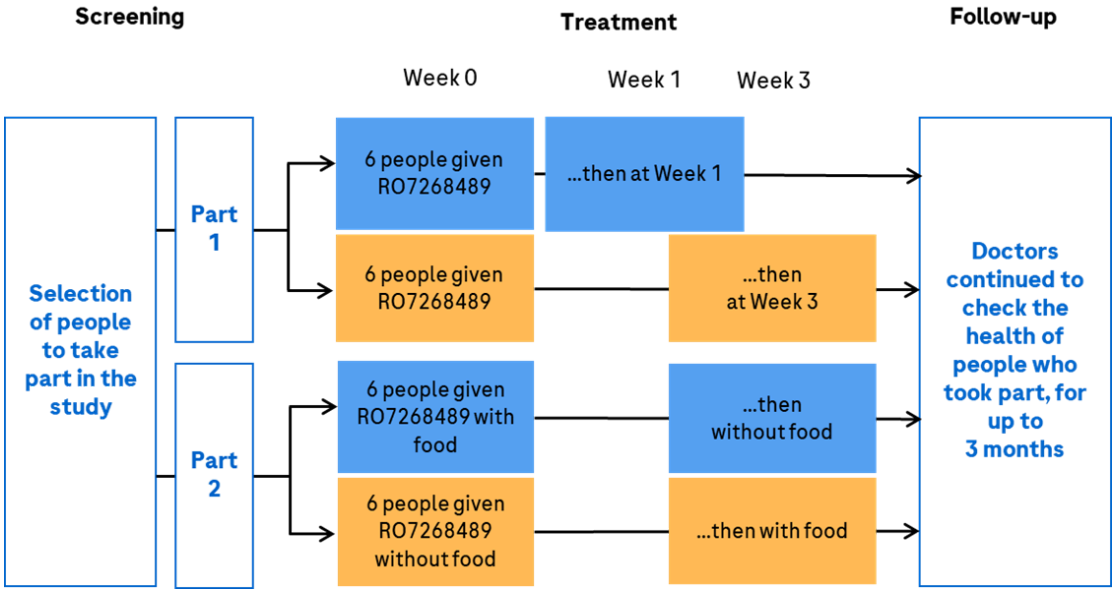
Part 2:

Part 2 of the study looked at whether taking RO7268489 with or without food affected what happened to RO7268489 in the body.

People took the first dose of RO7268489 either with or without food. They then took the second dose 3 weeks later, switching from how they took their first dose: if they took the first dose with food, they took the second dose without food, and vice versa.

During both parts of the study, researchers took samples of blood and cerebrospinal fluid (CSF). CSF is a special fluid that surrounds and protects the brain and spinal cord.

When the study finished, the people who took part were asked to go back to their 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?

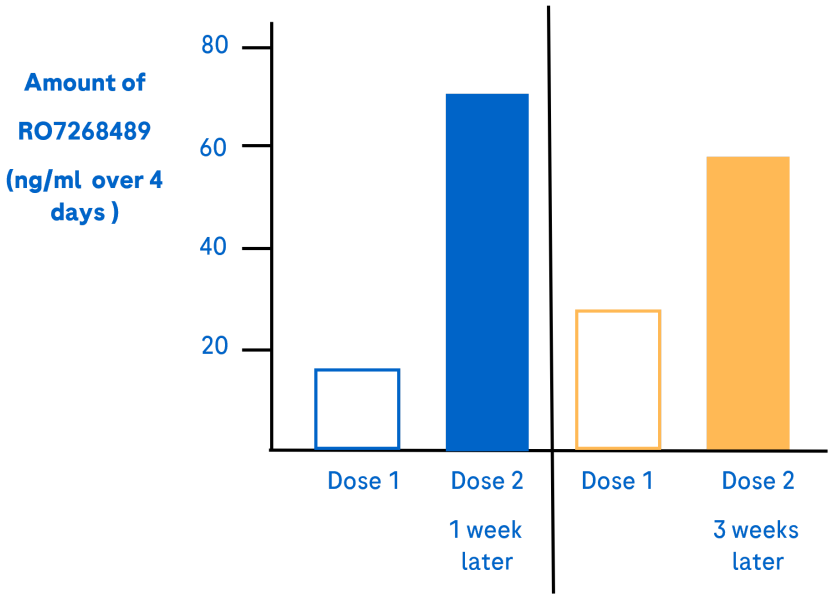
Question 1: What happened to RO7268489 in the body when a second dose was taken 1 or 3 weeks after the first dose?

