NOVARTIS

Clinical Trial Results Summary

A clinical trial to compare the effects of 2 dosing plans of brolucizumab in people with uncontrolled wet age-related macular degeneration

Thank you!

Thank you to the participants who took part in the clinical trial for **wet age-related macular degeneration**. 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: CRTH258ADE01

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

Sponsor: Novartis

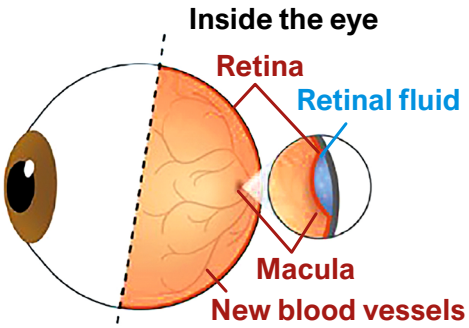
If you were a participant and have any questions about the results, please talk to the doctor or staff at the trial site.

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 compare the effects of 2 dosing plans of brolucizumab in people with uncontrolled **wet (or neovascular) age-related macular degeneration**. To find this out, trial doctors gave **brolucizumab** as injections directly into the participants' eyes and observed them for any improvement.

Wet age-related macular degeneration (wet AMD) or neovascular age-related macular degeneration (nAMD) is a progressive eye disorder that causes loss of eyesight in the macula as a person grows older. Eyesight is lost because new blood vessels form inside the eye, as shown in the figure. The new blood vessels that form are very delicate and leak blood and fluid into the eye. This causes swelling of the macula and slowly leads to vision loss.



The retina is the part at the back of the eye that is sensitive to light. The macula is the central part of the retina that is responsible for central vision and helps to see fine details clearly.

Brolucizumab is a drug approved in many countries including the United States, Europe and Switzerland for the treatment of **wet AMD**. 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 inside the eye. **Brolucizumab** blocks VEGF, helping to slow or stop damage from leaky blood vessels in the macula and slow down vision loss.

In this trial, researchers wanted to compare the effects of 2 dosing plans of **brolucizumab** on vision in participants with **wet AMD**.

Trial drug
Brolucizumab

Pronounced as
BROE-lue-SIZ-ue-mab

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

- How did the vision test scores change in the last 3 months of treatment, compared to the start of the trial, in the 2 **brolucizumab** dosing plans?
- 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 July 2021 and ended in January 2024. The participants were in the trial for about 1 year. The trial was completed with fewer participants than initially planned. This was due to difficulties in recruiting the required number of participants with **wet AMD**.

Who was in this trial?

52 participants with **wet AMD** received treatment in this trial – 20 men and 32 women. Participants' ages ranged from 58 to 93 years. Their average age was 78 years.

The participants could take part in this trial if they:

- were aged 50 years or older,
- had confirmed problems in their vision due to **wet AMD**,
- had fluid in the retina,
- had shown responses to earlier anti-VEGF treatment for **wet AMD**, and
- had a vision test score between 83 and 38 letters.

52 participants from 2 countries received treatment:

- Germany (47 participants)
- Switzerland (5 participants)

What treatments did the participants receive?

The treatment in this trial was:

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

The trial had 2 dosing plans:

- **Dosing plan 1**: **brolucizumab 6 mg** given as an injection once a month for the first 3 months, then once every 3 months.
- **Dosing plan 2: brolucizumab 6 mg** given as an injection at the start of the trial, then once every 3 months.

In this trial, only one eye was treated with **brolucizumab**, known as treated eye or study eye. In the other eye, known as the fellow eye, participants received treatments for other eye disorders or standard treatment for **wet AMD** as decided by the trial doctors.

Researchers used a computer to randomly assign participants to their treatment.

The participants, researchers, and trial staff knew what treatment the participants were receiving. All participants received **brolucizumab**.

The participants could continue the trial treatment as long as they were benefiting from it.

What happened during the trial?

Before treatment — Up to 2 weeks

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

During treatment — 11 Months

A total of 52 participants received treatment. Participants were equally assigned to receive 1 of the 2 dosing plans.

- **Dosing plan 1:** 25 participants received **brolucizumab 6 mg** as an injection directly into the eye once a month for the first 3 months, then once every 3 months.
- **Dosing plan 2:** 27 participants received **brolucizumab 6 mg** as an injection directly into the eye at the start of the trial, then once every 3 months.

After treatment — 1 Month

Trial staff checked participants' general health and monitored for any medical problems up to 1 month after the participants' last dose of trial treatment.

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

What were the main results of this trial?

