Clinical Trial Results

NOVARTIS

Research Sponsor: Novartis

Drug Studied: LFG316

Protocol #: CLFG316B2101

Thank you!

Thank you for taking part in the clinical trial for the drug LFG316, also called tesidolumab. You and all of the patients helped researchers learn more about how LFG316 works in people with kidney failure who are at risk of antibody-mediated rejection after a kidney transplant. Antibody-mediated rejection is also called ABMR.

Novartis sponsored this trial and believes it is important to share the results of the trial with you and the public. 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 participated in the trial and have questions about the results, please speak with the doctor or staff at your trial site.

What has happened since the trial ended?

You were in the trial for about 3 months. But, the entire trial took about 1 year to finish. This is because the patients started and stopped treatment at different times. The trial started in August 2016 and ended in July 2017. The researchers ended the trial earlier than planned because the sponsor decided to stop studying LFG316 in patients with ABMR.

At first, the researchers planned to include 18 patients in this trial. After reviewing results from other LFG316 trials, the sponsor decided to stop studying LFG316 in patients with ABMR. The sponsor decided to include only 9 patients in this trial. But, it was hard to find enough patients to join, so the sponsor ended the trial early. Only 8 patients in the United States joined and finished the trial. After the trial ended, the sponsor reviewed the data and created a report of the results. This is a summary of that report.

Why was the research needed?

Before a drug can be approved for patients to take, researchers do clinical trials to find out how safe it is and how well it works. Researchers are looking for a better way to treat patients with kidney failure who are at risk of developing ABMR after a kidney transplant. People who have had blood transfusions, been pregnant, or had a transplant before have a bigger risk of developing ABMR. There are currently no approved treatments for ABMR.

Some patients do not qualify for a transplant because they have “donor-specific antibodies”. Antibodies are normally made by the immune system to identify substances like bacteria and viruses that are not made by the body. Sometimes, researchers can use antibodies as medicines to treat certain conditions. But, donor-specific antibodies often cause the body to reject a kidney transplant because they identify the transplant as something not made by the body. ABMR develops when the body rejects and attacks the transplanted kidney. This rejection can cause the transplanted kidney to fail.

Before the transplant, patients can be treated with medicines like intravenous immunoglobulin therapy, also called IVIG. IVIG can lower the amount of antibodies in the blood. This can help make sure the body does not reject the transplanted organ. But, it is not always enough to stop ABMR from developing in the patient.

Researchers think a certain type of protein made by the immune system may be involved in ABMR. The trial drug LFG316 is an antibody that was designed to block this protein.

In this trial, the researchers wanted to find out if IVIG changed the amount of LFG316 in the blood in a small number of patients. Because LFG316 is an antibody, the researchers wanted to know if IVIG would lower the amount of LFG316. To find out, the trial doctors gave some patients both IVIG and LFG316 and gave some patients LFG316 only. The researchers compared the blood test results from patients who got both IVIG and LFG316 with patients who got LFG316 only. This information would help doctors decide if LFG316 could be used safely with other drugs like IVIG.

The main questions the researchers wanted to answer in this trial were:

- Did IVIG change the amount of LFG316 in the patients’ blood?
- What medical problems did the patients have?

What kind of trial was this?

To answer the questions in this trial, the researchers asked for the help of men and women with kidney failure who needed a kidney transplant. These patients were also at risk of ABMR after receiving a kidney transplant. The patients in this trial were 39 to 61 years old.

This was an “open-label” trial. This means each patient knew what treatment they were getting. The trial staff and sponsor staff also knew what treatment each patient was getting. The sponsor staff did not know the identity of any of the patients.

A computer program was used to randomly assign the treatment each patient received. Researchers do this so that comparing the results of each treatment is done as fairly as possible. In some cases, the trial doctor decided which treatment certain patients got. The trial doctor did this if he or she thought that a patient’s overall health would be better in a certain treatment group.

What happened during the trial?

Before the treatment started, the trial doctors did tests to make sure the patients could take part in the trial. The trial doctors:

- took blood and urine samples from the patients
- checked the patients' blood pressure and heart rate
- checked the patients' heart health using an electrocardiogram, also called an ECG
- gave patients vaccines and antibiotics, if needed

The trial doctors may have given the patients medicine to lower the activity of their immune system. They did this based on which treatment the patients were assigned.

