NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the effects of LCZ696 on erectile function compared to enalapril in men with heart failure and erectile dysfunction

Protocol number: CLCZ696BDE03

Thank You!

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.

Thank you for taking part in this trial for the drug combination of sacubitril/valsartan, also known as LCZ696. You helped researchers learn more about how LCZ696 works in people with heart failure and erectile dysfunction.

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

? If trial participants have any questions about the trial results, please talk to the doctor or staff at the trial site.

How long was this trial?

This trial started in April 2019 and ended in May 2021. The entire duration, from enrolling the first participant to the last participant completing the trial was around 2 years. Each participant was in this trial for an average of 3 months.

The sponsor ended this trial early because of the low enrollment of participants. When the trial ended, researchers created a report of the trial results. This summary is based on that report.

Why was the research needed?

Heart failure is a condition in which the heart has difficulty pumping blood to meet the body's requirements. Participants can have symptoms of feeling tired, shortness of breath, dizziness, and swollen ankles and legs. Men with heart failure can also have erectile dysfunction. In heart failure, 7 in 10 men have experienced erectile dysfunction. Erectile dysfunction is a condition in which a man fails to get or maintain an erection sufficient for sexual intercourse.

In this trial, researchers wanted to learn about the effects of LCZ696 compared to enalapril in improving erectile function in men with heart failure and erectile dysfunction. The main question the researchers wanted to answer in this trial was whether the participants' erectile function improved after 12 weeks of treatment with LCZ696 compared to enalapril.

Treatments given in this trial were LCZ696 and enalapril.

LCZ696 is a drug that has been approved for the treatment of heart failure. It is a combination of 2 substances, sacubitril and valsartan.

Enalapril is an active comparator drug which has also been approved for the treatment of heart failure. A comparator drug is an already approved and licensed drug available in the market for a disease condition. In case of more similar drugs for a disease condition, one of them will be chosen to be used as a comparator drug for a clinical trial.

Who was in this trial?

Men could take part in this trial if they:

- were between 18 to 75 years of age,
- were diagnosed with chronic heart failure and decreased pumping ability of the heart,
- had mild to moderate erectile dysfunction,
- were sexually active for at least 6 months before the start of the trial, and

- were not taking any medicines for erectile dysfunction for at least 4 weeks before the start of the trial.

A total of 27 men from Germany participated in this trial.

The participants were randomly assigned to treatment groups using a computer system. This process is called randomization. It means that each participant could be assigned to any group, and it helps to make sure the groups are distributed fairly. Thirteen participants received LCZ696 plus matching placebo, and the other 14 participants received enalapril plus matching placebo.

This was a double-blind trial, where none of the participants, trial doctors, or trial staff knew what treatment the participants were receiving.

The average age of the participants was 65 years. Participants' age ranged from 40 to 75 years.

What treatments did the participants take?

Trial drugs		Comparator	
	**LCZ696,** 200 mg twice a day by mouth.		**Enalapril,** 10 mg twice a day by mouth.
	**Placebo,** which looked like the trial drug, but did not have any medicine in it. Using a placebo helps researchers better understand the effect of a trial drug by making sure that the changes were not happening by chance.		**Placebo,** which looked like the trial drug, but did not have any medicine in it. Using a placebo helps researchers better understand the effect of a trial drug by making sure that the changes were not happening by chance.

What happened during this trial?

Before treatment

- Trial doctors confirmed that participants could take part in this trial.

Up to
2 weeks

During treatment

- Participants received **LCZ696 + matching placebo** or **Enalapril + matching placebo**.
- Each participant had an equal chance of ending up in either group.
- Treatment dose was increased every 2 weeks till the target dose was reached.
- The target dose was then maintained till the end of the trial.

