NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the safety of XXB750 in people with heart failure

Thank you!

Thank you to the participants who took part in the clinical trial for heart failure. Every participant helped the researchers learn more about the trial drug **XXB750**.

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. We hope this helps the participants understand their important role in medical research.

Trial information

Trial number: CXXB750A12101

Novartis drug studied: **XXB750**

Sponsor: Novartis

If you were a participant and have any questions about the results, please talk to the doctor or staff at the trial site.

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

What was the main purpose of this trial?

The purpose of this trial was to learn about the safety of different doses of **XXB750** for people with heart failure.

Heart failure happens when the heart cannot pump enough blood to meet the body's needs. The participants in this trial had heart failure with **reduced or mildly reduced ejection fraction**. This means the heart's lower left side does not pump blood well.

XXB750 is a trial drug designed to allow more blood flow through the body and lower blood pressure. Researchers think this could treat certain types of heart failure.

During this trial, participants continued to take their **standard medicines** for heart failure that lower blood pressure. These include:

- Angiotensin-converting enzyme (ACE) inhibitors
- Angiotensin receptor blockers (ARBs)
- Sacubitril and valsartan

The trial's purpose was to answer this main question:

- What medical problems, also called adverse events, happened during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial. Adverse events **may** or **may not** be caused by treatments in the trial.

How long was this trial?

The trial began in May 2022 and ended in January 2024.

Who was in this trial?

27 participants who had heart failure with reduced or mildly reduced ejection fraction were in this trial – 20 men and 7 women. Participants' ages ranged from 50 to 79 years. Their average age was 65 years.

The number of participants by race is shown below.

Race

8	Black or African American
19	White

Participants were split into 2 groups. Participants were in either Group 1 or Group 2 based on the standard medicines for heart failure they were taking:

- **Group 1**: Taking either ACE inhibitors or ARBs as standard medicines for heart failure
- **Group 2**: Taking sacubitril and valsartan as standard medicines for heart failure

The participants could take part in this trial if they:

- Were taking standard medicines for heart failure for at least 4 weeks before joining the trial
- Did not have another type of heart failure
- Were not in the hospital for heart failure in the last 3 months before joining the trial

27 participants from 2 countries received treatment:

- The United States | 22 participants
- The Netherlands | 5 participants

What treatments did the participants receive?

The treatments in this trial were:

2 different doses of **XXB750**:

- **Low dose XXB750** – 120 milligrams (mg)
- **High dose XXB750** – 240 mg

Placebo looks like the trial drug but does not have any trial drug in it. Using a placebo helps researchers better understand the effect of a trial drug.

XXB750 and placebo were given as injections under the skin.

- Group 1 received their treatment 1 time
- Group 2 received their treatment 3 times, each treatment was about 1 month apart

Researchers used a computer to randomly assign participants to their treatment.

The participants and trial staff did not know what treatment the participants were receiving. Some trials are done this way because knowing what treatment the participants receive can affect the results of the trial. Doing a trial this way helps to make sure that the results are looked at with fairness across all treatments.

Participants continued their standard medicines for heart failure during this trial.

What happened during this trial?

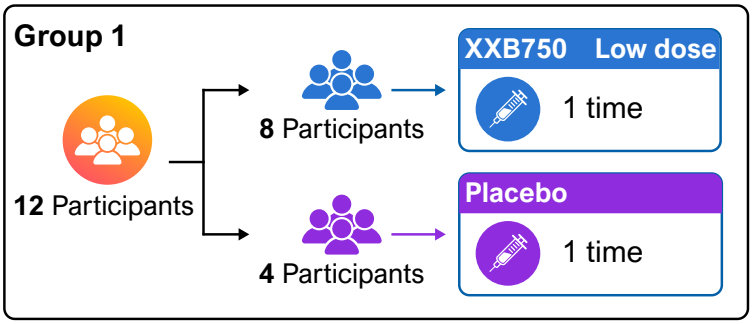
Before treatment — About 1 month

The trial staff checked to make sure the participants could be in this trial.

