NOVARTIS

Clinical Trial Results Summary

A clinical trial comparing the effects of brolucizumab and aflibercept in people with neovascular age-related macular degeneration (Wet AMD)

Protocol number: CRTH258A2303

Thank You!

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.

Thanks to the participants for taking part in this trial for the drug **brolucizumab**, also known as **RTH258**. They helped researchers learn more about how **brolucizumab** works in people with neovascular age-related macular degeneration.

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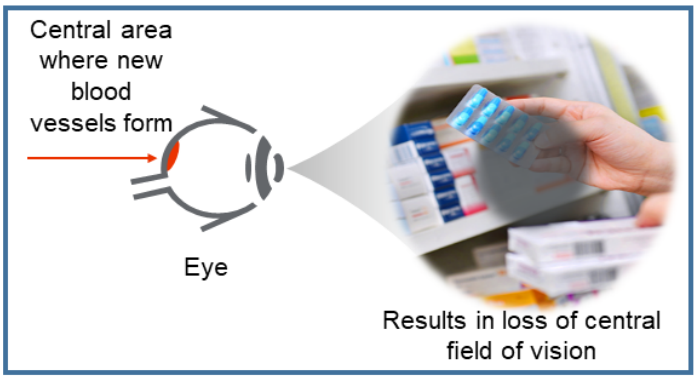
If the participants have any questions about the trial results, please talk to the doctor or staff at the trial site.

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

Why was the research needed?

Researchers were looking for a better way to treat **neovascular age-related macular degeneration**, also called **wet AMD**.



Wet AMD is a disease of the eye 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 leaked fluid can collect in the eye and cause eventual loss of central vision. Central vision is needed for seeing objects clearly and for common daily tasks such as reading and driving.

Brolucizumab is a medicine which is approved for the treatment of wet AMD in Australia, Canada, Japan, United States, and some countries in Europe. It works by blocking a protein that forms new blood vessels in the retina. However, there is still a need for better treatments that uses fewer injections to improve vision.

Drug	Pronounced as
Brolucizumab	BRO lu SIZ oo mab
Aflibercept	a FLI ber sept

Aflibercept is a medicine which works like **brolucizumab** and is approved for the treatment of wet AMD.

In this trial, the researchers wanted to see if the effects of **brolucizumab** in treating wet AMD is better than **aflibercept**.

How long was this trial?

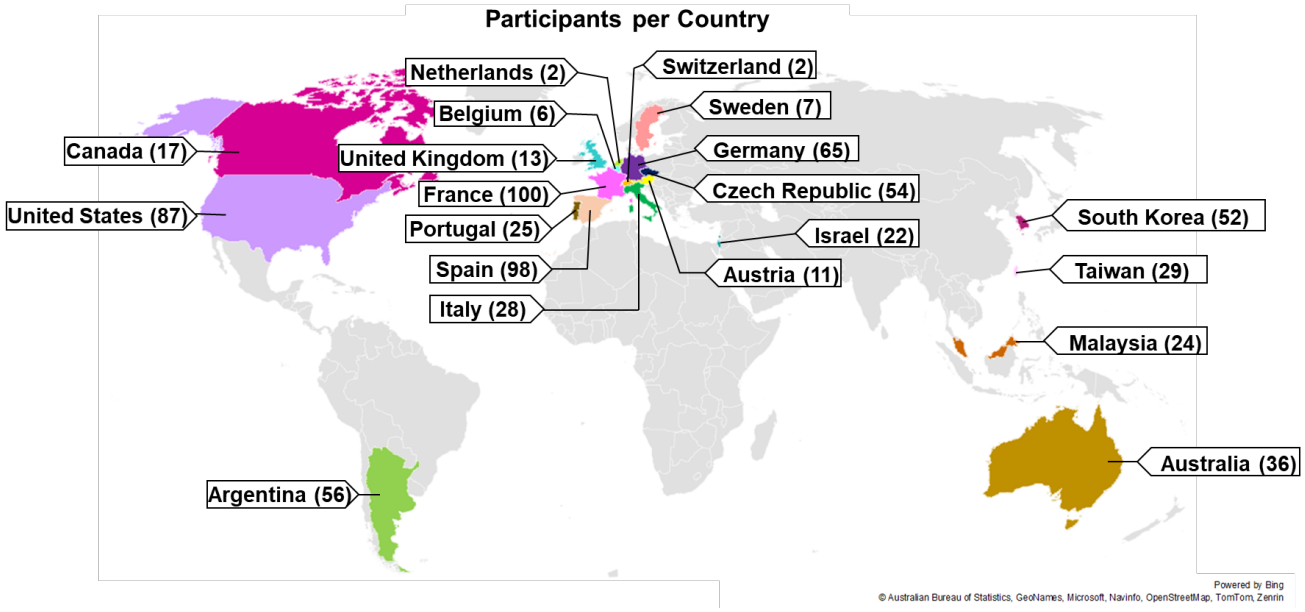
This trial started in September 2019 and ended in September 2022. The entire duration, from enrolling the first participant to the last participant completing the trial was around 3 years. An individual participant was in this trial for an average of 1 year and 3 months.

