Summary of Clinical Trial Results

A study to compare different doses of vicasinabin with a placebo – to find out how well vicasinabin works and how safe it is in people with type 1 or 2 diabetes and diabetic retinopathy

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 June 2020 and finished in July 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.

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.

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Glossary

- DR = Diabetic retinopathy
- DME = Diabetic macular oedema

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 retinopathy (DR) and the medicine studied – 'vicasinabin' (also known as 'RG7774' and 'RO6868847').

Key information about this study

- This study was done to test how well vicasinabin works to treat DR in people with type 1 or 2 diabetes mellitus, good vision, and who have not yet been treated for DR. Researchers also looked at how safe vicasinabin is.
- In this study, people were given either vicasinabin (the medicine being studied), OR a placebo – it was decided by chance which treatment each person was given.
- This study included 139 people in 6 countries.
- The main findings were that:
    - vicasinabin does not help improve damaged blood vessels at the back of the eye in people with DR
    - 30mg and 200mg doses of vicasinabin are safe enough to be given to people with DR
- No person taking vicasinabin or the placebo had serious unwanted effects related to study treatment.

1. General information about this study

Why was this study done?

Diabetes mellitus is a group of health conditions that cause a person's blood sugar to become too high. This happens when the body does not make enough insulin or does not respond to insulin the way it should. Insulin is a molecule in the body that turns food into energy and controls the quantity of sugar in the blood. There are 2 types of diabetes known as 'type 1' and 'type 2'. Type 1 diabetes is caused by the body attacking healthy cells that make insulin by mistake. Type 2 diabetes is caused by the body not responding to insulin as well as it should.

Diabetic retinopathy (DR) is a complication that can develop in some people living with diabetes. DR is a condition where high blood sugar levels from diabetes damages the back of the eye. This can cause blindness if not treated. There are 2 main types of DR:

- Early DR, also called non-proliferative DR (NPDR) — new blood vessels aren't growing (proliferating). The blood vessels in the eye swell and leak fluid. They can become blocked. This reduces the blood flow to the light-sensitive layer at the back of the eye, called the retina, and causes vision to become blurry
- Advanced DR, also called proliferative DR — new blood vessels and scar tissue have formed on your retina, which can cause serious vision problems

Standard treatments for DR are eye surgery, laser or medicines given through a needle inserted into the eye. Many people find treatment through a needle into the eye hard to bear. This study looked at a medicine called vicasinabin. Vicasinabin can be given as a tablet to be swallowed, which could reduce the burden of treatment for people with DR.

This study looked at how well vicasinabin worked to reduce certain signs of DR in people with type 1 or 2 diabetes, who had good vision and had not yet been treated for DR. Researchers also looked at how safe vicasinabin was.

What was the medicine being studied?

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

- You say this as 'vi–cah–sin-a-bin'.
- Vicasinabin may reduce inflammation at the back of the eye.
- Vicasinabin could slow down vision loss in people with DR.
- Vicasinabin was tested at different doses.

Vicasinabin was compared to a 'placebo'.

- You say this as 'plah – see – bo'
- The placebo looked the same as vicasinabin but did not contain any real medicine. This means it had no medicine-related effect on the body.
- Researchers compared the medicine being studied to a placebo so they could show which benefits or unwanted effects are actually caused by the medicine.

What did researchers want to find out?

- Researchers did this study to compare vicasinabin with a placebo – to see how well vicasinabin worked (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 questions that researchers wanted to answer were:

1. How many people showed improvement in damaged blood vessels at the back of the eye?
2. How many unwanted effects did people have and how serious were they?

Other questions that researchers wanted to answer included:

3. How many people had DR that got worse?
4. How much did people's eyesight change?

What kind of study was this?

This study was a 'Phase 2' study. This means that vicasinabin had been tested in a number of people without type 1 or 2 diabetes mellitus or DR before this study. In this study, people with type 1 or 2 diabetes and good vision, who had early DR but had not yet been treated for it, either took vicasinabin or a placebo – this was to find out about the safety of vicasinabin and if vicasinabin worked to reduce certain signs of DR.