During treatment, the patients got their treatment through a needle into a vein. The dose of LFG316 was measured in milligrams per kilogram of body weight, also called mg/kg. All patients got 20 mg/kg of LFG316. The dose of IVIG was measured in grams per kilogram of body weight, also called g/kg. Patients who got IVIG got 2 g/kg of IVIG.

The patients got 1 of 2 treatments:

- 6 patients got a single dose of IVIG, then a single dose of LFG316
- 2 patients got a single dose of LFG316 only

The trial doctors may have given the patients medicine to lower the activity of their immune system. If a patient got this medicine, the trial doctors waited for the medicine to leave the patient's body before giving the patient LFG316. This helped the trial doctors make sure that LFG316 did not interact with this medicine.

After treatment, the patients visited the trial site at least 8 more times. At each visit, the trial doctors:

- checked the patients' blood pressure and heart rate
- asked how the patients were feeling and about any other medicines they were taking
- took more blood samples

Patients waited at least 28 days after getting their last dose of LFG316 before getting their kidney transplant.

The chart below shows how the trial was done.

Before treatment	During treatment	After treatment
• Trial doctors checked that patients could take part in the trial • The patients gave blood and urine samples	• 6 patients got LFG316 and IVIG • 2 patients got LFG316	• The patients visited their trial site at least 8 more times • The patients gave more blood samples
Up to 31 days	1 day	56 days

During the trial, the sponsor decided to stop studying LFG316 in patients with ABMR. So, the researchers ended the trial early.

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. Other trials may provide new information or different results. You should not make medical decisions based on the results of a single trial without first talking to your doctor. Always talk to a doctor before making any changes to your medications or treatment plans.

Did IVIG change the amount of LFG316 in the patients' blood?

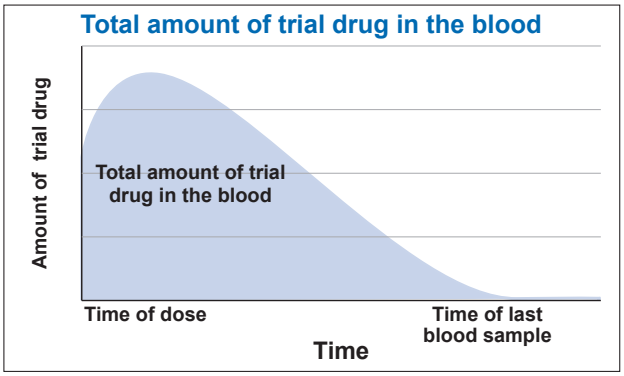
Yes. IVIG changed the amount of LFG316 in the patients' blood.

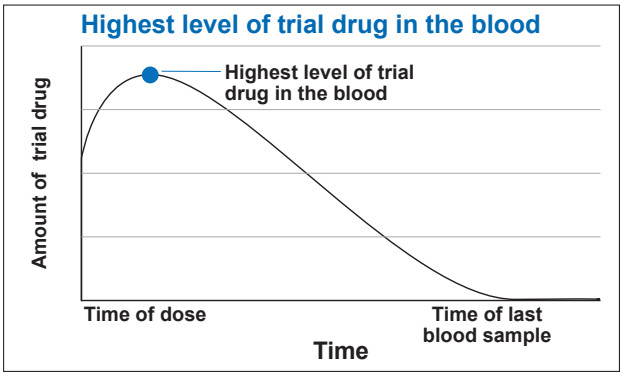
The researchers wanted to know how the amount of LFG316 in the blood changed when patients got both IVIG and LFG316. To answer this question, the researchers compared the amounts of LFG316 in the blood of patients who got IVIG with patients who did not get IVIG.

The researchers measured the amount of LFG316 at different times in the trial. This helped the researchers find:

- the total amount of LFG316 in the patients' blood during treatment
- the highest amount of LFG316 in the patients' blood after they got LFG316

The graphs below show an example of how the amount of a trial drug in the blood can change over time. It does not show actual results from this trial.

