Clinical Trial Results

NOVARTIS

Research sponsor: Novartis Pharmaceuticals Corporation

Drug studied: sacubitril/valsartan, also called LCZ696

Protocol number: CLCZ696BUS13 (PROVE-HF)

Short title: A study to learn how LCZ696 affects the heart structure and function in patients with heart failure with reduced left ventricle ejection fraction

Thank You!

Thank you for taking part in this trial to learn if the trial drug sacubitril/valsartan, also called LCZ696, works to improve the following two measures of heart failure in the body:

- The heart's structure and function
- A lab value, a biomarker called NT-proBNP, which indicates if heart failure is improving

You and all of the other participants helped researchers learn more about the trial drug LCZ696 and how to treat patients with heart failure.

This summary of the trial results was prepared to provide you with information on what researchers learned from the trial and to acknowledge the important role you played. If you have questions about the results, please speak with the doctor or staff at your trial site.

How long was this trial?

This two-year trial started in October 2016 and ended in October 2018. Each participant was in the trial for one year.

At the end of the trial, the sponsor looked at the data collected and put together the overall results. This is a summary of those results.

Why was the research needed?

Trial drug LCZ696 treats patients with a type of chronic heart failure where the heart is weak and cannot pump enough blood. Researchers are always looking for better ways to treat heart failure and its symptoms. This trial was done to evaluate how well the trial drug works on two specific measures of heart failure: a biomarker in the blood called NT-proBNP, and the structure of the heart.

Trial Drug

The trial drug given in this trial was sacubitril/valsartan, also called LCZ696. This was taken as a tablet by mouth.

Trial Purpose

In this trial, the unanswered questions researchers wanted to try to answer were:

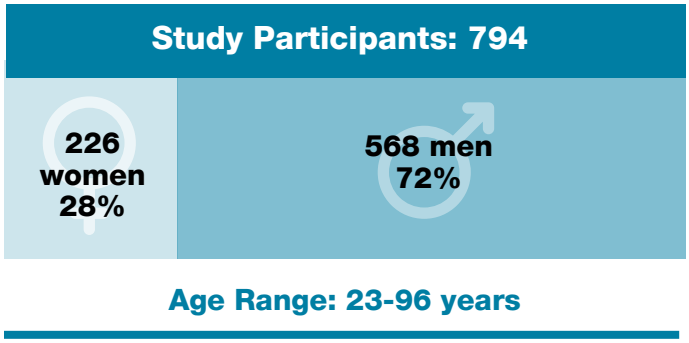
- How does the trial drug LCZ696 affect a blood biomarker called NT-proBNP that helps measure heart failure?
- How does the trial drug LCZ696 affect overall the physical structure of the heart and how it works (its function)?

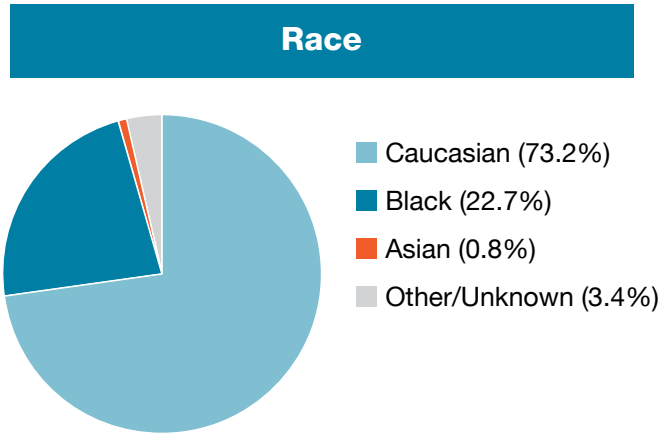
Who was in this trial?

Men and women, like you, with heart failure and those qualified to receive sacubitril/valsartan (trial drug LCZ696) as part of their standard treatment were asked to participate. Participants ranged in age from 23 to 96. The trial included 794 participants at 78 trial sites in the United States. Out of 794 participants, 226 (28%) were women and 568 (72%) were men.

A majority of patients (581, 73.2%) identified their race as Caucasian, 180 (22.7%) identified as Black and 6 patients (.8%) were Asian. In addition, 669 participants (84.3%) identified their ethnicity as non-Hispanic/Latino and 117 patients (14.7%) identified their ethnicity as Hispanic/Latino.

The figures below show who participated in the trial.





Non-Hispanic/Latino	(84.3%)
Hispanic/Latino	(14.7%)
Unknown	(1%)

What kind of trial was this?

This trial was an open-label trial where all 794 patients were given the same study drug. “Open-label” means the researchers and the participants both knew what the participants were taking.

What happened during this trial?

