NOVARTIS

The safety and effects of LKA651 for people with diabetic macular edema

Thank you!

Thank you to the participants who took part in the clinical trial for diabetic macular edema. Every participant helped the researchers learn more about **LKA651**.

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

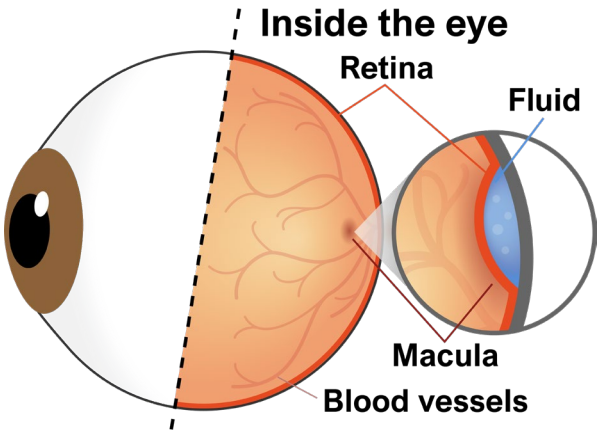
Trial number: CLKA651X2202
Drug studied: LKA651
Sponsor: Novartis

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 main purpose of this trial was to learn about the safety and effects of LKA651 when given with and without an approved treatment for diabetic macular edema.



Diabetic macular edema, or DME, is the build-up of fluid in the macula caused by diabetes.

- The **macula** is the part of the retina that helps focus vision
- The **retina** is the part at the back of the eye that is sensitive to light

Over time, high blood sugar can damage the tiny blood vessels at the back of the eye, which causes them to leak fluid into the macula. The fluid can cause swelling in the macula, blurry vision, or vision loss.

LKA651 is a trial drug designed to block a protein that may play a role in DME.

Ranibizumab is an approved treatment in certain countries to treat DME. It is designed to block a different protein than LKA651.

The main questions this trial was designed to answer:

- What adverse events did the participants have during this trial?
  An adverse event is any sign or symptom that the participants have during a trial.
- Could participants see more clearly after receiving LKA651 with or without ranibizumab?
- Did the amount of fluid in participants' retinas change after receiving LKA651 with or without ranibizumab?

How long was this trial?

The trial began in May 2019 and ended in August 2022. It was planned for the participants to be in the trial for about 6 months.

Who was in this trial?

91 participants with DME were in this trial – 59 men and 32 women. The participants were 37 to 79 years old. Their average age was 62.

Participants reported their race as:

- White | 82 participants
- Asian | 3 participants
- Black or African American | 3 participants
- American Indian or Alaska Native | 2 participants
- Native Hawaiian or Other Pacific Islander | 1 participant

Every participant in this trial:

- Did not receive certain eye treatments up to 3 months before joining the trial
- Did not have dangerously high blood sugar
- Did not have certain other eye conditions

This trial took place in:

- Germany | 6 participants
- Spain | 18 participants
- Turkey | 15 participants
- United States (US) | 52 participants

What trial treatments did the participants receive?

Participants were randomly assigned to one of these treatment groups:

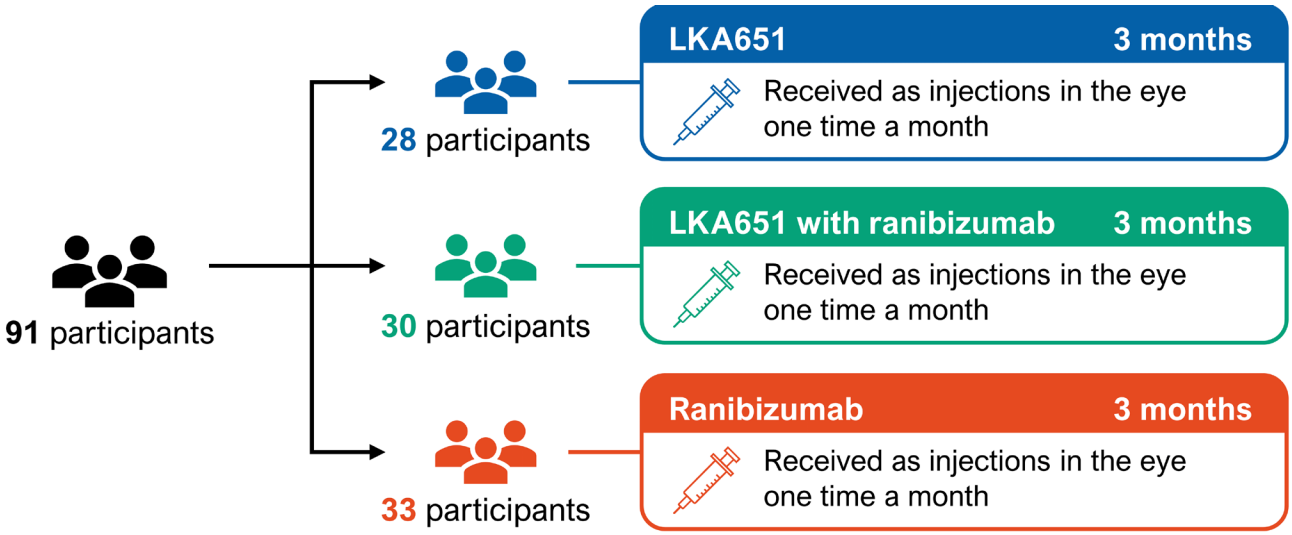
- **LKA651** – 5 milligrams (mg)
- **LKA651 with ranibizumab** – 1 mg of LKA651 and up to 0.5 mg of ranibizumab
- **Ranibizumab** – up to 0.5 mg

The participants received their assigned treatment as injections into the study eye 1 time a month for 3 months.

A computer program was used to randomly assign the treatments. This helped make sure the researchers compared the results as fairly as possible.

The participants, sponsor staff, and trial staff did not know what treatment each participant received during the trial. Some trials are done this way because knowing what treatment participants take can influence the results. Not knowing what treatment participants take helps make sure the results are looked at fairly.

The graphic below shows how many participants were assigned to each treatment.



To start, trial doctors first gave the trial treatments to 16 participants:

- 2 participants received LKA651
- 2 participants received ranibizumab
- 12 participants received LKA651 with ranibizumab

Then, the trial doctors and researchers checked that there were no safety concerns after 15 days. The remaining trial participants then received their assigned treatments.

What were the main results of this trial?

What adverse events did the participants have during this trial?

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 **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 about 4 months after completing treatment.

More than half of the participants (55 of 91 participants) had adverse events. 8 of the participants had adverse events that were considered serious, including 1 death.

The most common adverse event was a red spot in the white of the eye from a broken blood vessel. 1 participant left the trial due to an adverse event. There were more participants with adverse events who received LKA651 only.

The researchers concluded there were no new safety concerns for LKA651 when given with and without ranibizumab in this trial.

What serious adverse events did the participants have?

LKA651: 3 of 28 or 11% had a serious adverse event.

LKA651 with ranibizumab: 4 of 30 or 13% had a serious adverse event.

Ranibizumab: 1 of 33 or 3% had a serious adverse event.

The table below shows the types of serious adverse events that happened in **2 or more participants**. Additional serious adverse events happened in fewer participants.

	LKA651 28 participants	LKA651 with ranibizumab 30 participants	Ranibizumab 33 participants
Problems with the stomach and digestion Gastrointestinal disorders	0% 0 of 28	7% 2 of 30	0% 0 of 33
Viral or bacterial infections Infections and infestations	4% 1 of 28	0% 0 of 30	3% 1 of 33

During this trial, there was 1 death from bleeding in or around the brain (hemorrhagic stroke) in the **LKA651** group.

What other adverse events did the participants have?

LKA651: 20 of 28 or 71% had an adverse event.

LKA651 with ranibizumab: 16 of 30 or 53% had an adverse event.

