Clinical Trial Summary

A clinical trial to learn about the safety of trial drug LHW090 for people with high blood pressure and chronic kidney disease

Thank you!

Novartis, the sponsor of this clinical trial, thanks you and the other participants who helped make this clinical trial possible.

Trial overview

What was the purpose of this trial? Read more on **pg. 2**

Part 1 of this clinical trial was designed to learn about the safety of increasing amounts of the trial drug LHW090 for people with high blood pressure and chronic kidney disease. LHW090 is designed to help control high blood pressure.

Part 2 of this trial focused on the safety of LHW090 for the kidneys because people with high blood pressure often have kidney disease. Both parts were also designed to learn how much and how fast LHW090 got into the blood of participants.

Who was in this trial? Read more on **pg. 2**

Part 1: 11 men and women **Part 2:** 73 men and women

Every participant in this trial had chronic kidney disease and were being treated for high blood pressure.

What treatments did participants take? Read more on **pg. 3**

Participants were assigned to take one of these treatments as pills:

- LHW090
- Placebo – looks like the trial drug, but does not have any trial drug in it

This trial was designed to learn:

- What medical problems participants had
  Keeping track of medical problems helped learn about the safety of LHW090.
- If LHW090 increased the chance of kidney injury
- How much and how fast LHW090 got into the blood

What were the main results of this trial? Read more on **pg. 6**

The clinical trial team found that participants who took LHW090 had a similar number of medical problems compared to participants who took the placebo. The team also concluded that LHW090 did not increase the chance of kidney injury during this trial.

Trial number: CLHW090X2102

What was the purpose of this trial?

Researchers are looking for better ways to treat high blood pressure. The trial drug LHW090 is designed to help the body control high blood pressure. Before a drug can be approved for patients to take, researchers do many clinical trials to find out how safe it is and how it works.

Since many people with high blood pressure also have chronic kidney disease, this trial was designed to also check the safety of LHW090 for the kidneys.

This trial was designed to learn:

- What medical problems participants had
- If LHW090 increased the chance of kidney injury
- How much and how fast LHW090 got into the blood

Who was in this trial?

This trial had 2 parts: 11 participants began Part 1 and 73 participants began Part 2. Participants had the choice to be in one or both parts of this trial. Participants were 40 to 85 years old and 68 years old on average.

Every participant in this trial:

- Had moderately severe chronic kidney disease (stage 3)
- Was taking a medicine called an angiotensin receptor blocker (ARB) that treats high blood pressure

This trial took place in Germany and the United States.

For more information about who could and could not be in this clinical trial, visit novctrd.com. Use clinical trial number CLHW090X2102 to find the scientific summary.

What treatments did participants take?

The clinical trial team used a computer program to randomly assign each participant the treatment they took during this trial.

Part 1

Participants were assigned to take one of these treatments as pills:

- An increasing dose of LHW090:
  - 25 mg for 4 days
  - 50 mg for 4 days
  - 100 mg for 4 days
- Placebo for 12 days

Part 2

Participants were assigned one of these treatments as pills:

- 100 mg dose of LHW090 for 28 days
- 200 mg dose of LHW090 for 28 days
- Placebo for 28 days

A **placebo** looks like the trial drug, but does not have any trial drug in it. A placebo is used to help better show the actual effects of a trial drug. Participants and trial staff did not know what treatment each participant received during the trial.

Some trials are done this way because knowing what treatment people get can influence the results. Not knowing what treatment people get helps make sure the results are looked at fairly.

What happened during this trial?

The trial began in March 2017 and ended in October 2018. All participants in Part 1 completed this trial. 4 participants did not complete Part 2.

How the clinical team designed this trial:

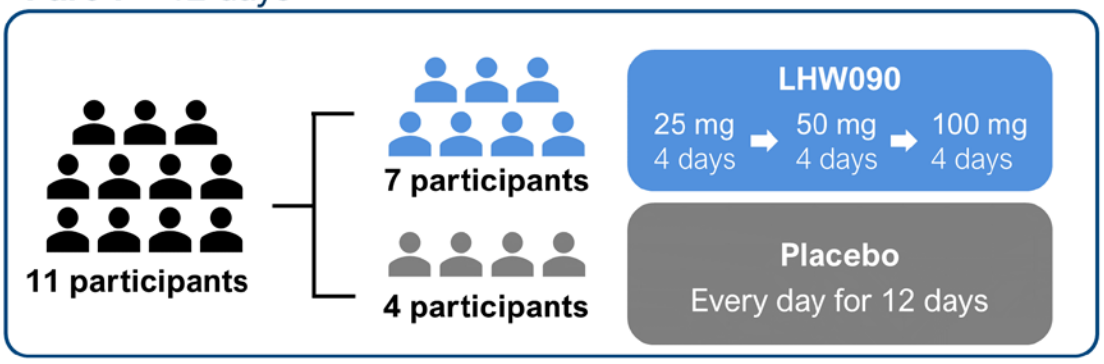
Before treatment

- Trial doctors checked each participant's health to make sure they could be in this clinical trial