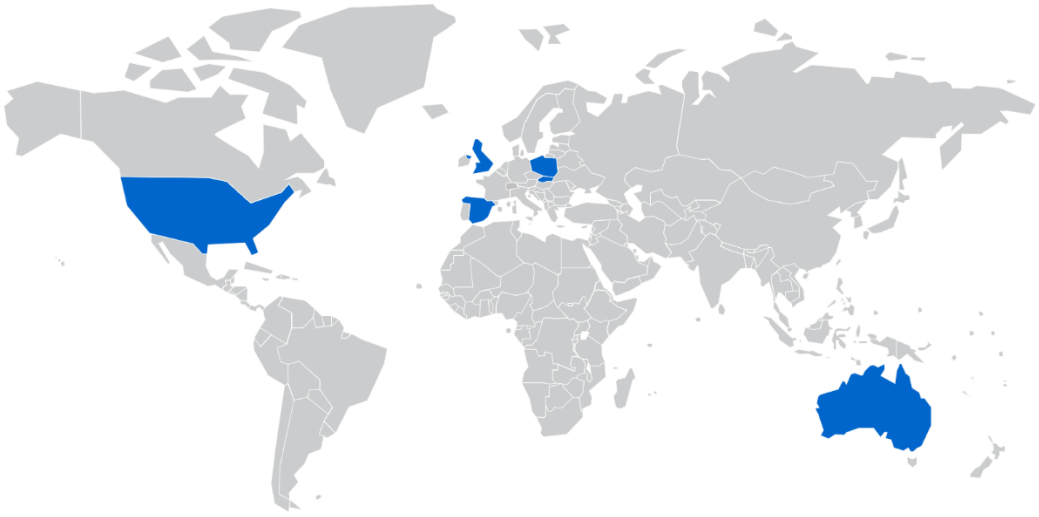
The study was 'randomised'. This means that it was decided by chance which of the medicines people in the study would have – like tossing a coin. Randomly choosing which medicine people take, makes it more likely that the types of people in both groups (for example, age, race) will be a similar mix. The groups tested different medicines, but all other aspects of their care were the same.

This study was 'double-masked'. This means that neither the people in the study nor the team running it knew which treatment was being given until the study ended. This was done to make sure that the results of the treatment are not affected by what people expected from the received treatment. However, the study doctor could find out which group a person was in during the study, if a person's safety was at risk.

When and where did the study take place?

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

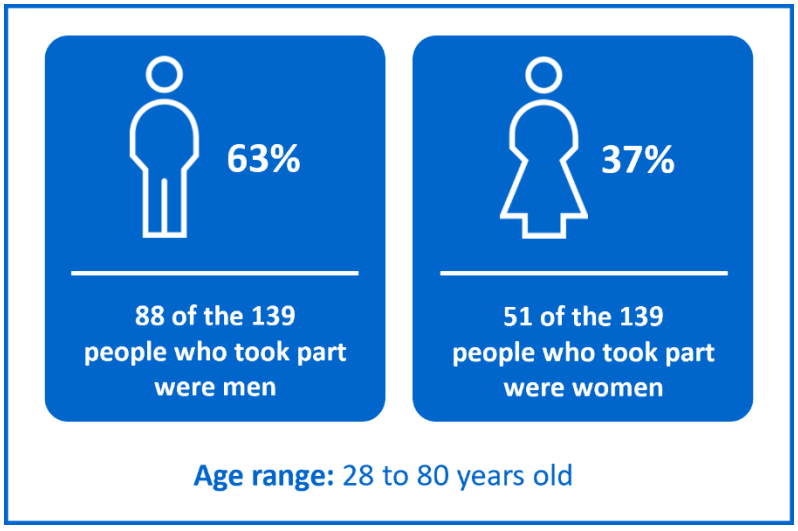
The study took place at 47 study centres – across 6 countries. The following map shows the countries where this study took place.



