NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of brolucizumab in adults with neovascular age-related macular degeneration (nAMD)

Thank you!

Thank you to the participants who took part in the clinical trial for nAMD. 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: CRTH258AFR01

Drug studied: RTH258, known as **brolucizumab**

Sponsor: Novartis

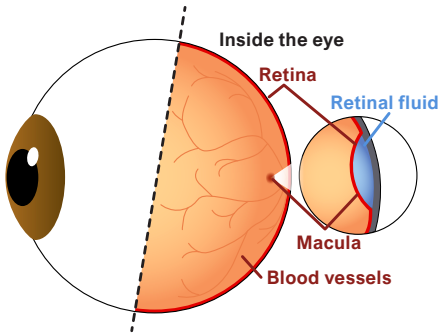
If you were a participant and have any questions about the results, please talk to the doctor or staff at the trial site.

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

What was the main purpose of this trial?

The purpose of this trial was to learn about the effects of **brolucizumab** in adults with **neovascular age-related macular degeneration (nAMD)**. To find this out, researchers gave **brolucizumab** as an injection directly into the participant's eye and observed the eyes for any improvement.

nAMD is a disorder that causes loss of eyesight in the central field of vision as a person grows older. Eyesight is lost because of new blood vessels forming inside the eye, as shown in the illustration. The new blood vessels that form are very delicate and leak blood and fluid into the eye. This causes swelling and slowly leads to eyesight loss.



Brolucizumab is a drug approved for the treatment of **nAMD** in France and in the United States. **Brolucizumab** belongs to the group of drugs called Anti-VEGF treatment. It works by blocking VEGF to slow the growth of the abnormal blood vessels in the eye. This slows or stops damage to the macula and slows down vision loss.
In this trial, researchers wanted to know the early and long-term effects of **brolucizumab** on the blood vessels that form in the retina of participant's with **nAMD** in France.

Trial drug
Brolucizumab

Pronounced as
BROE lue SIZ ue mab

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

- What effect did **brolucizumab** have on the area of the abnormal blood vessels in the retina at Week 12?
- What adverse events did the participants have during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial.

How long was this trial?

The trial began in January 2021 and ended in February 2023. It was planned for the participants to be in the trial for about 1 year after the start of the trial treatment.

Who was in this trial?

210 participants from France with **nAMD** received treatment in this trial. Participants' ages ranged from 52 to 93 years. Their average age was 78 years. The number of participants by gender is shown below.

Gender

81 Men	129 Women

The participants could take part in this trial if they:

- were aged 50 years or older,
- had a confirmed defect in their vision due to nAMD,
- had fluid in the retina, and
- never received any treatment for nAMD in their studied eye.

What treatment did the participants receive?

The treatment in this trial was:

Brolucizumab, given at a dose of 6 milligrams (mg) as a repeated injection into the eye.

The participants, trial doctors, or trial staff knew what treatment the participants were receiving.

What happened during this trial?

Before treatment — 1 day

Trial doctors checked the participants health and **nAMD** to make sure they could be in this clinical trial.

During treatment — 10 months

A total of 210 participants received treatment. The trial had 2 periods:

Period 1: loading or booster phase

- **Brolucizumab** 6 mg was given on Day 1 every 4 weeks up to Week 8 as an injection directly into the eye.
- At Week 12, participants' eyes were tested to find out the effects of **brolucizumab**.

Period 2: maintenance

- From Week 16 onward, brolucizumab 6 mg was given either once every 8 weeks or once every 12 weeks as per trial doctor's assessment of the disease.

Trial doctors checked the participants' disease condition and general health throughout the trial.

After treatment — 1 month

Participants returned to their trial site once after receiving their dose of treatment for follow-up visits.
No trial drug was given during this period.
Participants' health was monitored during this period.

