NOVARTIS

Clinical Trial Results Summary

A clinical trial to predict the long-term effect of brolucizumab in people with wet age-related macular degeneration (wAMD) by identifying early changes in the eye when scanned

Thank you!

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

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: CRTH258AIT04

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

Sponsor: Novartis

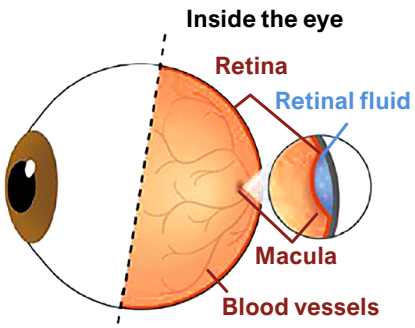
If you were a participant and have any questions about the results, please talk to the doctor or staff at the trial site.

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 whether identifying early changes in an eye scan could predict the long-term effect of **brolucizumab** in people from Italy with **wet age-related macular degeneration** (**wAMD**).

wAMD is a progressive 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 visual. 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 **wAMD** in Europe and United States. **Brolucizumab** belongs to the group of drugs called **anti-VEGF** treatment. It works by blocking a protein called **VEGF**, which is responsible for the growth of the abnormal blood vessels in the eye. Blocking **VEGF** slows or stops damage to the macula and slows down vision loss.

Trial drug
Brolucizumab
Pronounced as
BROE-lue-SIZ-ue-mab

In this trial, researchers wanted to know whether early changes in the eye, identified using a scanner, could predict the long-term effects of **brolucizumab** in participants with **wAMD**.

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

- Can parameters detectable by eye scanner predict the long-term effect of **brolucizumab** in participants with **wAMD** assessed after 16 weeks of treatment?
- **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 October 2021 and ended in October 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?

120 participants from Italy took part in this trial. Participants' ages ranged from 53 to 91 years. Their average age was 76 years. The number of participants by gender is shown below.

Gender

50 Men	70 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 **wAMD**,
- had fluid in the retina, and
- were able to read at least 23 letters in a vision test.

What treatments did the participants receive?

The treatment in this trial was:

Brolucizumab, 6 milligrams (mg) given as an injection into the treated eye every 4 weeks for the first 3 doses (until Week 16), and then either every 8 weeks or every 12 weeks, based on the doctor's decision (until Week 48).

Along with the above treatment, the participants could take standard treatments for **wAMD**, or treatments for any other disease in the non-treated eye. In this trial, participants, researchers and trial staff all knew what treatment each participant took.

What happened during this trial?

Before treatment — Up to 2 weeks

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

During treatment — Up to 11 months

A total of 120 participants received treatment. The trial had 2 parts:

Part 1

- **Brolucizumab** 6 mg was given every 4 weeks from Day 1 up to Week 8 as an injection directly into the treated eye.
- At Week 16, each participants' treated eye was checked to learn about the effects of **brolucizumab**.

Part 2

- 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.

After treatment — 1 month

Trial doctors monitored participants' overall health until 1 month after the end of the treatment.

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

What was the main result of this trial?

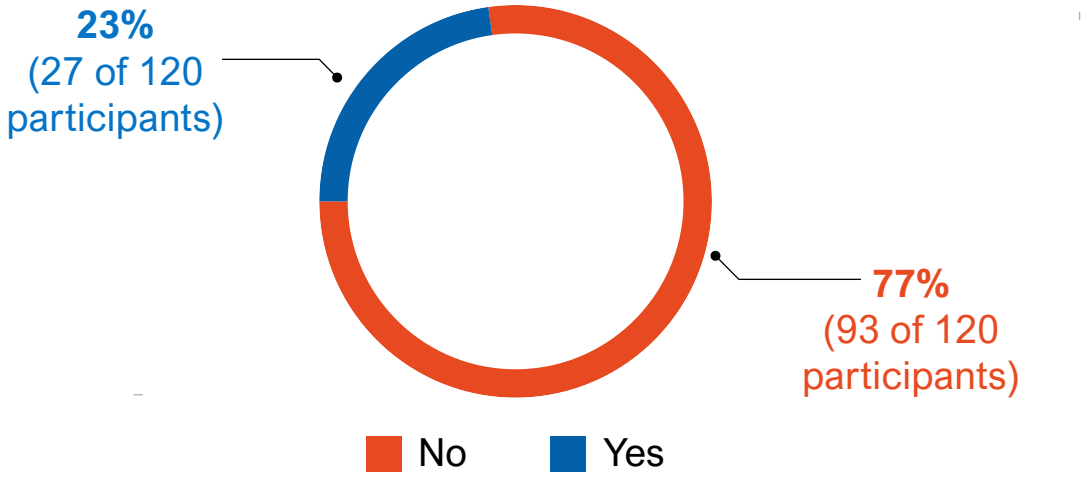
Can parameters detectable by eye scanner predict the long-term effect of brolucizumab in participants with wAMD assessed after 16 weeks of treatment?

