Clinical Trial Results

NOVARTIS

Research Sponsor: Novartis
Drug Studied: LHW090
Protocol #: CLHW090X2202

Thank you!

Thank you for taking part in the clinical trial for the drug LHW090. You and all of the participants helped researchers learn more about how LHW090 works in people with resistant hypertension. Resistant hypertension is high blood pressure that stays high even after taking 3 or more medicines to lower it.

Novartis sponsored this trial and believes it is important to share the results of the trial with you and the public. An independent non-profit organization called CISCRP prepared this summary of the trial results for you. We hope it helps you understand your important role in medical research.

If you participated in the trial and have questions about the results, please speak with the doctor or staff at your trial site.

What has happened since the trial ended?

You were in the trial for about 11 weeks. But, the entire trial took almost 2 years to finish. This is because the participants started and stopped at different times. The trial started in November 2015 and ended in August 2017.

The trial included 64 participants in Denmark, France, Germany, the Netherlands, Switzerland, and the United States. When the trial ended, the sponsor reviewed the data collected and created a report of the results. This is a summary of that report.

Why was the research needed?

Researchers are looking for a better way to treat people who have high blood pressure. Before a drug can be approved for patients to take, researchers do clinical trials to find out how safe it is and how well it works. This information is important to know before other trials can be done that help find out if LHW090 improves the health of people with high blood pressure.

High blood pressure can damage the heart, kidneys, eyes, and blood vessels. Some people's blood pressure remains high, even after treatment with 3 or more medicines. This is called resistant hypertension. People with resistant hypertension are at an increased risk of a heart attack, stroke, and kidney failure.

In this trial, the researchers wanted to find out how LHW090 works in a small number of participants with resistant hypertension. The researchers wanted to learn if LHW090 could lower the participants' blood pressure.

The body breaks down LHW090 into a substance called LHV527. LHV527 helps the body increase levels of a hormone made by the heart called atrial natriuretic peptide, also called ANP. Increasing ANP levels in the blood may lower blood pressure by causing blood vessels to relax. It also may help the kidneys get rid of more salt and water.

In this trial, the researchers compared LHW090 with a placebo. A placebo looks like the trial drug but does not have any medicine in it. Using a placebo helps researchers better understand the actual effects of a trial treatment.

The main questions the researchers wanted to answer in this trial were:

- Did LHW090 lower the participants' blood pressure?
- How much LHW090 and LHV527 got into the participants' blood?
- What medical problems did the participants have?

What kind of trial was this?

To answer the questions in this trial, the researchers asked for the help of men and women with resistant hypertension. The participants in this trial were 40 to 84 years old.

The first part of the trial was "single-blind". This means the trial staff and sponsor staff knew what the participants were taking, but the participants did not. During the first part of the trial, all of the participants took the placebo. This part was done to make sure the participants would take the trial drug as directed.

The second part of the trial was "site and subject double-blind". This means none of the participants or trial staff knew what treatment each participant took. But, the sponsor staff did know what each participant took. Some trials are done this way because if the participants and trial staff know what treatment the participants are taking, it can affect the results of the trial. Doing a trial this way helps make sure the results are looked at fairly. During the second part of this trial, the participants took either LHW090 or the placebo.

For both parts of the trial, the sponsor staff did not know the identity of any of the participants.

A computer program was used to randomly choose the treatment each participant took in the second part of the trial. Researchers do this so that comparing the results of each treatment is done as fairly as possible.

What happened during the trial?

Before the trial treatment started, the trial doctors did tests to make sure the participants could take part in the trial. The trial doctors checked the heart health of the participants using an electrocardiogram, also called an ECG. The participants gave blood and urine samples. They also had their blood pressure and heart rate checked.

During the first part of the trial, the participants took a placebo once a day for 2 weeks. During this time, the participants continued to take their blood pressure medicines that they were already taking. After 2 weeks, the participants who took the placebo as directed at least 80.0% of the time were allowed to enter the second part of the trial. The first part of the trial was designed this way so that the researchers could make sure the participants would take their treatments regularly in the second part of the trial.

During the second part of the trial, the participants visited the trial site at least 12 times. They took their treatment once a day for 4 weeks. Doses were measured in milligrams, also called mg. The participants took either 100 mg or 200 mg capsules of LHW090 or the placebo by mouth. During the second part of the trial, the participants also continued to take their blood pressure medicines.