Who was in this trial?

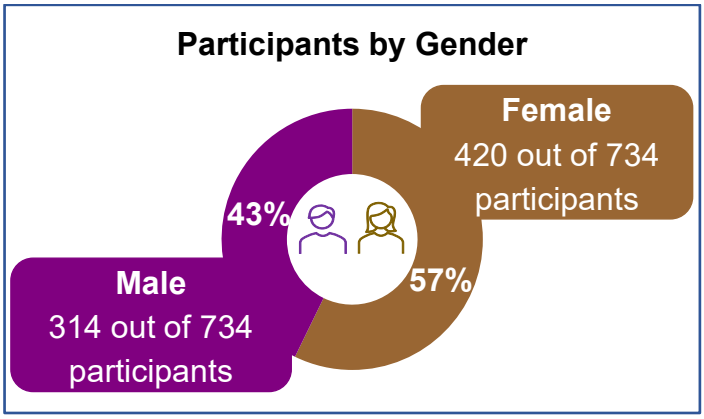
The participants could take part in this trial if they:

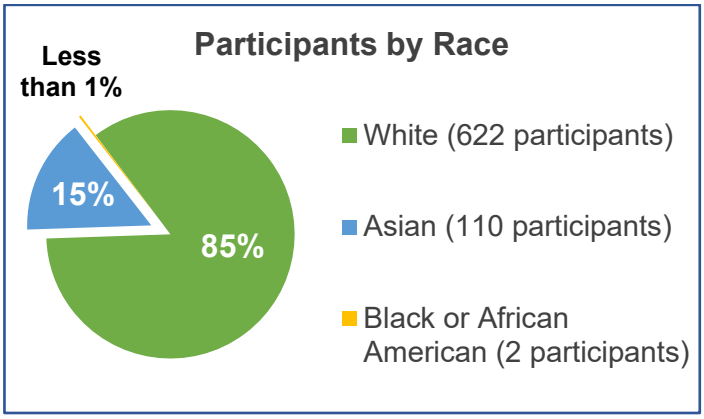
- were aged 50 years or older,
- had been diagnosed with wet AMD,
- had not received any other treatment or surgery for wet AMD, and
- had no other serious eye conditions or heart disease.

A total of 734 participants from 20 countries received treatment.



Participants' age ranged from 51 to 95 years. The average age of the participants was 76 years.





What treatments did the participants receive?

The treatments in this trial were:

Treatment drug	Comparator
 **Brolucizumab** was given as an injection in the eye at a dose of 6 mg.	 **Aflibercept** was given as an injection in the eye at a dose of 2 mg.

Participants in both groups received one injection at the start of the study (on Day 1), at Week 4, at Week 8, and at Week 16. After Week 16, they received one injection every 8 weeks, every 12 weeks or every 16 weeks, as evaluated by the trial doctor.

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, none of the participants, trial doctors, or trial staff knew what treatment the participants were receiving. Some trials are done this way because knowing what treatment each participant is getting can affect the results of the trial. Doing a trial this way helps to make sure that the results are looked at with fairness towards all treatments.

What happened during this trial?

Before treatment

The trial doctors checked if participants could take part in this trial.

Participants were randomly assigned to one of the following 2 treatment groups using a computer system. Each participant had an equal chance of ending up in either group.

- **Brolucizumab** (366 participants)
- **Aflibercept** (368 participants)

Up to 2 weeks

During treatment

Participants in both treatment groups underwent the following treatment process:

- The participants received one injection on Day 1, Week 4, Week 8, and Week 16.
- After Week 16, participants received treatment injections every 8 weeks, 12 weeks, or 16 weeks as per the study doctor's assessment.
- Participants were discontinued from the trial if they needed study treatment more frequently than **every 8 weeks**.

