Clinical Trial Results

NOVARTIS

Research Sponsor:	Novartis
Location of Headquarters:	Basel, Switzerland
Telephone Number:	1-888-669-6682 (US only) +41613241111 (outside of US)
Drug Studied:	LCZ696
National Clinical Trial #:	NCT01870739
Eudra Clinical Trial #:	2012-005720-15
Protocol #:	CLCZ696A2224
Trial Date:	October 2013 to June 2015
Short Trial Title:	A trial to test if LCZ696 reduces stiffness in the aorta in people with high blood pressure
Full Scientific Summary:	www.novctrd.com

Thank you!

As a clinical trial participant, you belong to a large community of participants around the world. You helped researchers answer important health questions and discover new medical treatments.

Thank you for taking part in the clinical trial for the drug LCZ696. You helped researchers learn more about how LCZ696 works in people with high blood pressure and stiffness in the aorta, the largest artery in the body. This trial started in October 2013 and ended in June 2015.

Novartis, the sponsor of this trial, thanks you for your help and thinks it is important for you to know the results of your trial. An independent non-profit organization called CISCRP prepared this summary of the trial results for you with the help of a medical writing organization. We hope it helps you understand your important role in medical research.

If you have questions about the results, please speak with the doctor, research nurse, or other team member at your trial site.

CISCRP
THE CENTER FOR INFORMATION & STUDY ON CLINICAL RESEARCH PARTICIPATION

What's happened since the trial ended?

You were in this trial for about 1 year, but the trial took a little over 1½ years to complete. The trial included 115 participants from 4 sites: Germany (2), Switzerland (1), and the United Kingdom (1). When the trial ended in June 2015, 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 were looking for a better way to treat people with high blood pressure. Some people with high blood pressure experience stiffness in the walls of the main artery of the body called the aorta. The stiffer the blood vessel walls are, the harder the heart has to work to pump blood into the arteries.

Researchers in this trial wanted to see if a drug called LCZ696 could help lower blood pressure and reduce stiffening in the aorta. Researchers compared LCZ696 with a drug called olmesartan. Olmesartan is approved to treat high blood pressure.

The main questions researchers asked in the trial were:

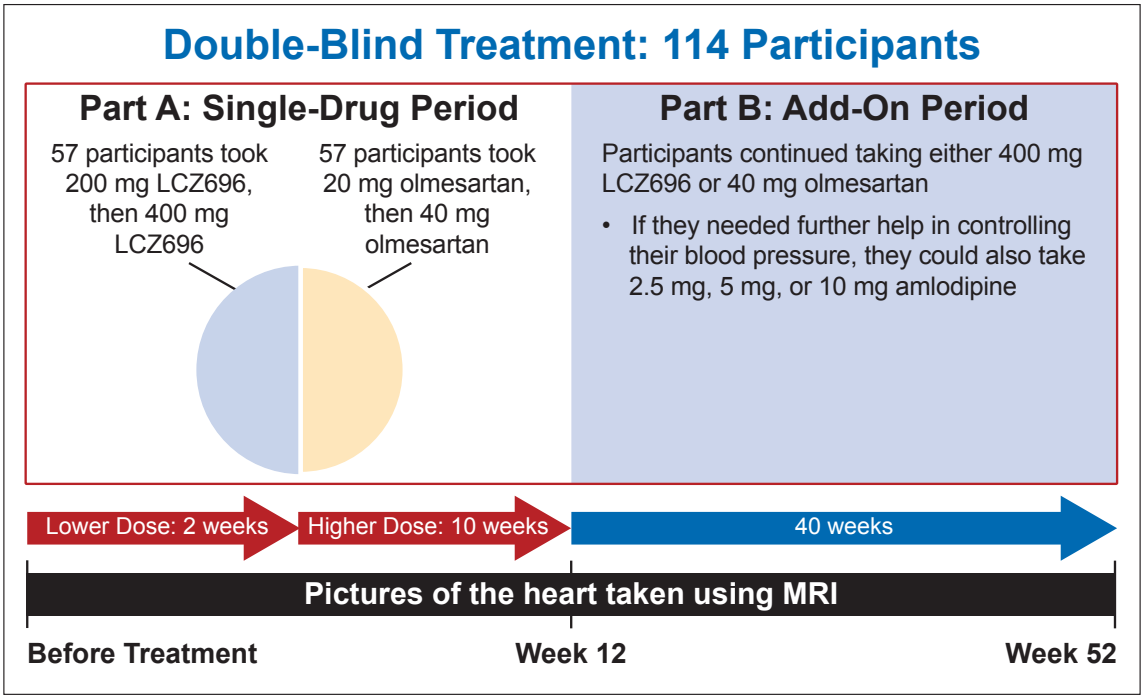
- Did LCZ696 reduce stiffening of blood vessels more than olmesartan after 52 weeks of treatment?
- Did LCZ696 help in other ways?
- How safe was LCZ696 and what were the medical problems?

