NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of brolucizumab compared to laser treatment in people with proliferative diabetic retinopathy

Thank you!

Thank you to the participants who took part in the clinical trial for **proliferative diabetic retinopathy**. Every participant helped the researchers learn more about the trial drug **RTH258**, also called **brolucizumab**.

Novartis sponsored this trial and believes it is important to share what was learned from the results of this trial with the participants and the public. We hope this helps the participants understand their important role in medical research.

Trial information

Trial number: CRTH258D2301

Novartis drug studied: **RTH258**, also called **brolucizumab**

Sponsor: Novartis

If you were a participant and have any questions about the results, please talk to the doctor or staff at the trial site.

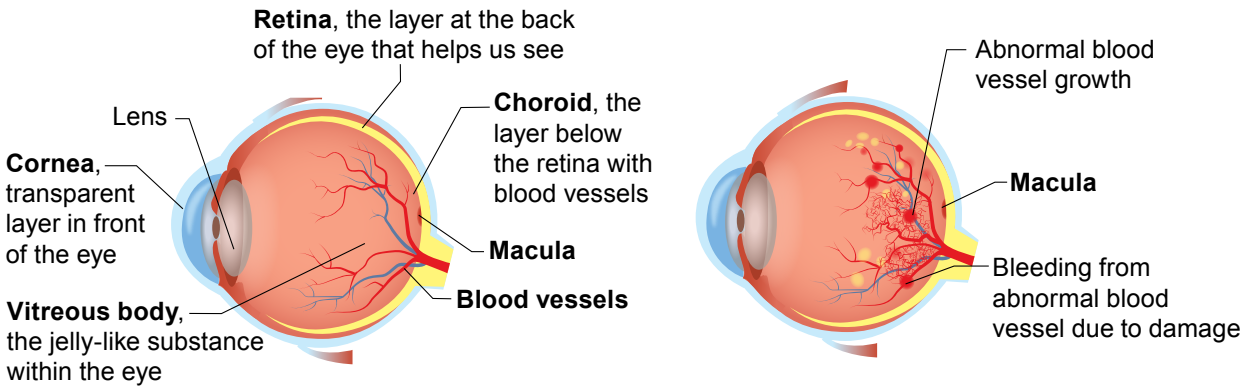
This summary only shows the results of a single clinical trial. Other clinical trials may have different results.

What was the main purpose of this trial?

The purpose of this trial was to learn about the effects of **brolucizumab** in people with **proliferative diabetic retinopathy (PDR)**. To find this out, researchers compared the effects of **brolucizumab** to **panretinal photocoagulation (PRP) laser** to see which one works better.

PDR is an advanced stage of diabetic retinopathy. In **PDR**, the blood vessels in the retina become damaged and stop working. New, abnormal blood vessels grow in the retina. These new vessels are weak and can bleed into the eye, causing the retina to separate from the back of the eye, which can lead to vision loss.

Diabetic retinopathy is an eye problem that happens when high blood sugar levels damage the blood vessels in the retina. This damage can reduce blood flow to the retina and may cause vision loss.



Normal eye | **Proliferative diabetic retinopathy**

Brolucizumab is a drug approved in many countries including the United States, Europe, and Asia for the treatment of a similar condition called diabetic macular edema. It works by blocking a protein called vascular endothelial growth factor (VEGF). This protein helps to form new blood vessels inside the eye. When VEGF increases, abnormal blood vessels are formed in the retina. By blocking VEGF, **brolucizumab** helps to slow or stop damage from the leaky blood vessels in the retina and slow down vision loss.

Trial drug

RTH258 also called Brolucizumab

Pronounced as

BROE-lue-SIZ-ue-mab

PRP is a type of laser treatment which can shrink abnormal blood vessels in the retina. This is one of the standard treatments available for this condition.

The trial's purpose was to answer these main questions:

- Did vision improve from the start of the trial until Week 54 for participants on **brolucizumab** compared to those on **PRP laser**?
- What medical problems, also called adverse events, happened during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial. Adverse events **may** or **may not** be caused by treatments in the trial.

How long was this trial?

The trial began in November 2020 and ended in August 2024. The participants were in the trial for about 2 years.

Who was in this trial?

689 participants with **PDR** received treatment in this trial – 413 men and 276 women. Participants' ages ranged from 20 to 82 years. Their average age was 54 years.

The number of participants by race is shown below.