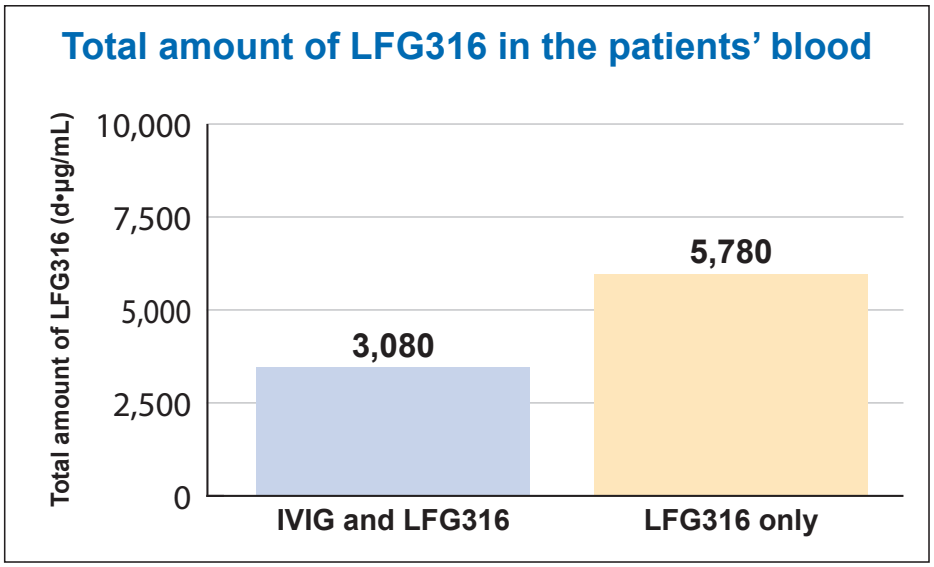




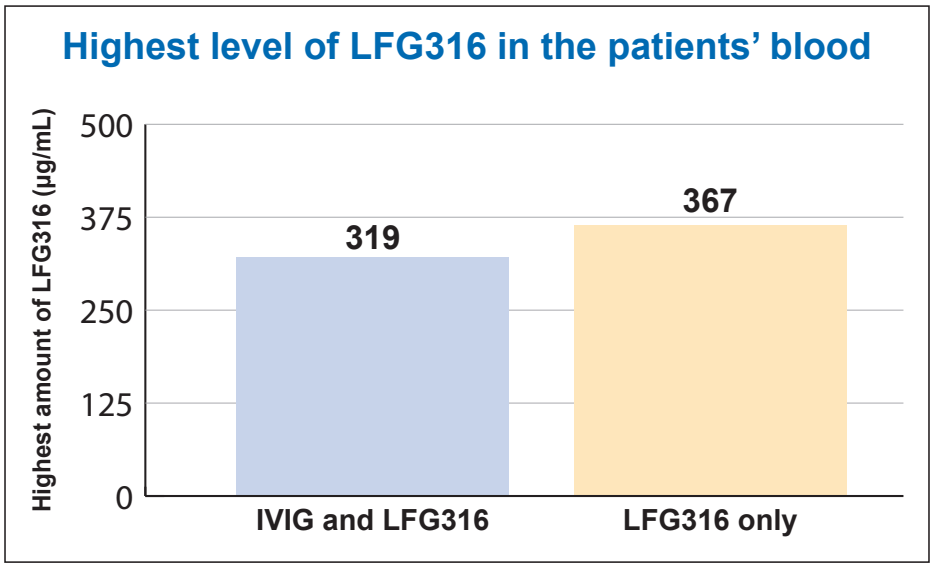
After 56 days, the researchers found that:

- The total amount of LFG316 in the blood during the treatment period was higher in patients who got LFG316 only compared with patients who got IVIG and LFG316.
- The highest amount of LFG316 in the blood was similar in patients who got either treatment. The difference between the treatments was too small for researchers to know if IVIG changed the highest amount of LFG316 in the blood.

The chart below shows the total amount of LFG316 in the blood in patients who got IVIG and in patients who did not get IVIG. This amount is measured in days multiplied by micrograms per milliliter of blood, also called d•µg/mL.



The chart below shows the highest level of LFG316 in the blood in patients who got IVIG and in patients who did not get IVIG. This amount is measured in micrograms per milliliter of blood, also called µg/mL.



For more measurements of LFG316 taken in the blood during this trial, please see the scientific summary that can be found on the website noted at the end of this summary.

What medical problems did the patients have?

Medical problems that happen in clinical trials are called “adverse events”. An adverse event is any unwanted sign or symptom that patients have during a trial. An adverse event is considered “serious” when it is life threatening, causes lasting problems, or the patients need hospital care.

These problems may or may not be caused by the trial drug. A lot of research is needed to know whether a drug causes a medical problem. During a trial, all medical problems are reported and written down, whether or not they are caused by the trial drug. So, when new drugs are being studied, researchers keep track of all medical problems that patients have during each trial.

