Clinical Trial Summary

A clinical trial to learn about the safety of the trial drug LKA651 for people with macular edema

Thank you!

Novartis, the sponsor of this clinical trial, thanks the participants who helped make this clinical trial possible.

Overview of results

Trial number: CLKA651X2104

In this clinical trial, researchers learned about the safety of a trial drug named **LKA651** when given as an injection (shot) into the eye of participants with macular edema. Macular edema is a buildup of fluid in the macula, an area at the back of the eye. Macular edema can cause blurry vision and sometimes vision loss.

What should I know about clinical trials?

A clinical trial is a type of research designed to learn more about how our bodies respond to drugs or other treatments. Do not use the results of only one clinical trial to make decisions about your health care.

Researchers wanted to learn:

- About any medical problems that happened
- How many participants had medical problems after getting one injection of the trial drug LKA651 in their eye
- If LKA651 moved from the eye into the blood

Who was in this clinical trial?

28 adult men and women with macular edema began this clinical trial.

What type of clinical trial was this?

This was a Phase 1 clinical trial, which tests a trial drug's safety by giving different amounts of the drug to a small number of participants.

How was safety tested?

Trial doctors checked for any medical problems, called **adverse events**, that happened during this clinical trial. Participants also reported adverse events.

What did researchers learn in this clinical trial?

There were no serious adverse events. 18 participants had 26 types of adverse events. No one stopped taking part in the trial due to an adverse event. Overall, the safety findings in this clinical trial support further testing of LKA651 in other clinical trials.

Table of Contents

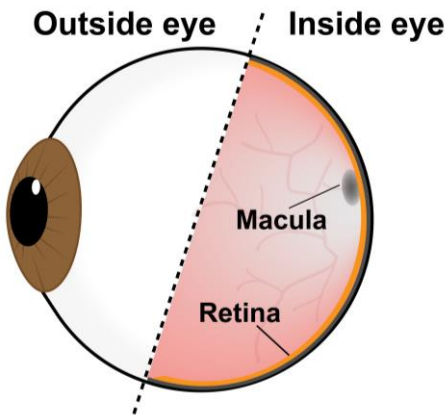
Researchers need many clinical trials to learn if a drug or other treatment is safe and works well. This is a summary of the overall results of this clinical trial, not the results for each participant in the clinical trial.

Do not use only the results of this clinical trial to make health decisions. Always talk to a doctor before making any changes to your treatments.

Why was this clinical trial needed?

Researchers are looking for a better way to treat macular edema. **Macular edema** is the build-up of fluid in the macula, an area near the center of the retina. The retina is the light-sensitive tissue at the back of the eye, and the macula is the part that helps focus vision on details in objects, like text and faces.

Location of the macula



The symptoms of macular edema can include:

- Blurry or wavy vision near or in the center of the field of vision – this can range from slightly blurry vision to vision loss
- Washed out or faded colors in vision

Macular edema often happens from one of the following diseases:

- Diabetes – long-term high blood sugar that can damage the blood vessels in the eye
- Age-related macular degeneration – an eye condition that causes slow, steady vision loss. This is a leading cause of vision loss for participants 50 years of age and older.
- Retinal vein occlusions – blockage in the small veins that carry blood away from the retina

In this clinical trial, the researchers wanted to learn:

- About any medical problems that happened
- How many participants had medical problems after getting one injection of the trial drug LKA651 in their eye
- If LKA651 moved from the eye into the blood

Who was in this clinical trial?

28 adult men and women with macular edema began this clinical trial. They were between 51 and 84 years old and 67 years old on average.

Every participant in this clinical trial had macular edema. They were also in good overall health and had eyes that were otherwise healthy based on a doctor's exam.

No one could be in this clinical trial if they had poorly controlled diabetes (blood sugar levels that were too high) or if they had certain other eye problems, such as glaucoma.

Researchers conducted this clinical trial in the United States, including Puerto Rico.

This clinical trial began in September 2016 and ended in February 2018. The participants in this clinical trial began on different dates. Every participant who began also completed this clinical trial.

What type of clinical trial was this?

This was a **Phase 1** clinical trial, which tests a trial drug's safety by giving different amounts of the drug to a small number of participants.

In this trial, researchers used a computer program to randomly assign each participant the treatment they got in the trial. Some participants got one injection of LKA651 in one eye and some participants got a sham injection in one eye. A **sham injection** is a syringe without a needle that has no active drug inside. Research staff placed the sham injection against the eye for the same amount of time as the injection of LKA651. Before giving the LKA651 or sham injection, research staff numbed the eye.

