Summary of Clinical Trial Results

A study to investigate a new medicine called faricimab for treating people with damage to the back of the eye caused by diabetes (diabetic macular edema)

See Section 8 (page 14) at the end of this summary for the full title of the study.

About this summary

This summary describes the results of a clinical trial (also called a study), written for:

- Members of the public, and
- People taking part in the study.

This summary is based on information known at the time of writing (November 2023). More information may now be available.

The study started in November 2020 and finished in December 2022. This summary presents the results that were analyzed in January 2023.

No single study can tell us everything about the risks and benefits of a medicine. 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 are taking part in this study

The people who took part were helping doctors to answer important questions about people with damage to the back of the eye caused by diabetes (diabetic macular edema).

Key information about this study

- This study investigated a medicine called faricimab in people with damage to the back of the eye caused by diabetes. This condition is called diabetic macular edema (DME for short).
- In this study, people were given faricimab eye injections once a month for 6 months.
- This study included 99 people across 7 countries in North America, South America, and Europe.
- This summary describes the key results from the study. People treated with faricimab eye injections gained vision and had reduced fluid in their retinas.
- Faricimab side effects were mostly mild and manageable.
- No new or unexpected side effects have been reported, and no one needed to stop treatment due to side effects.

Contents of the summary

Glossary

Angiopoietin-2 (Ang-2 for short): a protein that plays a role in the growth and leakiness of blood vessels, and in inflammation.

Diabetic macular edema (DME for short): damage to the back of the eye (the retina) caused by high blood sugar levels in people with diabetes.

Intraretinal fluid: fluid that collects within the retina.

Macula: the central part of the retina that provides sharp, clear vision for activities such as reading, driving, and recognizing faces.

Macular edema: swelling in the retina due to leaking blood vessels.

Retina: the thin layer of light-sensitive nerve cells that lines the back of the eye and sends signals through the optic nerve to the brain for processing.

Vascular endothelial growth factor-A (VEGF-A for short): a protein that plays a role in the growth and leakiness of blood vessels.

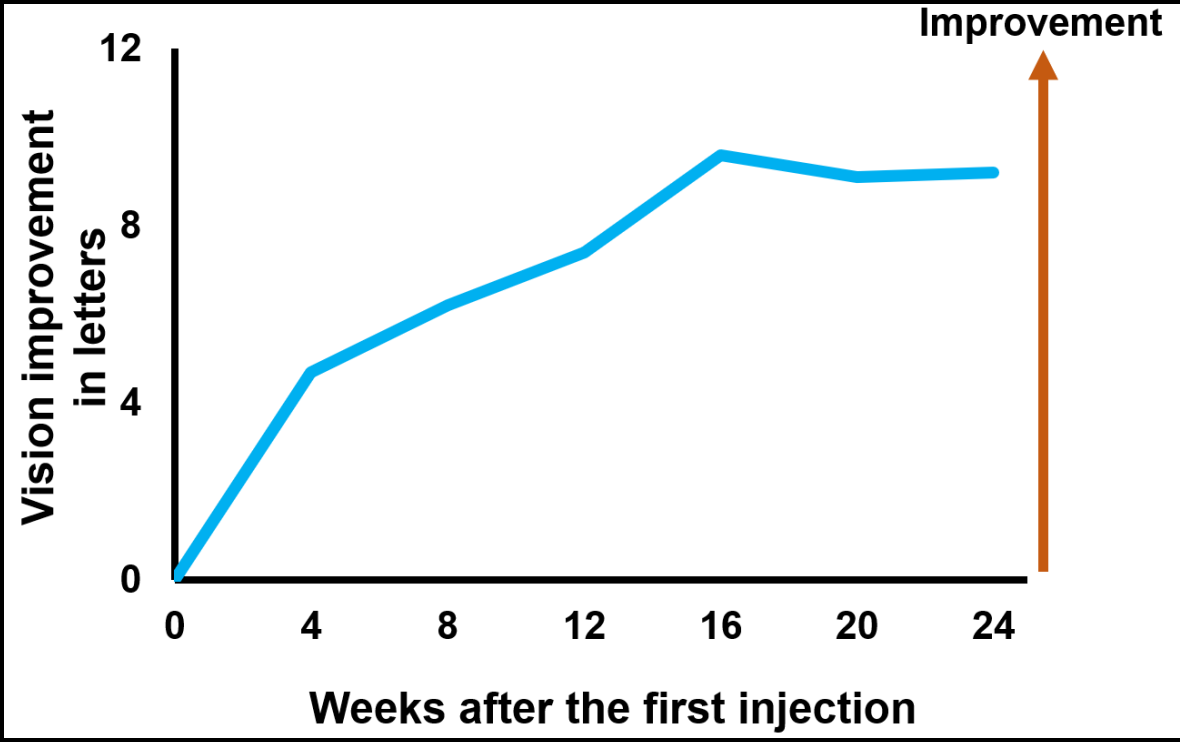
Section 1: What are the results of the study?