To answer these questions, researchers asked for the help of men and women like you. The participants in this trial were 23 to 80 years old and had high blood pressure. Their blood pressure results also indicated stiffness in the walls of their aorta.

What kind of trial was this?

This trial was "double-blind". This means none of the participants, trial doctors, or staff knew what treatment each participant received. Some trials are done this way because knowing what treatment each participant is getting can affect the results of the trial. That way, no one was biased when trying to understand the results. When the trial ended, the research sponsor found out which treatment participants took so they could create a report of the trial results.

The figure below shows how the trial was done.



What happened during the trial?

Trial doctors did a full check-up of all participants to make sure they were good candidates for the trial. They also took blood samples and used magnetic resonance imaging (MRI) scans to take detailed pictures of the heart and aorta.

Because some participants were already taking medications to treat high blood pressure, everyone initially took a placebo for 4 weeks during a “washout period”. A placebo looks like the study drug but has no medicine in it. Washout periods help get rid of the effect that previous medications may have had.

Part A lasted 12 weeks.

- For the first 2 weeks, participants were randomly assigned, like flipping a coin, to take either 200 milligrams (mg) LCZ696 or 20 mg olmesartan. Researchers were interested in seeing if participants could handle these doses without having medical problems.
- Then, for the next 10 weeks, participants took higher doses of the study drugs, either 400 mg LCZ696 or 40 mg olmesartan.

Part B lasted 40 weeks.

- During this longer part of the trial, participants continued taking either 400 mg LCZ696 or 40 mg olmesartan. However, if these drugs were not controlling their blood pressure well enough, participants could also begin taking 2.5 mg, 5 mg, or 10 mg of amlodipine. This is a drug also approved to lower high blood pressure.
- Throughout the trial, trial doctors took blood samples and checked participants' weight, temperature, blood pressure, and heart rate. Trial doctors also checked participants' arteries using MRI scans.

What were the results of the trial?

This is a summary of the overall findings and may not be the same for all participants. Researchers look at results of many studies to decide which drugs work best and are safer for patients. The results presented here are for a single trial. Other trials may provide new information or different results. You should not make therapeutic changes to your treatment based on the results of a single trial without first talking to your doctor.