Up to 62 weeks

After treatment

Participants' health was monitored throughout the trial. All participants underwent a final assessment 4 weeks after their last injection.

Up to 4 weeks

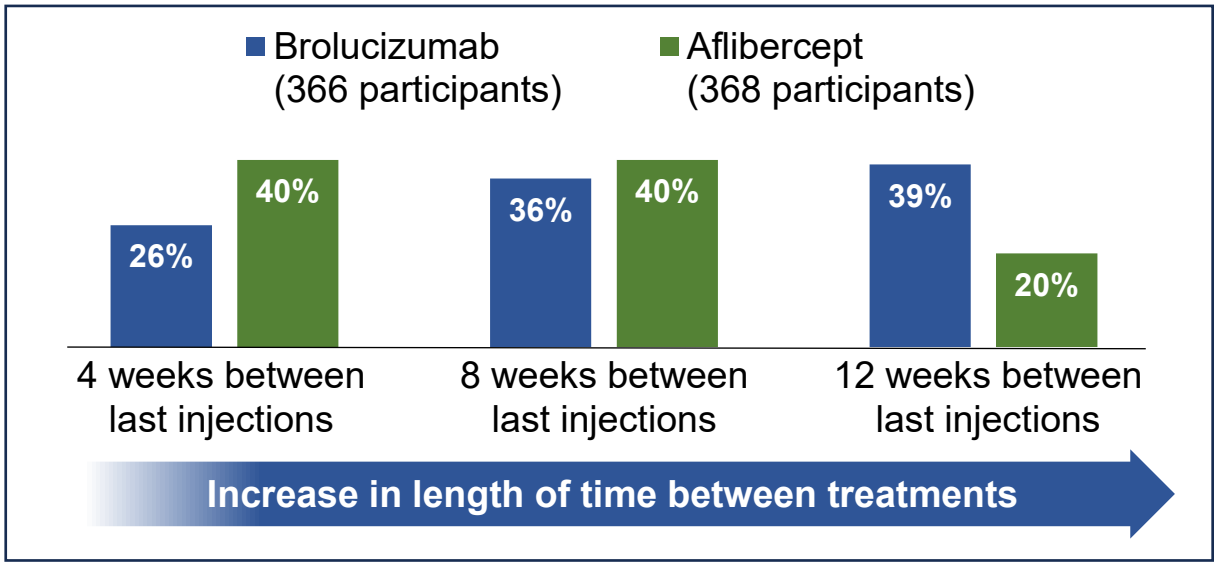
What were the main results of this trial?

When increasing time between last injections, how many participants treated with brolucizumab compared to aflibercept remained symptom-free by Week 32?

To answer this, researchers calculated how many participants treated with **brolucizumab** compared to **aflibercept** were symptom-free with either 4 weeks, 8 weeks, or 12 weeks between their last injections, by Week 32. The time between last injections was determined by the trial doctor, based on participant's wet AMD symptoms, up to the end of the trial.

At Week 32, a higher percentage of participants who received **brolucizumab** had a longer symptom-free time compared to those who received **aflibercept**.

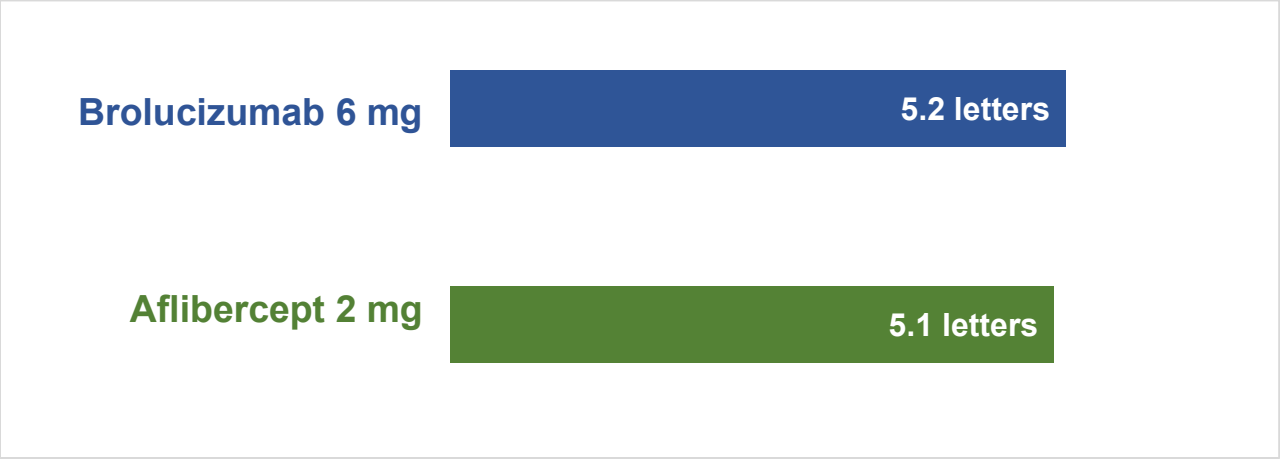
Percentage (%) of Symptom-Free Participants with 4, 8, or 12 weeks between last injections up to Week 32