Question 1: Was there a change in a person's best vision after 24 weeks compared with the start of the study?

Doctors looked at whether a person's vision changed from the start of the study. For this, the people had their vision tested by finding out how many letters they could read on a standardized eye chart. This chart has rows of letters, bigger on the top and then gradually smaller towards the bottom. The study doctors compared the results of eye tests taken after 24 weeks with eye tests taken at the start of the study.

On average, people who received faricimab every month saw 9 more letters on an eye chart than when they started the study (their vision improved). The improvement in vision from the start of the study to the end is shown below in Figure 1.

Figure 1: How well did faricimab improve vision for people with DME?

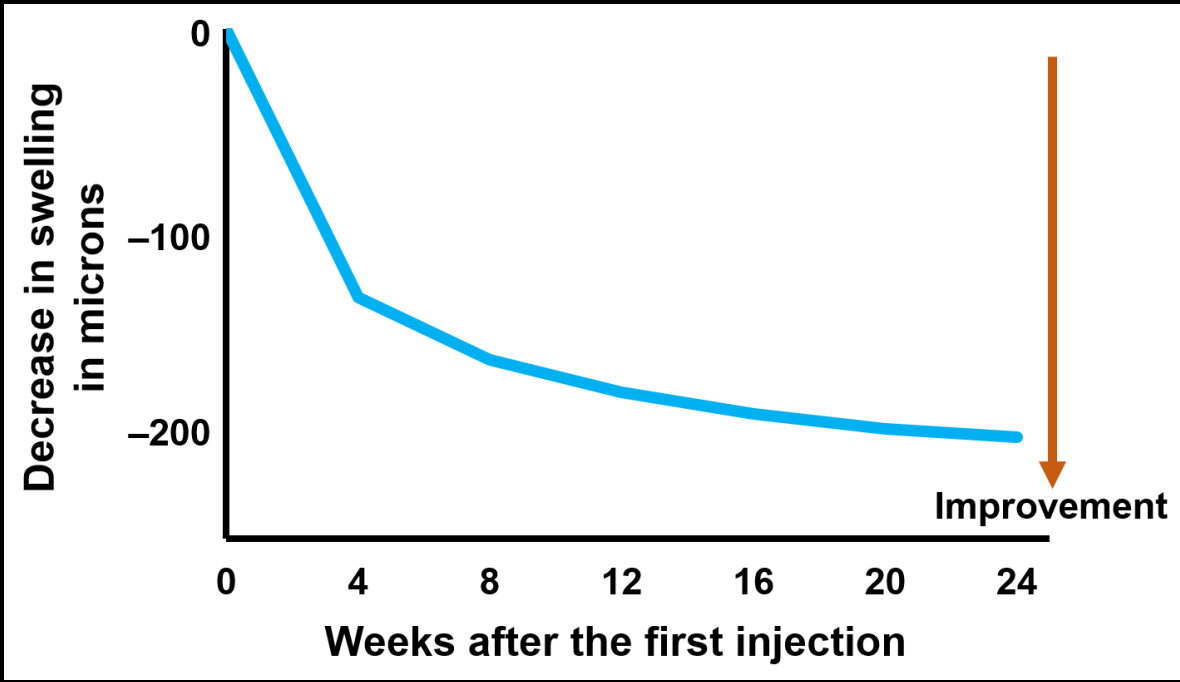


Question 2: How well did faricimab reduce swelling in the back of the eye?

