NOVARTIS

Clinical Trial Results Summary

A clinical trial extension to learn more about the effects of brolucizumab in people with neovascular age-related macular degeneration (Wet AMD) who have completed the CRTH258A2303 trial

Thank you!

Thank you to the participants who took part in the clinical trial for neovascular (wet) age-related macular degeneration. 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: CRTH258A2303E1

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

Sponsor: Novartis

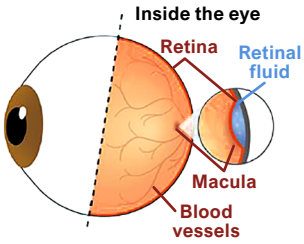
If you were a participant and have any questions about the results, please talk to the doctor or staff at the trial site.

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 about the effects of **brolucizumab** in people with **neovascular age-related macular degeneration**, also called **wet AMD**. To find this out, researchers examined participants who had completed the CRTH258A2303 trial, also known as TALON trial, and then received **brolucizumab** for a longer duration.

Wet AMD is an eye disease that develops in some people as they grow older. In this disease, the back of the eye, also called the retina, can form new abnormal vessels that carry blood and fluid. These newly formed vessels are very weak and can leak this blood and fluid. This can cause a blind spot or distortion in the central vision. Central vision is needed for seeing objects clearly and for common daily tasks such as reading and driving.



Results in loss of central vision

Brolucizumab is a medicine which is approved for the treatment of **wet AMD** in several countries. It works by blocking a protein called **VEGF** that forms new blood vessels in the retina. However, for many patients the treatment with medicines that block **VEGF** requires frequent injections and hence, many visits to the doctor's office. There is a need to reduce the treatment burden and control the symptoms of **wet AMD**, and researchers wanted to know whether **brolucizumab** could do this.

Trial drug
Brolucizumab

Pronounced as
BROE-lue-SIZ-ue-mab

The trial purpose was to answer these main questions:

- What was the longest time between injections where participants were without **wet AMD** symptoms up to week 56?
- 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 December 2020 and ended in March 2023. It was planned for each participant to be in the trial for about 1 year and 1 month after receiving their first trial treatment.

Who was in this trial?

248 participants with **wet AMD** who had successfully completed the CRTH258A2303 core trial received treatment during this trial. Participants' ages were between 52 and 95 years. Their average age was 76 years. The number of participants by gender and race is shown below.