In Part 1 of the study, researchers looked at how much RO7268489 could be detected in blood and CSF samples taken after each dose. Both doses were taken without food.

In the blood:

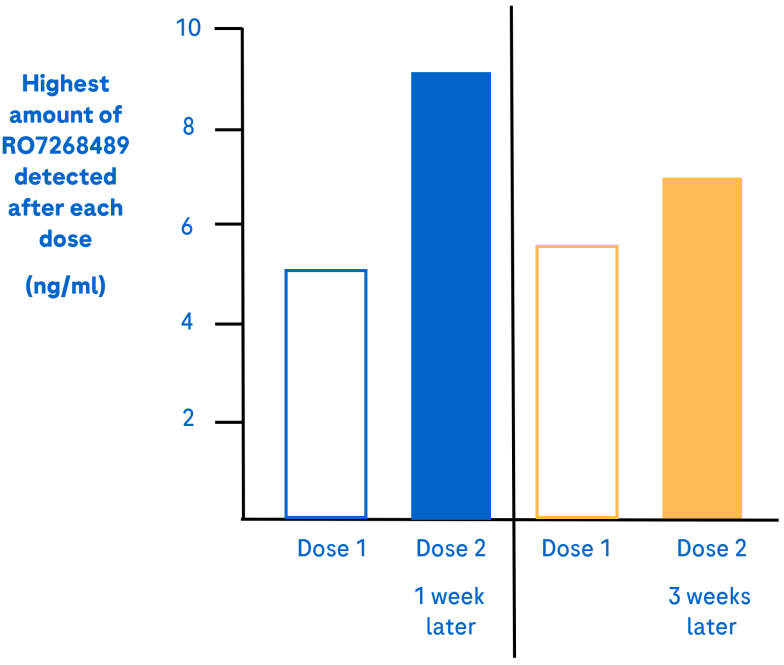
- More RO7268489 was detected after the second dose (given 1 or 3 weeks after the first dose) – which suggests that RO7268489 stays attached to MAGL for some time.

How much RO7268489 was in the blood over the 4 days after each dose was given?



- The highest amount of RO7268489 in the blood was seen when the doses were 1 week apart, compared with 3 weeks apart.
    - After 1 week between doses, 4 times more RO7268489 was detected than after the first dose.
    - After 3 weeks between doses, 2 times more RO7268489 was detected than after the first dose.

What was the highest amount of RO7268489 in the blood?



- It took about 30 minutes for the highest amount of RO7268489 to be detected in the blood after both the first and second doses were given without food.
    - The time between the first and second dose (1 or 3 weeks) did not affect this.
- The highest level of processed RO7268489 (broken down into smaller parts) was 7 to 9 times lower than the highest level of unprocessed RO7268489. However, over 4 days after both doses, there was no difference in the amount of processed and unprocessed RO7268489 available in the body.

In CSF:

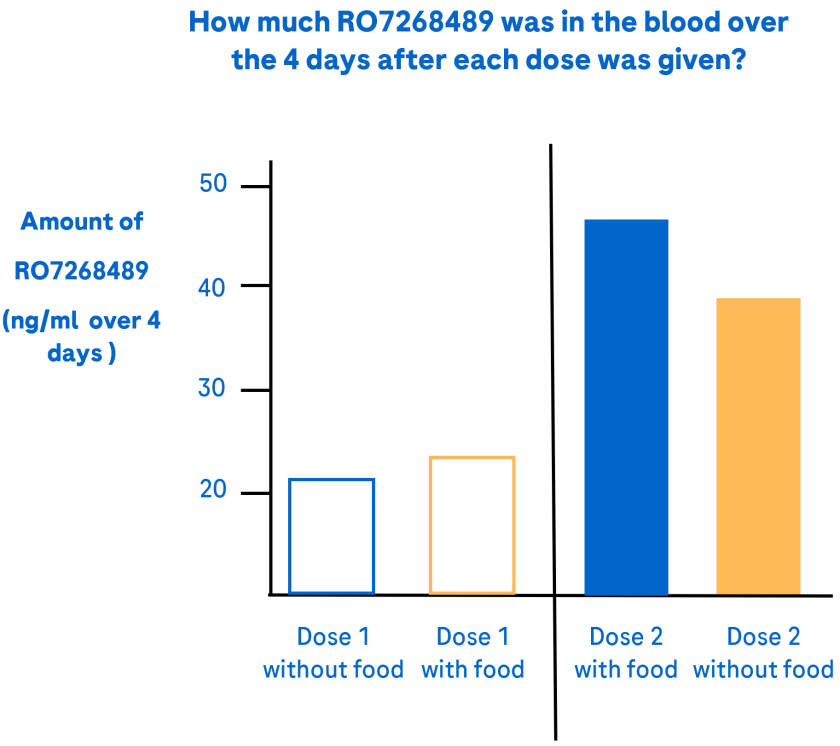
- There was 5 to 10 times more RO7268489 detected in blood than CSF during the study.

