Roche

Summary of Clinical Trial Results

An extension study to look at the long-term safety of faricimab for people with diabetic macular oedema

See Section 8 (page 14) at 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 2020 and finished in October 2023. 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.

Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about diabetic macular oedema (DME) and the medicine studied – 'faricimab'.

Key information about this study

- This study was an 'extension study'. This means that the people who took part had already completed another study looking at the same medicine before.

Why was this study done?

- In this extension study, people were given the medicine being studied (called 'faricimab').
- This extension study was done to look at how safe it is for people to have faricimab injections into the eye as a long-term treatment for DME.

Who took part in this study?

- This study included 1474 people in 30 countries. Of these, 1464 people were given at least 1 dose of faricimab and were included in the safety results.

What were the results?

- The main findings were that faricimab was well-tolerated, and no new safety issues were identified.
- Less than 1% of people (2 out of 1464 people) had serious unwanted effects that were thought to be related to faricimab and affected their eye.
- Less than 1% of people (3 out of 1464 people) had other, non-eye related serious unwanted effects that were thought to be related to faricimab.

1. General information about this study

Why was this study done?

Diabetic macular oedema (DME) is a condition where high blood sugar levels from diabetes cause fluid to leak into the central area at the back of the eye. This can cause blurry vision.

This extension study (called 'RHONE-X' or 'GR41987') was done to find out how safe a medicine called 'faricimab' was for treating DME when given over a long period of time. It was an extension of 2 previous studies of DME, called 'parent studies' in this document.

The parent study names were 'YOSEMITE' or 'GR40349', and 'RHINE' or 'GR40398'.

What was the medicine being studied?

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

- You say this as 'far-ih-see-mab'.
- Faricimab works by slowing the growth of new blood vessels in the eye and reducing the amount of fluid that leaks from blood vessels.
- This may mean that faricimab treatment could prevent damage to eyes and protect vision in people with DME.

What did researchers want to find out?

In the parent studies, researchers had looked at how well different timings of faricimab treatment worked and how safe they were compared to an existing medicine (called 'aflibercept'). People were given faricimab either every 2 months, or as they needed it depending on their eyesight. The

parent studies showed that vision improved for people with DME, allowing them to go longer between treatments.

In this extension study, some of the people who had taken part in the parent studies continued taking faricimab on a long-term basis, after the parent studies had finished.

- Researchers wanted to gather information on:
  - How safe faricimab was in the long-term
  - How people's bodies coped with faricimab in the long-term

The main questions that researchers wanted to answer were:

1. How many people had eye-related unwanted effects and how serious were they?
2. How many people had other, non eye-related unwanted effects and how serious were they?

What kind of study was this?

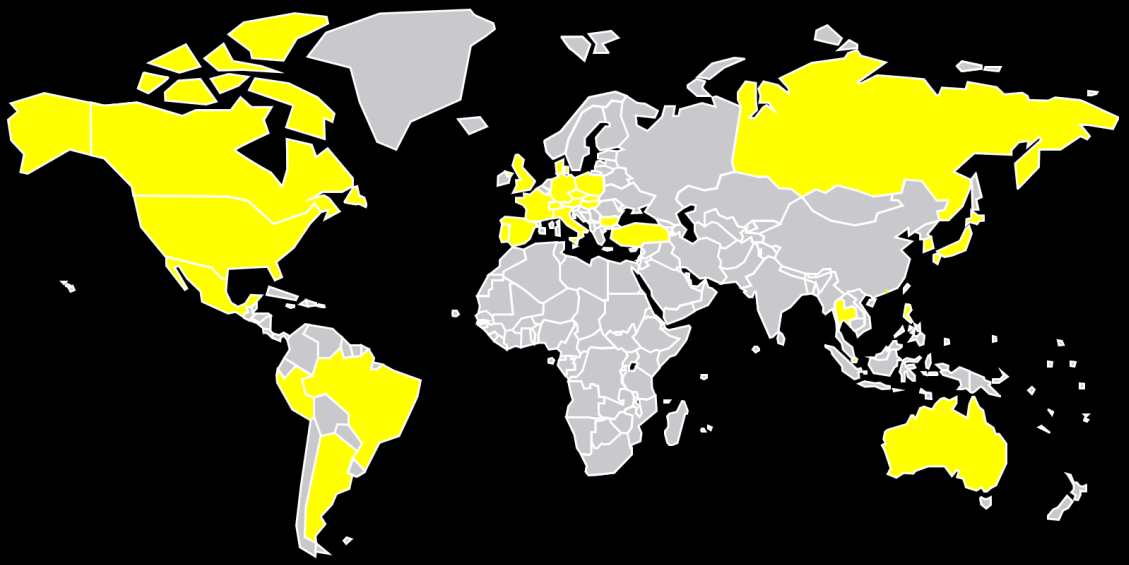
This study was an extension of 2 'Phase 3' studies. This means that faricimab had been tested in a number of people with DME before this study. In this study, people with DME continued to take faricimab – this was to find out about the long-term safety of faricimab.