Race

335 White or Caucasian	305 Asian	38 Black or African American
5 Native Hawaiian or Pacific Islander	4 American Indian or Alaska Native	1 More than 1 race
1 Unknown		

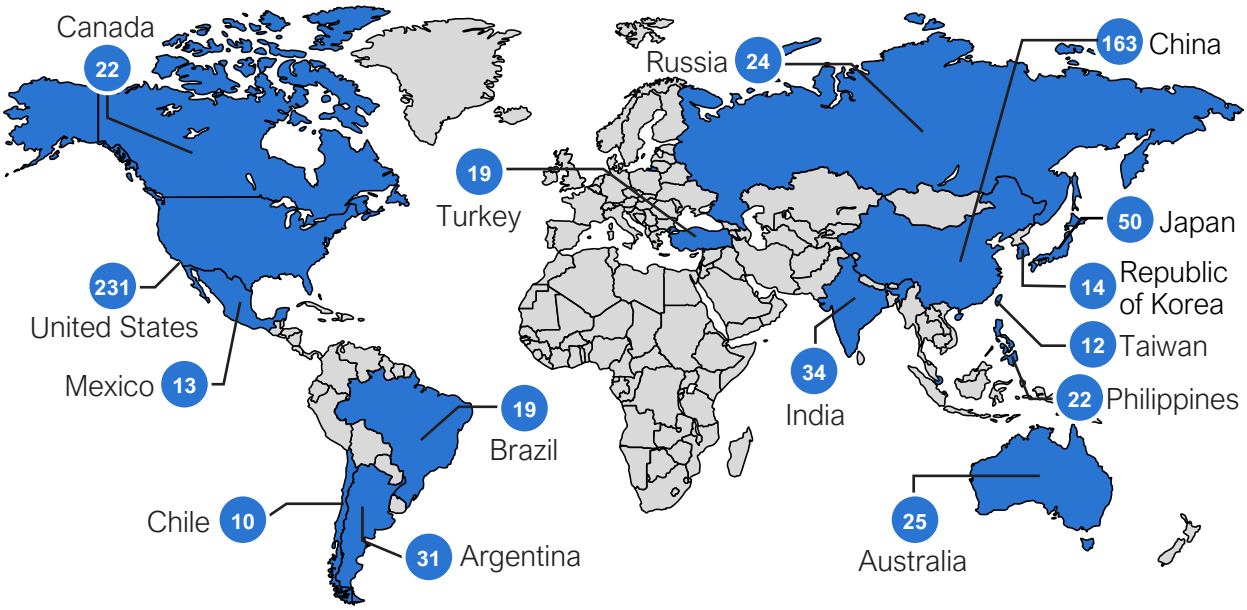
The participants could take part in this trial if they:

- had diabetes,
- were on medications for diabetes that remained the same for at least 3 months,
- had PDR in the study eye not previously treated with laser treatment,
- did not have any other eye disease in the study eye that would affect the results of the trial.

In this trial, only one eye was treated with **brolucizumab** or **PRP laser**, known as the treated eye or study eye.

In the untreated eye, also known as the fellow eye, participants could receive treatment for other eye disorders, or standard treatment for **PDR**, as decided by the trial doctors.

689 participants from 15 countries received treatment. The map below shows the number of participants who took part in each country.



What treatments did the participants receive?

The treatments in this trial were:

Brolucizumab, also called **RTH258**, was given at a dose of 6 milligrams (mg) as injections directly into the eye.

For the first 3 doses, participants received an injection once every 6 weeks. After that, they received an injection once every 3 months. Starting from Month 11, participants could extend the time between injections from every 6 weeks, up to a maximum of every 6 months based on the trial doctor's review. If their disease worsened, participants could go back to receiving injections once every 6 weeks or once every 3 months.

PRP laser was given in 1 to 4 sessions for the first 3 months, with each session lasting about 30 minutes. Participants received additional **PRP laser** in 2 to 4 sessions as decided by the trial doctors.

Researchers used a computer to randomly assign participants to their treatment. Participants had an equal chance of receiving **brolucizumab** or **PRP laser**. The participants, researchers, and trial staff knew what treatment the participants were receiving.

What happened during this trial?

Before treatment — 3 weeks

The trial staff checked to make sure the participants could be in this trial.

During treatment — Up to 1 year and 9 months

689 participants received treatment. Participants were equally assigned to receive 1 of the 2 treatments.

- 347 participants received **brolucizumab** as an injection directly into the study eye.
- 342 participants received **PRP laser** in 1 to 4 sessions for the first 3 months.

After treatment — 6 weeks

Trial staff checked participants' general health and for any medical problems for up to 6 weeks after participants' last trial treatment.

Trial staff checked the participants' general health throughout the trial.

What was the main result of this trial?

Did vision improve from the start of the trial until Week 54 for participants on brolucizumab compared to those on PRP laser?