In people with DME, leaky blood vessels cause swelling in the back of the eye. Study doctors assessed this swelling by measuring the thickness of the retina in microns, which is a scale to measure very small things. For example, the average width of a human hair is 75 microns, and the normal thickness of the central part of the retina (the macula) is about 250 microns. On average, people who took part in this study had a macula thickness of around 464 microns before receiving faricimab eye injections. A decrease in swelling means there is less damage to the eye.

After 24 weeks, on average, faricimab had reduced swelling by 200 microns. The decrease in swelling from the start of the study to the end is shown below in Figure 2.

Figure 2: How well did faricimab reduce swelling in the back of the eye for people with DME?

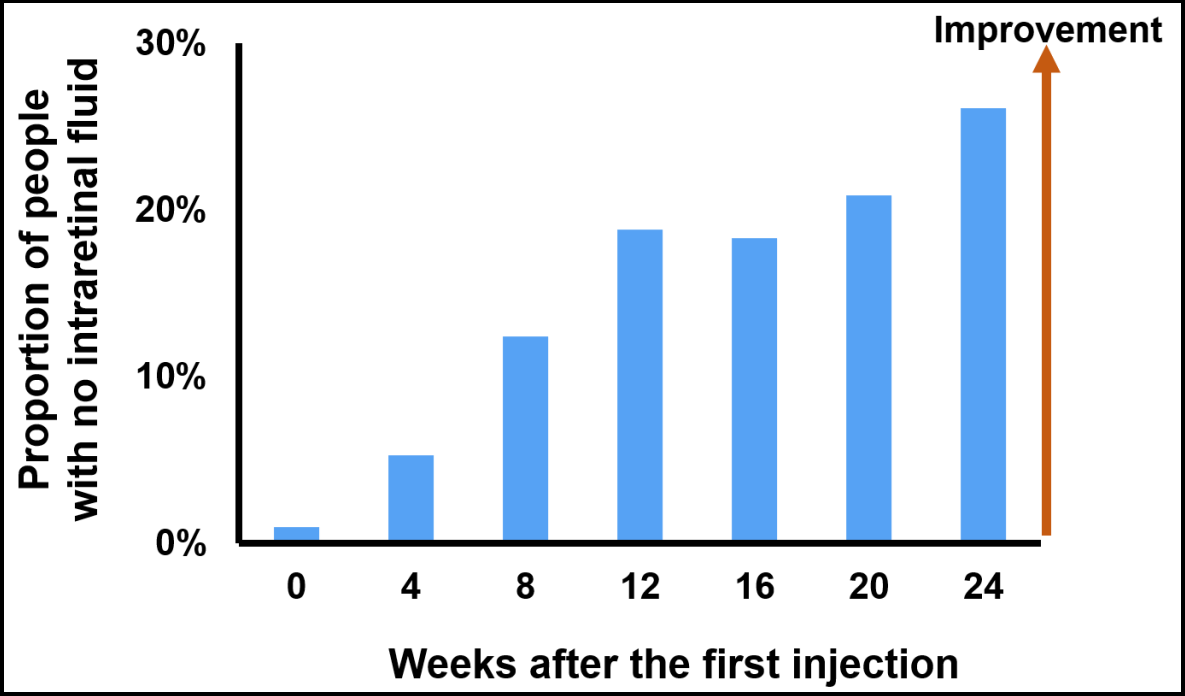


Question 3: How well did faricimab reduce fluid buildup in the retina?

Intraretinal fluid is fluid that collects within the retina. The presence of intraretinal fluid is a hallmark of DME.

Before receiving faricimab, nearly all (99%) people in this study had intraretinal fluid. After 24 weeks, 26% of people no longer had intraretinal fluid. The increase in the percentage of people with no intraretinal fluid from the start of the study to the end is shown below in Figure 3.

Figure 3: How well did faricimab reduce fluid buildup in the retina for people with DME?



