Clinical Trial Results

NOVARTIS

Research Sponsor: Novartis

Location of Headquarters: Basel, Switzerland

Drug Studied: LFG316

Protocol #: CLFG316A2203

Full Trial Title: A multicenter, randomized, sham-control, proof-of-concept study of intravitreal LFG316 in patients with geographic atrophy associated with age-related macular degeneration

Trial Date: January 2012 to June 2015

Thank you!

As a clinical trial patient, you belong to a large community of patients around the world. You helped researchers answer important health questions and discover new medical treatments.

Thank you for taking part in the clinical trial for the drug LFG316. You helped researchers learn more about how LFG316 works in people with age-related macular degeneration, also called AMD. This trial started in January 2012 and ended in June 2015.

Novartis, the sponsor of this trial, thanks you for your help and thinks it is important for you to know the results of your trial. An independent non-profit organization called CISCRP prepared this summary of the trial results for you. We hope it helps you understand your important role in medical research.

If you have questions about the results, please speak with the doctor, research nurse, or other team member at your trial site.

CISCRP
THE CENTER FOR INFORMATION & STUDY ON CLINICAL RESEARCH PARTICIPATION

What's happened since the trial ended?

This trial had 2 parts - Part A and Part B. If you participated in Part A, you were in this trial for up to 2 years. If you participated in Part B, you were in the trial for about 4 months. The trial took about 3½ years to complete. The trial included 158 participants from 19 sites in the United States. When the trial ended in June 2015, the sponsor reviewed the data and created a report of the results. This is a summary of that report.

Why was the research needed?

Researchers were looking for a better way to treat age-related macular degeneration, or AMD. This disease causes vision problems by damaging the part of the inner eye that is needed for detailed vision. This part of the eye is called the "macula". Some people may develop an advanced form of AMD called "geographic atrophy", also called GA. People with GA have lesions, or damaged areas, that form on the macula. These lesions may become larger over time.

Researchers have found that people with AMD have higher activity of an immune system protein called C5. In this trial, researchers wanted to know if the trial drug LFG316 could block C5.

The trial drug LFG316 is a type of antibody. Antibodies are normally made by the body's immune system to fight off infection. Researchers are now able to use antibodies as medications to treat a variety of conditions, including AMD and GA.

The main questions researchers asked in the trial were:

- Did LFG316 move from the eye into the bloodstream?
- Did multiple injections of LFG316 help reduce the growth of GA lesions after 12 months of treatment compared to no treatment at all?
- Did LFG316 help in other ways?
- What medical problems did participants have during the trial?

To answer these questions, researchers asked for the help of men and women like you. The participants in this trial were 61 to 90 years old and had AMD with GA lesions.

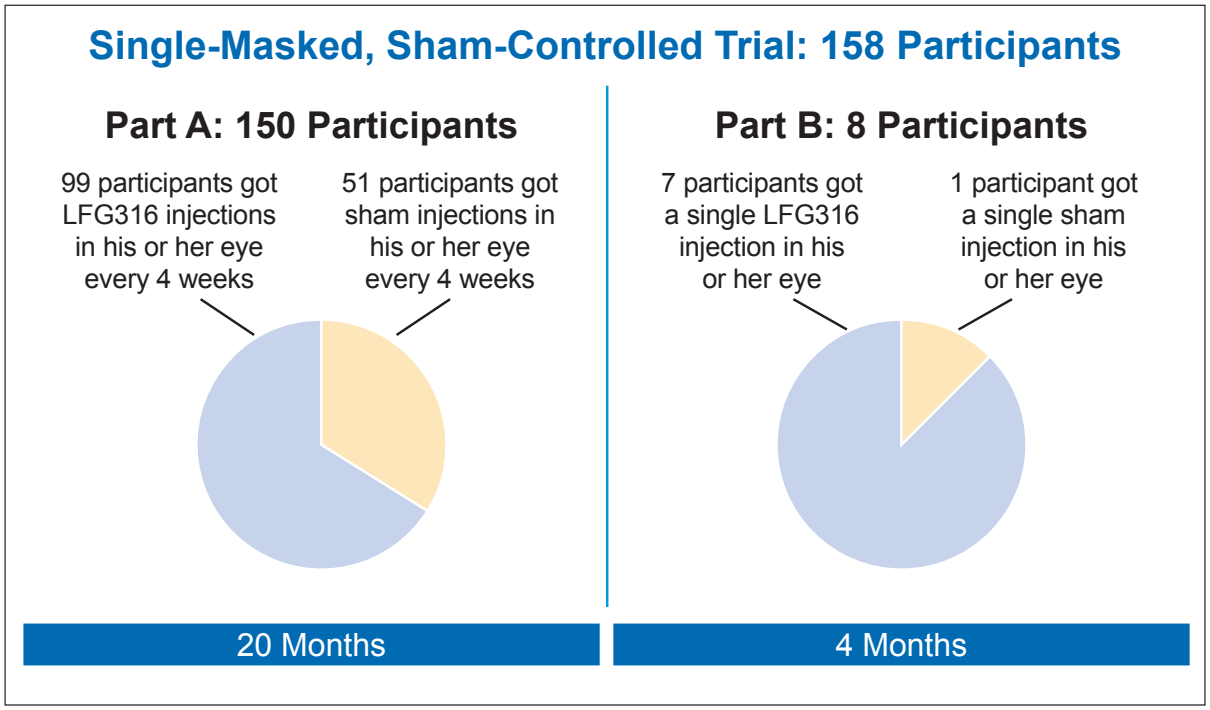
What kind of trial was this?