How did the vision test scores change in the last 3 months of treatment, compared to the start of the trial, in the 2 brolucizumab dosing plans?

Compared to the start of the trial, the vision test scores in the last 3 months of treatment improved by 4 letters in participants on **brolucizumab dosing plan 1** compared to those on **dosing plan 2**.

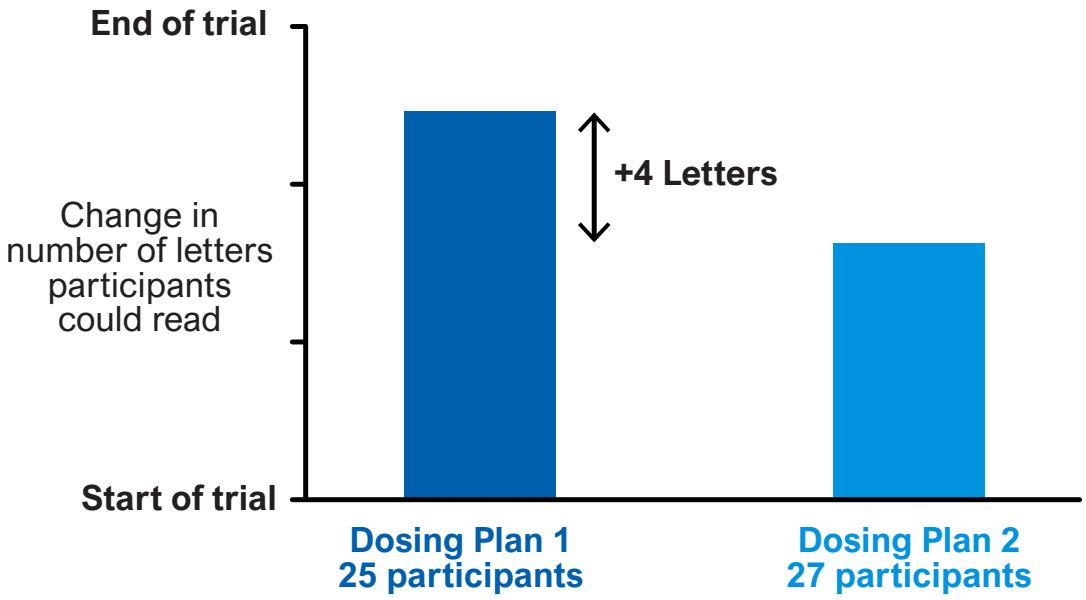
Researchers measured the average vision test scores for participants in the 2 dosing plans using the ETDRS chart. They then compared the vision test scores between the 2 groups.

In participants on **brolucizumab dosing plan 1**, vision test scores improved by 4 more letters compared to those on **dosing plan 2**.

What is the ETDRS chart?

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

Change in vision test scores from the start of the trial to the last 3 months of treatment



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 1 month 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.

A total of 49 out of 52 participants (94%) had adverse events, which include serious and non-serious. 11 participants had adverse events that were considered serious. No participant left the trial due to an adverse event. 1 participant died. The researchers concluded there were no new safety concerns for **brolucizumab** in this trial.

How many participants had adverse events?

	Dosing Plan 1 **Brolucizumab 6 mg** 25 participants	Dosing Plan 2 **Brolucizumab 6 mg** 27 participants
Had at least 1 **adverse event**	**23 of 25** 92%	**26 of 27** 96%
Had at least 1 **serious adverse event**	**5 of 25** 20%	**6 of 27** 22%
Died	**0 of 25** 0%	**1 of 27** 4%

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 shown below.

What serious adverse events did the participants have?

11 participants had serious adverse events. 1 participant in **dosing plan 2** died.

The table below shows the serious adverse events that happened in all participants.

Number of Participants (%) With Ocular Serious Adverse Events

	Dosing Plan 1 **Brolucizumab 6 mg** 25 participants	Dosing Plan 2 **Brolucizumab 6 mg** 27 participants
Swelling in the treated eye Eye inflammation-Study eye	**1 of 25** 4%	**1 of 27** 4%
Inflammation of the colored part of the treated eye Iridocyclitis-Study eye	**0 of 25** 0%	**1 of 27** 4%
Bleeding at the back of the treated eye Retinal haemorrhage-Study eye	**0 of 25** 0%	**1 of 27** 4%
Abnormal blood vessels are formed at the back of the treated eye Retinal neovascularization-Study eye	**0 of 25** 0%	**1 of 27** 4%
Inflammation of blood vessels at the back of the treated eye Retinal vasculitis-Study eye	**0 of 25** 0%	**1 of 27** 4%