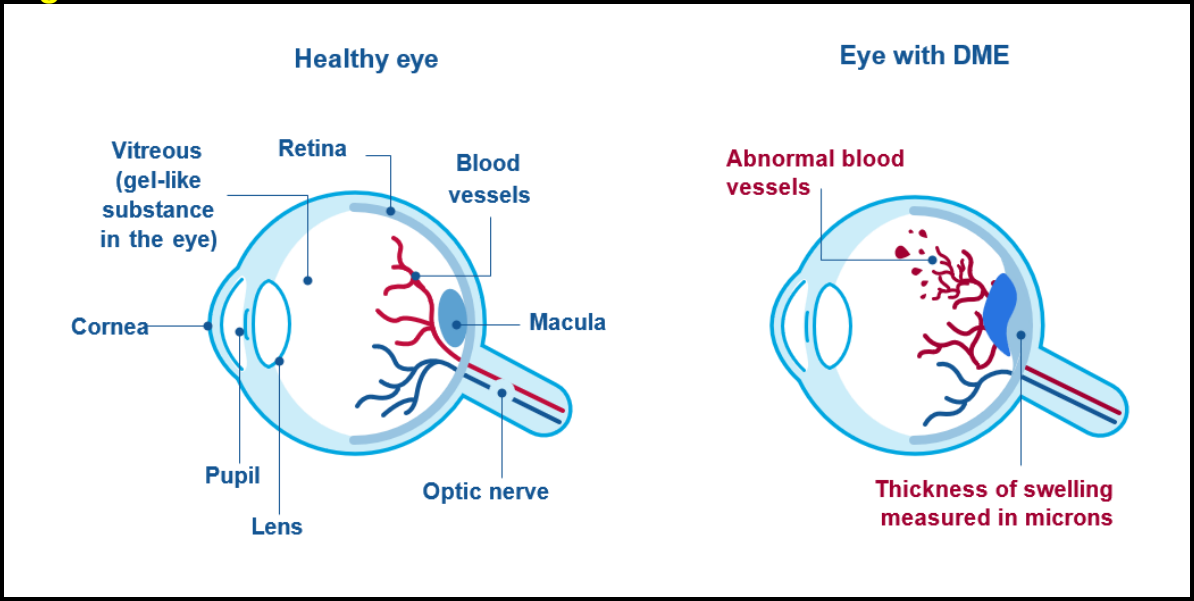
This section only shows results from this study considered to be of interest to patients.

Section 2: General information about this study

Question 1: Why was this study done?

DME is a major cause of vision loss and blindness in people with diabetes. DME affects the central part of the retina that provides sharp, clear vision (the macula). The macula swells with fluid that has leaked from abnormal blood vessels.

Figure 4: What is DME?



This figure shows a healthy eye and an eye with DME. On the left is a drawing of a healthy eye, showing the pupil and lens at the front of the eye, and the blood vessels, retina, macula, and optic nerve at the back of the eye. On the right is a drawing of an eye with DME. Abnormal blood vessels leak fluid into the macula, which causes swelling and damage at the back of the eye.

The preferred first-line anti-VEGF treatments for DME are medicines such as aflibercept (Eylea®) and ranibizumab (Lucentis®), which are injected into the eye. These medicines block one pathway that causes fluid leakage and growth of abnormal blood vessels. This pathway involves the vascular endothelial growth factor A (VEGF-A) protein, which plays a role in the growth and leakiness of blood vessels. Other treatments for DME include steroid injections into the eye to reduce swelling, and laser treatments to stop blood vessels from leaking.

Approved medicines have improved vision for many people with DME, but they usually require eye injections every 1 to 2 months over a long

period of time. Newer medicines, such as faricimab (Vabysmo™), which block multiple pathways, may allow people to control their DME symptoms with less frequent injections.

Question 2: What was the medicine being studied?

Faricimab is the medicine that was being tested in this study. Faricimab is injected into the eye.

- You say this as *"far-ih-see-mab".*
- Faricimab blocks the two pathways involving the proteins VEGF-A and Ang-2. Blocking VEGF-A reduces fluid leakage and can prevent new abnormal blood vessels growing in the eye. Like VEGF-A, blocking Ang-2 also reduces fluid leaking from blood vessels. Reducing the amount of fluid leaking from blood vessels may reduce the amount of swelling in the macula. Blocking Ang-2 also reduces inflammation and the scarring of the retina. By having a medicine that blocks two different pathways, it might be of more benefit than a medicine that blocks just one pathway.
- By blocking two pathways that cause DME, faricimab may more effectively strengthen blood vessels and improve vision with fewer eye injections.

