NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the effects of MBG453 in combination with azacitidine and venetoclax in people with acute myeloid leukemia who cannot receive chemotherapy

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 **MBG453**, also called sabatolimab.

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: CMBG453C12201

Novartis drug studied: **MBG453**, also called sabatolimab

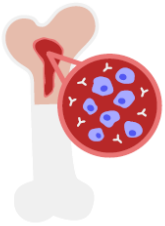
Sponsor: Novartis

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 **MBG453** in combination with **azacitidine** and **venetoclax** in people with **acute myeloid leukemia** who cannot receive intensive chemotherapy.



Acute myeloid leukemia (AML) is a blood cancer that starts in myeloid cells located in the bone marrow. Bone marrow is the tissue inside bones that helps make blood cells. Usually, myeloid cells develop into mature (fully developed and normal) blood cells such as red blood cells (cells that transport oxygen), white blood cells (cells that protect the body against infections), and platelets (cells that help blood clot). In people with **AML**, these myeloid cells develop into abnormal blood cells (not fully developed, also called immature) that do not function properly.

Common symptoms of **AML** are tiredness, weakness, frequent infections, fever, easy bruising, and bleeding.

Intensive chemotherapy is a treatment option for **AML**, but it is not suitable for elderly people and/or those with other health issues, as it can cause severe complications. Those who are unable to receive intensive chemotherapy, according to their doctors, are called **AML unfit**. Researchers are looking for treatment options that can help people who are **AML unfit**.

MBG453, also called sabatolimab, is a trial drug designed to help the immune system fight cancer by blocking a protein called TIM-3. TIM-3 is found on certain immune cells, such as T cells, and normally helps keep the immune system from attacking healthy parts of the body. In **AML**, TIM-3 becomes overactive, making it harder for the immune system to see and fight cancer cells. By blocking TIM-3, **MBG453** may help re-activate the immune system so it can better recognize and destroy cancer cells.

Trial drug
MBG453 also called sabatolimab
Pronounced as
Saba-To-li-mab

In this trial, participants also received **azacitidine** and **venetoclax**, along with **MBG453**. **Azacitidine** and **venetoclax** are approved treatments for **AML** in some countries. These medicines work by blocking the growth of cancer cells.

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

- What was the best dose of **MBG453** in combination with **azacitidine** and **venetoclax** for participants with **unfit AML**?
- How many participants had **complete remission** at least one year after treatment with 800 mg of **MBG453** in combination with **azacitidine** and **venetoclax**?

  In this trial, a participant was considered to have **complete remission** when the signs and symptoms of their disease had disappeared, and their blood tests showed the disease was under control. This included:

  - the bone marrow had less than 5% of immature (not fully developed) blood cells
  - the blood had normal levels of neutrophils (a type of white blood cell) and platelets
  - there were no immature cells in the blood
  - there were no signs of the disease outside the bone marrow, such as in the brain or soft tissues
- What medical problems, also called adverse events, happened during this trial?

  Adverse events reported in this trial were any sign or symptom that participants had 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 September 2020 and ended early in October 2024. It was planned that participants would continue the trial treatment for as long as it was beneficial, unless the trial was stopped by the sponsor or the participants decided to leave the trial early.

This trial was designed to have 2 parts.

- **Part 1** was to find the best dose of **MBG453** in combination with **azacitidine** and **venetoclax** that would be used in Part 2 of the trial. This was done by assessing the safety in two groups of participants with different doses of **MBG453**.
- **Part 2** was to further assess the effects of the best dose of **MBG453** in combination with **azacitidine** and **venetoclax** in larger groups of participants.

However, the sponsor decided to stop studying **MBG453** earlier than planned. This was because the results from another **MBG453** trial did not show the expected effects. The decision was not due to any safety concerns with **MBG453**.

Who was in this trial?

90 participants with **unfit AML** received treatment in this trial – 51 men and 39 women. Participants' age ranged from 55 to 88 years. Their average age was 76 years.

The number of participants by race is shown below.