Ranibizumab: 19 of 33 or 58% had an adverse event.

In this trial, the researchers separated the other adverse events that happened into 3 categories:

- In the **study eye**, which is the eye that the trial treatment was injected into
- In the **non-study eye**, which is the other eye that trial treatment was not injected into
- Not in the eyes

The tables on the next page show the adverse events that happened in **3 or more participants** for each category. Additional adverse events happened in fewer participants.

Adverse events in the study eye

	LKA651 28 participants	LKA651 with ranibizumab 30 participants	Ranibizumab 33 participants
A red spot in the white of the eye from a broken blood vessel Conjunctival hemorrhage	4% 1 of 28	13% 4 of 30	6% 2 of 33
A build-up of fluid in the retina from diabetes Diabetic retinal edema	7% 2 of 28	3% 1 of 30	6% 2 of 33
Damage to the blood vessels in the retina from diabetes Diabetic retinopathy	4% 1 of 28	3% 1 of 30	3% 1 of 33
Loss of ability to see fine details Visual acuity reduced	11% 3 of 28	0% 0 of 30	0% 0 of 33
Bleeding in the eye Vitreous hemorrhage	4% 1 of 28	0% 0 of 30	6% 2 of 33

Adverse events in the non-study eye

	LKA651 28 participants	LKA651 with ranibizumab 30 participants	Ranibizumab 33 participants
A build-up of fluid in the retina from diabetes Diabetic retinal edema	7% 2 of 28	0% 0 of 30	6% 2 of 33
A red spot in the white of the eye from a broken blood vessel Conjunctival hemorrhage	0% 0 of 28	7% 2 of 30	3% 1 of 33
Damage to the blood vessels in the retina from diabetes Diabetic retinopathy	4% 1 of 28	3% 1 of 30	3% 1 of 33

Adverse events not in the eyes

	LKA651 28 participants	LKA651 with ranibizumab 30 participants	Ranibizumab 33 participants
High blood pressure Hypertension	11% 3 of 28	3% 1 of 30	9% 3 of 33
High blood sugar Hyperglycemia	7% 2 of 28	3% 1 of 30	3% 1 of 33
Low level of red blood cells Anemia	4% 1 of 28	7% 2 of 30	3% 1 of 33
COVID-19	7% 2 of 28	0% 0 of 30	3% 1 of 33
UTI Urinary tract infection	4% 1 of 28	3% 1 of 30	3% 1 of 33

Other eye safety results: The trial doctors also performed a full eye exam for all participants before and after treatment. A part of this exam included checking for changes in:

- intraocular pressure, which is the pressure inside the eye
- the foveal avascular zone, which is the center of the retina and responsible for detailed vision

For all treatment groups, intraocular pressure and the foveal avascular zone stayed about the same both before treatment and at the end of treatment.

Could participants see more clearly after receiving LKA651 with or without ranibizumab?

LKA651 with or without ranibizumab did not have a meaningful effect on the participants' sight when compared to ranibizumab alone.

To learn this, the trial staff measured the number of letters participants could correctly identify on a vision test. This is called Best Corrected Visual Acuity, or BCVA. The researchers then looked at participants' BCVA after 3 months of treatment.

The results were reported as a total letter score of 0 to 100. A **higher letter score** means a participant can see **more clearly**.

Participants' letter score after treatment

The average letter score of participants after receiving their assigned treatment for 3 months.

Identifying more letters means a participant can see more clearly

When compared to ranibizumab alone, the researchers concluded that LKA651 with and without ranibizumab **did not have a meaningful effect** on whether participants could see more clearly.

Did the amount of fluid in participants' retinas change after receiving LKA651 with or without ranibizumab?

