NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects and safety of brolucizumab compared to aflibercept in adults with vision loss due to diabetic macular edema (DME)

Thank you!

Thank you to the participants who took part in the clinical trial for DME. 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: CRTH258B2304

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

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.

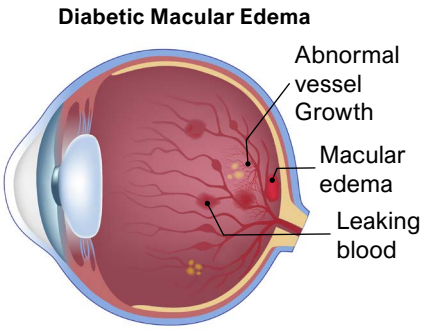
This summary only shows the results of a single clinical trial. Other clinical trials may have different findings.

What was the main purpose of this trial?

The purpose of this trial was to learn about the effects and safety of **brolucizumab** in people with **diabetic macular edema (DME)**. To find this out, researchers compared the effects of **brolucizumab** to a drug called **aflibercept**.

DME is an eye disease that affects vision in people with diabetes, and is the most common cause of vision loss in people with diabetes. High blood sugar due to diabetes damages small blood vessels in the eye. The fluid from damaged blood vessels starts to build up at the central part of the back of the eye (the macula), making it swell. As the macula is essential for clear vision, its swelling leads to blurry vision. Eventually, these changes can become permanent.

Currently, DME is treated with drugs such as **aflibercept** and ranibizumab. These drugs block a protein called vascular endothelial growth factor which causes abnormal growth and leakage of blood vessels at the back of the eye. Other treatments include medicines called steroids, which reduce swelling, and laser treatments to stop blood vessels from leaking.



Source: EveryDayHealth.com

Brolucizumab is approved outside of China to treat eye diseases including DME. Researchers wanted to find out if it is effective and safe in treating DME in Chinese participants.

Aflibercept is a drug approved and available on the market in China and other countries to treat DME. It was used as a reference to compare the effects of the study drug **brolucizumab**.

Trial drug
Brolucizumab

Pronounced as
BROE-lue-SIZ-ue-mab

Comparator drug
Aflibercept

Pronounced as
A-fli-ber-sept

The trial purpose was to answer the main question:

- Did vision test scores show similar improvement for participants on **brolucizumab** compared to those on **aflibercept** after 52 weeks of treatment?
- **What medical problems, also called as 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 August 2019 and ended in January 2023. It was planned for the participants to be in the trial for about 1 year after receiving the trial treatment.

Who was in this trial?

263 participants from China with DME received treatment in this trial.

Participants' ages ranged from 26 to 78 years. Their average age was 60 years. The number of participants by gender and race is shown below.

Gender

- 141 Men
- 122 Women

Race

- 263 Asian

The participants could take part in this trial if they:

- had diabetes,
- had difficulty with their vision due to DME, and
- did not have any other eye disease that could interfere with the result of the trial.

What treatments did the participants receive?

The treatments in this trial were:

Brolucizumab was given at a dose of 6 mg as an injection into the eye every 6 weeks, 8 weeks or 12 weeks.

Aflibercept was used as a reference to compare with **brolucizumab** in this trial. It was given at a dose of 2 mg as an injection into the eye every 4 weeks or every 8 weeks.

Researchers randomly assigned participants to the above treatment groups using a computer.

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 the participants receive can affect the results of the trial. Doing a trial this way helps to make sure that the results are looked at with fairness across all treatments.

What happened during this trial?

Before treatment [2 weeks]

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

During treatment [48 weeks]

263 eligible participants were randomly and equally assigned to one of the following 2 treatment groups:

Brolucizumab 6 mg (132 participants)	**Aflibercept** 2 mg (131 participants)
• was given every 6 weeks until Week 24 and then • was given every 12 weeks or every 8 weeks until Week 48, as per the trial doctor.	• was given every 4 weeks until Week 16 and then • was given every 8 weeks until Week 48.

The treatment was given as an injection into the eye.
Trial doctors checked the participants' disease condition and general health throughout the trial.

After treatment [1 month]

Participants' health was monitored during this period.

What were the main results of this trial?