Did vision test scores show similar improvement for participants treated with brolucizumab compared to aflibercept by Week 32?

To answer this, researchers measured how well the participants could see using a score called best-corrected visual acuity score, or vision test scores. By Week 32, vision test scores were similar in participants treated with **brolucizumab** and **aflibercept**.

Improvement of Vision Test Scores By 32 Weeks of Treatment



What were the other results of this trial?

When increasing time between injections, how many participants treated with brolucizumab compared to aflibercept remained symptom-free by Week 64?

The number of symptom-free participants treated with **brolucizumab** compared to **aflibercept** with 4, 8,12 or 16 weeks between last injections by Week 64 are listed in the following table.

Symptom-free participants (%) by the time between their last injections

Participants' time between their last injections	Brolucizumab 6 mg (366 out of 734 participants)	Aflibercept 2 mg (368 out of 734 participants)
16-week	104 (28%)	45 (12%)
12-week	82 (22%)	88 (24%)
8-week	95 (26%)	81 (22%)
4-week	85 (23%)	154 (42%)

Did vision test scores show similar improvement for participants on brolucizumab compared to those on aflibercept by Week 64?

By Week 64, vision test scores improved on average by **4.7** letters for participants treated with **brolucizumab** and by **4.9** letters for participants treated with **aflibercept**.

What medical problems did the participants have during the trial?

Medical problems that happen in clinical trials are called “adverse events”.

A lot of research is needed to know whether a drug causes an adverse event. **During a trial, all adverse events are recorded, whether or not they are thought to be caused by the trial drug.** When new drugs are being studied, researchers keep track of all adverse events participants have.

An adverse event is any sign, symptom, or disease that participants have during a trial.

An adverse event is considered “serious” when it is life-threatening, causes lasting problems, or the participant needs hospital care. ***These problems may or may not be caused by the trial drug.***

This section is a summary of the adverse events that happened during the treatment and 30 days after the last treatment in this trial. The websites listed at the end of this summary may have more information about all the adverse events that happened 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

	Brolucizumab 6 mg (366 out of 734 participants)	Aflibercept 2 mg (368 out of 734 participants)
At least 1 adverse event to the treated eye	114 (31%)	102 (28%)
At least 1 serious adverse event	10 (3%)	3 (1%)
Stopped drug due to adverse event	18 (5%)	3 (1%)

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

	Brolucizumab 6 mg (366 out of 734 participants)	Aflibercept 2 mg (368 out of 734 participants)
At least 1 adverse event on body apart from the treated eye	182 (50%)	185 (50%)
At least 1 serious adverse event	49 (13%)	50 (14%)
Stopped drug due to adverse event	0	3 (1%)
Death	4 (1%)	2 (1%)

What were the most common serious adverse events?

The most common serious adverse events that happened in more than 2 participants in any group are presented below.

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

	Brolucizumab 6 mg (366 out of 734 participants)	Aflibercept 2 mg (368 out of 734 participants)
Inflammation in the eye wall (Uveitis – Study Eye)	3 (1%)	0

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

	Brolucizumab 6 mg (366 out of 734 participants)	Aflibercept 2 mg (368 out of 734 participants)
Heart failure (Cardiac failure)	3 (1%)	1 (<1%)
Worsening of chest infection due to COVID-19 virus (COVID-19 pneumonia)	5 (1%)	1 (<1%)

What were the most common other adverse events?

The most common other adverse events that happened in at least 4% (4 out of 100) of participants in any group are presented below.

