

Clinical Trial Results Summary

A trial to learn about the safety and effects of LLF580 in participants with obesity and high levels of a type of fat in their blood called triglycerides

Thank you



Thank you to the participants who took part in the clinical trial for the trial drug LLF580. All of the participants helped the researchers learn more about how LLF580 works and how safe it is to receive.

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.

Research Sponsor: Novartis
Drug Studied: LLF580
Trial Number: CLLF580X2102

Overview of this trial



What was the purpose of this trial?

In this clinical trial, the researchers studied:

- The safety of a trial drug called LLF580.
- If LLF580 affected the levels of fat in the participants' blood such as triglycerides.
- If LLF580 affected the participants' body weight.
- The participants' bone health by measuring proteins in the blood that are present when bone is formed and broken down.



Who was in the trial?

61 men and women participated in this clinical trial.

The participants were 21 to 64 years old, had obesity, and had high levels of a type of fat in their blood called triglycerides.



What treatments did the participants receive?

The participants in this trial received LLF580 or a placebo.

The placebo looked like the trial drug but had no trial drug in it. Using a placebo helps researchers better understand the actual effects of a trial drug.



What were the main results of the trial?

Overall the researchers learned that:

- Compared to the placebo group, the participants in the LLF580 group had lower levels of certain fats in their blood, including triglycerides.
- There was no difference in body weight between the LLF580 group and the placebo group.
- Most of the participants had medical problems during this trial, including the participants receiving either LLF580 or placebo.
 - The most common medical problem was nausea. This happened more in the LLF580 group than in the placebo group.
 - Some medical problems were serious.
 - 2 participants in the LLF580 group and 1 participant in the placebo group left the trial due to a medical problem.
- The researchers looked at proteins in the blood that are present when the bone forms and when it breaks down. The researchers found:
 - Lower levels of proteins related to bones being formed in the LLF580 group compared to the placebo group.
 - Similar levels of proteins related to when bones are broken down in both groups.

More details about the results of this trial are included later in this summary.

What was the purpose of the trial?



Researchers are trying to find better ways to treat conditions caused by high levels of fats like cholesterol and triglycerides in the blood. High levels of these types of fats in the blood can increase the risk of other serious conditions, like heart attacks and strokes.

Obesity can cause higher levels of fat in the blood. It can also increase the risk of other serious conditions, like diabetes and fatty liver disease.

The trial drug, LLF580, was designed to act like a hormone in the body that reduces levels of fats like triglycerides and last longer in the blood. In this trial, the researchers wanted to find out if LLF580 could help lower the levels of triglycerides in the participants' blood, and if there was any effect on weight loss.

Before a trial drug can be approved for patients to take, researchers do clinical trials to find out how safe it is and how it works.

The main question the researchers wanted to answer in this trial was:

- What medical problems did the participants have during this trial?

Keeping track of the medical problems helped to learn about the safety of LLF580.

Other questions the researchers wanted to answer were:

- Did LLF580 affect the levels of fats in the participants' blood?
- Did LLF580 affect body weight?
- Did LLF580 affect the levels of proteins related to bone health in the participants' blood?

Who was in the trial?



To answer the questions in this trial, the researchers asked for the help of men and women who had high levels of triglycerides in their blood and obesity. Obesity is when someone is overweight for their height from too much body fat.

This trial included 61 participants in the United States.

The trial participants were 21 to 64 years old when they joined. Their average age was 46 years old.

What trial treatments did the participants receive?



The clinical trial team used a computer program to randomly assign each participant to receive one of these trial treatments:





- LLF580 – the trial drug
- Placebo

The placebo looked like LLF580 but had no trial drug in it. Using a placebo helps researchers better understand the actual effects of a trial drug. Using a computer program to assign treatments helps make sure that comparing the results of the treatments is as fair as possible.

The participants in this trial received their trial treatment through a needle put under the skin, also known as an injection.