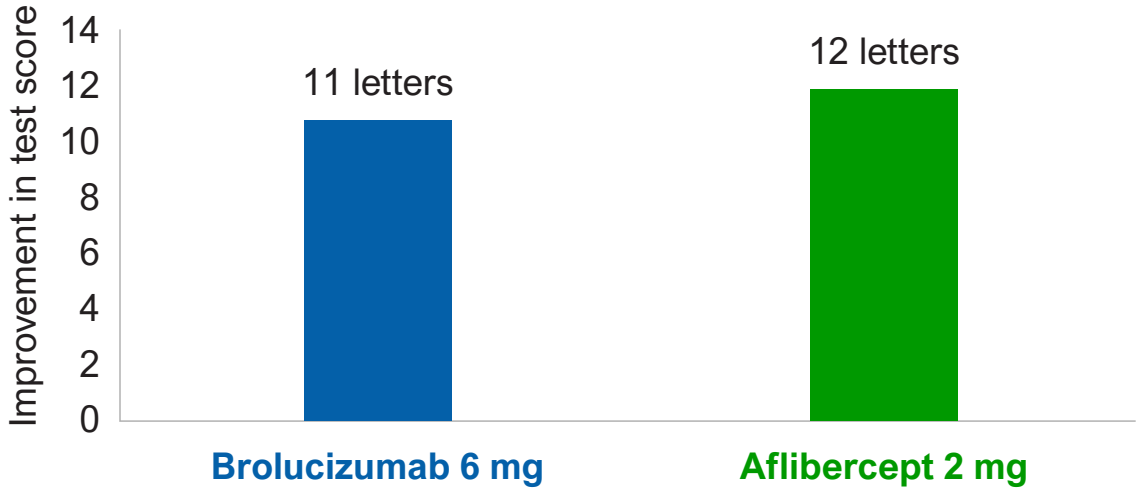
Did vision test scores show similar improvement for participants on brolucizumab compared to those on aflibercept after 52 weeks of treatment?

Vision test scores showed a similar improvement for participants on **brolucizumab** compared to those on **aflibercept** by Week 52.

Researchers calculated the vision test scores based on the number of letters participants could read during the test. They then compared the improvement in participants' scores, from the start of the trial until Week 52 or last visit of the trial.

The results showed that the vision test score improved by 11 letters for the participants on **brolucizumab** and 12 letters for the participants on **aflibercept** after 52 weeks of treatment. Therefore, researchers concluded that the vision test scores showed similar improvement for the participants in both groups.

Improvement in vision test score by Week 52



What was the other result of this trial?

Was the average reduction in the swelling of the macula similar in participants on brolucizumab compared to the participants on aflibercept by Week 52?

The swelling of the macula was more reduced in participants on **brolucizumab** compared to those on **aflibercept**.

The average reduction in the swelling of the macula was greater in participants on **brolucizumab** compared to participants on **aflibercept** by Week 52.

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 trial treatment, and up to 30 days after the last dose of 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.

Adverse events in the treated eye occurred in 104 of 263 (40%) participants. Adverse events on the body apart from the treated eye occurred in 168 of 263 (64%) participants. 50 participants had adverse events that were considered serious. 1 participant died due to kidney failure. 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?

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 132 participants	Aflibercept 2 mg 131 participants
Had at least 1 adverse event on the treated eye	57 of 132 43%	47 of 131 36%
Had at least 1 serious adverse event	4 of 132 3%	4 of 131 3%
Stopped treatment due to an adverse event	3 of 132 2%	1 of 131 1%

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

Participants who:	Brolucizumab 6 mg 132 participants	Aflibercept 2 mg 131 participants
Had at least 1 adverse event on the body apart from the treated eye	94 of 132 71%	74 of 131 56%
Had at least 1 serious adverse event	21 of 132 16%	17 of 131 13%
Stopped treatment due to an adverse event	1 of 132 1%	2 of 131 2%
Died during the trial	0 of 132 0%	1 of 131 1%

What serious adverse events did the participants have?

50 participants had serious adverse events. 1 participant on **aflibercept** died.

The table below shows the most common serious adverse events that happened in **1% or more** participants in any treatment group.