- Australia
- Poland
- Slovakia
- Spain
- United Kingdom
- Unites States

2. Who took part in this study?

In this study, 139 people with diabetes mellitus and early DR that had not been treated took part.



People could take part in the study if:

- They were at least 18 years old
- They were being treated for type 1 or 2 diabetes mellitus
- They had early DR that had not been treated before
- They were never treated before for another eye condition known as 'diabetic macular oedema' (DME) and were not expected to need DME treatment during the study
- They had good eyesight when using glasses or contact lenses
- Their eyes were clear enough to take photographs of the back of their eyes

People could not take part in the study if:

- They had anti-VEGF (also known as 'anti-vascular endothelial growth factor') treatment as a tablet or a drip into a vein within 6 months of joining the study
- They had certain other medical conditions, such as liver disease, kidney disease, heart problems, certain infections, or uncontrolled high blood pressure
- They had received treatment in another study within 2 months of joining this study

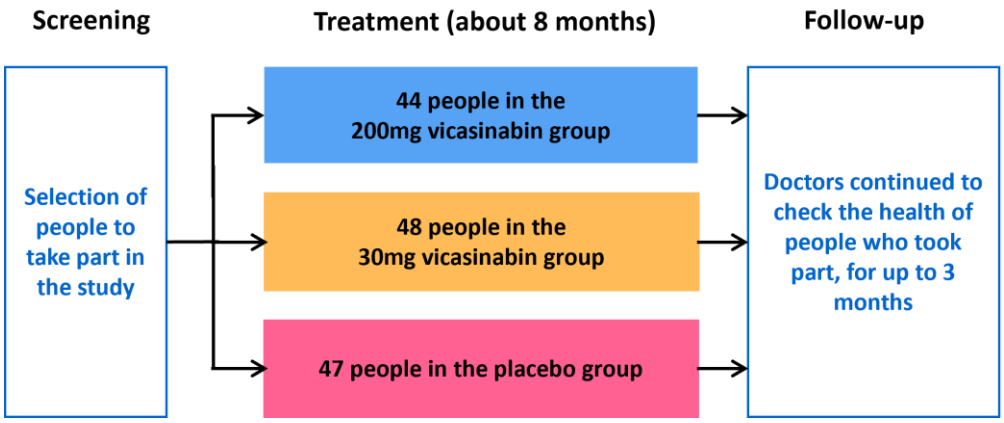
3. What happened during the study?

During the study, people were selected by chance to get either vicasinabin 200mg, vicasinabin 30mg or placebo. The treatments were selected at random – by a computer.

The treatment groups were:

- **Vicasinabin** (the medicine being studied) – given as tablets to be swallowed once a day. People took 1 or 3 tablets, depending on the treatment group they were in (30mg or 200mg)
- **Placebo** – given as a tablet to be swallowed once a day

People in the study took the treatments for about 8 months (36 weeks). 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.



1 person in the 200mg vicasinabin group left the study before they were given treatment, so they are not included in the results.

4. What were the results of the study?

Question 1: How many people showed improvement in damaged blood vessels at the back of their eye?

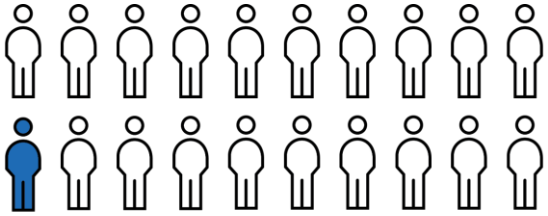
Researchers looked at DR severity scores (DRSS) – a measurement of how much the blood vessels in the back of the eyes are damaged due to diabetes. A better DRSS shows that blood vessels are more healthy and there is less damage at the back of the eye. This means there is a smaller risk of having loss of vision.

Some people in this study are not included in these results, as they did not complete the study.