During treatment

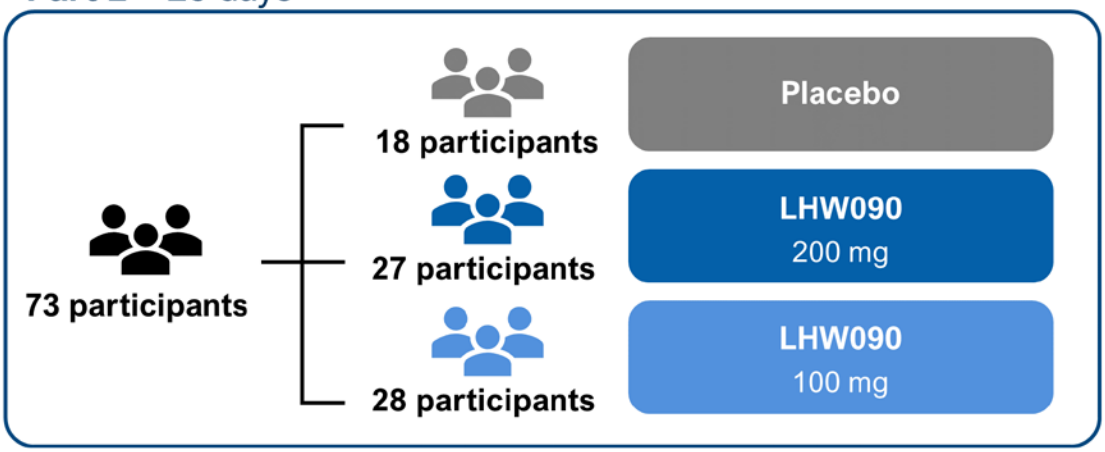
- Trial staff took blood and urine samples and checked each participant's health
- Participants took their assigned treatment as pills

Part 1 – 12 days



The sponsor reviewed the safety results from Part 1 before starting Part 2

Part 2 – 28 days



After treatment

For both Part 1 and Part 2

- Participants had a final visit to check their health about 7 days after their last dose
- Participants were called one month later to check on their health

What were the main results of this trial?

What medical problems happened during the trial?

Medical problems that happen during 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.

Adverse events may or may not be caused by treatments in the trial. Many trials are needed to know if a drug or treatment causes an adverse event. Trial doctors keep track of all adverse events that happen in trials, even if they do not think the adverse events might be related to the trial treatments.

Trial doctors looked for any adverse events when they checked participants’ blood and urine samples and during the visits to the trial site. Participants also reported adverse events. The clinical team compared the number of participants with adverse events who took LHW090 to those who took the placebo.

The clinical trial team found that participants who took LHW090 had a similar number of medical problems compared to participants who took the placebo.

Adverse events during Part 1

Participants who had:	**LHW090** (out of 7 participants)	**Placebo** (out of 4 participants)
Adverse events	14% (1)	50% (2)
Serious adverse events	0% (0)	0% (0)
Left this trial due to adverse events	0% (0)	0% (0)

Adverse events during Part 2

Participants who had:	**LHW090** 100 mg (out of 28 participants)	**LHW090** 200 mg (out of 27 participants)	**Placebo** (out of 18 participants)
Adverse events	46% (13)	59% (16)	50% (9)
Serious adverse events	11% (3)	0% (0)	0% (0)
Left this trial due to adverse events	7% (2)	4% (1)	0% (0)

What serious adverse events happened during this trial?

No serious adverse events were reported during Part 1 of this trial.

3 participants who took the 100 mg dose of LHW090 during Part 2 reported serious adverse events. These were:

- **Angioedema**: Rapid swelling beneath the skin
- **Radius fracture**: A broken wrist
- **Skin laceration**: A torn or jagged wound to the skin

No participants died during this trial.

What types of adverse events did participants report?

Some participants reported adverse events that were not serious. This section reports the most common adverse events participants had during this trial.

Adverse events by type in Part 1

	LHW090 Out of 7 participants	Placebo Out of 4 participants
Unusual dreams	0	25% (1)
Hair loss	0	25% (1)
Diarrhea	14% (1)	0
Dry mouth	0	25% (1)
Discolored skin from bleeding	0	25% (1)
Change in color of feces	0	25% (1)
Headache	0	25% (1)
Bleeding at infusion site	0	25% (1)
Muscle spasms	0	25% (1)
Itchy skin	14% (1)	0

This summary only includes adverse events reported by 4 or more of the participants in Part 2. There were other adverse events, but these happened in fewer participants.

Adverse events by type in Part 2

	LHW090 Out of 55 participants	Placebo Out of 18 participants
Itchy skin	13% (7)	6% (1)
Diarrhea	11% (6)	6% (1)
Low blood pressure	7% (4)	0
Itchy nose	7% (4)	0

Did LHW090 increase the chance of kidney injury?