When and where did the study take place?

The study started in August 2020 and finished in October 2023. This summary was written after the study had ended.

The study took place at 318 study centres – across 30 countries in the Americas, Australia, Asia and Europe. The countries were

Argentina, Australia, Austria, Brazil, Bulgaria, Canada, Czech Republic, Denmark, France, Germany, Hong Kong, Hungary, Israel, Italy, Japan, Mexico, Peru, Poland, Portugal, Russia, Singapore, Slovakia, South Korea, Spain, Switzerland, Taiwan, Thailand, Turkey, United Kingdom and the United States. The following map shows the countries where this study took place.

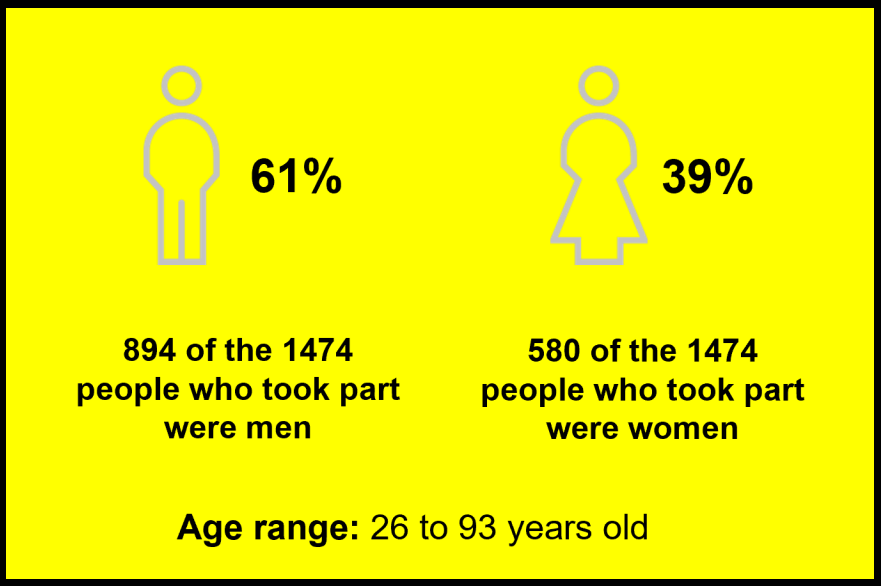


2. Who took part in this study?

In this study, 1474 people with DME took part. People who took part in the study were between 26 and 93 years of age.

894 of the1474 people (61%) were male and 580 of the 1474 people (39%) were female.

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



People could take part in the study if:

- They had completed treatment with faricimab or aflibercept in either of the YOSEMITE or RHINE parent studies
- They did not stop taking faricimab or aflibercept during a parent study

People could not take part in the study if:

- They had another eye condition or other medical condition that would potentially prevent them from being given faricimab
- They were pregnant or breastfeeding

3. What happened during the study?

The parent studies were 'masked'. This means the people in the parent studies and the study doctors did not know if people were given an injection of faricimab or aflibercept treatment or a 'sham' injection at each visit.

