NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of LCZ696 in people with non-obstructive hypertrophic cardiomyopathy

Thank you!

Thank you to the participants who took part in the clinical trial for **non-obstructive hypertrophic cardiomyopathy (nHCM).** Every participant helped the researchers learn more about the trial drug **LCZ696**, also called sacubitril and valsartan.

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.

Trial information

Trial number: CLCZ696I12201

Novartis drug studied: LCZ696, also called sacubitril and valsartan

Sponsor: Novartis

If you were a participant and have any questions about the results, please talk to the doctor or staff at the trial site.

This summary only shows the results of a single clinical trial. Other clinical trials may have different results.

What was the main purpose of this trial?

The purpose of this trial was to learn about the effects of **LCZ696** in people with nHCM.

Non-obstructive hypertrophic cardiomyopathy, or **nHCM,** is a condition that causes the heart muscle to become thicker. **Non-obstructive** means that blood flow is not blocked, but the thicker muscle makes it harder for the heart to pump blood. This means it pumps less blood and oxygen to the body.

Symptoms of nHCM may include:

- Chest pain
- Fast, fluttering, or pounding heartbeats
- Trouble breathing
- Swollen legs

Symptoms are worse during or right after physical activity because the heart cannot pump enough blood and oxygen to the body. Because of this, people with nHCM are often unable to exercise or do physical activity at a level that is normal for their age.

LCZ696 is a drug designed to relax and open blood vessels, which can lower blood pressure and the build-up of fluids in the body. It is approved in the European Union, United States, and other countries to treat a type of heart failure. **Heart failure** is another heart condition where the heart can't pump enough blood and oxygen to the body.

LCZ696 is not currently approved to treat nHCM, but researchers think it might allow the heart to pump more blood and oxygen to the body.

The trial's purpose was to answer these main questions:

- Did participants' hearts pump more oxygen to the body during exercise after taking LCZ696?
- What medical problems, also called adverse events, happened during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial.

How long was this trial?

The trial began in January 2020 and ended in August 2023.

Who was in this trial?

46 participants with nHCM received treatment in this trial – 34 men and 12 women. Participants' ages ranged from 20 to 79 years. Their average age was 56 years.

The number of participants by race is shown below.

Race

6 Asian	40 White

The participants could take part in this trial if they:

- Did not need to take certain medicines that lower blood pressure
- Did not have certain other heart conditions

46 participants from 6 countries received treatment. The map below shows the number of participants who took part in each country.

What treatments did the participants receive?

The treatments in this trial were:

LCZ696 – 50, 100, or 200 milligrams (mg) taken by mouth as tablets twice a day.

Placebo – Taken by mouth as tablets twice a day. A **placebo** looks like the trial drug but does not have any trial drug in it. Using a placebo helps researchers better understand the effects of a trial drug.

Participants took treatment during 2 parts of this trial:

- **Part 1** (4 weeks): Each participant took the **placebo** for 2 weeks and then **LCZ696** for another 2 weeks. The researchers checked each participant for any safety concerns before they continued to Part 2.
- **Part 2** (about 11 months): The researchers used a computer to randomly assign participants who completed Part 1 to receive either **LCZ696** or the **placebo**. The participants took their assigned treatment for about 11 months.

In Part 1, the researchers and trial staff knew when the participants took the **placebo** and **LCZ696**. The participants did not know when they were taking each treatment.

In Part 2, none of the participants, researchers, or trial staff knew what treatment the participants took. Some trials are done this way because knowing what treatment the participants take can affect the results of the trial. Doing a trial this way helps to make sure that the results are looked at with fairness across all treatments.

Participants could continue taking other medicines for nHCM during this trial.