None of the participants, trial staff, or sponsor staff knew what treatment each participant received. Some trials are done this way because knowing what treatment the participants are receiving can influence the results. Not knowing what treatment participants get helps make sure the results are looked at fairly.

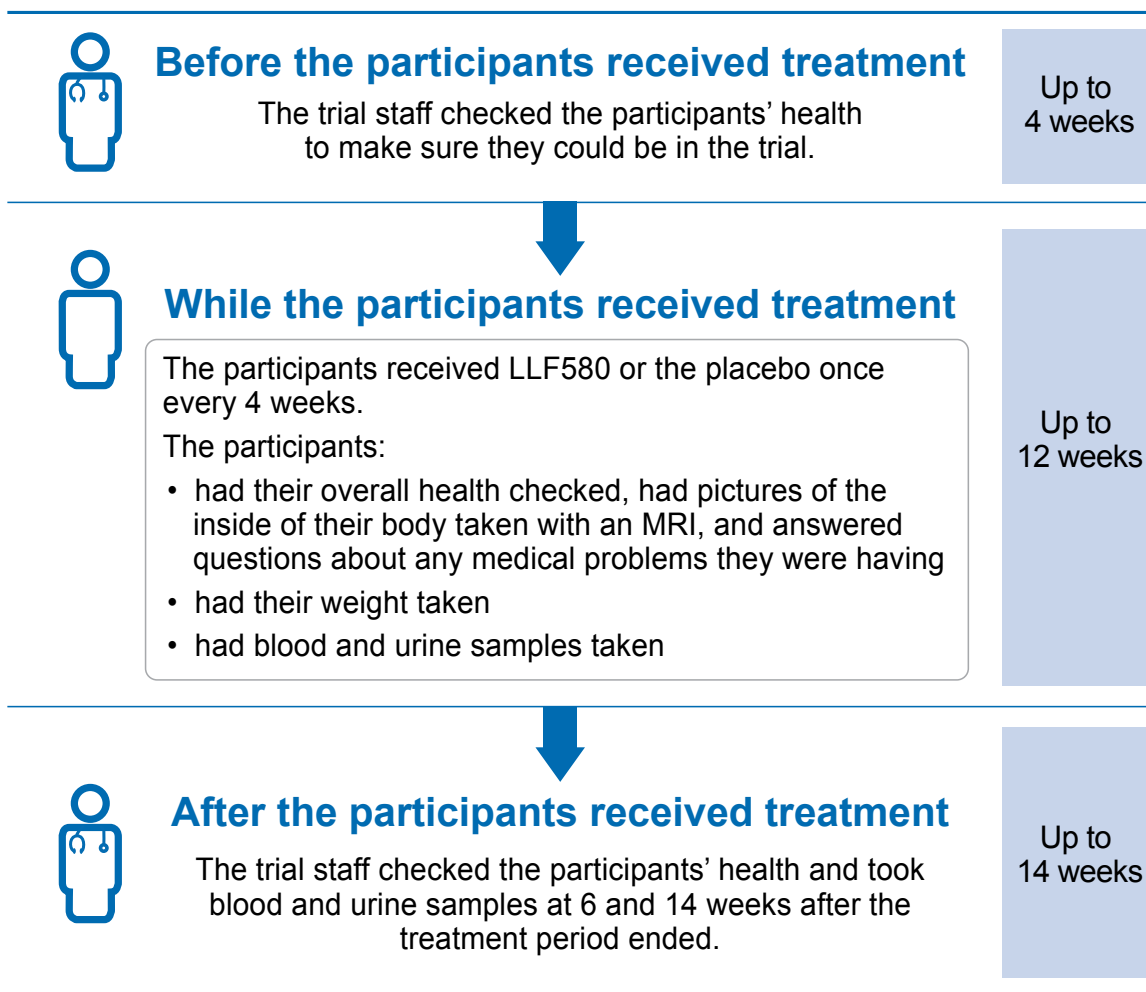
The chart below shows the treatments that each group of participants took:

	LLF580	Placebo
	30 participants	31 participants
	300 mg of LLF580	The placebo
	Through an injection	
	Once every 4 weeks for a total of 3 doses	

What happened during this trial?