During treatment — Group 1: About 1 week; Group 2: About 2 months

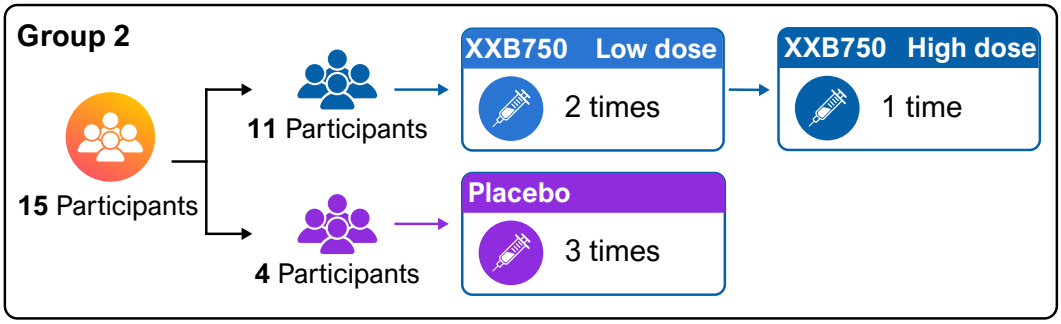
In **Group 1**, participants arrived at the trial site 1 or 2 days before they received treatment and stayed at the site for about 5 days after treatment. Participants received treatment 1 time.

The graphic below shows how many participants in Group 1 were assigned each treatment.



In **Group 2**, participants arrived at the trial site 1 day before they received their first treatment. For the other treatments, participants arrived at the trial site on the day they received them. Participants stayed at the site for about 3 days after each treatment. Each treatment was about 1 month apart.

The graphic below shows how many participants in Group 2 were assigned each treatment.



After treatment — About 3 months

Trial staff checked participants for any medical problems for up to about 3 months after participants' last dose of trial treatment.

Trial staff checked the participants' general health throughout the trial.

What were the main results of this trial?

What medical problems, also called adverse events, happened during this trial?

Trial doctors keep track of all medical problems, also called **adverse events**, that happen in trials. They track adverse events even if they think the adverse events are not related to the trial treatments.

Many trials are needed to know if a drug or treatment causes an adverse event.

This section is a summary of the adverse events that happened from the start of treatment until about 3 months after the last dose of treatment.

An **adverse event** is:

- Any **sign or symptom** that the participants have during a trial
- Considered **serious** when it is life-threatening, causes lasting problems, the participant needs hospital care, or results in death

Adverse events **may** or **may not** be caused by treatments in the trial.

In Group 1, most of the participants (8 of 12) had adverse events during the trial. 2 participants had adverse events that were considered serious. No participants died. No participants left the trial due to an adverse event.

In Group 2, most of the participants (10 of 15) had adverse events during the trial. 3 participants had adverse events that were considered serious. No participants died. 1 participant left the trial due to an adverse event.

The researchers concluded there were no new safety concerns for **XXB750** in this trial.

How many participants had adverse events?

	Group 1		Group 2	
	Low Dose XXB750 8 participants	**Placebo** 4 participants	**Low and High Dose XXB750** 11 participants	**Placebo** 4 participants
Had at least 1 **serious adverse event**	2 of 8 25%	0 of 4 0%	3 of 11 27%	0 of 4 0%
Had at least 1 **other adverse event**	5 of 8 63%	2 of 4 50%	7 of 11 64%	3 of 4 75%
Left the trial due to an adverse event	0 of 8 0%	0 of 4 0%	1 of 11 9%	0 of 4 0%
Died	0 of 8 0%	0 of 4 0%	0 of 11 0%	0 of 4 0%

What serious adverse events did the participants have?

2 participants in Group 1 had serious adverse events. 3 participants in Group 2 had serious adverse events. No participants died.

The table below shows the serious adverse events that happened during the trial.