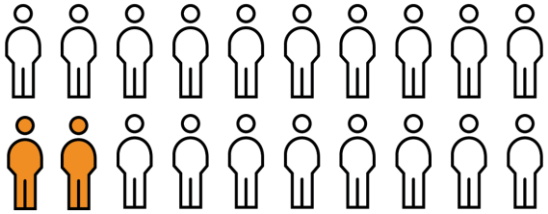
The number of people who had an improvement in the back of the eye was similar between the vicasinabin and placebo groups:

- 2 out of 35 people (6%) given 200mg vicasinabin showed improvement
- 4 out of 42 people (10%) given 30mg vicasinabin showed improvement
- 3 out of 38 people (8%) who were given a placebo showed improvement

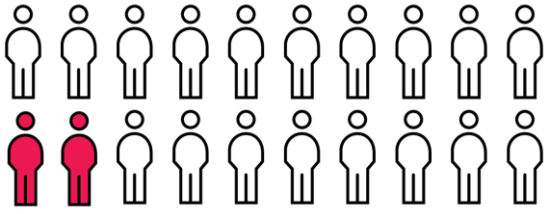
In summary:



Around 1 in every 20 people (6%) who were given 200mg of vicasinabin had less eye damage



Around 2 in every 20 people (10%) who were given 30mg of vicasinabin had less eye damage

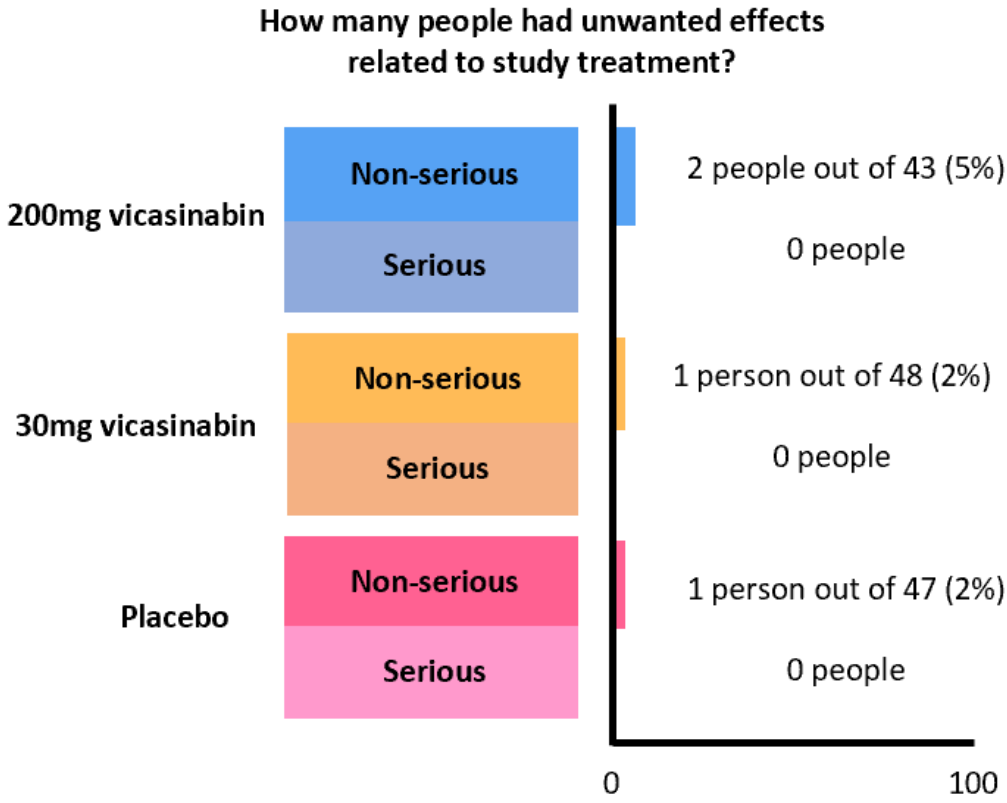


Around 2 in every 20 people (8%) who were given a placebo had less eye damage

Question 2: How many unwanted effects did people have and how serious were they?