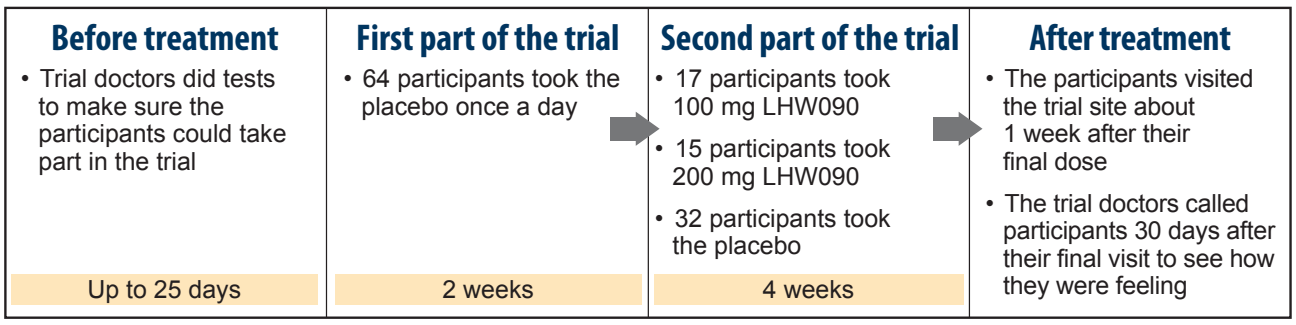
Throughout the trial, the trial doctors:

- checked the participants' blood pressure and heart rate at each visit
- asked the participants how they were feeling and about any other medicines they were taking at each visit
- asked the participants about their mental health at some visits
- took blood and urine samples and checked the participants' heart health at some visits
- fitted the participants with a device that monitored their blood pressure for 24 hours at some visits

About 1 week after the last trial treatment, the participants had their final visit at the trial site. The trial doctors checked the physical health, mental health, and heart health of the participants. The trial doctors also asked how the participants were feeling and what medicines they were taking. The participants gave more blood and urine samples.

The trial doctors called participants 30 days after their final visit to see how they were feeling.

The chart below shows how the trial was done.



What were the results of the trial?

This is a summary of the overall results from the 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. Always talk to a doctor before making any treatment changes.

Did LHW090 lower the participants' blood pressure?

Yes. After 4 weeks of treatment, LHW090 lowered the participants' blood pressure more than the placebo did.

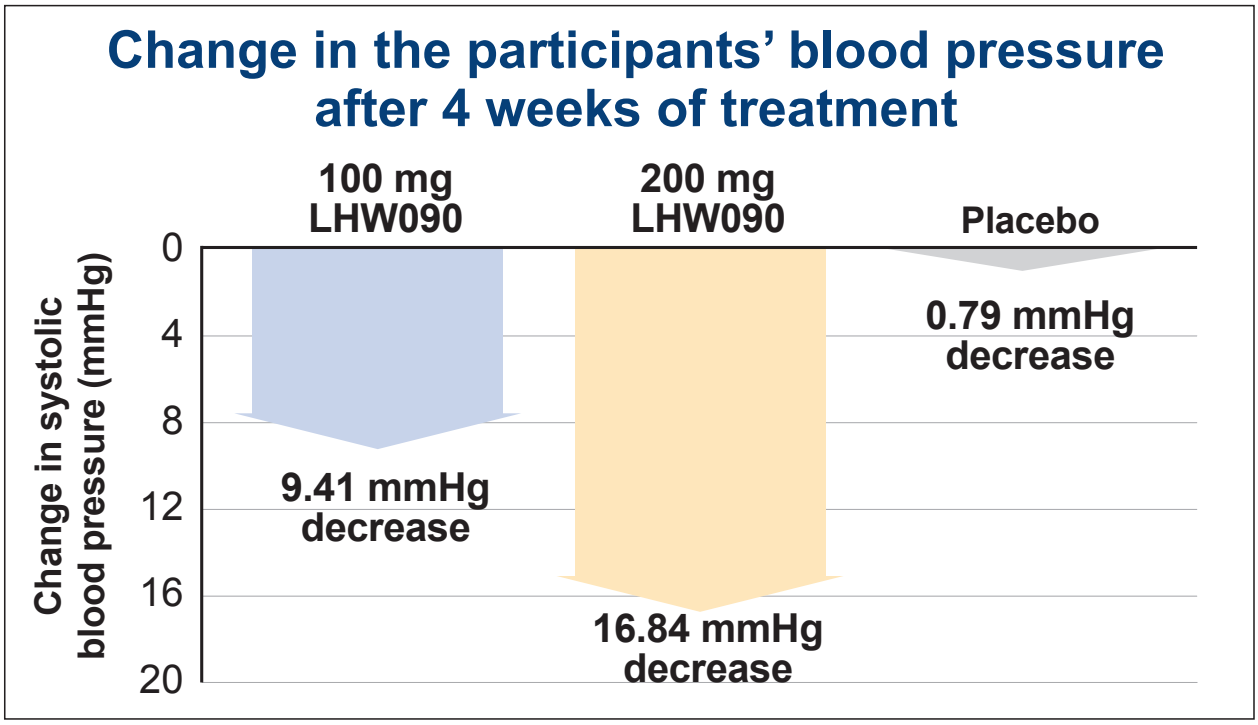
In a blood pressure reading, the top number is known as the "systolic blood pressure". It measures the pressure in the blood vessels when the heart beats. The bottom number in a blood pressure reading measures the pressure in the blood vessels when the heart rests between beats. This is known as the "diastolic blood pressure".

In the trial, the researchers were interested in the systolic blood pressure changes the participants had during the daytime. Blood pressure is measured in millimeters of mercury, also called mmHg. A decrease in mmHg meant lower blood pressure in the participants.

