NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects and safety of DFV890 and MAS825 in people with a type of heart disease

Thank you!

Thank you to the participants who took part in the clinical trial for **coronary heart disease with clonal hematopoiesis of indeterminate potential (CHIP)**. Every participant helped to learn more about the trial drugs **DFV890** and **MAS825**.

Novartis sponsored this trial. We believe 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: CADPT15A12201

Novartis drugs studied: **DFV890** and **MAS825**

Sponsor: Novartis

If you were a participant and have any questions about the results, please talk to your 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 more about the effects and safety of **DFV890** and **MAS825** for people with coronary heart disease. Participants in this trial also had clonal hematopoiesis of indeterminate potential, also called CHIP.



Coronary heart disease is a condition where the blood vessels to the heart become narrow or blocked. In coronary heart disease, fatty substances called plaques build up inside the blood vessels, which narrow them and block blood flow. This means less blood and oxygen get to the heart, which can prevent it from pumping as much blood as it should.

Symptoms of coronary heart disease may include:

- Chest pain
- Trouble breathing
- Feeling weak or tired



Participants in this trial also had **clonal hematopoiesis of indeterminate potential**, also called **CHIP**. CHIP refers to changes, or mutations, in the cells that become blood cells. These cells are called stem cells. The changes happen as a person gets older. The changed stem cells often grow and copy themselves more quickly than the other stem cells. The blood cells continue to work, but CHIP causes inflammation and raises a person's chance of getting other health conditions, including coronary heart disease.

People with coronary heart disease and CHIP may have a higher chance of having a heart attack or stroke.



DFV890 is a trial drug created to lower inflammation by lowering the levels of certain proteins that cause inflammation.



MAS825 is a trial drug created to lower inflammation by blocking the activity of certain proteins that cause inflammation.

What is inflammation?

Inflammation is one of the ways the immune system protects the body from disease and infection. Inflammation happens when the immune system brings many cells and proteins to an area of the body. However, too much inflammation can be harmful.

The **immune system** is made up of many cells and proteins that help the body fight disease and infection.

Researchers think lowering inflammation may lower the chance of a heart attack or stroke in people with coronary heart disease and CHIP.

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

- Did DFV890 or MAS825 change signs of inflammation in the blood?
- What medical problems, also called adverse events, happened during this trial?
  - **Adverse events** reported are any sign or symptom that participants had during this trial. Adverse events **may** or **may not** be caused by treatments in this trial.

How long was this trial?

The trial began in February 2024 and ended in November 2024. The participants started the trial on different dates.

At the end of this trial, Novartis created a report of the trial results. This summary is based on that report.

Who was in this trial?

31 participants with coronary heart disease and CHIP received treatment in this trial – 24 males and 7 females. Participants' ages ranged from 59 to 80 years. Their average age was 70 years.

The table below shows the number of participants by race.

Race	
2	Black or African American
29	White

The participants could take part in this trial if they:

- Had a heart attack more than 1 month before joining
- Had no changes in their dose of statins in the last month, if they were taking statins

The participants took part in:

- Canada | 8 participants
- Germany | 21 participants
- United States | 2 participants

What treatments did the participants receive?

The treatments in this trial were:

DFV890, taken by mouth as tablets once a day. This trial looked at 4 doses of DFV890:

- 10 milligrams (mg)
- 25 mg
- 50 mg
- 100 mg

MAS825 – Received as an injection under the skin one time at the start of treatment.

Placebo, which looks like the trial drug but does not have any drug in it. Researchers use a placebo to better understand the effect of a trial drug. To make sure participants did not know which treatment they were receiving, this trial had 2 types of **placebo**:

- One looked like **DFV890** and was taken by mouth as tablets once a day
- The other looked like **MAS825** and was received as an injection under the skin one time at the start of treatment

Participants could continue taking certain medicines for heart disease during the trial, such as statins.

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

The participants, researchers, 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.

What happened during this trial?