A similar number of people in the vicasinabin and placebo groups had unwanted effects that were related to study treatment but not considered serious.

None of the people in the study had unwanted effects caused by the study treatment that were serious. This included in the eye or in any other part of the body.



More information about the number, type and seriousness of unwanted effects is provided in Section 5.

Question 3: How many people had DR that got worse?

Another piece of information that researchers collected was how many people had DR that worsened during the study and could cause loss of vision.

This was measured by counting the number of people with:

- DR becoming worse
- Appearance of new DME, or if DME was present at the start of the study, how many people needed treatment for it
- New blood vessels at the front of the eye

The number of people with DR that got worse during the study was similar between the vicasinabin and placebo groups:

- 5 out of 43 people (12%) given 200mg vicasinabin
- 6 out of 48 people (13%) given 30mg vicasinabin
- 4 out of 47 people (9%) given a placebo

Question 4: How much does eyesight change?

Another piece of information that researchers collected was how much a person's best corrected visual acuity (known as 'BCVA') changed. BCVA is the best eyesight a person can have when using glasses or contact lenses. It is measured using a letter chart.

After about 8 months of treatment, BCVA remained the same as at the beginning of the study for the vicasinabin and placebo groups.

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, nobody had a serious unwanted effect caused by the study treatment.

No-one in this study died due to the study treatment.

No person during the study decided to stop taking their medicine because of unwanted effects that were related to the study medicine.

Most common unwanted effects

During this study, around 3 out of every 100 people (3%) had an unwanted effect related to study treatment, that was not considered serious. No-one had unwanted effects from the study treatment that affected their eyes.

3 out of 91 people (3%) taking vicasinabin had an unwanted effect that was not considered serious, compared with 1 out of 48 people (2%) taking a placebo.

The most common unwanted effects are shown in the following table – these are the 6 most common unwanted effects. Some people had more than one unwanted effect – this means that they are included in more than one row in the table.

Most common unwanted effects reported in this study	**People taking 200mg vicasinabin** (43 people total)	**People taking 30mg vicasinabin** (48 people total)	**People taking a placebo** (47 people total)
Frequent bowel movements	2% (1 out of 43)	0% (0 out of 48)	0% (0 out of 47)
Sensation of wanting to vomit (nausea)	0% (0 out of 43)	2% (1 out of 48)	0% (0 out of 47)
Allergic reaction (hypersensitivity)	2% (1 out of 43)	0% (0 out of 48)	0% (0 out of 47)
Low level of sugar in the blood (hypoglycaemia)	0% (0 out of 43)	0% (0 out of 48)	2% (1 out of 47)
Dizziness	0% (0 out of 43)	2% (1 out of 48)	0% (0 out of 47)
Impairment or unusual functioning of one or more senses (sensory disturbance)	0% (0 out of 43)	2% (1 out of 48)	0% (0 out of 47)

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 139 people with DR. These results helped researchers learn more about DR and vicasinabin.

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.

- **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?

At the time of writing this summary, no more studies looking at vicasinabin 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/NCT04265261
- https://www.clinicaltrialsregister.eu/ctr-search/search?query=2019-002067-10
- https://forpatients.roche.com/en/trials/metabolic-disorder/dr/a-study-to-investigate-the-efficacy-and-safety-of-rg777-36226.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/metabolic-disorder/dr/a-study-to-investigate-the-efficacy-and-safety-of-rg777-36226.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 randomized, double-masked, 48-week, parallel group, placebo-controlled, proof of concept study to investigate the efficacy and safety of RG7774 in patients with diabetes mellitus type 1 or type 2 with treatment naïve diabetic retinopathy”.

The study is known as ‘CANBERRA’.

- The protocol number for this study is: BP41321.
- The ClinicalTrials.gov identifier for this study is: NCT04265261.
- The EudraCT number for this study is: 2019-002067-10.