Gender

119 Men	129 Women

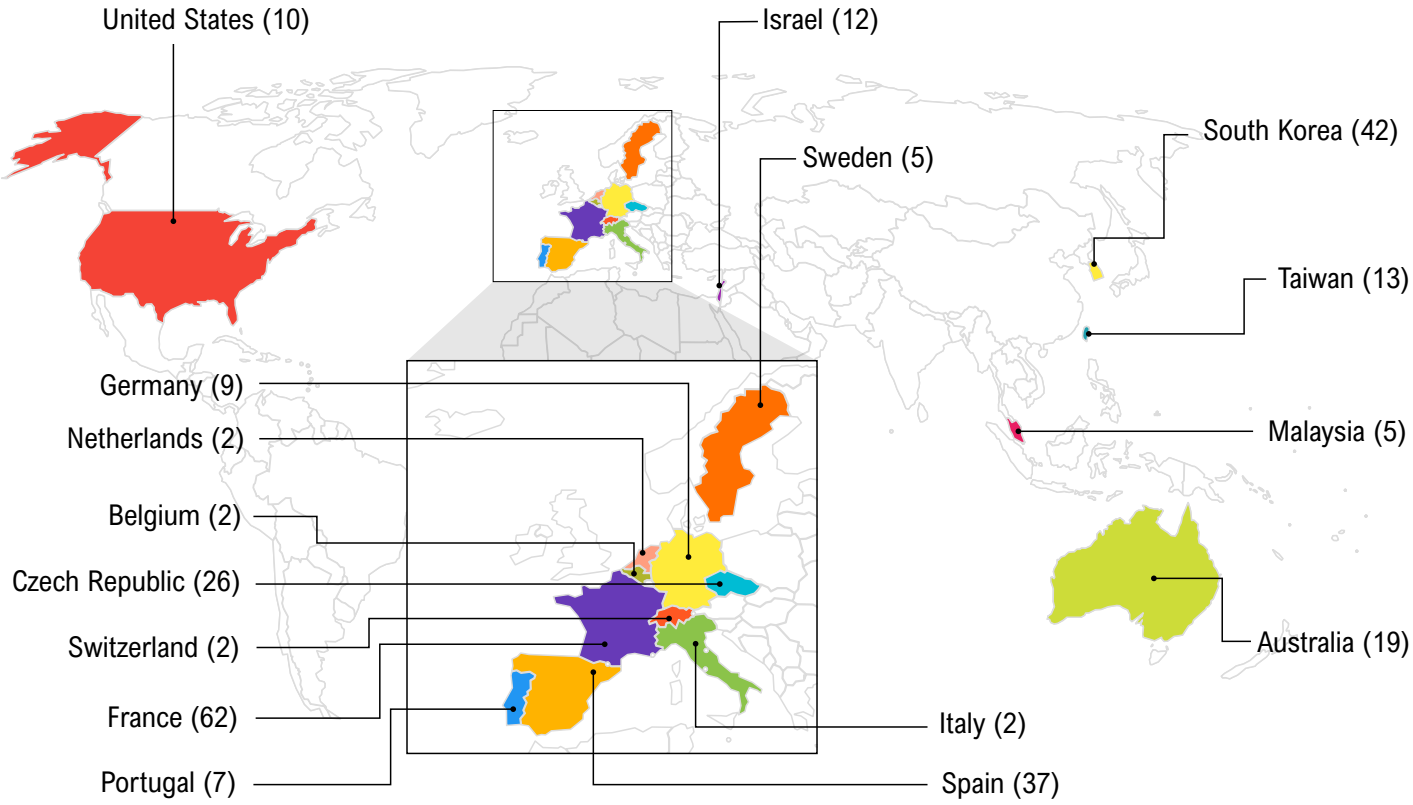
Race

61 Asian	187 White

The participants could take part in this trial if they:

- were 50 years of age or older,
- had successfully completed the core trial,
- were healthy enough to participate in the trial, as assessed by the trial doctors,
- were appropriately treated with anti-**VEGF** injections in the study eye, and
- required study treatment no less than every 4 weeks.

255 participants from 16 countries entered this trial, and of those 248 received treatment. The map below shows the number of participants who took part in each country.



What treatments did the participants receive?

The treatment in this trial was:

Brolucizumab 6 milligram (mg), given as an injection into the study eye every 4, 8, 12, 16, or 20 weeks between injection treatments.

Along with the treatments above, the participants could take standard treatments for **wet AMD** in the other eye (non-study eye). Medicines to reduce inflammation in the form of eye drops were allowed in both eyes.

In this trial, the participants, trial doctors and trial staff knew what treatment the participants received.

What happened during this trial?

In this trial, the study eye was the same eye that received **brolucizumab** or aflibercept treatment in CRTH258A2303 core trial.

Before treatment [Day 1]

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

*The first day of this extension trial (Day 1) for a participant was also the last day they participated in the completed core trial.

During treatment [Up to 54 weeks]

All 248 participants were treated as follows:

Brolucizumab 6 mg

- was given every 8 weeks, every 12 weeks, every 16 weeks, or every 20 weeks, based on when the last injection was given in the core trial and the trial doctor's assessment of **wet AMD** and eye health in the study eye.
- The time between injection was shortened by 4 weeks if any signs of disease came back.

Trial doctors checked the participants' **wet AMD**, eye health and general health throughout the trial.

After treatment [4 weeks]

Participants' **wet AMD** and health was monitored during this period.