Before treatment

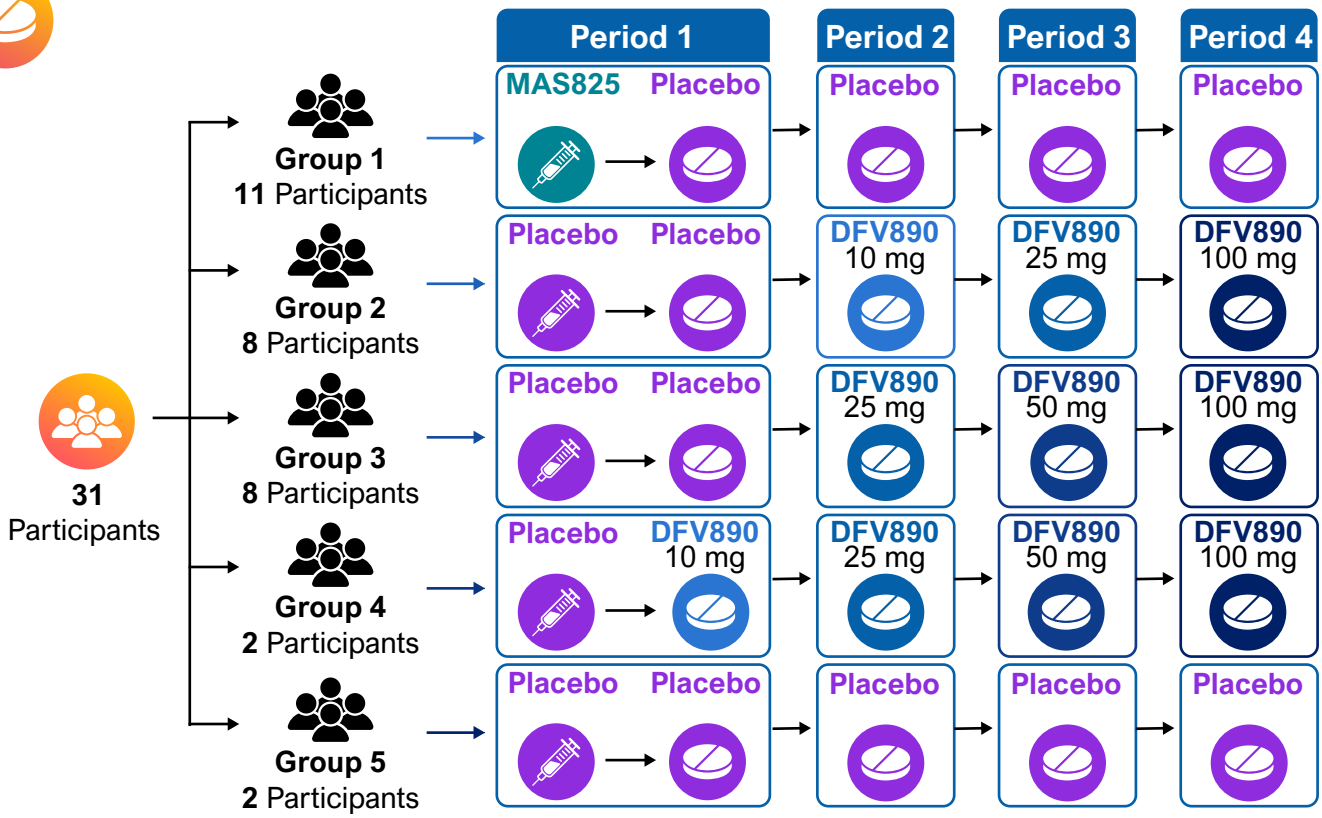
About 1 month

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

During treatment

About 3 months

31 participants received treatment during 4 treatment periods. Each treatment period lasted 3 weeks. They were assigned to 1 of 5 groups.
The graphic below shows which treatment the groups received during each period.



After treatment

About 1 month

Trial staff checked participants' general health and for any medical problems for up to about 1 month 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?

Did DFV890 or MAS825 change signs of inflammation in the blood?

Signs of inflammation went down 3 weeks after participants started receiving **DFV890** or **MAS825** compared to **placebo**.