This section is a summary of the adverse events that happened during this trial.

How many patients had adverse events?

Both patients who got only LFG316 had adverse events. Most of the patients who got IVIG and LFG316 had adverse events.

None of the patients in either treatment group had a serious adverse event or left the trial because of an adverse event. None of the patients died during the trial.

The table below shows how many patients had adverse events during this trial.

Adverse events during this trial

	IVIG and LFG316 (Out of 6 patients)	LFG316 (Out of 2 patients)	Total (Out of 8 patients)
How many patients in this trial had adverse events?	66.7% (4)	100.0% (2)	75.0% (6)
How many patients in this trial had serious adverse events?	0.0% (0)	0.0% (0)	0.0% (0)
How many patients left this trial because of adverse events?	0.0% (0)	0.0% (0)	0.0% (0)

What were the most common adverse events?

Pain in the arms, legs, hands, or feet was the most common adverse event during this trial. This happened in 25.0% of patients, which was 2 out of 8 patients. The table below shows all the adverse events that happened during the trial. The trial doctors did not think any of the adverse events were related to LFG316.

Adverse events that happened during this trial

Adverse event	IVIG and LFG316 (Out of 6 patients)	LFG316 (Out of 2 patients)	Total (Out of 8 patients)
Pain in the arms, legs, hands, or feet	16.7% (1)	50.0% (1)	25.0% (2)
Acid reflux	16.7% (1)	0.0% (0)	12.5% (1)
Back pain	16.7% (1)	0.0% (0)	12.5% (1)
Cough	16.7% (1)	0.0% (0)	12.5% (1)
Drowsiness	16.7% (1)	0.0% (0)	12.5% (1)
Ear pain	16.7% (1)	0.0% (0)	12.5% (1)
Itching	16.7% (1)	0.0% (0)	12.5% (1)
Low blood pressure during a medical procedure	16.7% (1)	0.0% (0)	12.5% (1)
Nausea	16.7% (1)	0.0% (0)	12.5% (1)
Numbness or tingling in the arms, legs, hands, or feet	16.7% (1)	0.0% (0)	12.5% (1)
Pain in the bones, muscles, or joints	16.7% (1)	0.0% (0)	12.5% (1)
Restless legs syndrome	0.0% (0)	50.0% (1)	12.5% (1)
Runny nose	16.7% (1)	0.0% (0)	12.5% (1)
Skin discoloration	16.7% (1)	0.0% (0)	12.5% (1)
Tiredness	16.7% (1)	0.0% (0)	12.5% (1)
Wet cough	16.7% (1)	0.0% (0)	12.5% (1)

For more information about the adverse events in this trial, please see the scientific summary that can be found on the website noted at the end of this summary.

How has this trial helped patients and researchers?

The information described above helped the researchers better understand if LFG316 works in people with kidney failure who are at risk of ABMR after a kidney transplant and who are treated with IVIG. It also helped the researchers learn how other antibodies could be given to people who are getting IVIG. More trials to study LFG316 in patients with ABMR are currently not planned.

The results presented here are for a single trial. More research is needed to find out which treatments can be used for patients with ABMR. This summary shows only the main results from this one trial in a small number of patients. Other trials may provide new information or different results. It takes volunteers in many trials all around the world to advance medical science.

Where can I learn more about this trial?

More information about the results of this trial can be found in the scientific results summary available on the Novartis Clinical Trial Results website (www.novctrd.com). Once on the site, click **"READ MORE"** under **"Clinical trial results"** at the bottom of the page. After agreeing to enter the Novartis website, type **"CLFG316B2101"** into the keyword search box and click **"Search"**. If you have questions about the results, please speak with the trial doctor or trial staff at your trial site.

You can find more information about this trial on the website listed below:

- www.clinicaltrials.gov. Once you are on the website, type **"NCT02878616"** into the **"Other terms"** search box and click **"Search"**.

If more clinical trials are planned, they will be listed on the above public website or www.novartisclinicaltrials.com. Search for **"LFG316"**.

Full trial title: Open-label, parallel-group, drug-drug interaction study in end-stage renal disease patients awaiting kidney transplant to investigate the potential effect of IVIG treatment on the pharmacokinetics and pharmacodynamics of LFG316

Thank you

Clinical trial patients belong to a large community of patients around the world. They help researchers answer important health questions and test new medical treatments.

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.

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