NOVARTIS

The safety of MHU650 for people with macular edema caused by certain eye conditions

Thank you!

Thank you to the participants who took part in the clinical trial for macular edema caused by certain eye conditions. Every participant helped the researchers learn more about **MHU650**.

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: CMHU650A12101
Drug studied: MHU650
Sponsor: Novartis

What was the main purpose of this trial?

The purpose of this trial was to learn about the safety of MHU650 for people with macular edema caused by certain eye conditions. This was the first trial where people received MHU650.

Macular edema is swelling or damage to the macula caused by fluid leaking into the retina.

The retina is a part of the eye that is responsible for vision. The **macula** is the center part of the retina. Swelling or damage in the macula can cause vision problems.

MHU650 is a trial drug designed to block 2 proteins that can cause fluid to build up in the eye.

The main questions this trial was designed to answer were:

- **What medical problems did the participants have during this trial?**
  Keeping track of the medical problems helped to learn about the safety of MHU650.
- **How much MHU650 got into the blood when injected into the eye?**

Main results: About half of the participants (10 out of 21 participants) had medical problems. 1 participant had medical problems that were considered serious. None of the participants died. Most of the medical problems were related to the eyes. The most common type of medical problem was bleeding in the top part of the eye where the injection was received. The researchers concluded that there were no safety concerns for MHU650 in this trial.

Additional results are also provided later in this summary.

How long was this trial?

The trial began in December 2020 and ended in May 2022. It was planned for the participants to be in the trial for about 2 months after starting treatment. The trial staff followed up with participants after 1 month to check for any safety concerns.

Who was in this trial?

21 participants were in this trial – 13 males and 8 females. Their average age was 64.

17 participants reported their race as White (Caucasian), and 4 participants reported their race as Asian. 10 participants reported their ethnicity as Hispanic/Latino.

Every participant in this trial had a specific eye condition that causes macular edema.

The 3 specific eye conditions that the researchers studied were:

- **Diabetic macular edema** – swelling in the retina caused by blood vessels that are damaged due to diabetes
- **Neovascular age-related macular degeneration** – damage in the retina from aging
- **Retinal vein occlusion** – damage in the retina caused by a blocked vein sometimes associated with high blood pressure

This trial took place in the United States, including Puerto Rico.

Visit **novctrd.com** for more information about:

- Who could and could not be in this trial
- Which medicines they could or could not take during the trial

Use trial number **CMHU650A12101** to find the scientific summary.

What trial treatment did the participants receive?

Each participant was assigned to 1 of 4 groups. In each group, participants received the following treatment as an injection into the eye 1 time:

- **MHU650** – 1 of 4 dose levels from 0.25 to 7.5 milligrams.

Group 1 received the lowest dose. Group 4 received the highest dose.

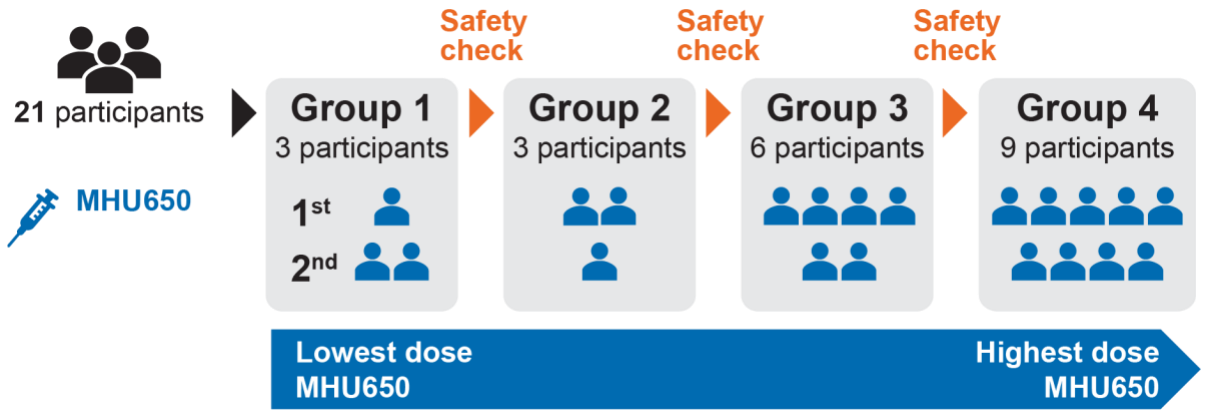
The participant, trial staff, and researchers knew which dose level the participant received.

The trial doctors and researchers closely checked for safety concerns with each dose level. If they found no safety concerns, they started the next group with a higher dose level.