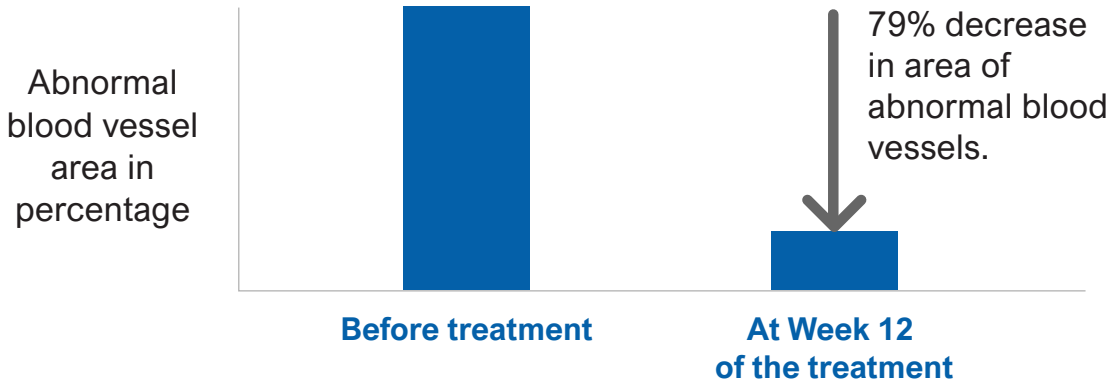
What was the main result of this trial?

What effect did brolucizumab have on the area of the abnormal blood vessels in the retina at Week 12?

Brolucizumab reduced the area of the abnormal blood vessels in the retina by 79% at Week 12.

To find this out, trial doctors took a scan of the eyes at regular periods and checked the area of the abnormal blood vessels in the retina. The area of the abnormal blood vessels before the start of the treatment was considered as 100%. This was then compared with the change in the area of abnormal blood vessels after the treatment.

Percentage change in area of abnormal blood vessels



Researchers found that the area of the abnormal blood vessels inside the retina decreased by 79% at Week 12 following treatment with **brolucizumab**.

What were the other results of this trial?

Did the treatment with brolucizumab reduce the thickness of the central part of the retina at Week 48?

Yes, treatment with **brolucizumab** reduced the thickness of the central part of the retina by 31%, which was an improvement at Week 48.

How many participants had a dry retina at Week 48 following treatment with brolucizumab?

62% of all the participants (99 out of 159) had a dry retina at Week 48 following treatment with **brolucizumab**.

How many participants had their brolucizumab injections once every 12 weeks during the maintenance period?

43% of all the participants (65 out of 153) had their **brolucizumab** injections once every 12 weeks during the maintenance period.

Did vision in participants on brolucizumab improve at Week 48 compared to the start of the trial?

Yes, after 48 weeks of treatment with **brolucizumab**, the average vision test score improved by 8 ETDRS letters compared to the start of the trial.

What is ETDRS chart?

It is a chart that has rows of letters from large to small size. It helps to monitor improvement or any change in vision especially during a treatment.

What adverse events did the participants have?

Trial doctors keep track of all **adverse events** that happen in trials, 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 up to 1 month after the last injection.

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.

64% of all the participants (135 of 210) had adverse events.
20 participants had adverse events that were considered serious.
26 participants had inflammation inside the treated eye.
1 participant died. 28 participants left the trial due to an adverse event.
The researchers concluded there were no new safety concerns for **brolucizumab** in this trial.

How many participants had adverse events?

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 number of participants with ocular or non-ocular adverse events is presented in the table below.

Number of Participants (%) With Ocular Adverse Events

Participants who:	Brolucizumab 6 mg 210 participants
Had at least 1 serious adverse event	8 of 210 (4%)
Had at least 1 adverse event in the treated eye	95 of 210 (45%)
Had at least 1 episode of inflammation in the treated eye	26 of 210 (12%)
Stopped treatment due to an adverse event	25 of 210 (12%)

Number of Participants (%) With Non-Ocular Adverse Events

Participants who:	Brolucizumab 6 mg 210 participants
Had at least 1 serious adverse event	13 of 210 (6%)
Had at least 1 adverse event on the body apart from the treated eye	77 of 210 (37%)
Stopped treatment due to an adverse event	3 of 210 (1%)
Died during the trial	1 of 210 (<1%)

What serious adverse events did the participants have?