The trial started in February 2018 and ended in November 2019. Each participant was in the trial for up to 30 weeks.

The chart below shows what happened during this trial to find the main results.



What were the main results of the trial?

This is a summary of the overall results from this trial. The individual results of each participant might be different and are not in this summary.

The results from several trials are needed to decide which treatments are safest and work best. Other trials may provide new information or different results. Always talk to a doctor before making changes to your healthcare.

What medical problems happened during the trial?

Medical problems that happen in clinical trials are called “adverse events”. An adverse event is any unwanted sign or symptom that participants have during a trial. An adverse event is 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 the treatments in the trial.

A lot of research is needed to know whether a treatment causes an adverse event. Doctors keep track of all the adverse events that happen in trials, even if they do not think the adverse events might be related to the treatments.

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



Most of the participants had medical problems during this trial, including the participants receiving either LLF580 or the placebo. The most common medical problem was nausea. This happened in more participants who received LLF580 than in those who received the placebo. Some medical problems were serious. 2 participants in the LLF580 group and 1 participant in the placebo group left the trial due to a medical problem.

Summary of adverse events

	LLF580 (30 participants)	Placebo (31 participants)
Serious adverse events	6.7% 2 of 30	3.2% 1 of 31
Other adverse events	93.3% 28 of 30	77.4% 24 of 31
Left the trial due to adverse events	6.7% 2 of 30	3.2% 1 of 31









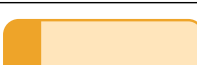
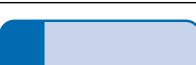
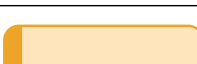


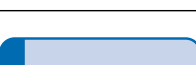



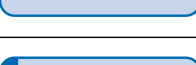

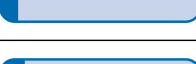
Serious adverse events

LLF580	Placebo
<p>6.7% of participants who received LLF580 had a serious adverse event. This was 2 out of 30 participants. The serious adverse events were:</p> <ul style="list-style-type: none">• inflammation of the gallbladder (cholecystitis)• a rare type of cancer that starts in a type of white blood cell called B-cells (Burkitt's lymphoma)	<p>3.2% of participants who received the placebo had a serious adverse event. This was 1 out of 31 participants. The serious adverse events were:</p> <ul style="list-style-type: none">• lung infection that causes inflammation of the airways in the lungs (pneumonia)• blood condition caused by the body's over reaction to infection (sepsis)• a respiratory condition that happens when the lungs can't get enough oxygen into the blood (respiratory failure)

No other serious adverse events were reported, including no deaths.

What were the other adverse events?

The adverse events in the below table happened in **4 or more participants**. There were other adverse events, but these happened in fewer participants.

Most common other adverse events		
Adverse events	LLF580 (30 participants)	Placebo (31 participants)
Nausea	60.0% 18 of 30 	6.5% 2 of 31 
Diarrhea	26.7% 8 of 30 	12.9% 4 of 31 
Vomiting	30.0% 9 of 30 	3.2% 1 of 31 
Heart burn (Dyspepsia)	13.3% 4 of 30 	3.2% 1 of 31 
Infection of the upper airways (Upper respiratory tract infection)	16.7% 5 of 30 	12.9% 4 of 31 
Back pain	10.0% 3 of 30 	6.5% 2 of 31 
Pain in the muscles, joints, and bones (Musculoskeletal pain)	3.3% 1 of 30 	9.7% 3 of 31 
Decreased appetite	16.7% 5 of 30 	0.0% 0 of 31 
Increased appetite	10.0% 3 of 30 	6.5% 2 of 31 
Fluid filled sacs in the kidney (Renal cyst)	10.0% 3 of 30 	9.7% 3 of 31 

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 the summary.