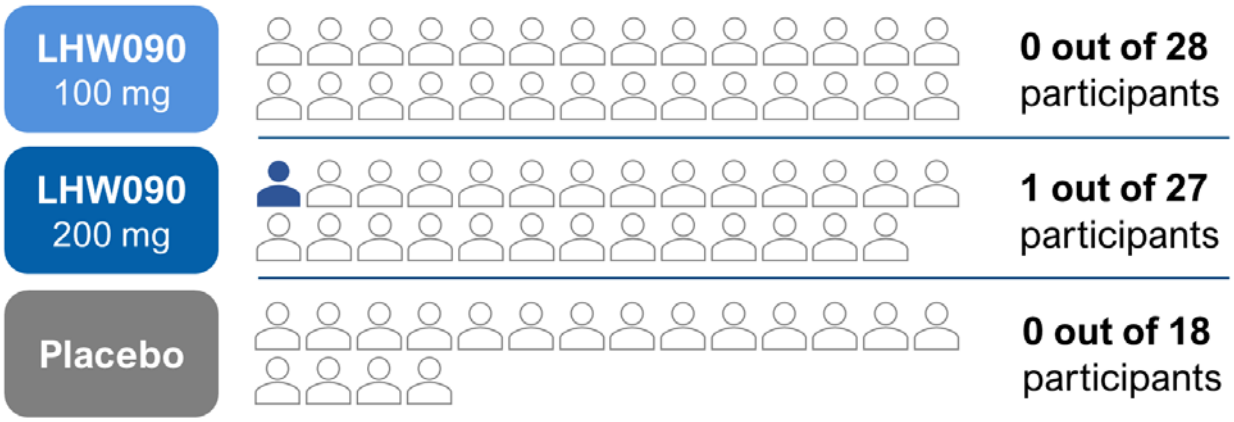
The clinical trial team concluded that LHW090 did not increase the chance of kidney injury in this trial**.**

To find this out, trial doctors measured the level of creatinine in participants' blood throughout Part 2. Creatinine is a waste produced by the body. Healthy kidneys remove creatinine to keep a normal level in the blood.
If creatinine increases, it can be a sign of kidney injury.

When trial doctors measured creatinine, they looked for increases of 0.3 mg/dL or more. 1 participant who took the 200 mg dose of LHW090 had this increased level of creatinine for a short time. Trial doctors closely watched the participant until their creatinine returned to the level it was before treatment. The participant completed treatment with LHW090.

To learn if LHW090 increased the chance of kidney injury, the clinical team looked at how many participants had an increased level of creatinine and which treatment they took. They found no meaningful difference between participants who took LHW090 and participants who took the placebo.

Participants with increased creatinine



What other results were learned?

How much and how fast did LHW090 get into the blood?

The clinical team learned that LHW090 got into participants' blood about 1 to 2.5 hours after they took any dose of LHW090.
The levels of LHW090 in the blood increased with larger doses.

The clinical team measured the amount of LHW090 in participants' blood. They compared the levels of LHW090 found in this trial to levels found in a previous trial in healthy participants. They found the amount of LHW090 was higher in participants with chronic kidney disease.

This information helps the team decide when a dose should be given and what dose is safe and effective.

What was learned from this trial?

This trial helped learn more about the safety of LHW090 for the kidneys. This is important because many people with high blood pressure also have chronic kidney disease.
The clinical trial team concluded that:

- Safety results were similar between participants who took LHW090 and the placebo in this trial
- LHW090 did not increase the chance of kidney injury in this trial
- LHW090 got into participants' blood about 1 to 2.5 hours after they took any dose of LHW090. The levels of LHW090 in the blood increased with larger doses.

The results presented here are for one trial. One trial cannot give a complete picture of the benefits and risks of a trial drug. The results of many trials are needed to find out which treatments can be used for people with chronic kidney disease. This summary shows only the main results from this trial. Other trials may provide new information or different results.

Where can I learn more about this and future clinical trials?

If you were in this trial and have questions about the results, please speak with the doctor or staff where you took part in this trial.

This is a summary of the results for one clinical trial.

You can find detailed results and more information about this clinical trial on the Novartis Clinical Trial Results website:

1. Visit novctrd.com
2. Click on “Clinical trial results and trial summary for patients” at the top right of the page
3. Read and scroll down, then click “I accept” to agree to use the information and the website
4. Select “Search by study number” on the bottom left of the page
5. Type **CLHW090X2102** in the search box and click search

This clinical trial was registered on the following websites:

- ClinicalTrials.gov – https://clinicaltrials.gov/
  To find this trial, type **CLHW090X2102** in the **Other terms** search box
- European Union Clinical Trials Register – https://www.clinicaltrialsregister.eu/ctr-search
  To find this trial, type **CLHW090X2102** in the search box

If more clinical trials are planned, they will appear on the public websites listed above or at www.novartisclinicaltrials.com. When there, search for LHW090.

Full trial title:

A two part randomized, double-blind, parallel-group, placebo-controlled study to evaluate the renal safety, tolerability and pharmacokinetics of LHW090 in patients with moderately impaired renal function on angiotensin receptor blockers

Thank you!

Novartis would like to thank all of the people who participated in this clinical trial. The participants made this clinical trial possible and helped researchers answer important health questions and learn about a possible medical treatment. Many volunteers and many clinical trials are needed to advance medical science.

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