	Group 1		Group 2	
	Low Dose XXB750 8 participants	**Placebo** 4 participants	**Low and High Dose XXB750** 11 participants	**Placebo** 4 participants
Congestive heart failure Cardiac failure congestive	0 of 8 0%	0 of 4 0%	2 of 11 18%	0 of 4 0%
Sudden heart failure Cardiac failure acute	1 of 8 13%	0 of 4 0%	1 of 11 9%	0 of 4 0%
Blood in the urine Hematuria	1 of 8 13%	0 of 4 0%	0 of 11 0%	0 of 4 0%
Chest pain not caused by the heart Non-cardiac chest pain	1 of 8 13%	0 of 4 0%	0 of 11 0%	0 of 4 0%
Fluid filled sac in the pancreas Pancreatic cyst	0 of 8 0%	0 of 4 0%	1 of 11 9%	0 of 4 0%
Heart Attack Acute myocardial infarction	0 of 8 0%	0 of 4 0%	1 of 11 9%	0 of 4 0%

What other adverse events did the participants have?

7 participants in Group 1 had other adverse events. 10 participants in Group 2 had other adverse events.

The table below shows the other adverse events that happened in **2 or more** participants. Additional adverse events happened in fewer participants.

	Group 1		Group 2	
	Low Dose XXB750 8 participants	**Placebo** 4 participants	**Low and High Dose XXB750** 11 participants	**Placebo** 4 participants
Low blood pressure Hypotension	2 of 8 25%	1 of 4 25%	0 of 11 0%	1 of 4 25%

What were the other results of this trial?

How much and how fast did XXB750 get into the participants' blood?

Overall, the researchers found that:

- The total amount and peak level of **XXB750** went up as the dose went up
- It took about 6 to 14 days for **XXB750** to reach peak level in the blood
- It took about 12 to 14 days for the blood level of **XXB750** to go down by half

To learn this, the trial staff took many blood samples from each participant after they received **XXB750**.

Researchers will use these results to decide how often and how much **XXB750** should be given in future trials.

What was learned from this trial?

Researchers learned about the safety of different doses of **XXB750** for people with heart failure with reduced or mildly reduced ejection fraction.

The researchers concluded there were no new safety concerns for **XXB750** in this trial.

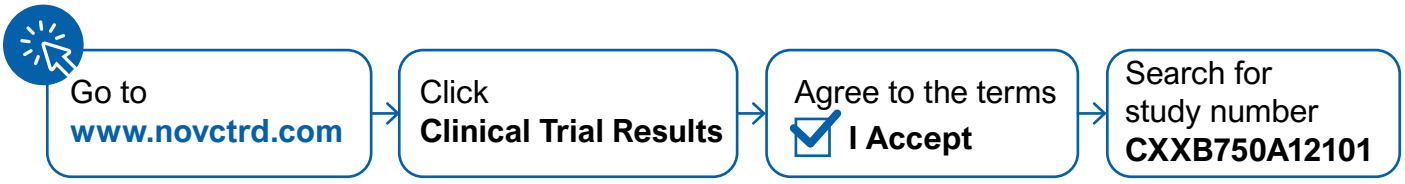
They also learned about how much and how fast **XXB750** got into the participants' blood. See the conclusions above.

When this summary was written, the sponsor had plans for future trials of **XXB750** in people with heart failure.

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**

Follow these steps to find the scientific summary:



For more information about this trial, go to this website:

- **clinicaltrials.gov** – search using the number **NCT05328752**
- **clinicaltrialsregister.eu/ctr-search/search** – search using the number **2021-006683-24**

Other trials of **XXB750** may appear on the public website above. When there, search for **XXB750**.

Full clinical trial title: A randomized, participant- and investigator-blinded, sponsor open-label, placebo-controlled, single and multiple dose study to investigate the safety and tolerability of XXB750 in heart failure participants with reduced or mildly reduced ejection fraction (HFrEF/HFmrEF)

Novartis is a global healthcare company based in Switzerland that provides solutions to address the evolving needs of patients worldwide.

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www.novartis.com/clinicaltrials