NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of HDM201 in people with acute myeloid leukemia that went away after a bone marrow transplant

Thank you!

Thank you to the participants who took part in the clinical trial for acute myeloid leukemia. Every participant helped the researchers learn more about the trial drug **HDM201**, also called **siremadlin**.

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: CHDM201K12201

Novartis drug studied: **HDM201**, also known as **siremadlin**

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 **HDM201** alone or with another treatment in people with acute myeloid leukemia (AML). This trial included participants whose AML went away after receiving a bone marrow transplant, but had a high chance of having AML come back (high risk of **relapse**). The trial planned to learn about the effects of **HDM201** on preventing AML from coming back.

Acute myeloid leukemia (AML) is cancer that starts in cells that turn into blood cells in the bone marrow. Bone marrow is the tissue inside of bones that helps make blood cells. AML most often affects cells that turn into white blood cells.

AML can be treated with a **bone marrow transplant**, also called a stem cell transplant, which is a procedure that replaces damaged bone marrow with healthy bone marrow.

HDM201, also called **siremadlin**, is a trial drug designed to block a protein that can help cancer cells grow. By blocking this protein, researchers think it may treat certain types of cancer, including AML.

Another treatment for AML that has come back after a bone marrow transplant is **donor lymphocyte infusion**. For this treatment, doctors take healthy white blood cells (lymphocytes) from a donor and give them to the person through a needle into a vein (IV infusion).

Trial drug
HDM201 also called siremadlin

Pronounced as
sie-ur-mad-lin

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

- What was the highest dose of HDM201 that was safe for participants with AML to take?
- How many participants did not have their AML relapse 6 months after taking HDM201?
- 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 February 2023 and ended early in October 2023. The participants were in the trial for up to about 6 months.

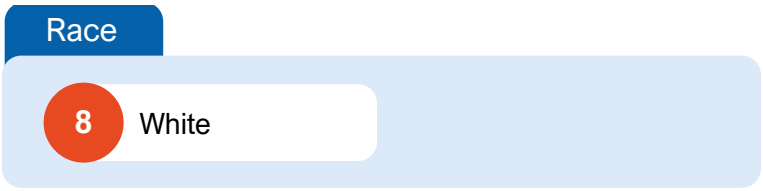
This trial was designed to have 2 parts:

- **Part 1:** A small group of participants were given increasing doses of **HDM201** alone to help researchers choose a dose to use in Part 2.
- **Part 2:** Researchers planned to give the chosen dose of **HDM201** to more participants to learn the effects of **HDM201** on preventing AML from coming back. These participants would have received **HDM201** alone or with a donor lymphocyte infusion. However, the sponsor decided to stop enrollment early, and Part 2 did not start.

In October 2023, the sponsor ended this trial early due to strategic business reasons. The decision was not due to safety concerns.

Who was in this trial?

8 participants with AML received treatment in this trial – 5 men and 3 women. Participants' ages ranged from 21 to 74 years. Their average age was 52 years. The number of participants by race is shown below.



The participants could take part in this trial if they:

- Had received a bone marrow transplant from another person and did not have certain problems after the transplant
- Had a high chance of having AML come back after transplant (high risk of relaupse)
- Had not received certain treatments for AML after their transplant

8 participants from 3 countries received treatment. The participants took part in:

- Germany | **5** participants
- Italy | **2** participants
- Spain | **1** participant

What treatments did the participants receive?

The treatment in this trial was:

HDM201, 30 milligrams (mg), taken by mouth as capsules during 4-week cycles. Participants took **HDM201** on Days 1 through 5 of each cycle.

What is a cycle?
A **cycle** is a treatment period that is repeated.

The participants, researchers, and trial staff knew what treatment each participant took. All participants took **HDM201**.

It was planned for the participants to continue trial treatment for up to 2 years, as long as they were benefiting from it.

What happened during this trial?

Before treatment — **About 1 month**

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

During treatment — **Up to about 5 months**

In **Part 1**, 8 participants took 30 mg of **HDM201** by mouth as capsules on Days 1 through 5 of each 4-week treatment cycle.

Researchers planned to give participants different doses of **HDM201** based on the results of the starting dose. However, because the trial ended early, no higher doses of **HDM201** were given.

Part 2 did not start.

After treatment — **Until the trial ended**

Trial staff checked participants' general health and for any medical problems for up to 30 days after the participants' last dose of trial treatment.

If a participant's cancer did not get worse during trial treatment, they had follow-up visits with trial staff to check on their cancer until their cancer got worse or the trial ended.

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

What were the main results of this trial?

What was the highest dose of HDM201 that was safe for participants with AML to take?

Overall, 30 mg **HDM201** once a day on Days 1 through 5 of each 4-week cycle was safe for the participants in this trial. However, as this trial ended early, researchers could not learn the highest dose of **HDM201** that was safe to use in Part 2.