Starting dose		**Next higher dose**		**Target dose**
50 mg LCZ696 + placebo or 2.5 mg Enalapril + placebo	→	100 mg LCZ696 + placebo or 5 mg Enalapril + placebo	→	200 mg LCZ696 + placebo or 10 mg Enalapril + placebo

Up to
12 weeks

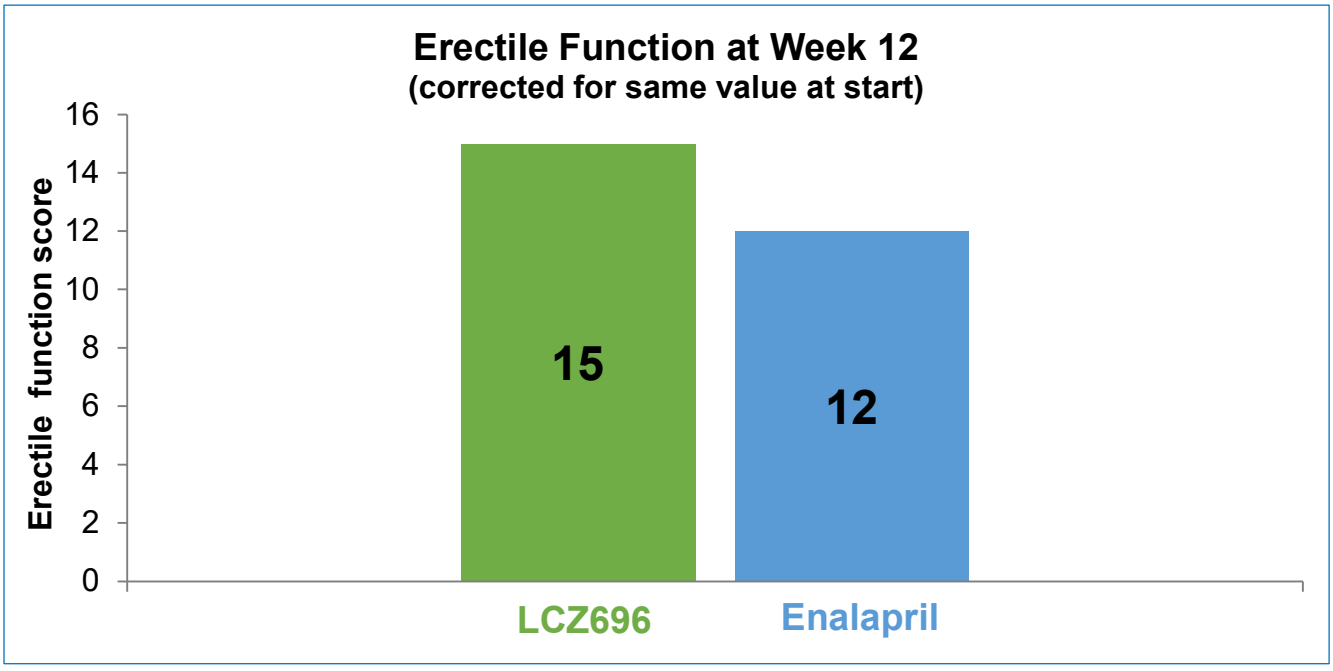
What were the main results of this trial?

?

Did the participants' erectile function improve after 12 weeks of treatment with LCZ696 compared to enalapril?

To answer this question, researchers asked participants to score their erectile function using a questionnaire called International Index for Erectile Function (IIEF-15). IIEF-15 consists of 15 questions assessing different aspects associated with erectile dysfunction like erectile function, sexual desire, or satisfaction. For each question, a score of 0-5 can be achieved with 5 being the best and 0 being the worst score. For erectile function score, 6 questions are important, which were evaluated and summed.

The erectile function score improved slightly at Week 12 in the LCZ696 group compared to the enalapril group. However, the number of participants was too low to confirm the changes in the score.



What medical problems did the participants have during the trial?

Medical problems that happen in clinical trials are called “adverse events”.

A lot of research is needed to know whether a drug causes an adverse event. During a trial, all adverse events are recorded, whether or not they are thought to be caused by the trial drug. When new drugs are being studied, researchers keep track of all adverse events participants have.

This section is a summary of the adverse events that happened during this trial. The websites listed at the end of this summary may have more information about all the adverse events that happened in this trial.

An adverse event is an unwanted sign, symptom, or disease that participants have during a trial.

An adverse event is considered “serious” when it is life-threatening, causes lasting problems, or the participant needs hospital care.

These problems may or may not be caused by the trial drug.

How many participants had adverse events?

No participant died during the trial.

Number of Participants (%) With Adverse Events

	LCZ696 (Out of **13** participants)	**Enalapril** (Out of **14** participants)
At least 1 adverse event	8 (62%)	6 (43%)
At least 1 serious adverse event	1 (8%)	1 (7%)
Stopped drug due to adverse event	1 (8%)	1 (7%)

What serious adverse events did the participants have?