A sham procedure uses the blunt end of an empty syringe (without a needle) and presses it against the anaesthetised eye

to simulate a real injection. This was done to make sure that the results of the treatment were not affected by what people expected to happen. The parent studies were still masked when this extension study started.

During the first 4 months of the extension study, to keep the parent studies masked people attended monthly treatment visits and were given either:

- Faricimab (the medicine being studied) – as an injection into the eye, or
- Sham (a procedure with no effect that mimics the procedure being studied)

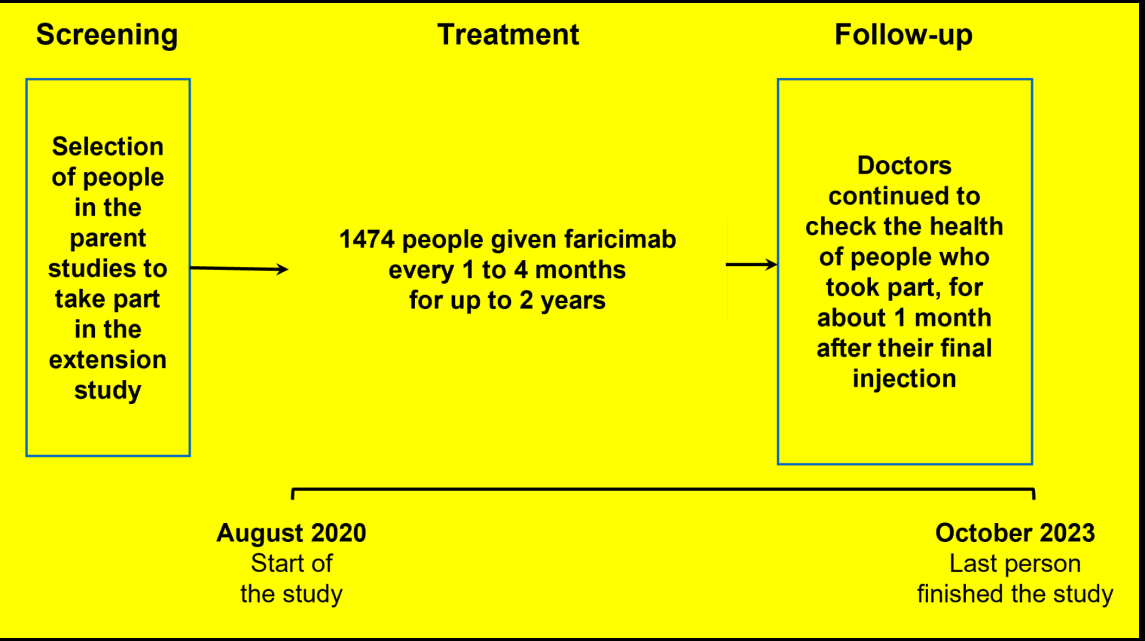
After the first 4 months, the study was 'open-label'. An open-label study means everyone involved, including the people in the study and the study doctor, know which study treatment is given and how often.

Treatment was given at a 'personalised treatment interval'. This means how often a person needed to be injected was decided based on two eye measurements. These measurements informed doctors about the health of the eye and the person's eyesight.

In the open-label period, everyone was given:

- Faricimab (the medicine being studied) – as an injection into the eye, every 1 to 4 months, as needed

People in the study took the treatments for up to 2 years. 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 eye health. Look below to see more information about what happened in the study.



4. What were the results of the study?

Question 1: How many people had eye-related unwanted effects and how serious were they?

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.
- Not all of the people in this study had all of the unwanted effects.
- Unwanted effects may be mild to very serious and can be different from person to person.
- An unwanted effect is considered 'serious' if it is life- or sight-threatening, needs hospital care, or causes lasting problems.

- 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.