Using a sham injection helped researchers better understand the actual effects of the trial drug. Only the research staff giving the sham injection knew who got the trial drug or the sham injection. A trial doctor who did not give the injections checked people's eyes. Some clinical trials are done this way because knowing what treatment participants get can affect the results. Not knowing what treatment participants get helps make sure the results are looked at fairly.

What happened during this clinical trial?

Before treatment

During a 60-day period, trial doctors checked each participant's health and eyes to make sure they could be in this clinical trial. Trial doctors also made sure participants stopped any current treatment that wasn't allowed during this clinical trial.

During treatment

Researchers randomly assigned participants in the groups getting LKA651 and the sham injection into 5 smaller groups. These groups got a different dose (amount) of LKA651 or the sham injection. Each participant got either one injection of LKA651 or the sham injection in one of their eyes.

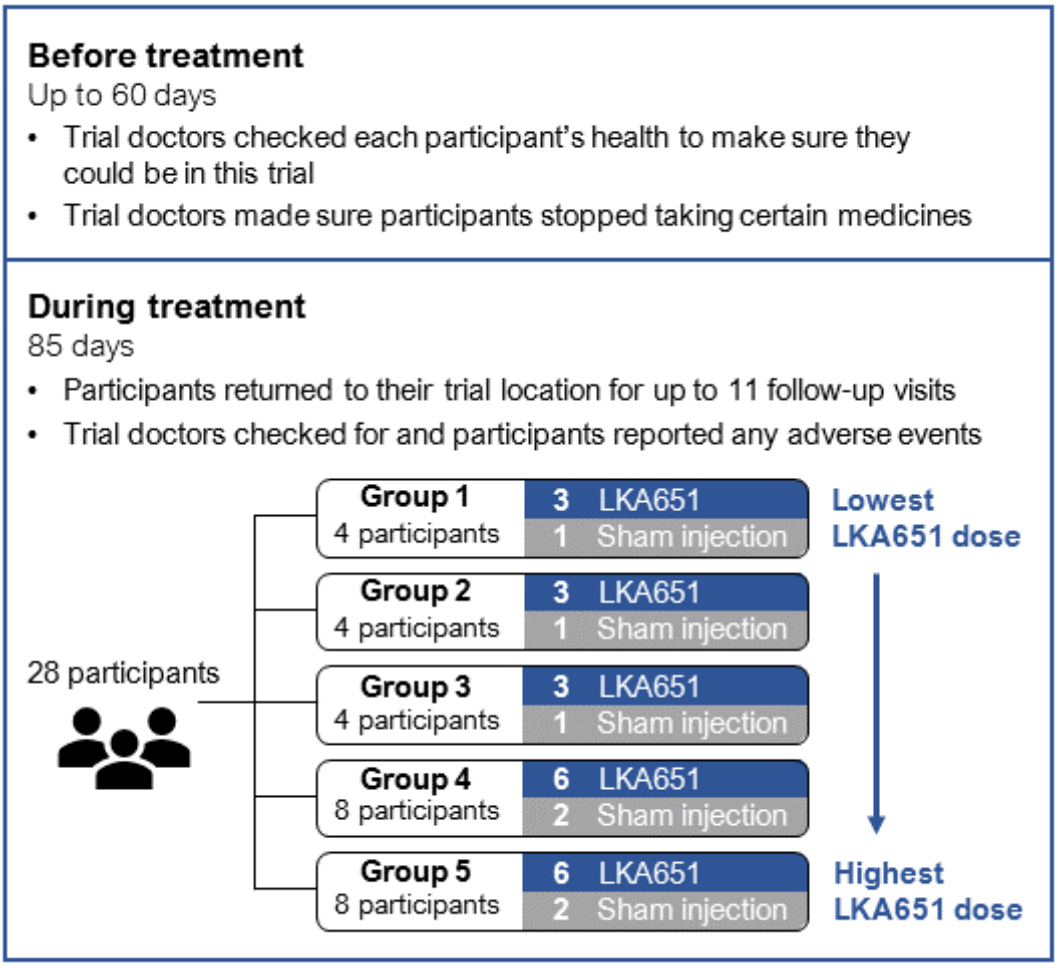
The researchers started by testing the lowest dose of LKA651 with the first group, then checked for any medical problems. Since this was the first test of LKA651 in people, trial doctors closely looked for any problems in the first participant to get the trial drug.

Trial doctors waited 15 days after every participant in a group got either LKA651 or the sham injection before giving the next higher dose to the next group. This was to make sure no serious problems happened before giving a higher dose to the next group. After trial doctors checked the results of one dose, they gave a higher dose to the next group and continued to increase the dose through all 5 groups.