One participant (8%) in the LCZ696 group had serious adverse events of **sudden and sharp increase in blood pressure** (hypertensive crisis).

One participant (7%) in the enalapril group had serious adverse events of **heart attack** (cardiac arrest).

What other adverse events did the participants have?

The non-serious adverse events that happened in this trial are presented below.

Number of Participants (%) With Most Common Non-Serious Adverse Events

Groups (Number of participants)	LCZ696 (Out of **13** participants)	Enalapril (Out of **14** participants)
Accumulation of fluids in the body (Fluid retention)	0	1 (7%)
Bruise (Haematoma)	1 (8%)	0
Decreased level of potassium in the blood (Blood potassium decreased)	1 (8%)	0
Infection of airways of the lungs (Bronchitis)	1 (8%)	0
Joint pain (Arthralgia)	1 (8%)	0
Low blood pressure (Hypotension)	1 (8%)	1 (7%)
Pain and swelling in joints (Gout)	0	1 (7%)
Shortness of breath (Dyspnoea)	0	1 (7%)
Swelling in lower legs and hands (Oedema peripheral)	0	1 (7%)
Tooth decay (Dental caries)	1 (8%)	0
Tooth pain (Toothache)	1 (8%)	0

How many participants stopped trial drug due to adverse events?

One participant (8%) in the LCZ696 group stopped the trial drug due to adverse events of **sudden and sharp increase in blood pressure** (hypertensive crisis) and **irregular heartbeats** (ventricular tachycardia).

One participant (7%) in the enalapril group stopped the trial drug due to adverse events of **heart attack** (cardiac arrest) and **accumulation of fluid in the body** (fluid retention).

How was this trial useful?

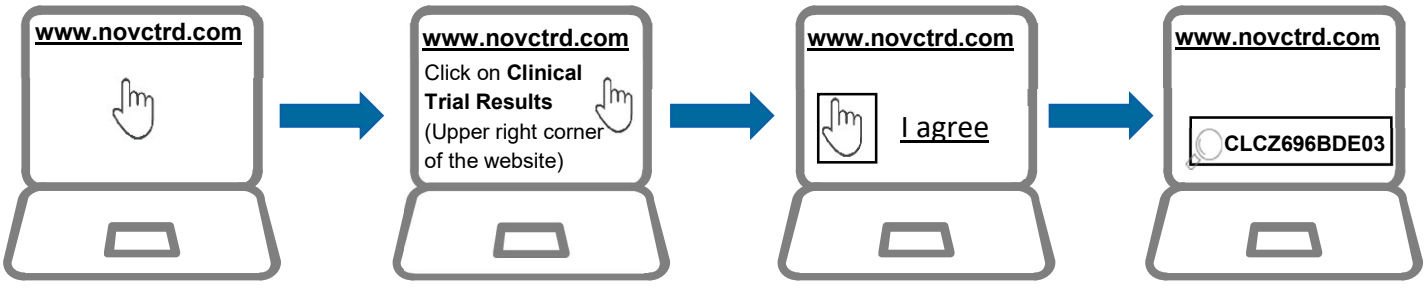
The trial helped researchers to learn about the effects and safety of LCZ696 compared to enalapril on erectile function in men with heart failure and erectile dysfunction. However, due to the low number of participants, the improvement in erectile dysfunction was not meaningful in the LCZ696 group compared to the enalapril group. The researchers found no new safety concerns for LCZ696 during this trial.

The trial ended early because of the low enrollment of the participants.

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).

Please follow the below steps:



You can find more information about this trial on the following websites:

- www.clinicaltrials.gov Use the NCT identifier NCT03917459 in the search field.
- https://www.clinicaltrialsregister.eu/ctr-search/search Use the EudraCT identifier 2018-000220-33 in the search field.

Full clinical trial title: A randomized, double-blind, active-controlled study to assess the effect of sacubitril/valsartan compared with enalapril to improve erectile function in patients with heart failure with reduced ejection fraction (HFrEF) and erectile dysfunction (ED)

Thank you

Thank you for taking part in this trial. As a clinical trial participant, you belong to a large community of people around the world. You helped researchers answer important health questions and test new medical treatments.

NOVARTIS

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.novartisclinicaltrials.com