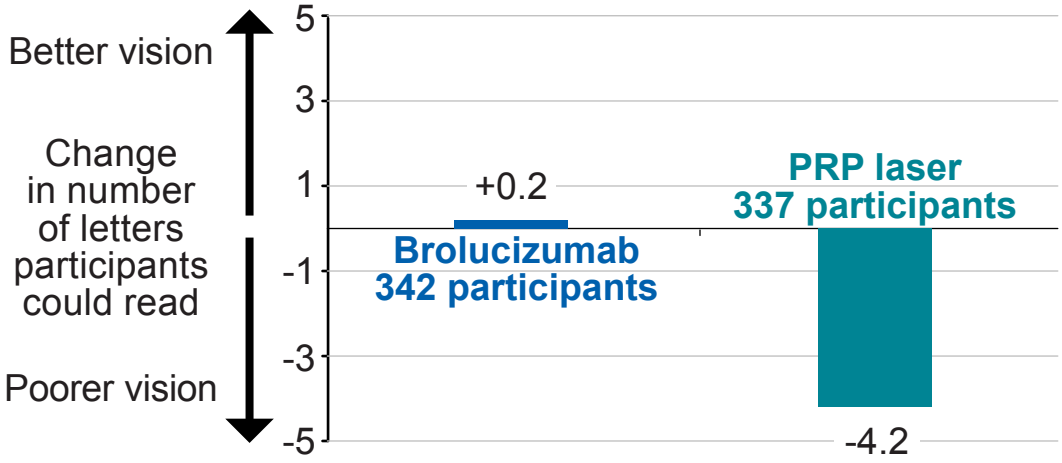
From the start of the trial until Week 54, participants on **brolucizumab** maintained their vision test scores, while those on **PRP laser** had a decrease in their vision test scores.

Researchers measured participants' vision using the ETDRS chart until Week 54. Following this the average vision test scores in the study eye for participants on **brolucizumab** and **PRP laser** were compared between the 2 groups.

What is ETDRS chart?
A test chart that has rows of letters from large to small size. It helps to monitor any changes in vision, especially during treatment.

Participants who were given **brolucizumab** kept their vision stable, while those on **PRP laser** had their vision go down.

Change in vision test scores at Week 54



Data from 342 out of 347 participants on **brolucizumab**, and 337 out of 342 on **PRP laser** were available at Week 54 and were used to compare the vision test scores.

What were the other results of this trial?

Did vision change from the start of the trial until Week 96 for participants on brolucizumab compared to those on PRP laser?

Participants on **brolucizumab** kept their vision stable at Week 96, whereas those on **PRP laser** had their vision go down.

How many participants developed serious eye problems that could affect sight due to diabetic retinopathy at Week 54 and Week 96?

At Week 54, a total of 117 out of 347 (34%) participants on **brolucizumab** developed serious eye problems that could affect sight, compared to 258 out of 342 (75%) of the participants on **PRP laser**.

At Week 96, a total of 144 out of 347 (42%) participants on **brolucizumab** developed serious eye problems that could affect sight, compared to 270 out of 342 (79%) of the participants on **PRP laser**.

At Week 54, how many participants in the brolucizumab group did not have signs of proliferative diabetic retinopathy (PDR), compared to those in the PRP laser group?

At Week 54, a total 187 out of 294 (64%) participants in the **brolucizumab** group did not have signs of **PDR**, compared to 65 out of 290 (22%) of the participants on **PRP laser**.

At Week 54, when checking for signs of PDR, not all participants on **brolucizumab** and **PRP laser** had available results.

At Week 54, how many participants on brolucizumab had swelling in the center of the macula, compared to those on PRP laser?

At Week 54, a total of 108 out of 347 (31%) participants treated with **brolucizumab** had swelling in the center of the macula, compared to 248 out of 341 (73%) of the participants treated with **PRP laser**.

At Week 54, when checking for swelling in the center of the macula, 1 participant on **PRP laser** did not have available results.

What is the macula?
The macula is the central part of the retina that helps to see fine details clearly.

What medical problems, also called adverse events, happened during this trial?

Trial doctors keep track of all medical problems, also called **adverse events**, that happen in trials. They track adverse events even if they think the adverse events are not related to the trial treatments.

Many trials are needed to know if a drug or treatment causes an adverse event.

This section is a summary of the adverse events that happened from the start of treatment until 6 weeks after the last treatment.

An **adverse event** is:

- Any **sign or symptom** that the participants have during a trial
- Considered **serious** when it is life-threatening, causes lasting problems, the participant needs hospital care, or results in death

Adverse events **may** or **may not** be caused by treatments in the trial.