This trial was "sham-controlled". This means that some participants got an injection containing LFG316 into one eye, while some participants got a "sham" injection into one eye. The sham injection was not a real injection. Participants who got the sham had an empty syringe without a needle or trial drug placed against his or her eye. Sham injections are used to make sure that any changes researchers find during the trial did not happen by chance. No matter which treatment participants received, the treatment was only given in one eye.

Participants did not know if they were getting LFG316 or the sham injection, but the trial doctors did. When the trial ended, the research sponsor created a report of the trial results.

What happened during the trial?

This trial had 2 parts - Part A and Part B. Participants were enrolled in either Part A or Part B - not both. The figure below shows how the trial was done.



All participants had full check-ups and a physical examination to make sure they could take part in the trial. Trial doctors took blood samples and checked participants' temperature, blood pressure, as well as their heart health using an electrocardiogram, or EKG. Trial doctors also performed eye examinations to check participants' eye health and vision at each visit.

Part A lasted for about 20 months:

- Participants were randomly assigned to get LFG316 injections or sham injections.
- Participants got either 5 milligrams (mg) LFG316 injections or sham injections every 4 weeks for up to a total of 18 injections.
- Participants had a visit 1 month after their last treatment and a final visit 4 months after their last treatment.

Part B lasted for about 4 months:

- Participants were randomly assigned to get a single, 10mg injection of LFG316 or a single sham injection.
- Participants had a final visit about 12 weeks after the injection.

What were the results of the trial?

This is a summary of the overall results of your trial, not your individual results. The results presented here are for a single trial. Researchers look at the results of many studies to decide which drugs work best and are safest for patients. Other trials may provide new information or different results. You should not make therapeutic changes to your treatment based on the results of a single trial without first talking to your doctor. Further clinical studies with LFG316 [are/are not] currently planned.

Did LFG316 move from the eye into the rest of the body?

Single injection:

Yes. After a single injection, a small amount of LFG316 did move into the bloodstream. It took about 9 days for LFG316 to reach its highest amount in the blood. This level of LFG316 in the blood is too small to block C5 in the body or affect other organs in the body.

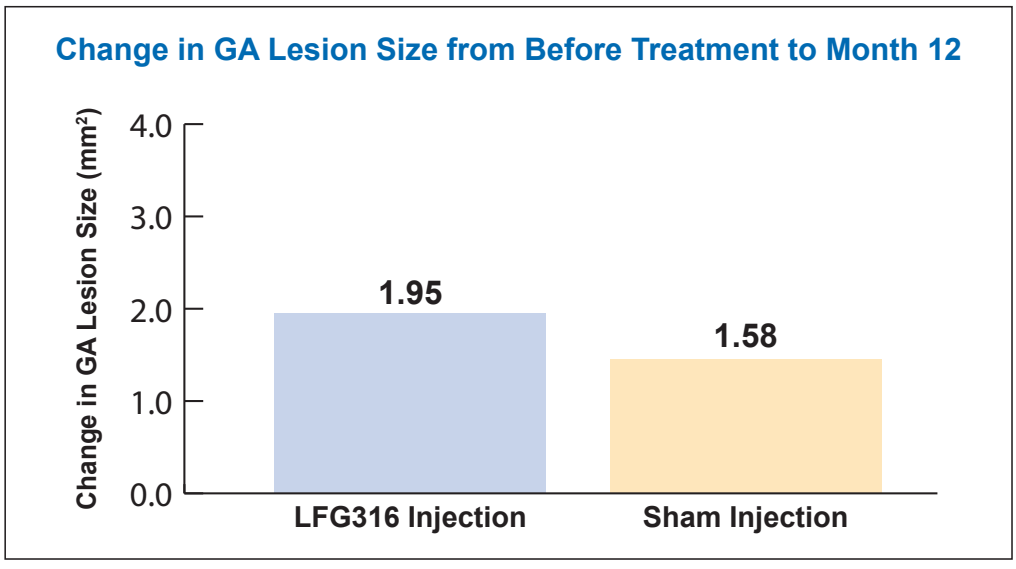
Multiple injections:

Yes. Researchers also measured the levels of LFG316 in the blood after multiple injections of LFG316. They found that a small amount of LFG316 did move from the eye and was found in the blood within 24 hours after the injection. The highest amount of LFG316 to collect in the blood happened 24 hours after the first dose. This level of LFG316 in the blood is too small to block C5 in the body or affect other organs in the body.

Did multiple injections of LFG316 help reduce the growth of GA lesions after 12 months of treatment compared to no treatment at all?

No. Researchers measured the size of GA lesions on the macula throughout the trial. To measure the size of the lesions, researchers took a picture of the back of the eye and measured the lesion in the picture. At Month 12 of Part A, participants in the LFG316 group had an average GA lesion growth of 1.95 square millimeters (mm2) compared to their lesion size before the trial started. Participants in the sham group had an average GA lesion growth of 1.58 mm2 compared to before the trial started. Overall, the results did not show that one treatment was better than the other. The 23.3% difference seen between the treatment groups could have been due to chance. The results did not show that one treatment was better than the other.

The figure below shows the average change in GA lesion size from before treatment to Month 12.



Did LFG316 help in other ways?

- Researchers also wanted to know if the size of lesions changed at 6 and 18 months following multiple doses of LFG316. They found that LFG316 did not reduce growth of the GA lesions at those time points. Overall, the results did not show that one treatment was better than the other. The differences seen could have been due to chance.

Growth of GA Lesions	6 Months After Treatment	18 Months After Treatment
LFG316 Injections	0.99 mm^2	2.78 mm^2
Sham Injections	0.88 mm^2	2.03 mm^2

- Since people with AMD have vision problems, researchers used an eye chart to measure participants' vision at different time points in the trial. They found that LFG316-treated participants were able to read slightly more letters than sham-treated participants.

Number of Letters Participants Could Read on the Eye Chart with Treated Eye	6 Months After Treatment	12 Months After Treatment	18 Months After Treatment
LFG316 Injections	48.4 letters	47.5 letters	44.7 letters
Sham Injections	42.5 letters	43.0 letters	43.8 letters

- Researchers also measured the levels of C5 in the blood after participants got multiple injections of LFG316. They found that neither LFG316-treated nor sham-treated participants had a change in their C5 levels throughout the trial.

What medical problems did participants have during the trial?

A lot of research is needed to know whether a drug causes a medical problem. So when new drugs are being studied, researchers keep track of all medical problems that patients have. These medical problems are called "adverse events". An adverse event is any sign or symptom that may or may not be caused by the trial drug.

How many participants had adverse events during the trial?

The table on the next page shows how many participants had adverse events that were related to the eye and how many had adverse events that were not related to the eye.

Adverse Events in this Trial

	Part A			Part B		
	LFG316 (5 mg) Out of 99 participants	Sham Out of 51 participants	Total Out of 150 participants	LFG316 (10 mg) Out of 7 participants	Sham Out of 1 participant	Total Out of 8 participants
Related to the eye	83 (83.8%)	35 (68.6%)	118 (78.7%)	3 (42.9%)	1 (100.0%)	4 (50.0%)
Not related to the eye	88 (88.9%)	37 (72.5%)	125 (83.3%)	1 (14.3%)	1 (100.0%)	2 (25.0%)

In Part A, 83 participants treated with LFG316 had adverse events related to the eye. Only 8 of those participants had 9 adverse events that the study doctors thought were related to the injection procedure and the presence of drug particles in the eye and not due to the effects of LFG316 itself. The 9 adverse events were:

- 2 cases of increased pressure in the eye
- Worsening of increased eye pressure
- Black spots in vision
- Eye floaters
- Droplets of silicone in the gel that fills the back of the eye
- Swelling of the colored part of the eye
- General swelling of the middle layer of the eye
- Brightness in vision

For the adverse events not related to the eye, the trial doctors did not think these adverse events were related to treatment with LFG316. In Part A, 6 participants (4.0%) left the trial because of adverse events.