20 participants had serious adverse events. 1 participant died.

The table below shows the most common serious adverse events that happened in **2 or more** participants.

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

	Brolucizumab 6 mg 210 participants
Inflammation of gel like part (vitreous cavity) of the eye Vitritis-Study eye	**4 of 210 (2%)**
Inflammation in the eye wall Uveitis-Study eye	**3 of 210 (1%)**

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

	Brolucizumab 6 mg 210 participants
Stroke Cerebrovascular accident	**2 of 210 (<1%)**

What other adverse events did the participants have?

130 participants had other adverse events.

The table below shows the other adverse events that happened in **5 or more** participants.

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

	Brolucizumab 6 mg 210 participants
Worsening of nAMD in the untreated eye Neovascular age-related macular degeneration-Fellow eye	**10 of 210 (5%)**
Pain in the treated eye Eye pain-Study eye	**8 of 210 (4%)**
Dark small shadowy shapes in the treated eye that obstruct the vision Vitreous floaters-Study eye	**8 of 210 (4%)**
Dryness in both eyes Dry eye-Both eye	**7 of 210 (3%)**
Inflammation of gel like part (vitreous cavity) of the treated eye Vitritis-Study eye	**6 of 210 (3%)**
Decreased clarity of vision in the treated eye Visual acuity reduced-Study eye	**5 of 210 (2%)**
Blurred vision in the treated eye Vision blurred-Study eye	**5 of 210 (2%)**

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

	Brolucizumab 6 mg 210 participants
High blood pressure Hypertension	**9 of 210 (4%)**
Covid-19	**8 of 210 (4%)**

What was learned from this trial?

Researchers learned about the effects of **brolucizumab** in people with nAMD in France.

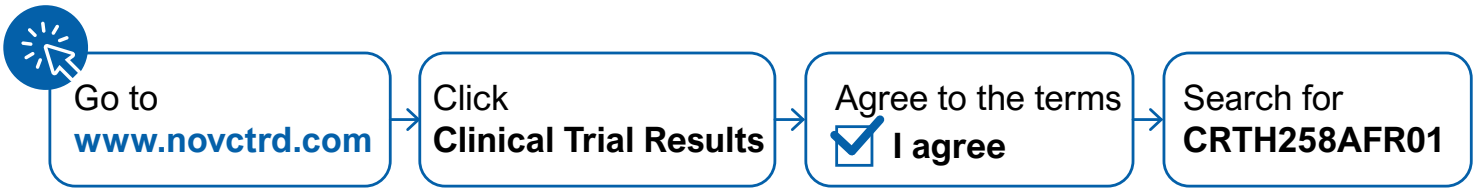
- The researchers found that treatment with **brolucizumab** 6 mg decreased the area of abnormal blood vessels inside the eyes in participants with nAMD
- Researchers found treatment with **brolucizumab** improved vision
- Researchers found that there was less inflammation reported in the treated eye than in previous trials with **brolucizumab**
- Researchers found no new safety concerns with **brolucizumab**

At the time this report was created, there were no plans for future trials with **brolucizumab** in people with nAMD.

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:



For more information about this trial, go to of these websites:

- **clinicaltrials.gov** – search using the number **NCT04239027**
- **clinicaltrialsregister.eu/ctr-search/search** – search using the number **2019-003338-17**

Full clinical trial title: A one-year, single-arm, open-label, multicenter study assessing the anatomic outcomes of brolucizumab assessed by OCT-A in adult patients with neovascular age-related macular degeneration (OCTOPUS)

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

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www.novartisclinicaltrials.com