Participants stayed at the trial location for several hours after the injection so that trial doctors could check their eyes and health. Everyone in the trial also gave blood samples during this visit before and after getting either LKA651 or the sham injection.

Everyone returned to their trial location up to 11 times for follow-up visits.

How researchers designed this trial:



What did researchers learn in this clinical trial?

18 participants had 26 types of adverse events during the testing of LKA651. None of the adverse events were serious. No one stopped taking part in the trial due to an adverse event. Overall, the safety findings in this clinical trial support further testing of LKA651 in other clinical trials.

What medical problems happened during the trial?

Medical problems that occur during a clinical trial are called adverse events. **An adverse event is any unwanted sign or symptom that participants report during a trial. These problems may or may not be caused by the clinical trial or the trial drug.** Researchers need many trials to know if a drug causes a medical problem. Researchers ask participants in the trial to report all adverse events during a trial.

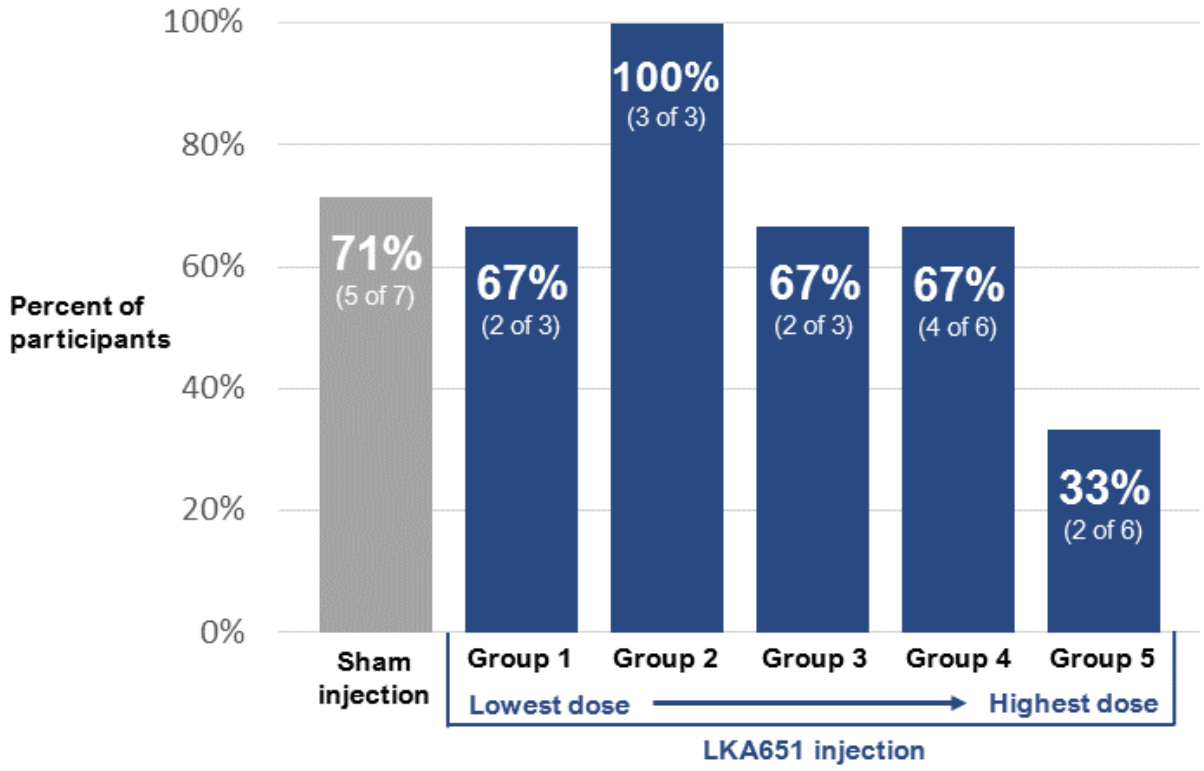
Trial doctors at each location kept track of adverse events. They looked for any adverse events when they checked participants' eyes and blood samples. Participants also reported adverse events. Then, the researchers compared the number of participants with adverse events who got LKA651 to those who got the sham injection.

Overall, the percent of participants with adverse events were similar for those who got LKA651 and those who got the sham injection. The number of participants who had adverse events were similar for the different doses of LKA651 tested in this trial.

What is a sham injection?

A **Sham injection** is a syringe without a needle that has no active drug inside.

Percent of participants who had adverse events during and after treatment



How many participants reported serious adverse events?

An adverse event is called serious when it is life-threatening, requires a hospital stay, can cause disability or permanent damage, or can cause a birth defect.

During this clinical trial, no one reported serious adverse events and no one died.

What adverse events did participants report?