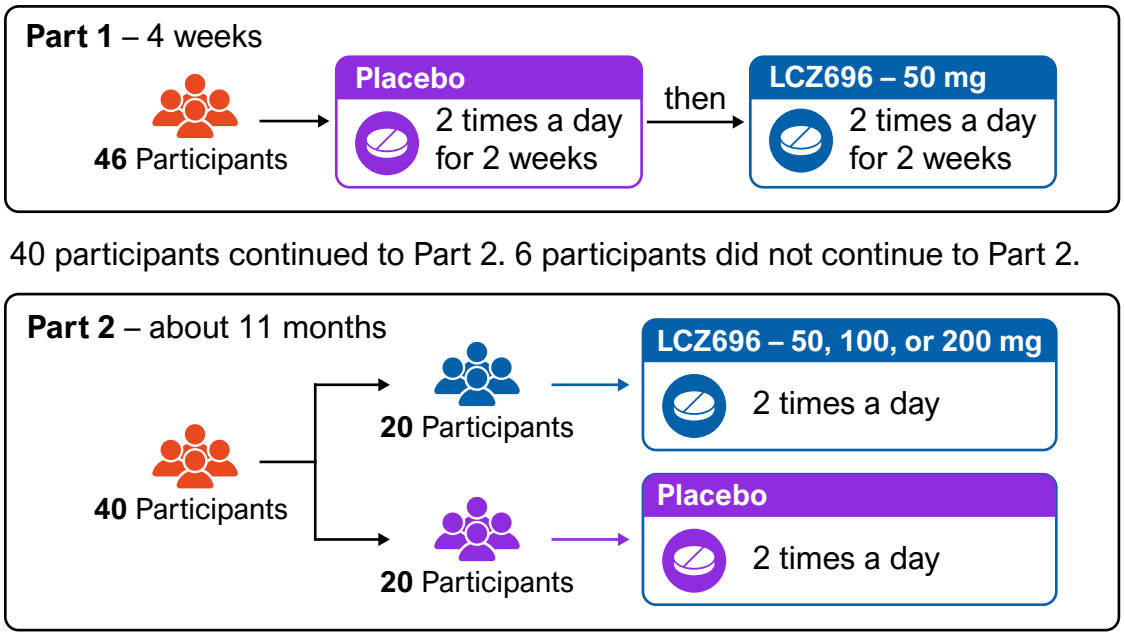
What happened during this trial?

Before treatment — About 1 month

The trial staff checked to make sure the participants could be in this trial.

During treatment — About 1 year

The participants took treatment during 2 parts of this trial. The graphic below shows how participants took treatment in each part.



In Part 2, participants assigned LCZ696 took 100 mg 2 times a day.
After 2 weeks:

- If a participant did not have safety concerns, their dose went up to 200 mg 2 times a day
- If a participant had safety concerns, their dose went down to 50 mg 2 times a day

Each participant continued to take the highest dose that did not cause safety concerns.

Trial staff checked the participants' general health throughout the trial.

After treatment — About 1 month

Participants returned to their trial site one time after receiving their last dose of treatment for trial staff to check their health.

What were the main results of this trial?

Did participants' hearts pump more oxygen to the body during exercise after taking LCZ696?

After taking LCZ696 for about a year, the participants' hearts pumped about the same amount of oxygen during exercise compared to participants who took the placebo.

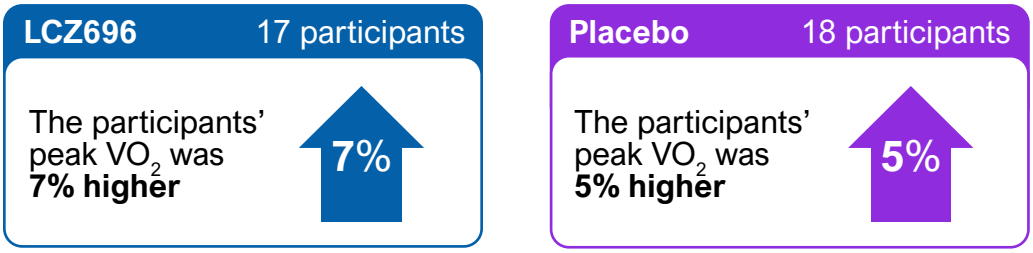
To learn this, each participant had **cardiopulmonary exercise testing,** or **CPET**, before and after taking LCZ696 or the placebo for about a year.

During CPET, researchers measured participants' **peak VO_2**. Peak VO_2 is the highest amount of oxygen the body uses while exercising. Peak VO_2 shows how well the heart pumps blood and oxygen to the body to use for energy. A **higher** peak VO_2 means the heart can pump **more** blood and oxygen to the body.

What happens during CPET?
During CPET, a person moves on a treadmill with increasing speed and incline. They continue until they reach the highest speed and incline they are able to do. While on the treadmill, they wear a face mask that records the amount of oxygen they breathe in and out.

Change in peak VO_2 after about 1 year of treatment

The graphic below shows the average change in the participants' peak VO_2 after about a year of treatment compared to before treatment.



The graphic only includes participants who took their treatment as planned.

What medical problems, also called adverse events, happened during this trial?

Trial doctors keep track of all **adverse events** that happen in trials, even if they think the adverse events are not related to the trial treatments.

Many trials are needed to know if a drug or treatment causes an adverse event.

This section is a summary of the adverse events that happened from the start of trial treatment until about 30 days after the last dose of treatment.

