NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of different doses of XXB750 in people with resistant hypertension

Thank you!

Thank you to the participants who took part in the clinical trial for **resistant hypertension**. 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: CXXB750B12201

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 effects of different doses of **XXB750** in people with **resistant hypertension**. To find this out, researchers compared the effects of different doses of **XXB750** to a **placebo**.

Resistant hypertension is a condition in which the **blood pressure** remains high despite the use of 3 or more medicines to lower it. High blood pressure can damage the heart, kidneys, eyes, and blood vessels. People with **resistant hypertension** are at an increased risk of heart attack, stroke, and kidney failure.

Blood pressure is the force of moving blood against the walls of the blood vessels. It has two numbers:

- **systolic blood pressure** is the pressure when the heart beats
- **diastolic blood pressure** is the pressure when the heart rests between beats.

XXB750 is a trial drug developed to relax the blood vessels, which helps to lower blood pressure.

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

During this trial, all the participants continued taking their **routine blood pressure-lowering medicines**.

The trial's purpose was to answer these main questions:

- What was the change in participants' systolic blood pressure after 12 weeks of treatment with **XXB750**, as compared to a **placebo**?
- 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 November 2022 and ended in August 2024. Individual participants were in this trial for about 5 months.

Who was in this trial?

191 participants with **resistant hypertension** were enrolled in this trial. 189 participants received treatment in this trial – 131 men and 58 women. 2 participants were mistakenly enrolled in the trial even though they did not meet the study-specific requirements. These participants did not receive any trial treatment. Participants' ages ranged from 35 to 92 years. The average age was 61 years.

The number of participants by race is shown below.

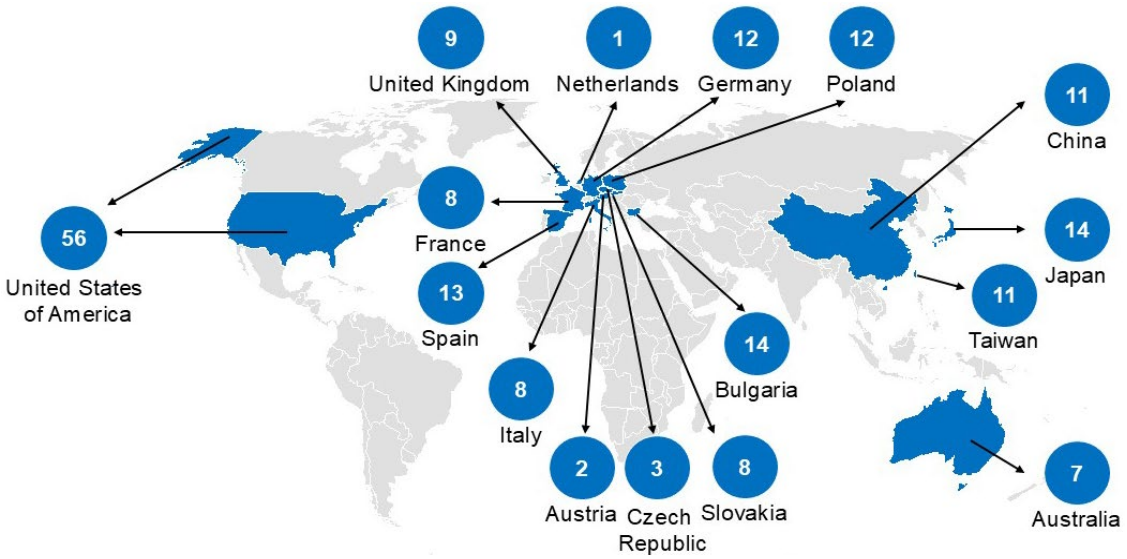
Race

27 Black or African American	37 Asian
116 White	9 Other

The participants could take part in this trial if they:

- were at least 18 years of age
- had high blood pressure despite taking 3 or 4 blood pressure-lowering medicines

189 participants from 16 countries received treatment. The following map shows the number of participants who took part in each country.



What treatments did the participants receive?

The treatments in this trial were:

XXB750, which was given as an injection under the skin once every 4 weeks.

This trial looked at 4 different doses of **XXB750**. This trial looked at 4 different doses of **XXB750**. Each participant was assigned to one dose group only as follows:

- **Dose 1: 30 milligrams (mg)**
- **Dose 2: 60 mg**
- **Dose 3: 120 mg**
- **Dose 4: 120 mg** as the first dose, followed by **240 mg**.

Placebo, which was given as an injection under the skin once every 4 weeks.

All participants received one injection of **placebo**, followed by **XXB750** or **placebo**.
Participants also took their **routine blood pressure-lowering medicines**.

What happened during this trial?

Before treatment — Up to 1 week

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

During treatment — Around 3 months

This trial was done in 2 parts:

- In the **first part** (lasting 2 weeks), all participants received 1 injection of **placebo** and kept taking their usual blood pressure medicines. In this part, the researchers and trial staff knew what treatment the participants were receiving but the participants did not.