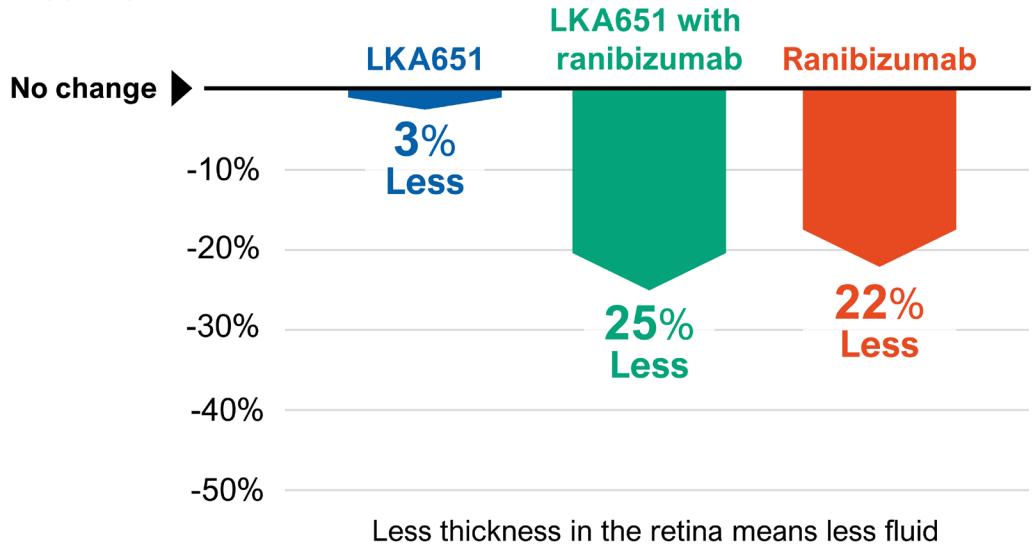
LKA651 with or without ranibizumab did not have a meaningful effect on the amount of fluid in participants' retinas when compared to ranibizumab alone.

To learn this, trial staff used imaging tests to measure the thickness of participants' retinas.

The researchers compared the participants' retina thickness from before and 3 months after starting trial treatment. **Less thickness** in the retina means **less fluid** in the retina.

Percent change in retina thickness

The average change in retina thickness after 3 months of treatment compared to before treatment.



The researchers concluded that LKA651 with or without ranibizumab **did not have a meaningful effect** on the participants' retina thickness when compared to ranibizumab alone.

What other results were learned?

How long after finishing the trial treatment did the participants have to be treated again for DME?

To find this out, the researchers followed up with each participant for about 4 months after their last dose of trial treatment. They did this to see if a participant needed to be treated for DME again. If a participant received an approved DME treatment, the researchers noted the length of time until they needed treatment again.

A little more than half of the participants in each treatment group received an approved DME treatment during the 4 months. Among these participants, it took about:

- 2 months for participants who received **LKA651** to receive an approved DME treatment
- 1 month for participants who received **LKA651 with ranibizumab** or **ranibizumab alone** to receive an approved DME treatment

What was learned from this trial?

This trial helped researchers learn about the safety of LKA651 given with and without ranibizumab and its effects in people with DME.

The researchers concluded there were no new safety concerns for LKA651 when given with and without ranibizumab in this trial. They also learned that LKA651 with and without ranibizumab did not have a meaningful effect on the participants' sight or amount of fluid in the retina when compared to ranibizumab alone.

In addition, a little more than half of the participants in each treatment group received an approved DME treatment within 4 months after finishing treatment.

These are the results of a single trial. This was one of many trials a drug goes through. This type of trial helped researchers learn about the safety and effects of a trial drug in a small number of participants. At this time, no other trials are planned for LKA651 in DME.

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 study number **CLKA651X2202**
- **clinicaltrials.gov** – search using the number **NCT03927690**
- **clinicaltrialsregister.eu/ctr-search** – search using the number **2018-000031-28**

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

Full trial title:

A randomized, active-controlled, patient and investigator-masked, multiple dose proof-of-concept study of intravitreal LKA651 in patients with diabetic macular edema

? If you participated in the trial and have **questions** about the results, please speak with the trial doctors or staff at your trial site. Always talk to a doctor before making any changes to your health care.

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