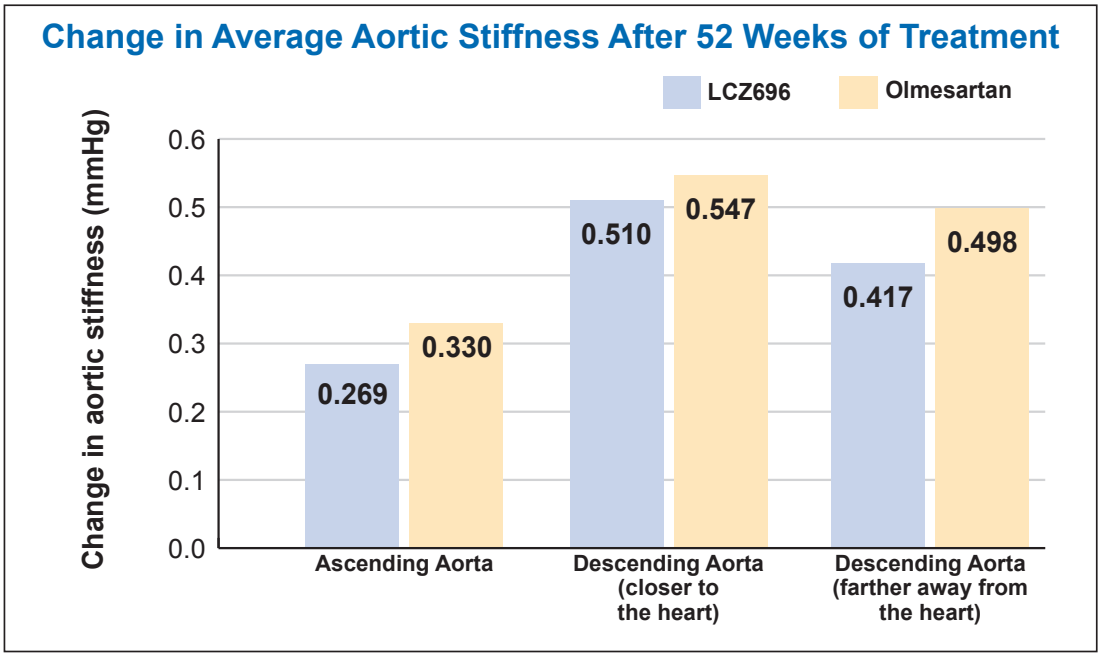
Did LCZ696 reduce stiffening of blood vessels more than olmesartan after 52 weeks of treatment?

No. LCZ696 did reduce stiffening, but the difference between LCZ696 and olmesartan was too small for researchers to know if LCZ696 reduced stiffening of blood vessels more than olmesartan after 52 weeks of treatment.

Using MRI scans, trial doctors looked at the stiffness of different parts of the aorta with each heartbeat. Trial doctors examined the ascending aorta, or the part of the aorta that receives blood from the heart. They also examined two parts of the descending aorta, or the part of the aorta that sends blood downward towards the lower part of the body.

Researchers measured the change in the average stiffness in the aorta. They found that all 3 areas of the aorta showed less stiffness after 52 weeks of treatment with either LCZ696 or olmesartan.

The graph below shows the change in average stiffness of the aorta after 52 weeks of treatment with LCZ696 or olmesartan. Researchers measured the change in the average stiffness in mmHg. The higher the number is, the less stiff the arteries are, which makes it easier for the heart to pump blood to the body.



Did LCZ696 help in other ways?

Researchers found that LCZ696 did not help more than olmesartan after 52 weeks of treatment in the following ways:

- Aortic strain (stretching/straining of the aortic wall).
- Aortic pulse wave velocity (speed of the pressure as it moves down the aorta).
- Central blood pressure (overall pressure in the aorta). However, the gap between the high and low blood pressure in the central aorta (beside the heart) was lower with olmesartan than with LCZ696.
- Augmentation pressure and index (how a pulse flowing through the aorta affects its pressure).

What medical problems did participants have?

A lot of research is needed to know whether a drug causes a medical problem. So when new drugs are being studied, researchers keep track of all medical problems that participants have. These medical problems are called “adverse events”. An adverse event is any sign or symptom that may or may not be caused by the study drug.

How many participants had adverse events during the trial?

A total of 89 participants (78.1%) had adverse events in the trial. Two participants (1.8%) left the study because of adverse events.

The table below shows how many participants had adverse events in the study.