To learn this, researchers kept track of how many participants had **dose limiting toxicities (DLTs)**.

Before this trial started, the researchers decided which medical problems were DLTs based on their type, severity, and timing. Trial doctors kept track of DLTs that happened during the first treatment cycle.

Of the 7 participants who completed one 4-week treatment cycle, 1 participant reported a DLT, which was:

- **Very low levels of platelets (help blood to clot) that could be life-threatening** (thrombocytopenia)

What are dose limiting toxicities (DLTs)?

DLTs are medical problems that:

- The trial doctors think could be related to the trial treatment
- Lead to a pause or lowering of the dose of treatment

How many participants had DLTs?

	HDM201 7 participants
Had a DLT	**1 of 7** 14%

This table does not include a participant who did not complete one 4-week treatment cycle.

How many participants did not have their AML relapse 6 months after taking HDM201?

As the trial ended early and Part 2 did not start, the researchers could not learn how many participants did not have their AML relapse 6 months after taking **HDM201**.

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

Trial doctors keep track of all medical problems called **adverse events** that happen in trials, 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 trial treatment up to 30 days 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.

All the participants (8 of 8) had adverse events. 2 participants had adverse events that were considered serious. No participants left the trial due to an adverse event. 2 participants died. The researchers concluded there were no unexpected safety concerns for **HDM201** in this trial.

How many participants had adverse events?

	HDM201 8 participants
Had at least 1 **serious adverse event**	**2 of 8** 25%
Had at least 1 **other adverse event**	**8 of 8** 100%
Left the trial due to an adverse event	**0 of 8** 0%
Died	**2 of 8** 25%

What serious adverse events did the participants have?

2 participants died. 2 participants had serious adverse events.

The serious adverse events were:

- **Low levels of platelets** (thrombocytopenia)
- **Infection in the belly area** (abdominal infection)
- **Frequent, loose, or watery stool** (diarrhea)
- **Physical health got worse** (general physical health deterioration)
- **Inflammation (swelling) in the esophagus, which is the tube that connects the throat to the stomach** (esophagitis)

What other adverse events did the participants have?

8 participants had other adverse events.

The table below shows the other adverse events that happened in **3 or more** participants. Additional adverse events happened in fewer participants.

	HDM201 8 participants
Low levels of platelets Thrombocytopenia	**7 of 8** 88%
Low levels of white blood cells Neutropenia	**6 of 8** 75%
Feeling sick to the stomach Nausea	**4 of 8** 50%
Frequent, loose, or watery stool Diarrhea	**4 of 8** 50%
Fever Pyrexia	**3 of 8** 38%
Low levels of red blood cells Anemia	**3 of 8** 38%
Rash	**3 of 8** 38%

What was learned from this trial?

Researchers learned about the effects of **HDM201** in people whose acute myeloid leukemia (AML) went away after a bone marrow transplant but had a high chance of coming back. The sponsor ended this trial early due to strategic business reasons.

The researchers concluded that:

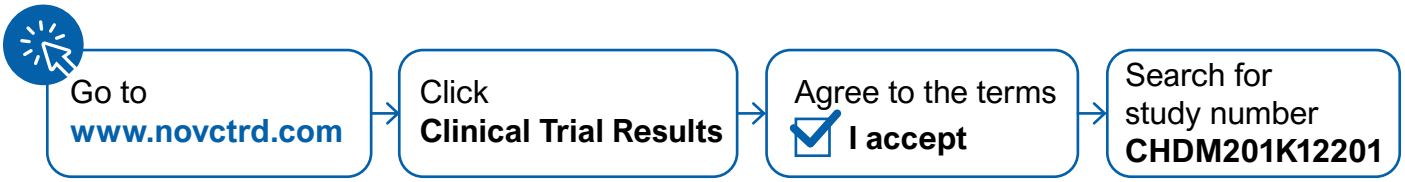
- Overall, 30 mg **HDM201** once a day on Days 1-5 of each 4-week cycle was safe for the participants with AML in this trial. However, as this trial ended early and Part 2 did not start, researchers could not learn the highest dose of **HDM201** that was safe to use.
- As Part 2 did not start, they could not learn the number of participants whose AML relapsed 6 months after taking **HDM201**
- There were no unexpected safety concerns for **HDM201** in this trial

When this summary was written, the sponsor had no plans for future trials of **HDM201** in people with AML.

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 **NCT05447663**
- clinicaltrialsregister.eu/ctr-search/search – search using the number **2021-003596-34**

Other trials of **HDM201** may appear on the public websites above. When there, search for **HDM201** or **siremadlin**.

Full clinical trial title: A phase Ib/II, open label study of siremadlin monotherapy and in combination with donor lymphocyte infusion as a treatment for patients with acute myeloid leukemia post-allogeneic stem cell transplantation who are in complete remission but at high risk for relapse.

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

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