To learn this, researchers looked at 2 signs of inflammation:

- **Interleukin-6**, or **IL-6** was measured for both **DFV890** and **MAS825**
- **Interleukin-18**, or **IL-18** was measured for **DFV890** only

Researchers measured the level of IL-6 and IL-18 in each participant's blood before treatment and after each 3-week treatment period. Then, researchers measured the average change in:

- **IL-6** after participants received **DFV890** or **MAS825** compared to **placebo**
- **IL-18** after participants received **DFV890** compared to **placebo**

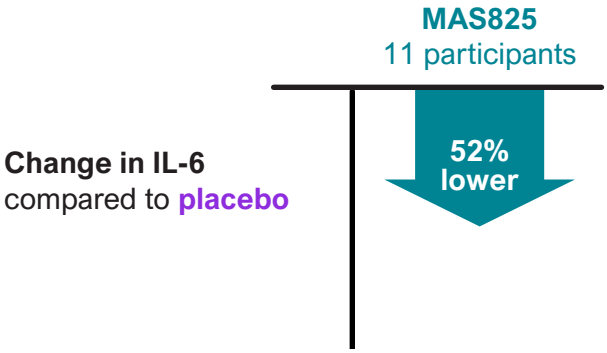
What are IL-6 and IL-18?

IL-6 and **IL-18** are proteins in the blood. The amount of the proteins goes up where there is inflammation in the body. High levels of these proteins may play a role in heart disease.

Did MAS825 change the level of IL-6 compared to placebo?

The level of IL-6 went down 3 weeks after participants received **MAS825** compared to **placebo**.

Change in IL-6 after receiving MAS825 compared to placebo



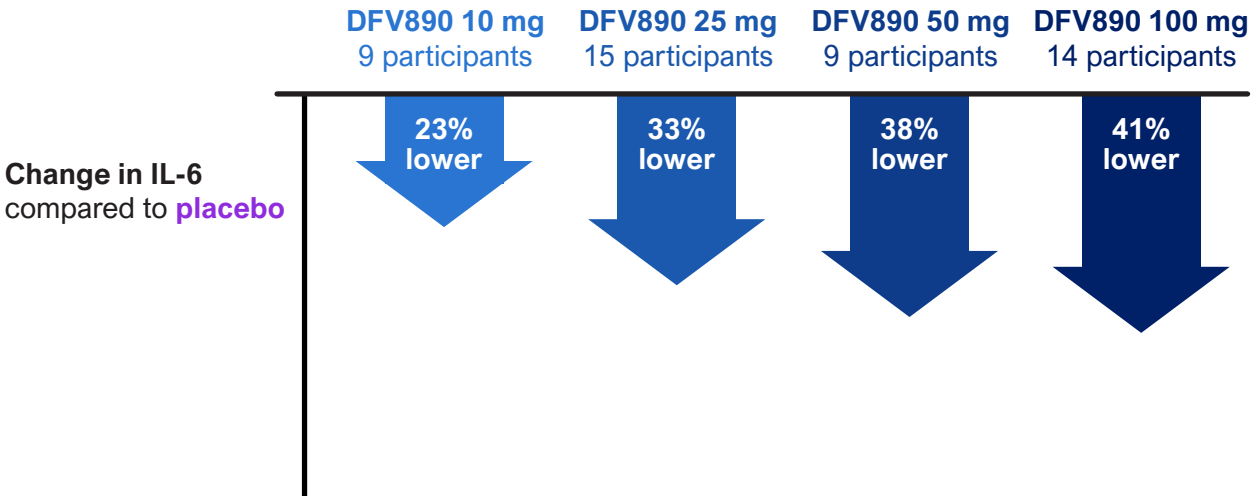
Did DFV890 change the level of IL-6 and IL-18 compared to placebo?

The levels of IL-6 and IL-18 went down 3 weeks after participants started taking **DFV890** compared to **placebo**:

- The level of IL-6 went down more after participant took higher doses of **DFV890**
- The level of IL-18 went down about the same across all doses of **DFV890**