Adverse Events in this Study

	Part A				Part B	
	LCZ696 200 mg (out of 57 participants)	Olmesartan 20 mg (out of 57 participants)	LCZ696 400 mg (out of 57 participants)	Olmesartan 40 mg (out of 56 participants)	LCZ696 400 mg ± Amlodipine (out of 54 participants)	Olmesartan 40 mg ± Amlodipine (out of 53 participants)
How many participants had adverse events?	13 (22.8%)	16 (28.1%)	21 (36.8%)	28 (50.0%)	31 (57.4%)	38 (71.7%)
How many participants had serious adverse events?	0 (0.0%)	2 (3.5%)	0 (0.0%)	2 (3.6%)	6 (11.1%)	5 (9.4%)

Did any participants have serious adverse events?

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

No participants died during this study.

A total of 15 participants (13.2%) experienced 22 serious adverse events. Inflammation of the stomach (gastroenteritis) and torn tendon were the only serious medical problems that occurred in 2 participants (1.8%) each. Study doctors did not think that any of the serious adverse events were related to the study medications.

For more information about serious adverse events in this study, please refer to the full scientific summary of the results available on the Novartis Clinical Trial Results website (www.novctrd.com).

What were the most common adverse events?

The table below shows the most common adverse events that occurred to at least 5% of all participants during the study.

Most Common Adverse Events in This Study

	Part A				Part B	
	LCZ696 200 mg (out of 57 participants)	Olmesartan 20 mg (out of 57 participants)	LCZ696 400 mg (out of 57 participants)	Olmesartan 40 mg (out of 56 participants)	LCZ696 400 mg ± Amlodipine (out of 54 participants)	Olmesartan 40 mg ± Amlodipine (out of 53 participants)
Common cold	0 (0.0%)	2 (3.5%)	4 (7.0%)	5 (8.9%)	11 (20.4%)	10 (18.9%)
Headache	0 (0.0%)	2 (3.5%)	2 (3.5%)	6 (10.7%)	2 (3.7%)	2 (3.8%)
Back pain	1 (1.8%)	0 (0.0%)	0 (0.0%)	5 (8.9%)	1 (1.9%)	5 (9.4%)
Dizziness	1 (1.8%)	2 (3.5%)	4 (7.0%)	1 (1.8%)	1 (1.9%)	0 (0.0%)
Increased levels of the liver protein albumin in the urine	2 (3.5%)	2 (3.5%)	2 (3.5%)	1 (1.8%)	1 (1.9%)	1 (1.9%)
Tiredness	1 (1.8%)	1 (1.8%)	1 (1.8%)	2 (3.6%)	1 (1.9%)	1 (1.9%)
Blood in the urine	1 (1.8%)	0 (0.0%)	0 (0.0%)	2 (3.6%)	3 (5.6%)	1 (1.9%)
Swelling of the lower limbs	0 (0.0%)	0 (0.0%)	1 (1.8%)	0 (0.0%)	1 (1.9%)	4 (7.5%)

Where can I learn more about this study?

Researchers look at the results of many studies to decide which drugs work best and are safer for patients. It takes volunteers in many trials all around the world to advance medical science.

A scientific summary of the results is 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. Then, click **"I accept"**. After agreeing to enter the Novartis website, type **CLCZ696A2224** into the keyword search box and click **"Search"**. If you have questions about the results, please speak with the doctor or staff at your trial site.

Official trial title: A randomized, double-blind, active-controlled, parallel group, 52-week study to evaluate the effects of LCZ696 compared to olmesartan on regional aortic stiffness in subjects with essential hypertension

Thank you

It is said that the greatest gift is one which is given anonymously, giving when you do not know whether you will get direct personal benefit.

This is the gift that you have given by taking part in a clinical trial. It is a brave and selfless act, one that advances medical knowledge and benefits public health.

Thank you for the gift of your participation in clinical research.

CISCRP
THE CENTER FOR INFORMATION & STUDY ON CLINICAL RESEARCH PARTICIPATION

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. CISCRP is not involved in recruiting participants for clinical trials, nor is it involved in conducting clinical trials.

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