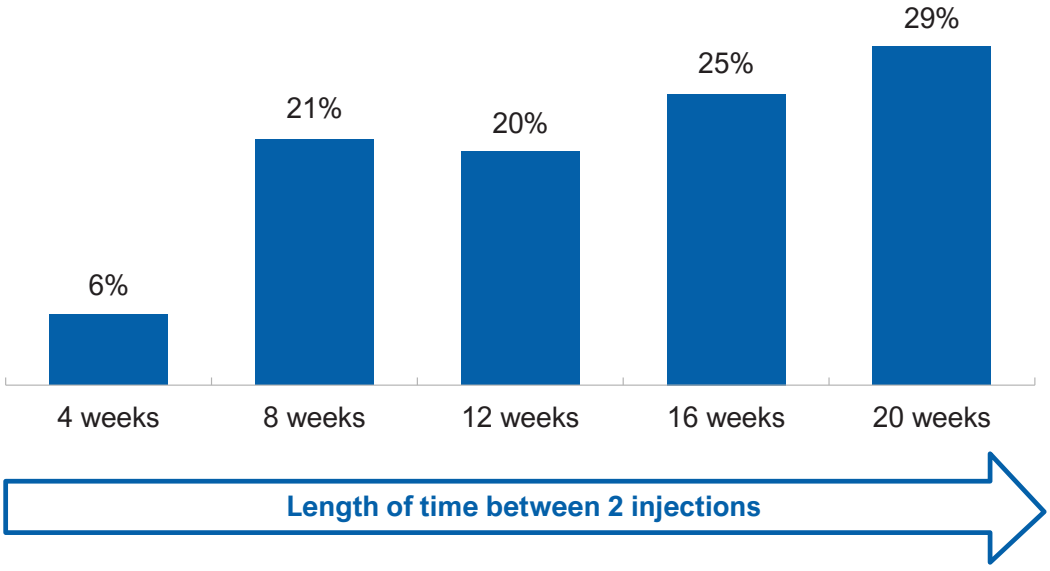
What were the main results of this trial?

What was the longest time between injections where participants were without wet AMD symptoms up to week 56?

20 weeks was the longest time between 2 injections where 29% of participants were without **wet AMD** symptoms up to week 56.

To answer this question, researchers counted the number of participants with no **wet AMD** symptoms in the study eye in each treatment interval (time between injections: 4 weeks, 8 weeks, 12 weeks, 16 weeks, or 20 weeks), through Week 56.

Participants with no wet AMD symptoms up to Week 56 at a specific time between injections

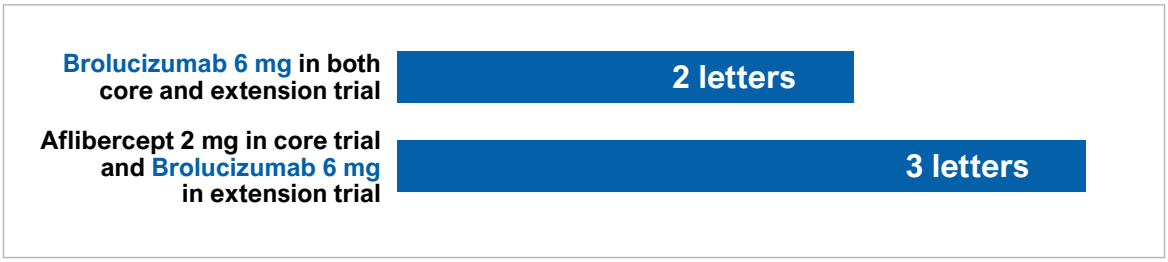


What was the change in vision test scores?

In this extension trial, vision test scores showed almost similar result for participants previously given **brolucizumab** compared to those previously given aflibercept in the core trial.

To answer this question, researchers measured how well the participants could see different sized letters on a chart at the end of the trial. This is called a best-corrected visual acuity score, or vision test score.

Change in Vision Test Scores By The End of The Trial



What were the other results of this trial?

What was the last time between injections where participants were without wet AMD symptoms at the end of the trial?

For participants previously treated with **brolucizumab**, 20 weeks was the last time between 2 injections with no **wet AMD** symptoms for 38% of participants. For participants previously treated with aflibercept, 16 weeks was the last time between 2 injections with no **wet AMD** symptoms for 28% of participants.

What was the change in vision test scores from start of the core trial to the end of this extension trial?

Vision test scores showed a similar improvement for participants on **brolucizumab** compared to those previously treated with aflibercept in the core trial.

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 during the treatment and up to 30 days after the last treatment in this trial.

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.