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

	Brolucizumab 6 mg 132 participants	Aflibercept 2 mg 131 participants
Clouding of the eye-untreated eye Cataract-Fellow eye*	5 of 132 4%	1 of 131 1%
Clouding of the eye-treated eye Cataract-Study eye*	2 of 132 2%	2 of 131 2%

*Fellow eye is the eye that did not receive any treatment
Study eye is the eye that received the treatment

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

	Brolucizumab 6 mg 132 participants	Aflibercept 2 mg 131 participants
Damage of the kidney caused by diabetes Diabetic nephropathy	1 of 132 1%	3 of 131 2%
Gradual loss of kidney function over time Chronic kidney disease	3 of 132 2%	0 of 131 0%
Nerve damage caused by diabetes Diabetic neuropathy	2 of 132 2%	0 of 131 0%
Stroke Cerebral infarction	2 of 132 2%	2 of 131 2%
Swelling of the thyroid gland on the neck Thyroid mass	2 of 132 2%	0 of 131 0%

What other adverse events did the participants have?

176 participants had other adverse events.

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

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

	Brolucizumab 6 mg 132 participants	**Aflibercept 2 mg** 131 participants
Decrease in clarity of vision-treated eye Visual acuity reduced-Study eye*	**12 of 132** 9%	**6 of 131** 5%
Decrease in clarity of vision-untreated eye Visual acuity reduced-Fellow eye*	**10 of 132** 8%	**8 of 131** 6%
Dryness and itching in the eye-treated eye Meibomian gland dysfunction-Study eye*	**8 of 132** 6%	**9 of 131** 7%
Dryness and itching in the eye-untreated eye Meibomian gland dysfunction-Fellow eye*	**8 of 132** 6%	**9 of 131** 7%
Eye disease due to lack of vitamin A in the body-untreated eye Xerophthalmia-Fellow eye*	**2 of 132** 2%	**8 of 131** 6%
Swelling at the back of the eye caused by diabetes-untreated eye Diabetic retinal oedema-Fellow eye*	**4 of 132** 3%	**11 of 131** 8%

*Fellow eye is the eye that did not receive any treatment
Study eye is the eye that received the treatment

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

	Brolucizumab 6 mg 132 participants	Aflibercept 2 mg 131 participants
Common cold Upper respiratory tract infection	9 of 132 7%	9 of 131 7%
High blood levels of fat Hyperlipidaemia	10 of 132 8%	9 of 131 7%
High blood pressure Hypertension	7 of 132 5%	12 of 131 9%

What was learned from this trial?

Researchers learned about the effects and safety of **brolucizumab** in Chinese people with vision loss due to DME.

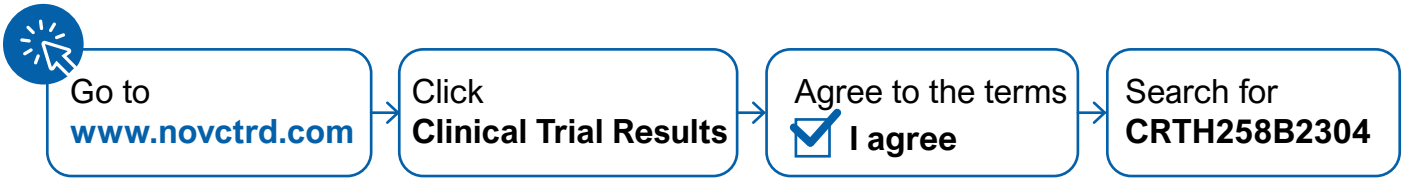
- The researchers found **brolucizumab 6 mg** had similar effects in improving vision of participants with DME when compared to **aflibercept 2 mg**.
- **Brolucizumab 6 mg** has the potential to reduce treatment burden, as it is injected less frequently than **aflibercept 2 mg**.
- Researchers found no new safety concerns for **brolucizumab**.

At the time this report is created, no further studies for DME 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**

Follow these steps to find the scientific summary:



For more information about this trial, go to of this website:

- **clinicaltrials.gov** – search using the number **NCT04058067**

Full clinical trial title: A One-Year, Randomized, Double-Masked, Multicenter, Phase III, Two-Arm Study Assessing the Efficacy and Safety of Brolucizumab versus Aflibercept in Adult Chinese Patients with Visual Impairment Due to Diabetic Macular Edema (KINGLET)

NOVARTIS

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.novartisclinicaltrials.com