In this trial, participants with no fluid inside the treated eye and receiving **brolucizumab** every 12 weeks until Week 48 were included. After 16 weeks of treatment, no parameters were found that could predict the response to long-term **brolucizumab** treatment in participants with **wAMD**.

To find this out, researchers assessed a few parameters using eye scanning procedures. From Day 1 to Week 16, they measured the retinal thickness by measuring the amount of fluid in the retina and checking the condition of the vessels at the back of the eye.

At Week 48, 23% of participants (27 of 120) were fluid-free and maintained **brolucizumab** dose frequency every 12 weeks, while 77% of participants (93 of 120) were not fluid free. Researchers found that the parameters did not predict the long-term effect of **brolucizumab** in participants with **wAMD**.

Participants who were fluid-free and maintained brolucizumab dose frequency every 12 weeks at Week 48



What were the other results of this trial?

What was the change in vision test score from Day 1 to Week 48?

Vision test score improved by about 6 ETDRS letters at Week 48 compared to Day 1.

What is ETDRS chart?

It is a test chart that has rows of letters from large to small size. It is used to test the vision in patients.

What was the change in quality of life from Day 1 to Week 48?

Based on questionnaires, there was no change in quality of life from Day 1 to Week 48.

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 end of the 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.

Participants who received at least one injection were analyzed in this section.

48% of participants (59 of 122) had adverse events. 11% of the participants had adverse events that were considered serious. No participants died. 7 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 are presented in the table below.

Number of Participants (%) With Ocular Adverse Events

Participants who:	**Brolucizumab** 122 participants
Had at least 1 adverse event in the treated eye	**25 of 122** 20%
Had at least 1 serious adverse event	**1 of 122** 1%
Left the trial due to an adverse event	**5 of 122** 4%

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

Participants who:	Brolucizumab 122 participants
Had at least 1 adverse event in the body, apart from the treated eye	40 of 122 33%
Had at least 1 serious adverse event	13 of 122 11%
Left the trial due to an adverse event	2 of 122 2%

What serious adverse events did the participants have?

14 participants had serious adverse events. No participants died.

None of the serious adverse events (ocular or non-ocular) happened in more than 2 participants.

What other adverse events did the participants have?

52 participants had other adverse events.

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

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

	Brolucizumab 122 participants
Break in the pigmented layer at the back of the treated eye Retinal Pigment Epithelial Tear- Study Eye	3 of 122 2%
Break in the tissue at the back of the treated eye Retinal Tear- Study Eye	2 of 122 2%

Clouding of the lens of the treated eye Cataract- Study Eye	**2 of 122** 2%
Inflammation of gel like part (vitreous cavity) of the treated eye Vitritis- Study Eye	**5 of 122** 4%
Inflammation of the treated eye Eye Inflammation- Study Eye	**2 of 122** 2%
Scar-like tissue over the central area in the back of the treated eye Macular Fibrosis- Study Eye	**2 of 122** 2%
Small break over the central area in the back of the treated eye Macular Hole- Study Eye	**3 of 122** 2%
Wet AMD in the untreated eye Neovascular age-related macular degeneration- Fellow Eye	**3 of 122** 2%

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

	Brolucizumab 122 participants
COVID-19	**13 of 122** 11%
Flu Influenza	**4 of 122** 3%

What was learned from this trial?

Researchers learned about the effects of **brolucizumab** in people from Italy with **wAMD**.

- Researchers concluded that imaging parameters did not predict the long-term effect of **brolucizumab** in participants with **wAMD**.
- Researchers found that treatment with **brolucizumab** improved vision test scores in participants with **wAMD**. However, there was no change in their quality of life.

At the time this report was created, there were no future trials planned with **brolucizumab** in people with **wAMD**. However, it cannot be ruled out if other trials will be planned in the future.

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** → Agree to the terms ☑ **I agree** → Search for **CRTH258AIT04**

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

- **clinicaltrials.gov** – search using the number **NCT04774926**
- **clinicaltrialsregister.eu/ctr-search/search** – search using the number **2020-002452-20**

Other trials will appear on the public websites above. When there, search for **RTH258** and/or **brolucizumab**.

Full clinical trial title: One year, single arm, open label, multicenter, phase IV study using multimodal imaging to guide disease activity assessment through innovative early predictive anatomical biomarkers of fluid resolution in wAMD patients treated with brolucizumab– *IMAGINE* study

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

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