	Dosing Plan 1 **Brolucizumab 6 mg** 25 participants	Dosing Plan 2 **Brolucizumab 6 mg** 27 participants
Decrease in clarity of vision in the treated eye Visual acuity reduced-Study eye	**0 of 25** 0%	**1 of 27** 4%
Infection inside the treated eye Endophthalmitis-Study eye	**1 of 25** 4%	**0 of 27** 0%
Increased fluid pressure in the treated eye Intraocular pressure increased-Study eye	**0 of 25** 0%	**1 of 27** 4%

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

	Dosing Plan 1 **Brolucizumab 6 mg** 25 participants	Dosing Plan 2 **Brolucizumab 6 mg** 27 participants
Reduced blood flow to the colon Colitis ischemic	**0 of 25** 0%	**1 of 27** 4%
Swelling in the colon Diverticulum intestinal	**0 of 25** 0%	**1 of 27** 4%
Bleeding in the stomach and gut Lower gastrointestinal hemorrhage	**0 of 25** 0%	**1 of 27** 4%

	Dosing Plan 1 **Brolucizumab 6 mg** 25 participants	Dosing Plan 2 **Brolucizumab 6 mg** 27 participants
Fever Pyrexia	**0 of 25** 0%	**1 of 27** 4%
Infection in the kidney Kidney infection	**0 of 25** 0%	**1 of 27** 4%
Severe infection that spreads from the urinary tract throughout the body Urosepsis	**0 of 25** 0%	**1 of 27** 4%
Swelling and pain in the joints Osteoarthritis	**0 of 25** 0%	**1 of 27** 4%
Kidney cancer Chromophobe renal cell carcinoma	**1 of 25** 4%	**0 of 27** 0%
Liver tumor Hepatic neoplasm	**1 of 25** 4%	**0 of 27** 0%
Repetitive involuntary movement Ballismus	**1 of 25** 4%	**0 of 27** 0%
Stroke Cerebrovascular accident	**1 of 25** 4%	**0 of 27** 0%

	Dosing Plan 1 Brolucizumab 6 mg 25 participants	Dosing Plan 2 Brolucizumab 6 mg 27 participants
Swelling of one or both kidneys Hydronephrosis	0 of 25 0%	1 of 27 4%

What other non-serious adverse events did the participants have?

The table below shows the most common other non-serious adverse events that happened in **3 or more** participants in any group. Additional adverse events happened in fewer participants.

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

	Dosing Plan 1 Brolucizumab 6 mg 25 participants	Dosing Plan 2 Brolucizumab 6 mg 27 participants
Blood spots on the white part of the treated eye Conjunctival haemorrhage-Study Eye	7 of 25 28%	5 of 27 19%
Worsening of nAMD in the untreated eye Neovascular age-related macular degeneration-Fellow Eye	3 of 25 12%	1 of 27 4%
Swelling at the back of the treated eye Retinal oedema-Study Eye	1 of 25 4%	3 of 27 11%
Decrease in clarity of vision in the treated eye Visual acuity reduced-Study Eye	1 of 25 4%	3 of 27 11%

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

	Dosing Plan 1 **Brolucizumab 6 mg** 25 participants	Dosing Plan 2 **Brolucizumab 6 mg** 27 participants
COVID-19	**6 of 25** 24%	**5 of 27** 19%
Common cold Nasopharyngitis	**6 of 25** 24%	**5 of 27** 19%
High blood pressure Hypertension	**3 of 25** 12%	**3 of 27** 11%

What was learned from this trial?

Researchers learned about the effects of 2 dosing plans of **brolucizumab** in people from Germany and Switzerland with **wet age-related macular degeneration** (**wet AMD**). The trial was completed with fewer participants than initially planned.

- The researchers learned that participants who received the **brolucizumab dosing plan 1** had better vision scores compared to those who received the **brolucizumab dosing plan 2**.
- Researchers did not find any new safety issues with **brolucizumab** in this trial.

When this summary was written, the sponsor had no plans for future trials for **brolucizumab** in people with **wet AMD**.

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 agree** → Search for **CRTH258ADE01**

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

- **clinicaltrials.gov** – search using the number **NCT04679935**
- **clinicaltrialsregister.eu** – search using the number **2019-004767-53**

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

Full clinical trial title: A 52-week, two arm, randomized, open-label, multicenter study assessing the efficacy and safety of two different brolucizumab 6 mg dosing regimens for patients with suboptimal anatomically controlled neovascular age-related macular degeneration (FALCON)

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