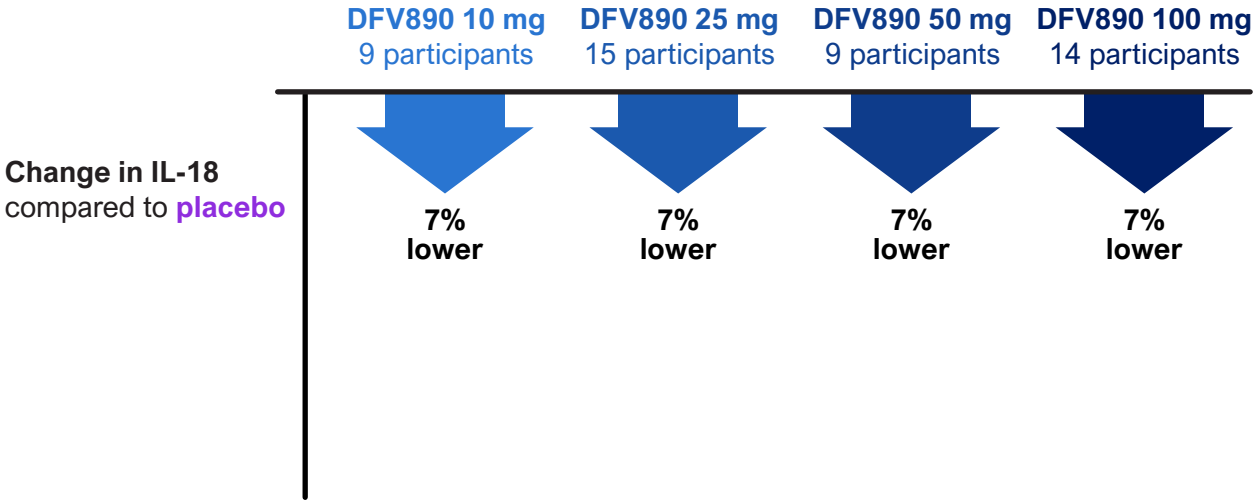
Change in IL-6 after taking DFV890 compared to placebo

The graphic below only includes participants who had data available.



Change in IL-18 after taking DFV890 compared to placebo

The graphic below only includes participants who had data available.



What were the other results of this trial?

How much DFV890 was in the blood at the end of each treatment period?

The average level of **DFV890** in the blood at the end of each treatment period was higher when participants took higher doses of **DFV890**.

To learn this, the trial staff took blood samples from participants at the end of each treatment period. They measured the amount of **DFV890** in the blood samples.

Researchers can use these results to decide how often and how much **DFV890** should be given in future trials.

How much MAS825 was in the blood over time?

The average level of **MAS825** measured in the blood was highest 3 weeks after participants received it. The level of **MAS825** went down over time.

To learn this, the trial staff took blood samples from participants many times during the trial. They measured the amount of **MAS825** in the blood samples.

Researchers can use these results to decide how often and how much **MAS825** should be given in future trials.

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 do this even if they think the adverse events are not related to the trial treatments.

Researchers need to do many trials to decide if a drug or treatment causes an adverse event.

This section is a summary of the adverse events that happened from the day participants started trial treatment until about 1 month after 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, requires hospital care, or results in death

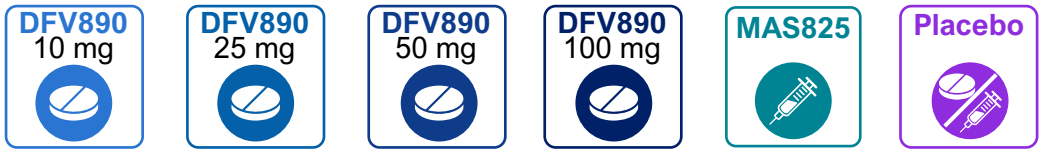
Treatments in the trial **may** or **may not** cause adverse events.

More than half of the participants (20 out of 31) had at least 1 adverse event.

- No participants had serious adverse events
- No participants died

The researchers concluded there were no new safety concerns for **DFV890** or **MAS825** in this trial.

The graphic below shows a summary of how many participants received each treatment.



What serious adverse events did the participants have?

None of the participants had serious adverse events.

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

20 participants had other adverse events.