In Part B, 1 participant (12.5%) left the trial because of adverse events. None of the adverse events (related to the eye or not) were thought to be related to treatment with LFG316.

Did any participants have serious adverse events?

An adverse event is called “serious” when it is life-threatening, causes lasting problems, or leads to hospitalization.

In Part A, 38 out of 150 participants (25.3%) experienced serious adverse events. The table below shows how many participants experienced serious adverse events.

	Part A		
	LFG316 Out of 99 participants	Sham Out of 51 participants	Total Out of 150 participants
How many participants had serious adverse events related to the eye?	3 (3.0%)	1 (2.0%)	4 (2.7%)
How many participants had serious adverse events not related to the eye?	24 (24.2%)	10 (19.6%)	34 (22.7%)

The 4 serious adverse events that were related to the eye included reduced sharpness in vision and infection of the inner parts of the eye, called endophthalmitis. None of these serious adverse events were thought to be related to treatment with LFG316 or sham by the trial doctors.

In Part A, 5 participants (4 treated with LFG316 and 1 treated with sham) died during the trial. None of the deaths were thought to be related to trial treatment by the trial doctors.

In Part B, 1 sham-treated participant out of the 8 total participants (12.5%) experienced 3 serious adverse events that were not related to the eye. None of these serious adverse events were thought to be related to LFG316 by the trial doctors. There were no deaths during Part B of the trial.

For more information about serious adverse events in this study, please refer to the full scientific summary of the results available on the Novartis Clinical Trial Results website (www.novctrd.com).

What were the most common non-serious adverse events?

The table below shows the most common non-serious adverse events (in at least 10% of participants in Part A and in at least 13% of participants in Part B) in this trial.

Most Common Non-Serious Adverse Events in this Trial

	Part A (Reported by about 10% of Participants or at least 15 participants out of 150)	**Part B (Reported by about 13% of Participants or at least 1 participant out of 8)**
Related to the eye	• Conjunctival hemorrhage (bright red patch appearing in the white of the eye beneath the clear lining of the eye) • Eye floaters • Eye pain • The feeling of having something foreign in the eye • Eye irritation • Vitreous detachment (separation of the gel that fills the back of the eye from the retina)	• Conjunctival hemorrhage (bright red patch appearing in the white of the eye beneath the clear lining of the eye) • Eye floaters • Abnormal tests on visual sharpness • Blurred vision • Retinal hemorrhage (bleeding in the retina) • Corneal dystrophy (abnormal material collects in the outer layer of the eye) • Charles Bonnet syndrome (visual hallucinations in people with vision loss)
Not related to the eye	• Infection in the nose, throat, and upper airways (upper respiratory tract infection) • High blood pressure	• Infection of the nose, throat, and airways • Muscle weakness • High cholesterol • Acid reflux disease • Falling • Bruising • Atrial fibrillation (an irregular, rapid heart rate)

For a full list of the adverse events that occurred in this study, please refer to the full scientific summary of the results available on the Novartis Clinical Trial Results website (www.novctrd.com).

Where can I learn more about this trial?

Researchers look at the results of many trials to decide which drugs work best and are safest for patients. It takes volunteers in many trials all around the world to advance medical science.

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). Once on the site, click **"Clinical trial results"** at the bottom of the page. After agreeing to enter the Novartis website, type **CLFG316A2203** into the keyword search box and click **"Search"**. If you have questions about the results, please speak with the doctor or staff at your trial site.

Official trial title: A multicenter, randomized, sham-control, proof-of-concept study of intravitreal LFG316 in patients with geographic atrophy associated with age-related macular degeneration

This trial was registered on Clinicaltrials.gov - **National Clinical Trial #** NCT01527500.

Thank you

It is said that the greatest gift is one which is given anonymously, giving when you do not know whether you will get direct personal benefit.

This is the gift that you have given by taking part in a clinical trial. It is a brave and selfless act, one that advances medical knowledge and benefits public health.

Thank you for the gift of your participation in clinical research.

CISCRP

The Center for Information & Study on Clinical Research Participation (CISCRP) is a non-profit organization focused on educating and informing the public about clinical research participation. CISCRP is not involved in recruiting participants for clinical trials, nor is it involved in conducting clinical trials.

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