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

	Brolucizumab 6 mg (366 out of 734 participants)	Aflibercept 2 mg (368 out of 734 participants)
Blood spot on white part of the treated eye (Conjunctival haemorrhage-Study Eye)	23 (6%)	13 (4%)
Dark small shadowy shapes that obstruct the vision (Vitreous floaters-Study Eye)	14 (4%)	6 (2%)
Decrease in clarity of vision in the treated eye (Visual acuity reduced-Study Eye)	18 (5%)	19 (5%)
Drying of the treated eye (Dry eye-Study Eye)	8 (2%)	18 (5%)
Drying of the untreated eye (Dry eye-Non study Eye)	6 (2%)	16 (4%)
Pain in the treated eye (Eye pain-Study Eye)	17 (5%)	13 (4%)
Wet age-related disease in the untreated eye (Neovascular age-related macular degeneration-Non study Eye)	22 (6%)	17 (5%)

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

	Brolucizumab 6 mg (366 out of 734 participants)	Aflibercept 2 mg (368 out of 734 participants)
COVID-19 (COVID-19)	9 (2%)	16 (4%)
High blood pressure (Hypertension)	18 (5%)	17 (5%)

How many participants stopped trial drug due to adverse events?

During this trial, 18 out of 366 participants (5%) treated with **brolucizumab** and 6 out of 368 participants (2%) treated with **aflibercept** discontinued the trial treatment due to adverse events in the study eye.

The most common adverse event leading to study discontinuation in more than 1% of the participants was **inflammation in the eye wall** (uveitis) reported in 4 out of 366 participants (1%) in the **brolucizumab** group. Adverse events leading to study discontinuation in the **aflibercept** group happened in less than 1% participants.

How was this trial useful?

This trial helped the researchers understand if the effects of **brolucizumab** in treating **wet AMD** are better than **aflibercept**.

The researchers concluded that:

- the benefits of **brolucizumab** lasted longer than **aflibercept**.
- the time between **brolucizumab** injections could be extended without affecting how long participants remained symptom-free, which meant fewer injections into the eye.
- **brolucizumab** was as effective as **aflibercept** and that there is no major difference between the treatments when it came to improving vision.

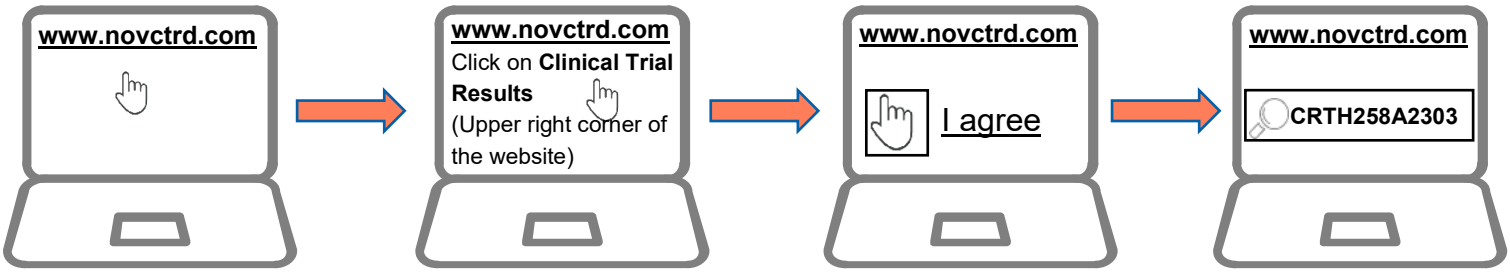
The safety profile of **brolucizumab** was similar to previous studies.

An additional clinical study with **brolucizumab** in people with wet AMD is currently ongoing in China, CRTH258A2307, and no new trials are planned.

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.

Please follow the steps below:



You can find more information about this trial on the following websites:

- www.clinicaltrials.gov Use the NCT identifier NCT04005352 in the search field.
- https://www.clinicaltrialsregister.eu/ctr-search Use the EudraCT identifier 2019-000716-28 in the search field.

Full clinical trial title: A 64-week, two-arm, randomized, double-masked, multicenter, phase IIIb study assessing the efficacy and safety of brolucizumab 6 mg compared to aflibercept 2 mg in a treat-to-control regimen in patients with neovascular age-related macular degeneration (TALON).

Thank you

Thank you for taking part in this trial. As a clinical trial participant, you belong to a large community of people around the world. You helped researchers answer important health questions and test new medical treatments.

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

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