Researchers looked at how safe long-term faricimab treatment was. The number of people in the study that could be included in these results was 1464 out of 1474. Some people were not included because they were not given any faricimab treatment (for example, they may have decided to leave the extension study before treatment was given).

- 29 out of 1464 people (2%) had unwanted effects that affected their eye, were not considered serious and were thought to be related to faricimab
- 2 out of 1464 people (less than 1%) had serious unwanted effects that affected their eye and were thought to be related to faricimab
    - Both people had recovered by the end of the study

More information about the type of unwanted effects that people had, is in Section 5.

Question 2: How many people had other, non eye-related unwanted effects and how serious were they?

Some people had unwanted effects that impacted them in other ways, other than their eye:

- 3 out of 1464 people (less than 1%) had serious non-eye related unwanted effects thought to be related to faricimab.
    - 2 of these people had recovered or were recovering by the end of the study
    - 1 person had not recovered by the end of the study

More information about the type of unwanted effects that people had, is in Section 5.

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?

Serious and common unwanted effects are listed in the following sections.

Serious unwanted effects

The serious unwanted effects related to faricimab treatment that affected the eye or other parts of the body are shown in the following tables. Some people had more than one unwanted effect – this means that they are included in more than one row in the table.

Most common serious unwanted effects reported in this study that affected the eye	People taking faricimab (1464 people total)
Inflammation inside the eye coming from the uvea causing redness and pain	Less than 1% (1 out of 1464)
Redness, swelling or pain of the coloured part of the eye and nearby areas	Less than 1% (1 out of 1464)

Most common serious unwanted effects reported in this study that affected other parts of the body	People taking faricimab (1464 people total)
Heart discomfort	Less than 1% (1 out of 1464)
Heart failure	Less than 1% (1 out of 1464)
Heart beating faster than usual	Less than 1% (1 out of 1464)
Stroke	Less than 1% (1 out of 1464)

No one in the study died due to unwanted effects that may have been related to faricimab.

During the study, some people decided to stop faricimab treatment because of unwanted effects that were related to faricimab:

- 2 out of 1464 people (less than 1%) stopped taking faricimab.

Most common unwanted effects

The most common unwanted effects thought to be related to faricimab treatment that affected the eye are shown in the following table.These are the most common unwanted effects that affected more than 2 people in the extension study, and were not considered serious. Some people had more than one unwanted effect – this means that they are included in more than one row in the table.

Most common non-serious unwanted effects reported in this study that affected the eye	People taking faricimab (1464 people total)
Higher than usual pressure in the eye	Less than 1% (11 out of 1464)
Redness, swelling or pain of the coloured part of the eye	Less than 1% (4 out of 1464)
The lens of the eye became cloudy	Less than 1% (3 out of 1464)
Inflammation of the gel-like substance inside the eye	Less than 1% (3 out of 1464)
Inflammation inside the eye coming from the uvea causing redness and pain	Less than 1% (2 out of 1464)
A disorder involving the gel-like substance inside the eye	Less than 1% (2 out of 1464)
Redness, swelling or pain of the coloured part of the eye and nearby areas	Less than 1% (2 out of 1464)

No one in the study had non-serious unwanted effects that were related to faricimab treatment and affected other parts of the body.

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 1474 people with DME. These results helped researchers learn more about DME and faricimab.

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 faricimab 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/NCT04432831
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-000402-29/results
- https://forpatients.roche.com/en/trials/eye-disorder/dme/a-study-to-evaluate-the-long-term-safety-and-tolerabili-41480.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/eye-disorder/dme/a-study-to-evaluate-the-long-term-safety-and-tolerabili-41480.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 Phase III, Multicenter, Open-Label Extension Study to Evaluate the Long-Term Safety and Tolerability of Faricimab in Patients with Diabetic Macular Edema'.

The study is known as 'RHONE-X'.

- The protocol number for this study is: GR41987.
- The ClinicalTrials.gov identifier for this study is: NCT04432831.
- The EudraCT number for this study is: 2020-000402-29.