  After 2 weeks, participants whose blood pressure remained high were allowed to enter the second part of the trial.

- During the **second part** of the trial, participants were randomly divided into 5 groups using a computer program. Each group received either **XXB750** or **placebo** by injection every 4 weeks (resulting in 3 injections during the second part), while continuing their routine blood pressure-lowering medicines. In this part, the participants, researchers, and trial staff did not know what treatment the participants were receiving.

30 mg of **XXB750**	32 participants
60 mg of **XXB750**	36 participants
120 mg of **XXB750**	37 participants
120 mg of **XXB750** followed by **240 mg** of **XXB750**	42 participants
Placebo	42 participants

Throughout the trial, doctors checked participants' blood pressure and heart rate. They also used a device called a 24-hour ambulatory blood pressure monitor on some visits to track blood pressure over 24 hours.

After treatment — Around 2 months

Trial staff checked participants' general health and for any medical problems for around 2 months after the treatment period.

What were the main results of this trial?

What was the change in participants' systolic blood pressure after 12 weeks of treatment with XXB750, as compared to a placebo?

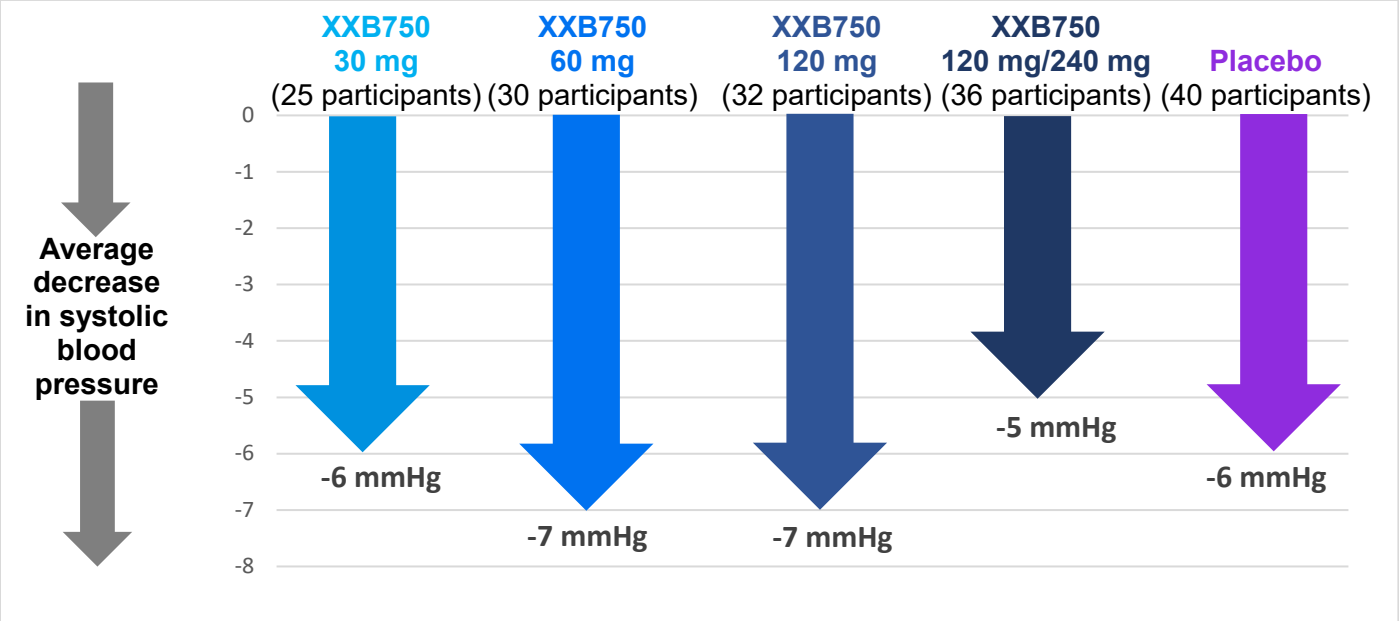
After 12 weeks of treatment, different doses of **XXB750** did not show a greater response than the **placebo**. The change in average systolic blood pressure with **XXB750** was similar to that seen with **placebo** across all doses tested.

To answer this question, researchers checked the systolic blood pressure changes the participants had over 24 hours after 12 weeks of treatment. Systolic blood pressure helps predict the risk of future heart problems or stroke.

Blood pressure is measured in mmHg. A decrease in mmHg meant lower blood pressure in the participants.

Some participants who entered the trial were not able to complete all the trial assessments. Results were available for 163 participants.

Average change in participants' systolic blood pressure after 12 weeks of treatment



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 2 months after the last 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.

95 of 189 participants had adverse events, including serious events.10 participants had adverse events that were considered serious. 4 participants left the trial due to an adverse event. None of the participants died.
The researchers concluded there were no new safety concerns for **XXB750** in this trial.

How many participants had adverse events?