An **adverse event** is:

- Any **sign or symptom** that the participants have during a trial
- 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 treatments in the trial.

In Part 1, some of the participants (8 of 46) had adverse events. No participants had adverse events that were considered serious, and no one died. 4 participants left the trial due to an adverse event.

In Part 2, about half of the participants (22 of 40) had adverse events. 3 participants had adverse events that were considered serious. No participants died. 1 participant left the trial due to an adverse event.

The researchers concluded there were no new safety concerns for LCZ696 in this trial.

How many participants had adverse events?

	Part 1		Part 2	
	LCZ696 43 participants	**Placebo** 46 participants	**LCZ696** 20 participants	**Placebo** 20 participants
Had at least 1 **serious adverse event**	**0 of 43** 0%	**0 of 46** 0%	**3 of 20** 15%	**0 of 20** 0%
Had at least 1 **other adverse event**	**4 of 43** 9%	**4 of 46** 9%	**12 of 20** 60%	**10 of 20** 50%
Left the trial due to an adverse event	**3 of 43** 7%	**1 of 46** 2%	**1 of 20** 5%	**0 of 20** 0%
Died during the trial	**0 of 43** 0%	**0 of 46** 0%	**0 of 20** 0%	**0 of 20** 0%

What serious adverse events did the participants have?

In Part 1, none of the participants had serious adverse events.

In Part 2, 3 participants who took LCZ696 had a total of 7 serious adverse events:

- **Abnormal electrical signals in the heart** (atrioventricular block second degree, left bundle branch block, or right bundle branch block)
- **Slow heart rate** (bradycardia)
- **Heart failure** (cardiac failure)
- **COPD** (chronic obstructive pulmonary disease)
- **Blocked blood flow in the vessels to the heart** (coronary artery disease)

What other adverse events did the participants have?

In Part 1, 8 participants had other adverse events.

In Part 2, 22 participants had other adverse events.

The table below shows the other adverse events that happened in **3 or more** participants. Additional adverse events happened in fewer participants.

	Part 1		Part 2	
	LCZ696 43 participants	**Placebo** 46 participants	**LCZ696** 20 participants	**Placebo** 20 participants
COVID-19	**0 of 43** 0%	**0 of 46** 0%	**0 of 20** 0%	**5 of 20** 25%
Feeling dizzy Dizziness	**0 of 43** 0%	**2 of 46** 4%	**2 of 20** 10%	**1 of 20** 5%
Low blood pressure Hypotension	**1 of 43** 2%	**0 of 46** 0%	**3 of 20** 15%	**0 of 20** 0%
Frequent, loose, or watery stool Diarrhea	**1 of 43** 2%	**1 of 46** 2%	**1 of 20** 5%	**0 of 20** 0%

What was learned from this trial?

Researchers learned about the effects of LCZ696 in people with nHCM.

The researchers concluded that:

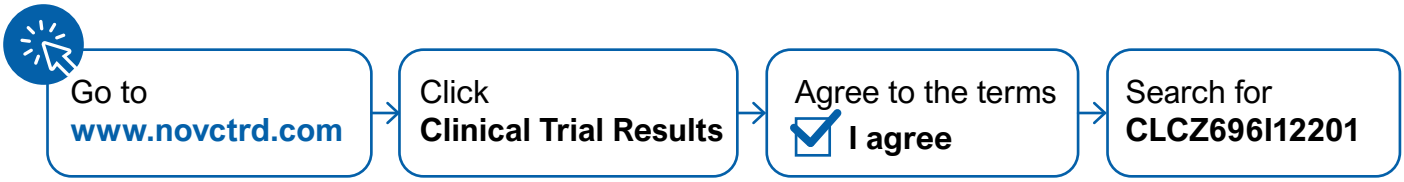
- Participants who took LCZ696 had their hearts pump about the same amount of oxygen during exercise compared to those who took the placebo
- There were no new safety concerns for LCZ696 in this trial

When this summary was written, the sponsor had no plans for future trials of LCZ696 in people with nHCM.

Where can I learn more about this trial?

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**

Follow these steps to find the scientific summary:



For more information about this trial, go to any of these websites:

- **clinicaltrials.gov** – search using the number **NCT04164732**
- **clinicaltrialsregister.eu/ctr-search/search** – search using the number **2019-003098-24**

Full clinical trial title: A multi-center, randomized, placebo-controlled patient and investigator-blinded study to explore the efficacy of oral sacubitril/valsartan in adult patients with non-obstructive hypertrophic cardiomyopathy (nHCM)

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

1-888-669-6682 (US) | +41-61-324 1111 (EU)

www.novartis.com/clinicaltrials