Question 3: What did the study doctors want to find out?

Study doctors wanted to find out if faricimab can improve vision and reduce swelling in the retina (see Section 1 "What are the results of the study?", page 4).

The study doctors also wanted to find out how safe faricimab is for people with DME. To test this, they looked at the number of side effects and how serious the side effects were (see Section 5 "What were the side effects?", page 10).

Question 4: What kind of study was this?

This was a 'Phase IIb' study. This means that before this study, faricimab was tested in a smaller number of people with DME.

The study was 'single-arm'. This means that the people in this study were all given the same medicine.

The study was ‘open-label. This means that both the people and the doctors involved in the study knew the people received faricimab.

Question 5: When and where did the study take place?

The study started in November 2020 and ended in December 2022.

This study took place at 24 centers in 7 countries, including Argentina, Canada, Germany, Italy, Poland, the United Kingdom, and the United States.

Section 3: Who is taking part in this study?

In total, 99 adults with DME took part in this study.

Around 6 out of 10 (61 people) were men and 4 out of 10 (38 people) were women. At the start of the study, people were, on average, 60 years of age.

People could take part in the study if they:

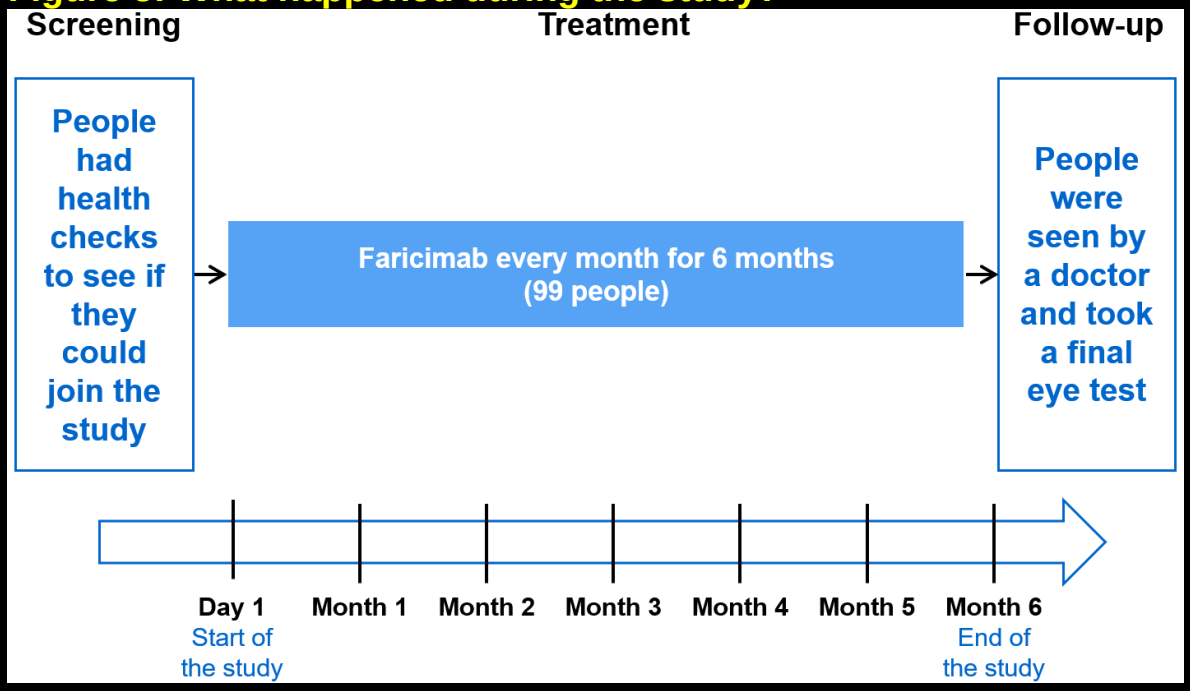
- Had swelling in the central part of the retina (the macula) with a thickness of 325 microns or more.
- Could read between 75 and 20 letters on a standard eye chart, which means that they have vision between 20/40 to 20/400.
- Had clear eyeballs and their pupils could be dilated with special eye drops to allow for good photos of the retina to confirm macular edema.