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

	10 mg DFV890 10 participants	25 mg DFV890 16 participants	50 mg DFV890 9 participants	100 mg DFV890 16 participants	MAS825 11 participants	Placebo 18 participants	100 mg DFV890 Follow-up 16 participants	MAS825 Follow-up 11 participants	Placebo Follow-up 2 participants
Common cold Nasopharyngitis	0 of 10 0%	0 of 16 0%	0 of 9 0%	0 of 16 0%	2 of 11 18%	2 of 18 11%	0 of 16 0%	0 of 11 0%	0 of 2 0%
Feeling weak and tired Fatigue	0 of 10 0%	1 of 16 6%	0 of 9 0%	0 of 16 0%	1 of 11 9%	1 of 18 6%	0 of 16 0%	0 of 11 0%	0 of 2 0%
Frequent, loose, or watery stool Diarrhea	0 of 10 0%	1 of 16 6%	0 of 9 0%	0 of 16 0%	1 of 11 9%	1 of 18 6%	0 of 16 0%	0 of 11 0%	0 of 2 0%
Joint pain Arthralgia	0 of 10 0%	1 of 16 6%	0 of 9 0%	0 of 16 0%	0 of 11 0%	2 of 18 11%	0 of 16 0%	0 of 11 0%	0 of 2 0%
Cough	0 of 10 0%	0 of 16 0%	0 of 9 0%	1 of 16 6%	0 of 11 0%	1 of 18 6%	0 of 16 0%	0 of 11 0%	0 of 2 0%
Headache	0 of 10 0%	0 of 16 0%	0 of 9 0%	0 of 16 0%	2 of 11 18%	0 of 18 0%	0 of 16 0%	0 of 11 0%	0 of 2 0%
Sudden feeling of warmth in the face, neck, and chest Hot flush	0 of 10 0%	1 of 16 6%	0 of 9 0%	1 of 16 6%	0 of 11 0%	0 of 18 0%	0 of 16 0%	0 of 11 0%	0 of 2 0%
Bruise Contusion	0 of 10 0%	0 of 16 0%	0 of 9 0%	0 of 16 0%	1 of 11 9%	0 of 18 0%	1 of 16 6%	0 of 11 0%	0 of 2 0%

What was learned from this trial?

Researchers learned more about the effects and safety of **DFV890** and **MAS825** in people with coronary heart disease and CHIP.

The researchers concluded that:

- Signs of inflammation went down 3 weeks after participants started receiving **DFV890** or **MAS825** compared to **placebo**
- The average level of **DFV890** in the blood at the end of each treatment period was higher when participants took higher doses of **DFV890**
- The level of **MAS825** measured in the blood was highest 3 weeks after participants received it

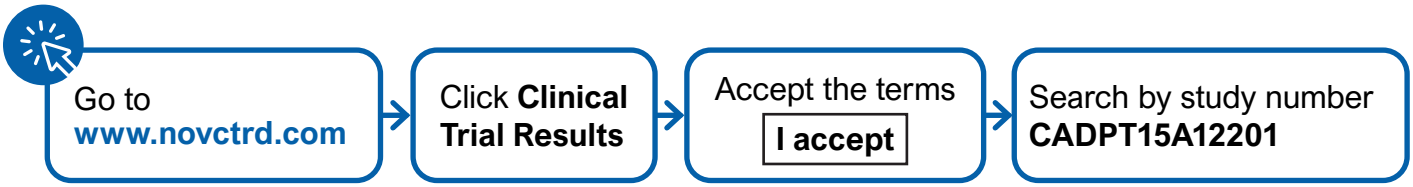
The researchers concluded there were no new safety concerns for **DFV890** or **MAS825** in this trial.

When this summary was written, Novartis had no plans for future trials of **DFV890** and **MAS825** in people with coronary heart disease and CHIP.

Where can I learn more about this trial?

To learn more about the results and adverse events in this trial, read the scientific summary of the results. It is 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 **NCT06097663**
- **euclinicaltrials.eu** – search using the number **2023-506741-34**

Other trials of **DFV890** and **MAS825** may appear on the public websites above. When there, search for **DFV890** and **MAS825**.

Full clinical trial title: A randomized, placebo-controlled, parallel-group, investigator- and participant-blinded Phase 2a study to investigate the efficacy, safety, and tolerability of DFV890 and MAS825 for inflammatory marker reduction in an adult population with coronary heart disease and Clonal Hematopoiesis of Indeterminate Potential (CHIP)



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

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