In this trial, researchers wanted to distinguish between adverse events that happened in the eye (ocular adverse events) and in other parts of the body (non-ocular adverse events).

The researchers concluded there were no new safety concerns for **brolucizumab** in this trial.

What serious adverse events did the participants have?

201 participants had serious adverse events. 17 participants died.

The tables below show the most common ocular and non-ocular serious adverse events that happened.

Number of Participants (%) With Most Common Ocular Serious Adverse Events

	Brolucizumab 347 participants	**PRP laser** 342 participants
Leakage of blood into the gel that fills the eye cavity in the treated eye Vitreous hemorrhage - Study eye	**4 of 347** 1%	**19 of 342** 6%
Clouding in the treated eye Cataract - Study eye	**1 of 347** <1%	**4 of 342** 1%
Leakage of blood into the gel that fills the eye cavity in the untreated eye Vitreous hemorrhage - Fellow eye	**14 of 347** 4%	**9 of 342** 3%

Number Of Participants (%) With Most Common Non-Ocular Serious Adverse Events

	Brolucizumab 347 participants	**PRP laser** 342 participants
Stroke Cerebral infarction	**5 of 347** 1%	**1 of 342** <1%
High blood pressure Hypertension	**5 of 347** 1%	**1 of 342** <1%
Lung infection Pneumonia	**4 of 347** 1%	**1 of 342** <1%
Heart attack Myocardial infarction	**1 of 347** <1%	**4 of 342** 1%
Gradual loss of kidney function over time Chronic kidney disease	**1 of 347** <1%	**4 of 342** 1%
Infection of the feet in people with diabetes Diabetic foot	**0 of 347** 0%	**4 of 342** 1%
Sudden heart attack Acute myocardial infarction	**0 of 347** 0%	**4 of 342** 1%

What other (not including serious) adverse events did the participants have?

The tables below show the most common other adverse events that happened.

Number Of Participants (%) With Most Common Ocular Other Adverse Events

	Brolucizumab 347 participants	**PRP laser** 342 participants
Leakage of blood into the gel that fills the eye cavity in the treated eye Vitreous hemorrhage – Study eye	**40 of 347** 12%	**78 of 342** 23%
Fluid in or under the retina in people with diabetes in the treated eye Diabetic retinal edema - Study eye	**8 of 347** 2%	**41 of 342** 12%
Fluid in or under the macula in the treated eye Macular edema - Study eye	**9 of 347** 3%	**34 of 342** 10%
Leakage of blood into the gel that fills the eye cavity in the untreated eye Vitreous hemorrhage - Fellow eye	**35 of 347** 10%	**48 of 342** 14%

Number Of Participants (%) With Most Common Non-Ocular Other Adverse Events

	Brolucizumab 347 participants	**PRP laser** 342 participants
Covid-19	**44 of 347** 13%	**53 of 342** 16%
High blood pressure Hypertension	**31 of 347** 9%	**29 of 342** 8%
Nose and throat infection Upper respiratory tract infection	**30 of 347** 9%	**18 of 342** 5%

What was learned from this trial?

Researchers learned about the effects of **brolucizumab** in people with **proliferative diabetic retinopathy (PDR)**.

The researchers concluded that, compared to participants in the **PRP laser** group, the **brolucizumab** group had:

- participants who maintained vision at Week 54 and Week 96,
- fewer participants with signs of PDR and swelling in the center of the macula at Week 54,
- fewer participants with serious eye problems that could affect their sight at Week 54 and Week 96.

There were no new safety concerns with **brolucizumab** in this trial.

When this summary was written the sponsor had no plans for future trials of **brolucizumab** in people with **PDR**.

Where can I learn more about this trial?

More information about the results and adverse events in this trial can be found in the scientific summary of the results available on the Novartis Clinical Trial Results website **www.novctrd.com**

Follow these steps to find the scientific summary:

Go to **www.novctrd.com** → Click **Clinical Trial Results** → Agree to the terms ☑ **I accept** → Search for **CRTH258D2301**

For more information about this trial, go to this website:

- **clinicaltrials.gov** – search using the number **NCT04278417**

Other trials of **brolucizumab** may appear on the public websites above. When there, search for **brolucizumab** or **RTH258**.

Full clinical trial title: A 96-week, two-arm, randomized, single-masked, multi-center, phase III study assessing the efficacy and safety of brolucizumab 6 mg compared to panretinal photocoagulation laser in patients with proliferative diabetic retinopathy (CONDOR)

Novartis is a global healthcare company based in Switzerland that provides solutions to address the evolving needs of patients worldwide.

1-888-669-6682 (US) | +41-61-324 1111 (EU)

www.novartis.com/clinicaltrials