Clinical Trial Results

NOVARTIS

Research Sponsor: Novartis
Drug Studied: LFG316
Protocol #: CLFG316X2202

Thank you

Thank you to the patients who took part in the clinical trial for the drug LFG316, also called tesidolumab. The researchers wanted to learn more about how LFG316 works in people with transplant associated microangiopathy, also called TAM. TAM is a disease that damages the small blood vessels and that can happen when a person gets a stem cell transplant.

Novartis sponsored this trial and believes it is important to share the results of the trial. An independent non-profit organization called CISCRP prepared this summary of the trial results.

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?

The patients were in the trial for up to about 1 year. The trial started in April 2016 and ended in June 2017. Based on the initial results, the researchers could not be sure that LFG316 was helping the patients. So, the researchers decided to stop the trial early.

The researchers planned to include 40 patients in this trial. But, the trial included only 7 patients in France, Germany, and the United States. 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?

Researchers are looking for a better way to treat patients with TAM. 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.

TAM is a form of microangiopathy that can happen when a person gets a stem cell transplant. Microangiopathy is a disease that can damage the small blood vessels in the body. Small blood vessels are lined with cells. When these cells are damaged, the blood flows more slowly through the small blood vessels. This can cause different medical problems.

TAM is a life-threatening disease that is difficult to treat. But, patients can sometimes recover on their own, with or without treatment. Researchers do not completely understand what causes TAM.

There are “standard of care” treatments for TAM, but some patients die even after getting these treatments. A treatment is considered “standard of care” when the medical community thinks it is the appropriate and widely used treatment for a disease. “Standard of care” is also called SOC.

In patients with TAM, researchers think that an immune system protein may be involved in damaging the small blood vessels. This leads to serious medical problems. LFG316 attaches to this protein, which may stop damage to the small blood vessels seen in TAM.

In this trial, the researchers wanted to find out how LFG316 worked in a small number of patients with TAM. To find out, the researchers planned to compare the blood test results from patients who got only the SOC with patients who got both the SOC plus LFG316. Giving all patients the SOC helps doctors make sure that all patients in the trial get a form of treatment.

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

- How many patients had a change in their blood counts?
- How much LFG316 got into the patients’ blood?
- How many patients died for reasons other than their TAM?
- Did TAM symptoms go away in more patients who got LFG316?
- 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 TAM who had a stem cell transplant. The patients in this trial were 31 to 66 years old. The researchers planned to include children in this trial, but the trial ended early before any children participated.

This was an "open-label" trial. This means each patient knew what they were getting. The trial staff and sponsor staff also knew what each patient was getting. The patients got either the SOC only or the SOC plus LFG316. The sponsor staff did not know the identity of any of the patients.

A computer program was used to randomly choose the treatment each patient received. Researchers do this so that comparing the results of each treatment is done as fairly as possible.

What happened during the trial?

Before treatment started, the trial doctors did tests to make sure the patients could take part in the trial. The patients gave blood and urine samples. They also had their blood pressure and heart rate checked. The trial doctors checked the heart health of the patients using an electrocardiogram, also called an ECG. If needed, some patients got vaccinations.

During treatment, patients got either the SOC only or the SOC plus LFG316. The researchers planned to give patients their assigned treatment for 16 weeks. If a patient had no improvement of their TAM during this time, the patient could switch to the other treatment.

Patients who got LFG316 got a dose based on their body weight. Doses were measured in milligrams per kilogram, also called mg/kg. These patients got LFG316 through a needle into their vein.

The patients got either the SOC only or the SOC plus LFG316 once a week. Patients who got LFG316 got:

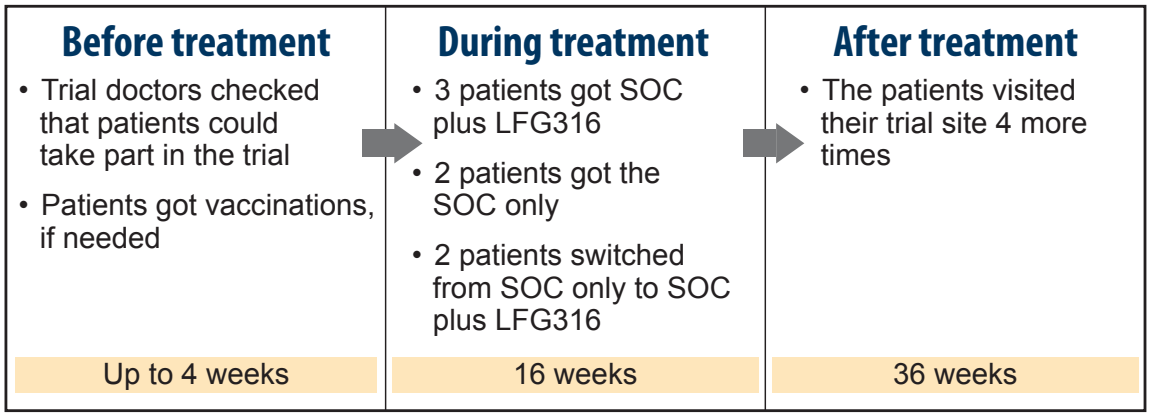
- 20 mg/kg for the first 3 weeks of treatment
- 10 mg/kg for another 13 weeks of treatment

Depending on their blood test results, they could go back to getting 20 mg/kg until the end of treatment. Throughout the trial, the trial doctors:

- checked the patients' blood pressure and heart rate
- asked the patients at each visit how they were feeling and about any other medicines they were taking
- took blood and urine samples and checked the patients' heart health
- gave antibiotics to the patients getting LFG316 to prevent infection

About 1 week after the last treatment, the patients visited their trial site. Then, they visited their trial site 3 more times. At these visits, the trial doctors checked the health of the patients. The trial doctors also asked how the patients were feeling and what medicines they were taking. The patients gave more blood and urine samples.