What other results were learned?

The researchers wanted to learn if LLF580 affected the participants in other ways. They studied how LLF580 affected the levels of fats in the participants' blood, their weight, and their bone health. The researchers compared these results in the participants who received LLF580 and in those who received the placebo.

Did LLF580 affect the levels of fats in the participants' blood?



Compared to the placebo group, the LLF580 group had lower levels of certain types of fats in the blood such as triglycerides.

The researchers wanted to find out if LLF580 helped reduce the amount of certain fats in the participants' blood, like triglycerides. To find this out, the trial doctors took blood samples at different times before and after the participants received the trial treatments.

Overall, compared to the participants who received the placebo, the participants who received LLF580 had the following fat levels in their blood:

- Lower levels of different types of fats, such as triglycerides and cholesterol.
- Higher levels of HDL, also known as high-density lipoprotein. HDL is sometimes called the “good” kind of fat, because it helps remove other types of fats from the blood.

Having low levels of triglycerides and cholesterol, as well as high levels of HDL, may help lower the risk of heart attacks and strokes.

Did LLF580 affect the participants' weight?



Overall there was no difference in body weight between the LLF580 group and the placebo group.

The researchers wanted to find out if LLF580 helped the participants lose weight. To find this out, the trial doctors weighed the participants at different times before and after the participants received the trial treatments.

The researchers found that some participants had changes in their body weight. They found that the placebo group on average showed an increase in body weight. However, the researchers found that overall there was no difference in body weight between the LLF580 group and the placebo group.

More research is needed to learn more about how LLF580 affects body weight.

Did LLF580 affect the levels of proteins related to bone health in the participants' blood?



There were lower levels of proteins related to when bones are being formed in the LLF580 group compared to the placebo group. However, there were similar levels of proteins related to when bones are being broken down in both groups.

To find this out, they measured the levels of certain proteins in the blood that are present when bone is being formed or being broken down. Looking at these levels of proteins can help the researchers find out if LLF580 affected the participants bone health.

Overall, the researchers found that:

- The levels of specific proteins present in the blood when bone is being formed decreased in both the LLF580 group and the placebo group. But, the researchers found that the participants who received LLF580 had lower levels of these proteins in their blood compared to the participants in the placebo group.
- The participants in the LLF580 group and the placebo group had similar levels of other specific proteins present in the blood when bone is broken down.

More research is needed to know if LLF580 affects bone health.

What was learned from this trial?



The information described above helped the researchers learn more about how safe LLF580 was in participants with obesity and higher levels of triglycerides. It also helped the researchers learn more about how LLF580 affected bone health and fats in the participants' bodies.

The results presented are for a single trial. This summary shows only the main results from this one trial in a small number of participants. Additional research is needed to confirm these results.

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.

- Go to www.novctrd.com.
- Once on the site, click “**Clinical Trial Results**” at the top right of the page.
- After accepting the terms, go to the bottom left of the page and click “**Study number**” from the drop-down menu.
- Type “**CLLF580X2102**” into the keyword search box and click “**Search**”.

If you would like to view the website in a language other than English, you can click the “**Google Translate**” button on the top right of the page.



If you participated in the trial and have questions about the results, please speak with the trial doctor or 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 “**CLLF580X2102**” into the “**Other terms**” search box and click “**Search**”.

If more clinical trials are planned, they will be listed on the above public websites or at www.novartisclinicaltrials.com. Search for “**LLF580**” or “**Obesity**” or “**hyperglyceridemia**” or “**non-alcoholic fatty liver disease**” or “**NAFLD**” or “**fatty liver**”.

Full trial title: A 12 Week Phase Ib Randomized Investigator and Subject Blinded Placebo Controlled Repeat-dose Study of LLF580

Protocol number: CLLF580X2102

Thank you

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



Novartis is a global healthcare company based in Switzerland that provides solutions to address the evolving needs of patients worldwide.

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