Overall, 129 out of 248 (52%) participants had adverse events. 26 participants had adverse events that were considered serious. 1 participant died due to a breathing issue. 7 participants left the trial due to an adverse event. The researchers concluded there were no new safety concerns for **brolucizumab** for this trial.

How many participants had adverse events?

Participants who:	Brolucizumab 6 mg 248 participants
Had at least 1 adverse event	**129 of 248** 52%
Had at least 1 adverse event to the eye (Ocular)	**82 of 248** 33%
Had at least 1 adverse event on the body apart from the eye (Non-ocular)	**82 of 248** 33%
Had at least 1 serious adverse event	**26 of 248** 10%
Stopped treatment due to an adverse event	**7 of 248** 3%
Died during the trial*	**1 of 248** <1%

*Not related to the treatment

What serious adverse events did the participants have?

26 participants had serious adverse events.

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

Serious adverse events of the eye (Ocular):
No serious ocular adverse events occurred in more than 1 participant.

Serious adverse events apart from the eye (Non-ocular):

	Brolucizumab 6 mg 248 participants
Irregular heartbeat (Atrial fibrillation)	**2 of 248** 1%
Falling down (Fall)	**2 of 248** 1%
Skin cancer (Basal cell carcinoma)	**5 of 248** 2%

What other adverse events did the participants have?

64 participants had other adverse events.

The table below shows the other adverse events that happened in **6 or more participants**.

Adverse events of the eye (Ocular):

	Brolucizumab 6 mg 248 participants
Clouding of the lens of the treated eye (Cataract-Study Eye)	**9 of 248** 4%
Clouding of the lens of the untreated eye (Cataract-Non study Eye)	**7 of 248** 3%
Decrease in clarity of vision in the treated eye (Visual acuity reduced-Study Eye)	**6 of 248** 2%
Pain in the treated eye (Eye pain-Study Eye)	**6 of 248** 2%
Wet AMD in the untreated eye (Neovascular age-related macular degeneration-Non study Eye)	**10 of 248** 4%

Adverse events on body apart from the eye (Non-ocular):

	Brolucizumab 6 mg 248 participants
Coronavirus disease (COVID-19)	**10 of 248** 4%
Common cold (Nasopharyngitis)	**8 of 248** 3%
Falling down (Fall)	**7 of 248** 3%

What was learned from this trial?

Researchers learned about the effects of **brolucizumab** in people with **wet AMD**.

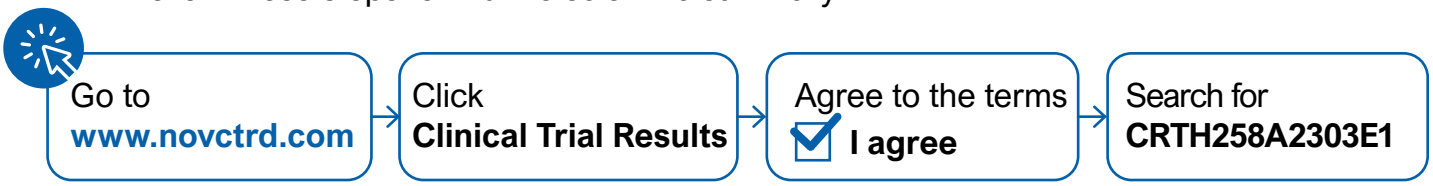
- The researchers found that **brolucizumab** 6 mg could control participants' **wet AMD** when the time between the 2 injections were prolonged comparing to the current existing treatment regimen.
- Most participants' time between 2 injections were increased by 4 weeks or more.
- The time between 2 injections could be increased up to 20 weeks for about one third of the participants.
- 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 **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:



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

- **www.clinicaltrials.gov** – search using the number **NCT04597632**
- **https://www.clinicaltrialsregister.eu/ctr-search** – search using the number **2020-002349-40**

Full clinical trial title: A 56-week phase IIIb/IV, open-label, one-arm extension study to assess the efficacy and safety of brolucizumab 6 mg in a Treat-to-Control regimen with maximum treatment intervals up to 20 weeks for the treatment of patients with neovascular age-related macular degeneration who have completed the CRTH258A2303 (TALON) study

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