Some participants reported medical problems or adverse events that were not serious. This section reports **all adverse events** that participants said they had during this clinical trial. These adverse events may or may not be caused by the clinical trial or the trial drug. Researchers need many trials to know if a drug causes an adverse event.

This summary includes all of the adverse events reported after participants got LKA651 or the sham injection. Because the number of participants who had adverse events were similar for the different doses of LKA651, this summary reports the adverse events for all doses of LKA651 combined.

Adverse events in the eye

Adverse event	Sham injection out of 7 participants	LKA651 injection out of 21 participants
Bleeding on the eye (conjunctival hemorrhage)	0	4 (19%)
Less clear vision	3 (43%)	1 (5%)
Swollen retina (retinal thickening)	2 (29%)	1 (5%)
Liquid in eye pulled away from the eye (vitreous detachment)	1 (14%)	1 (5%)
Basal cell cancer on upper eye lid (basal cell carcinoma)	0	1 (5%)
Bleeding in the retina (retinal hemorrhage)	0	1 (5%)
Cloudy lens of the eye (cataract)	0	1 (5%)
Eye pain	0	1 (5%)
Inflammation in the front of the eye (anterior chamber cells)	0	1 (5%)
Inflammation in the back of the eye (vitreal cells)	0	1 (5%)

Adverse events not in the eye

Adverse event	Sham injection out of 7 participants	LKA651 injection out of 21 participants
UTI (urinary tract infection)	1 (14%)	3 (14%)
Abnormal heartbeat (abnormal electrocardiogram)	0	1 (5%)
Blood infection (sepsis)	0	1 (5%)
Broken bone	0	1 (5%)
Common cold (upper respiratory tract infection)	0	1 (5%)
Damaged nerves from diabetes (diabetic neuropathy)	0	1 (5%)
Diabetes (general) that got worse	0	1 (5%)
Diabetes (type 2) that got worse	0	1 (5%)
Ear infection	0	1 (5%)
Flu (influenza)	0	1 (5%)
High blood pressure	0	1 (5%)
Higher amylase in blood (amylase breaks down starch for energy)	0	1 (5%)
Higher lipase in blood (lipase breaks down fats for energy)	0	1 (5%)
Joint pain	0	1 (5%)
Tooth pulled	0	1 (5%)
Toothache	0	1 (5%)

For more information about the adverse events that participants reported in this clinical trial, visit novctrd.com. Use clinical trial number CLKA651X2104 to find the scientific summary.

What other key results did researchers learn?

In this clinical trial, researchers also wanted to learn:

- **If LKA651 moved from the eye into the blood**

When researchers checked participants' blood, they found low levels of LKA651 in participants who were given higher doses.

Researchers concluded the low levels of LKA651 in their blood didn't have any effects.

How has this clinical trial helped?

The results of this clinical trial helped researchers learn more about the safety of LKA651. Overall, the safety findings in this clinical trial support further testing of LKA651 in other clinical trials.

The results presented here are for a single clinical trial. No single clinical trial can give a complete picture of the benefits and risks of a trial drug. The results of many trials are needed to find out which treatments can be used for participants with macular edema. This summary shows only the main results from this trial. Other clinical trials may provide new information or different results.

Where can I learn more about this and future clinical trials?

If you were in this clinical trial and have questions about the results, speak with the doctor or staff where you took part in this clinical trial.

This is a summary of the results for one clinical trial.

You can find detailed results and more information about this clinical trial on the Novartis Clinical Trial Results website:

1. Visit novctrd.com
2. Click on "**Clinical trial results and trial summary for patients**" at the top right of the page
3. Read and scroll down, then click "I accept" if you agree to use the Novartis website
4. Click on "**Search by study number**" at the bottom left of the page
5. Type "**CLKA651X2104"** in the keyword search box and click "search"

This clinical trial was registered on the following website:

- ClinicalTrials.gov – https://clinicaltrials.gov/ – National Clinical Trial Database. To find this trial, type "**CLKA651X2104"** into the "Other terms" search box.

If more clinical trials on this trial drug are planned, they will appear on the public website listed above or at www.novartisclinicaltrials.com. When there, search for LKA651.

Full trial title: A randomized, single-masked, sham-control, single ascending dose study to assess the safety, tolerability, pharmacokinetics and pharmacodynamic activity of intravitreal LKA651 in patients with macular edema from diabetic macular edema (DME), neovascular age-related macular degeneration (AMD), or retinal vein occlusions (RVO)

Thank you!

Novartis would like to thank all of the trial participants that made this clinical trial possible. The trial participants helped researchers answer important health questions and learn more about a possible medical treatment. Many volunteers and many clinical trials are needed to advance medical science.

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