The chart below shows how the trial was planned to be done.



The researchers ended the trial early because it was not clear if the patients were getting better. Only 2 patients completed 16 weeks of treatment.

What were the results of the trial?

This is a summary of the overall results from this trial. The individual results of each patient might be different and are not in this summary. Other trials may provide new information or different results. Always talk to a doctor before making any treatment changes.

Based on the initial data, the researchers decided to end the trial early. Because the trial ended early, researchers were not able to get the information they needed to answer most of the questions they had about LFG316.

How many patients had a change in their blood counts?

The researchers planned to measure the amounts of different types of blood cells in the patients. This is called a blood count. Looking at blood counts helps the researchers find out if LFG316 is helping patients with their TAM. The researchers measured the blood counts throughout the trial. Since the researchers ended the trial early, there were not enough patients to get enough data. So, the researchers did not compare the 2 treatments.

How much LFG316 got into the patients' blood?

The researchers wanted to know how much LFG316 got into the patients' blood and how long it stayed in the blood. This information helps the researchers decide when a dose should be given and what dose is safe and effective for patients.

The researchers found that in the 5 patients who got LFG316 as part of their treatment, LFG316 reached expected levels in the blood. No other conclusions could be made from the available data because the trial ended early.

How many patients died for reasons other than their TAM?

The researchers wanted to know how many patients died for reasons other than their disease. Three patients died during the trial. These deaths are discussed in the section below.

TAM is a serious and complex disease that can lead to other medical problems. This made it difficult for the trial doctors to know if these patients died from reasons other than their TAM.

Did TAM symptoms go away in more patients who got LFG316?

The researchers wanted to know how many patients in each treatment group had their TAM symptoms go away. The researchers planned to count how many patients had their TAM symptoms go away after 16 weeks of treatment. But, the researchers ended the trial early and there were not enough patients to get enough data. So, the researchers did not compare the 2 treatments.

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 patient needs 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.

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

How many patients had serious adverse events?

In this trial, 6 of the 7 patients had serious adverse events. This was 85.7% of patients. These 6 patients had a total of 31 serious adverse events during this trial. Most of these serious adverse events are common in patients with TAM who have had a transplant.

One patient had 3 serious adverse events that the trial doctors thought were related to the trial drug.

There were 3 patients who died during the trial. During treatment, 1 patient who was getting LFG316 died of a serious infection. The trial doctors thought this death was related to the trial drug. The other 2 patients died after they added LFG316 as part of their treatment. The trial doctors did not think that these 2 deaths were related to the trial drug.

How many patients had adverse events?

All the patients in this trial experienced at least 1 adverse event. Three patients who got LFG316 as part of their treatment stopped taking the trial treatment because of adverse events. This was 42.9% of all patients.

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

Adverse events during this trial

	LFG316 plus SOC (Out of 3 patients)	SOC only (Out of 2 patients)	SOC first, then LFG316 plus SOC (Out of 2 patients)	Total (Out of 7 patients)
How many patients in this trial had adverse events?	100.0% (3)	100.0% (2)	100.0% (2)	100.0% (7)
How many patients in this trial had serious adverse events?	100.0% (3)	50.0% (1)	100.0% (2)	85.7% (6)
How many patients stopped taking the trial treatment because of adverse events?	66.7% (2)	0.0% (0)	50.0% (1)	42.9% (3)

What were the most common adverse events?

Swelling of the lower limbs and tiredness were the most common adverse events during this trial. The table below shows the most common adverse events that happened in at least 50.0% of patients out of all the treatment groups during the trial. There were other adverse events, but these happened in fewer patients.

Most common adverse events during this trial

Adverse event	LFG316 plus SOC (Out of 3 patients)	SOC only (Out of 2 patients)	SOC first, then LFG316 plus SOC (Out of 2 patients)	Total (Out of 7 patients)
Swelling of the lower limbs	66.7% (2)	100.0% (2)	0.0% (0)	57.1% (4)
Tiredness	33.3% (1)	100.0% (2)	50.0% (1)	57.1% (4)

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

How has this trial helped patients and researchers?

The results presented here are from a single trial. More research is needed to find out which treatments can be used for patients with TAM. This summary shows only the main results from this one trial.

This trial studied LFG316 in a small group of patients with TAM. Because the trial ended early, the number of patients in each treatment group was too small to reach any clear conclusion. This trial could not show that LFG316 changed the blood counts of patients with TAM.

LFG316 will not be further studied for the treatment of TAM. The information learned in this trial may help researchers to study other possible treatments for TAM.

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 **"CLFG316X2202"** 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 websites listed below.

- www.clinicaltrials.gov. Once you are on the website, type **"NCT02763644"** into the **"Other terms"** search box and click **"Search"**.
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home & Search"**, then type **"2014-004972-49"** into the search box and click **"Search"**.

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

Full trial title: A randomized, open label, controlled, multiple dose study to evaluate the clinical efficacy, safety, tolerability, pharmacokinetics and pharmacodynamics of LFG316 in patients with transplant associated microangiopathy after hematopoietic precursor cell transplantation

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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