The trial doctors and researchers checked for safety concerns in the following ways:

1. Starting with Group 1, only 1 participant received the lowest dose of MHU650.
2. After 1 week with no safety concerns, the rest of the participants in Group 1 received their assigned dose level.
3. The doctors performed a safety check during the 15 days after all the participants in Group 1 received the trial treatment. If there were no safety concerns, Group 2 started with a higher dose level.
4. Once the doctors performed the 15-day safety check on 2 participants in Group 2, Group 3 started the next higher dose level. Group 4 started the highest dose level once doctors performed the safety check on 4 participants in Group 3.

The graphic below shows how this was done.



What were the main results of this trial?

This is a summary of the overall results of this trial. Individual results from each participant may be different and are not included in this summary.

Researchers need many trials to learn if a drug or other treatment is safe and works well. Other trials may provide new information or different results.

Always talk to a doctor before making any changes to your health care.

What medical problems did the participants have during this trial?

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

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.

An adverse event is:

- Any **unwanted 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.

The adverse events in this section include any that happened during treatment and up to 3 months after receiving treatment.

The researchers concluded that there were no safety concerns for MHU650 in this trial based on the following:

- About half of the participants had adverse events.
  - 8 participants had adverse events in the eye.
  - 4 participants had adverse events not in the eye.
  - 1 participant had adverse events that were considered serious.
- The most common type of adverse event was bleeding in the top part of the eye where the injection was received.

What serious adverse events did the participants have?

All dose levels of MHU650: 1 out of 21, or 5% of participants, had a total of 3 serious adverse events:

- **Part of the eye called the choroid pulling away from the eye socket |** Choroidal detachment
- **The retina pulling away from the eye socket due to fluid build up |** Serous retinal detachment
- **Inflammation in a part of the eye called the uvea |** Uveitis

No participants left the trial due to adverse events. None of the participants died.

What other adverse events did the participants have?

All dose levels of MHU650: 10 out of 21, or 48% of participants, had an adverse event.

The table below shows the adverse events that happened in this trial.

Adverse events in the eye

	MHU650 21 participants
Bleeding in the eye where the injection was received Conjunctival hemorrhage	**24%** 5 out of 21
Red eyes Conjunctival hyperemia	**5%** 1 out of 21
Dry eye	**5%** 1 out of 21
Worsening swelling or damage to the macula caused by fluid leaking into the retina Macular edema	**5%** 1 out of 21
Worsening damage in the retina caused by a blocked vein Retinal vein occlusion	**5%** 1 out of 21

Adverse events not in the eye

	MHU650 21 participants
Nausea	**5%** 1 out of 21
Allergic reaction to the dye used for imaging Contrast media allergy	**5%** 1 out of 21
Infection of the nose and throat Upper respiratory infection	**5%** 1 out of 21
Blood in the urine Hematuria	**5%** 1 out of 21
Cough	**5%** 1 out of 21

Additional safety measures

Before and after treatment with MHU650, the trial staff measured:

- The participants' ability to identify letters
- The thickness of the macula
- The fluid pressure inside the eye

Based on these measures, the researchers found no safety concerns for MHU650 for the participants in this trial.

What other results were learned?

How much MHU650 got into the blood when injected into the eye?

The trial staff took many blood samples from each participant at different times during the trial. This allowed the researchers to learn how much MHU650 got into the participants' blood over time.

The researchers found that the participants in Groups 1 and 2 did not have enough MHU650 in their blood to measure at any time after the injection. For Groups 3 and 4, the researchers found that the amount of MHU650 in the participants' blood:

- Was low
- Went up as the dose went up
- Was highest within about 3 days after receiving the injection
- Was gone from the blood about 15 days after receiving the injection

What was learned from this trial?

This was the first trial to help researchers learn about the safety of MHU650 for people with macular edema caused by certain eye conditions.

The researchers concluded that there were no safety concerns for MHU650 in this trial.

The researchers also learned that the amount of MHU650 that got into the blood was very low. It was highest at about 3 days after the injection with the higher doses and was gone from the blood about 15 days after the injection.

These are the results of a single trial. Other trials may have different results. This was one of many trials a drug goes through. This type of trial helped researchers learn about the safety of a trial drug in a small number of participants.

Where can I learn more about this and future trials?

For more information about this trial, go to any of the following websites:

- **novctrd.com** – search using the trial number **CMHU650A12101**
- **clinicaltrials.gov** – search using the number **NCT04635800**

If more trials are planned, they will appear on the public websites above. When there, search for **MHU650** or **macular edema**.

Full trial title: A first-in-human, open-label, single ascending dose study to assess safety and tolerability of intravitreal MHU650 in participants with macular edema from diabetic macular edema (DME), neovascular age-related macular degeneration (nAMD), or retinal vein occlusion (RVO)

If you participated in the trial and have **questions** about the results, please speak with the trial doctors or staff at your trial site.

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 (USA)

+41-61-324-1111 (EU)

www.novartisclinicaltrials.com