Section 4: What happened during the study?

People received 6 milligrams of faricimab, which was injected into their eye once every month for 6 months.

There is a diagram showing what happened during the study below (see Figure 5).

Figure 5: What happened during the study?



Section 5: What were the side effects?

Side effects (also known as adverse reactions) are medical problems (such as eye irritation or eye pain) that can happen during a study. This section describes the side effects reported during the study:

- Some side effects may be related to the medicines used, the injection procedure, or the disease itself.
- Not all of the people participating in this study had one or all of the side effects.
- Side effects can vary from mild to severe and may differ from person to person.

During the study, the side effects caused by faricimab were mostly mild, manageable, and resolved.

There were no side effects that caused people to stop receiving faricimab in this study.

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

Question 1: What serious side effects have been reported?

A side effect is considered serious if it is life-threatening, causes vision loss, needs hospital care, or causes lasting problems that are disabling.

During the study, there were no serious side effects reported in the eye treated with faricimab. Eight out of 99 (around 8%) people receiving faricimab had a non-eye related serious side effect.

Question 2: What were the most common side effects reported?

During this study, 23 out of 99 people (around 23%) had at least one side effect in the eye treated with faricimab.

Table 2 below shows the 6 most common side effects reported for this study.

Table 2: What are the most common side effects reported?

Most common side effects in the treated eye	99 people in total
Fatty deposits in the retina (retinal exudates)	5 out of 99 (5.1%)
Red spots on the white part of the eye caused by blood leaking from broken blood vessels (conjunctival hemorrhage)	4 out of 99 (4.0%)
Inflammation that makes the white part of the eye look red (conjunctival hyperemia)	3 out of 99 (3.0%)
Swelling of blood vessels within the eye that are at risk of bursting (retinal aneurysm)	3 out of 99 (3.0%)
Fibers in the gel-like fluid within the eye that pulled away from the retina (vitreous detachment)	3 out of 99 (3.0%)
Spots in vision (vitreous floaters)	3 out of 99 (3.0%)

All side effects in the eye treated with faricimab were mild or moderate in severity.

Mild side effects may cause discomfort but do not disrupt normal daily activities, while moderate side effects may cause discomfort that does affect or reduce normal daily activities.

Question 3: Were there any other side effects?

You can find information about other side effects (not shown in the sections above) on the websites listed at the end of this summary – see Section 8 (page 13).

Section 6: How is this study helping research?

The results described in this summary are from a single study of 99 people with DME. These results are helping study doctors learn more about faricimab and its effects in people with DME.

The main result is that people who received faricimab eye injections showed similar improvements in vision. Faricimab side effects were

mostly mild, easily treated, and comparable with what is already know about faricimab. No new or unexpected side effects were reported.

Section 7: Are there plans for other studies?

There are no plans for other faricimab studies in people with DME at this time.

Section 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/NCT04597918
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001174-30/PL
- https://forpatients.roche.com/en/trials/eye-disorder/dme/a-study-to-investigate-aqueous-humor-and-multimodal-ima-93975.html

Question 1: Who can I contact if I have questions about this study?

If you have any further questions after reading this summary:

- Visit the For Patients platform and fill out the contact form: https://forpatients.roche.com/en/trials/eye-disorder/dme/a-study-to-investigate-aqueous-humor-and-multimodal-ima-93975.html
- Contact a representative at your local Genentech or Roche office.

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

- Please speak with the study doctor or staff at the study hospital or clinic.

If you have questions about your own treatment:

- Please speak to the doctor in charge of your treatment.

Question 2: Who is organizing and paying for this study?

This study is being organized 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: “An Exploratory, Prospective, Multi-Center, Open-Label, Single-Arm, Interventional, Phase IIB Study to Investigate Aqueous Humor and Multimodal Imaging Biomarkers in Treatment-Naïve Patients with Diabetic Macular Edema Treated with Faricimab”.

The study is known as ‘ALTIMETER’.

The protocol number for this study is MR41926.

The ClinicalTrials.gov identifier for this study is NCT04597918.

The EudraCT number for this study is 2020-001174-30.