Before the treatment started, the trial doctors did tests to make sure participants could take part in the trial. This was the **screening** part of the trial. The patients:

- Had a physical examination
- Had laboratory tests
- Had a urine pregnancy test if female
- Reviewed their medications with the trial team
- Reviewed the informed consent with the trial team to ensure understanding of the trial

After screening, if the participant was eligible, the participant was given the study drug sacubitril/valsartan (LCZ696).

An echocardiogram (heart ultrasound) was done at the beginning of the study before starting study drug, after 6 months of study drug, and at the end of the study to see the change in the heart's physical structure and function. Blood work was done throughout the year at every visit to the trial site to measure biomarker NT-proBNP.

Each participant was in this trial for about 52 weeks and visited the trial site 10 times over the course of the year.

What were the results of the trial?

This is a summary of the overall results of this trial. The individual results of each participant might be different and are not in this summary. Other trials may provide new information or different results. Medical decisions should not be made based on the results of a single trial without first talking to a doctor. Always talk to a doctor before making any change to medications or treatment plans.

The trial answered the following questions:

Question	Answer
How does the trial drug change levels of biomarker NT-proBNP in the blood, a marker that is higher when heart failure is getting worse?	Participants showed a decrease in biomarker NT-proBNP, which means heart failure was improved. Within 2 weeks of starting LCZ696, NT-proBNP decreased significantly and persisted throughout the trial.
How does the trial drug affect overall heart structure and function?	Participants treated with LCZ696 showed improvement in the physical structure of the heart as well as how the heart works (function). Function was assessed through measuring ejection fraction. Ejection fraction is the measure of the heart's ability to pump blood.

What medical problems did the participants have?

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 death, causes lasting problems or requires hospital care. This trial showed that LCZ696 is generally safe and well tolerated. Adverse events reported in this trial were the same as what is normally seen in this patient population.

What were the most common adverse events in this trial?

The following table demonstrates the adverse events reported by at least 5% of the participants. Adverse events are medical problems or "side effects" that happen in clinical trials.

A participant could have experienced more than one adverse event, therefore the total adverse events in the chart below includes participants who may have experienced more than one adverse event. Adverse events reported in this trial were the same as what has been reported in this patient population. The most common adverse event participants reported during the trial was low blood pressure (hypotension). Although dizziness was reported at a lower percent than hypotension, it can be associated with hypotension as hypotension can cause dizziness.

Adverse Events	
Adverse Event Reported in at least 5% of Study Participants	**Total Participants 794**
Total Number of Affected Participants*	**443 (55.8%)**
Low blood pressure (hypotension)	17.4%
Dizziness	16.8%
Increased blood potassium (hyperkalaemia)	10.3%
Congestive heart failure (heart failure that prompts you to go to ER or seek urgent treatment)	8.9%
Upper respiratory tract infection (viral infection that affects the nose, throat, and airways)	7.4%
Tiredness (fatigue)	7.2%
Trouble breathing (dyspnea)	6.5%
Diarrhea	6.0%
Swelling of legs/arms (oedema peripheral)	5.8%
Sudden problems with kidney(s) (Acute kidney injury)	5.5%
Fall	5.4%
Impaired kidney function (blood creatinine increased)	5.2%

*Participants could have experienced more that than one adverse event.

How many participants had serious adverse events?

There were serious adverse events that occurred during the trial. These were not necessarily related to the trial drug. The most commonly reported adverse events that resulted in death were:

- Congestive heart failure
- Ventricular fibrillation (a life-threatening heart rhythm)
- Respiratory failure
- Sepsis (a reaction to infection that often requires hospitalization).

There were 30 participants who died during the trial or in the 30 days after treatment. There were very few serious adverse events suspected to be related to the trial drug.

How was this trial useful?

The trial helped researchers learn how trial drug LCZ696 changes biomarker NT-proBNP levels, the physical structure of the heart and how the heart works in patients with heart failure. The safety findings in this trial were similar to what researchers have seen in other trials of LCZ696.

Please remember, this summary only shows the results of a single clinical trial. Other clinical trials may have different results. Researchers and health authorities look at the results of many clinical trials to understand which drugs work, and if they are safe. It takes many people in multiple clinical trials around the world to advance medical science and healthcare. If you have any questions about these trial results, please talk to the doctor or staff at your trial site.

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). Once on the site, click “Clinical trial results” at the bottom of the page. After agreeing to enter the Novartis website, type CLCZ696BUS13 into the search by trial number box and click “Search”.

You can find more results of this trial on the following website: www.clinicaltrials.gov. Use the NCT identifier NCT02887183 in the search field.

Full Clinical Trial Title: A 52 week, open label evaluation of the effects of sacubitril/valsartan (LCZ696) therapy on biomarkers, myocardial remodeling and patient reported outcomes in heart failure with reduced left ventricular ejection fraction (PROVE-HF)

Thank you!

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

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