Question 2: What happens to RO7268489 in the body when it is taken with or without food?

During Part 2 of the study, researchers looked at how much RO7268489 could be detected in blood and CSF samples, and for how long, when it was taken with or without food. The second dose was taken 3 weeks after the first dose.

In the blood:

- There was no difference in the amount of RO7268489 in the blood over the first 4 days after each dose when it was taken with or without food.

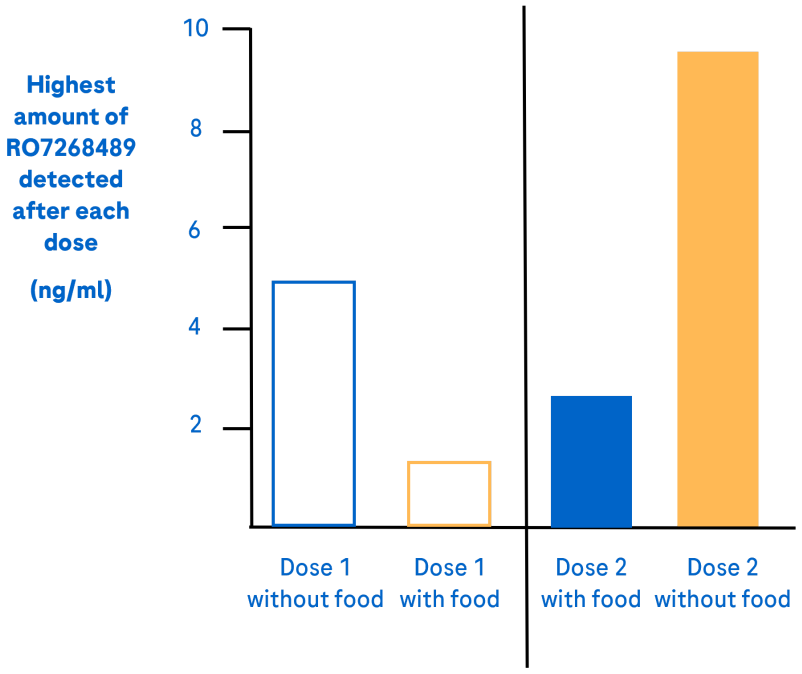


- 3 to 4 times more RO7268489 was detected in the blood when it was taken without food versus with food.

In summary, although it took longer for RO7268489 to reach its highest level in the blood when taken with food, the total amount of RO7268489 in the body and the amount of time it stayed in the body were about the same, whether taken with or without food.

- The highest amount of RO7268489 was detected in the blood more quickly when taken without food (after about half an hour) versus when taken with food (after 3 to 4 hours).
- The highest amount of processed RO7268489 (broken down into smaller parts) was 4 to 9 times lower than the highest amount of unprocessed RO7268489 detected. However, over the first 4 days after each dose, the total amount of processed and unprocessed RO7268489 in the blood was the same, whether taken with or without food.

What was the highest amount of RO7268489 in the blood?



In CSF:

- Whether taken with or without food, there was 5 to 10 times more RO7268489 in the blood than CSF.

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.

- They are described in this summary because the study doctor believes the unwanted effects were related to the treatments in 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.

During this study, no one decided to stop taking their medicine because of unwanted effects.

Most common unwanted effects

During this study, 1 out of 24 people (4%) had an unwanted effect that was not considered serious and was thought to be related to the study medicine.

This unwanted effect was sleeping for unusually long periods or having a strong desire for sleep. The person recovered the same day.

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 24 healthy people. 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--open-label--adaptive--two-period--single-oral-d.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--open-label--adaptive--two-period--single-oral-d.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, open-label, adaptive, two-period, single oral dose, Phase I study to assess the period effect (and the effect of food) on the pharmacokinetics of RO7268489 in healthy participants'.

- The protocol number for this study is: BP44618.
- The EU Trial number for this study is: 2023-503528-25-00.