	XXB750 30 mg 32 participants	XXB750 60 mg 36 participants	XXB750 120 mg 37 participants	XXB750 120 mg/240 mg 42 participants	Placebo 42 participants
Had at least 1 **adverse event**	20 of 32 63%	17 of 36 47%	14 of 37 38%	19 of 42 45%	25 of 42 60%
Had at least 1 **serious adverse event**	2 of 32 6%	3 of 36 8%	1 of 37 3%	3 of 42 7%	1 of 42 2%
Left the trial due to an adverse event	2 of 32 6%	0	0	2 of 42 5%	0

What serious adverse events did the participants have?

10 participants had serious adverse events.

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

	XXB750 30 mg 32 participants	XXB750 60 mg 36 participants	XXB750 120 mg 37 participants	XXB750 120 mg/ 240 mg 42 participants	Placebo 42 participants
Bone marrow cancer Plasma cell myeloma	0	1 of 36 3%	0	0	0
Decreased blood supply to the heart Coronary artery disease	0	1 of 36 3%	0	0	0
Device-related infection	0	1 of 36 3%	0	0	0
Dizziness	0	0	0	0	1 of 42 2%
Fainting Syncope	1 of 32 3%	0	0	0	0
Fluid around the lungs due to an infection Infectious pleural effusion	1 of 32 3%	0	0	0	0
Heart failure Cardiac failure	0	1 of 36 3%	0	0	0
Lung infection Pneumonia	1 of 32 3%	0	0	3 of 42 7%	0
Reduced quantity of fluids in the body Dehydration	0	0	1 of 37 3%	0	0

	XXB750 30 mg 32 participants	XXB750 60 mg 36 participants	XXB750 120 mg 37 participants	XXB750 120 mg/ 240 mg 42 participants	Placebo 42 participants
Low blood potassium levels Hypokalemia	0	0	1 of 37 3%	0	0
Muscle damage due to intense exercise Exertional rhabdomyolysis	0	0	1 of 37 3%	0	0
Sudden serious kidney problem Acute kidney injury	1 of 32 3%	0	0	0	0
Sudden bone infection Osteomyelitis acute	0	1 of 36 3%	0	0	0

What other (not including serious) adverse events did the participants have?

The table below shows the most common other adverse events that happened during this trial.

	XXB750 30 mg 32 participants	XXB750 60 mg 36 participants	XXB750 120 mg 37 participants	XXB750 120 mg 240 mg 42 participants	Placebo 42 participants
Blood creatine phosphokinase increased	0	0	0	0	3 of 42 7%
Cough	1 of 32 3%	0	3 of 37 8%	0	1 of 42 2%
COVID-19	1 of 32 3%	0	0	3 of 42 7%	4 of 42 10%
Diarrhea	0	0	0	0	3 of 42 7%
Dizziness	3 of 32 9%	2 of 36 6%	1 of 37 3%	2 of 42 5%	2 of 42 5%
Low blood potassium levels Hypokalemia	0	2 of 36 6%	3 of 37 8%	0	1 of 42 2%
Swelling in arms and legs Edema peripheral	0	3 of 36 8%	2 of 37 5%	1 of 42 2%	0
Urine infection Urinary tract infection	1 of 32 3%	0	4 of 37 11%	1 of 42 2%	4 of 42 10%

What was learned from this trial?

Researchers learned about the effects of different doses of **XXB750** in people with **resistant hypertension.**

The researchers concluded that, after 12 weeks of treatment, changes in average systolic blood pressure with **XXB750** were similar, compared to the **placebo**, regardless of the dose.

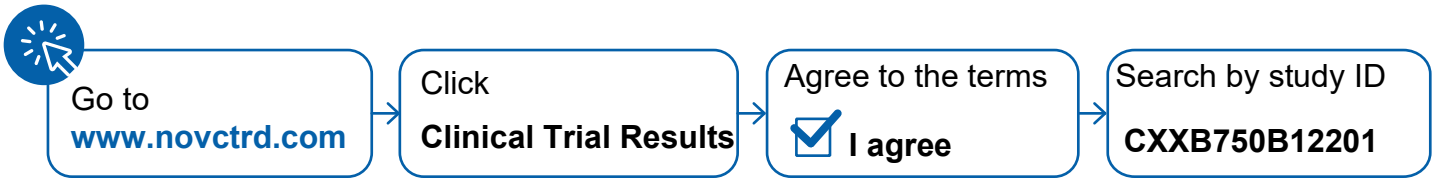
Researchers did not find any new safety concerns with the use of **XXB750** in combination with routine blood pressure-lowering medicines in this trial.

When this summary was written, the sponsor had no plans for future trials of **XXB750** in people with resistant hypertension.

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 any of these websites:

- clinicaltrials.gov – search using the number **NCT05562934**
- clinicaltrialsregister.eu/ - search using the number **2021-005738-41**

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

Full clinical trial title: A multi-center, randomized, double-blind, parallel-group 20-week dose-finding study to evaluate efficacy, safety, and tolerability of XXB750 in patients with resistant hypertension

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