The researchers found that on average, after 4 weeks of treatment:

- The systolic blood pressure of the participants who took 100 mg of LHW090 decreased by 9.41 mmHg.
- The systolic blood pressure of the participants who took 200 mg of LHW090 decreased by 16.84 mmHg.
- The systolic blood pressure of the participants who took the placebo decreased by 0.79 mmHg.

The chart below shows the change in the participants' systolic blood pressure during the daytime.



How much LHW090 and LHV527 got into the participants' blood?

The researchers wanted to know how much LHW090 and LHV527 got into the participants' blood.

The researchers learned that:

- The amount of LHW090 and LHV527 in the blood was higher in the participants who took 200 mg of LHW090 compared to the participants who took 100 mg of LHW090.
- It took 2 to 3 hours for LHW090 to reach its highest amount in the participants' blood.
- It took longer for LHV527 to show up in the participants' blood compared to LHW090. It took 3 to 4 hours for LHV527 to reach its highest amount in the participants' blood.
- LHW090 and LHV527 reached steady levels in the participants' blood by Day 28 of treatment.

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 lasting problems, or the participant needs hospital care. These problems may or may not be caused by the trial drug.

A lot of research is needed to know whether a drug causes a medical problem. During a trial, all medical problems are reported and written down, whether or not they are caused by the trial drug. So, when new drugs are being studied, researchers keep track of all medical problems that participants have during each trial.

Adverse events were recorded for both parts of the trial. But because the participants only took the trial drug in the second part of the trial, this section is a summary only of the adverse events that happened during the second part of the trial.

How many participants had adverse events?

A higher percentage of the participants who took 100 mg of LHW090 had adverse events during the second part of the trial compared to the participants who took 200 mg of LHW090 or the placebo.

Two participants who took 100 mg of LHW090 left the trial because of adverse events.

None of the participants had serious adverse events during the trial. None of the participants died during the trial.

The table below shows how many participants had adverse events during the second part of the trial.

Adverse events during the second part of the trial

	100 mg LHW090 (Out of 17 participants)	200 mg LHW090 (Out of 15 participants)	Placebo (Out of 32 participants)	Total (Out of 64 participants)
How many participants in the trial had adverse events?	70.6% (12)	20.0% (3)	40.6% (13)	43.8% (28)
How many participants in the trial had serious adverse events?	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
How many participants left the trial because of adverse events?	11.8% (2)	0.0% (0)	0.0% (0)	3.1% (2)

What were the most common adverse events?

Swelling of the lower limbs was the most common adverse event during the second part of the trial.

The table below shows the most common adverse events that happened in at least 2 participants out of all the treatment groups during the second part of the trial. There were other adverse events, but these happened in fewer participants.

Adverse events during the second part of the trial

	100 mg LHW090 (Out of 17 participants)	200 mg LHW090 (Out of 15 participants)	Placebo (Out of 32 participants)	Total (Out of 64 participants)
Swelling of the lower limbs	11.8% (2)	0.0% (0)	9.4% (3)	7.8% (5)
Itchy skin	17.6% (3)	0.0% (0)	0.0% (0)	4.7% (3)
Kidney failure	5.9% (1)	6.7% (1)	3.1% (1)	4.7% (3)
Back pain	0.0% (0)	0.0% (0)	6.3% (2)	3.1% (2)
Bruising	5.9% (1)	0.0% (0)	3.1% (1)	3.1% (2)
Fall	5.9% (1)	0.0% (0)	3.1% (1)	3.1% (2)
Infection of the nose, throat, and upper airways caused by a virus	0.0% (0)	0.0% (0)	6.3% (2)	3.1% (2)
Increased weight	5.9% (1)	0.0% (0)	3.1% (1)	3.1% (2)

For more information about the adverse events in the trial, please see the scientific summary that can be found on the websites noted at the end of this summary.

How has this trial helped participants and researchers?

The information described above helped the researchers better understand if LHW090 works in participants with resistant hypertension.

The results of many trials are needed to find out which treatments can be used for patients with resistant hypertension. This summary shows only the main results from this one trial. Other trials may provide new information or different results. It takes volunteers in many trials all around the world to advance medical science.

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 (www.novctrd.com). Once on the site, click **"READ MORE"** under **"Clinical trial results"** at the bottom of the page. After agreeing to enter the Novartis website, type **"CLHW090X2202"** into the keyword search box and click **"Search"**. If you have questions about the results, please speak with the trial doctor or trial staff at your trial site.

You can find more information about this trial on the websites listed below.

- www.clinicaltrials.gov. Once you are on the website, type **"NCT02515331"** into the search box and click **"Search"**.
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home & Search"**, then type **"2015-001890-42"** into the search box and click **"Search"**.

If more clinical trials are planned, they will be listed on the above public websites or www.novartisclinicaltrials.com. Search for **"LHW090"**.

Full trial title: A randomized, sponsor open, site and subject double blind, parallel group, placebo-controlled study to evaluate the safety and efficacy of LHW090 after 4 weeks treatment in patients with resistant hypertension

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 test new medical treatments.

CISCRP

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.

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