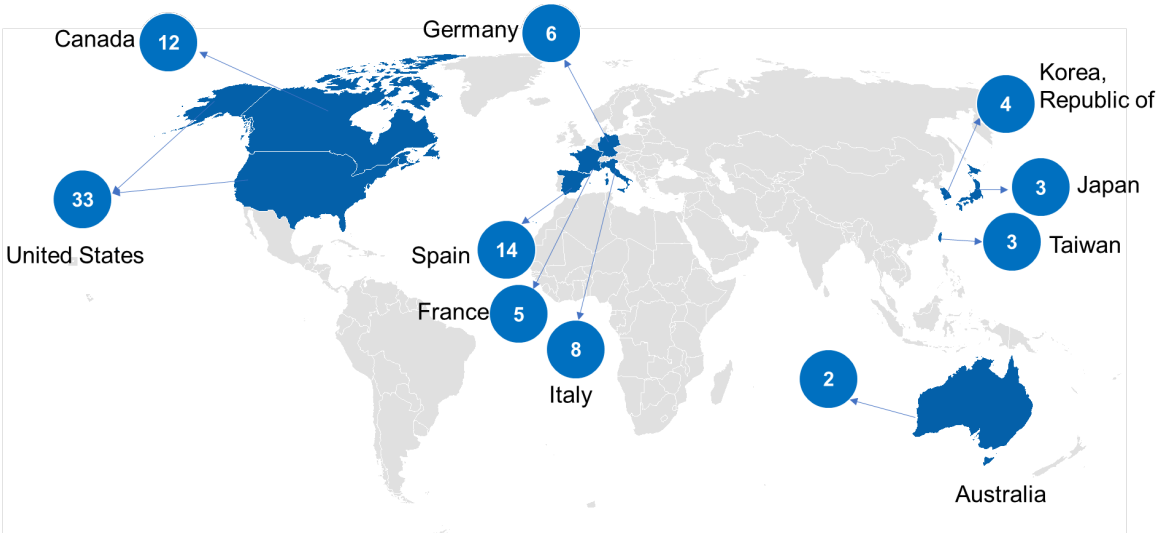
Race

13	Asian	2	Black or African American	74	White
1	Unknown				

The participants could take part in this trial if they:

- were more than 18 years old
- were newly diagnosed with **AML** and could not receive intensive chemotherapy
- were either fully active or at least able to do their daily jobs, except for heavy activities

90 participants from 10 countries received treatment. The map below shows the number of participants who took part in each country.



What treatments did the participants receive?

The treatments in this trial were given in **cycles**:

Participants received **MBG453** at a dose of 400 mg or 800 mg as an infusion into a vein over 30 minutes, on Day 8 of each treatment cycle.

Participants received **azacitidine** at a dose of 75 **mg/m^2*** as an injection under the skin or as an infusion into a vein.

It was given once a day on Days 1 to 7 of each treatment cycle, or on Days 1 to 5 and Days 8 and 9. Other schedules, per standard clinical practice, were also allowed.

A **cycle** is a treatment period that is repeated until the treatment ends.
In this trial, each **cycle** lasted for 28 days (roughly one month).

Participants took **venetoclax** at a dose of 400 mg as a tablet by mouth daily during each day of the treatment cycle.

***mg/m^2** is a unit for measuring the amount of trial drug per unit of body surface area.

The participants, researchers, and trial staff knew what treatment the participants were receiving.

What happened during the trial?

Before treatment

Up to 28 days

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

During treatment

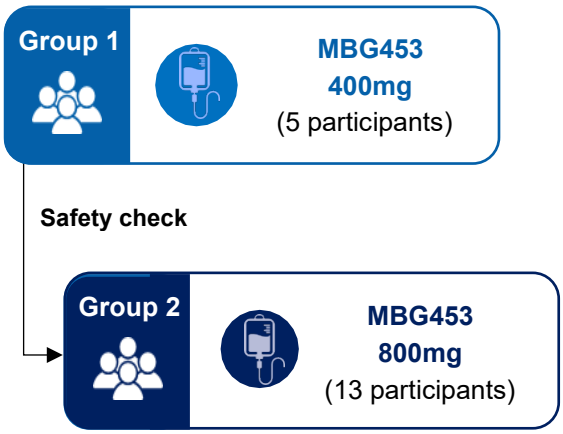
As long as participants benefit from the treatment

This trial was designed to have 2 parts:

Part 1: A total of 18 participants received treatment in Part 1 of this trial.

- Five participants in **Group 1** started treatment first and received a dose of 400 mg of **MBG453** in combination with **azacitidine** and **venetoclax**. There were no safety concerns after participants completed 8 weeks of treatment.
- Thirteen participants in **Group 2** received a higher dose of 800 mg of **MBG453** in combination with **azacitidine** and **venetoclax**. No safety concerns were observed.

800 mg was determined to be the best dose.



Part 2: A total of 72 participants received treatment in Part 2 of this trial.

Participants received 800 mg of **MBG453** in combination with **azacitidine** and **venetoclax**.

After treatment

Up to 5 months

Trial staff checked participants' general health and for any medical problems for up to 5 months after participants' last dose of trial treatment.

What were the main results of this trial?

What was the best dose of MBG453 in combination with azacitidine and venetoclax for participants with unfit AML?

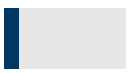
Researchers found that 800 mg of MBG453 in combination with azacitidine and venetoclax was the best dose for participant with **unfit AML** and chosen to be further tested during Part 2 of this trial.

To answer this question, researchers closely monitored participants for **dose-limiting toxicities** (**DLTs)** in each group during Part 1. The number of DLTs helped researchers decide the best dose of **MBG453** in combination with **azacitidine** and **venetoclax** that could be taken for further testing during Part 2.

The table below shows how many participants from Part 1 had DLTs during the first 8 weeks of treatment (2 cycles). To be included in the DLT results, participants had to receive an appropriate dose of trial treatment and have available results to report.
Thus, 4 out of 5 participants in the **MBG453 400 mg** group and 11 out of 13 participants in the **MBG453 800 mg** group were evaluated for DLT.

What are dose-limiting toxicities (DLTs)?
DLTs are medical problems that:

- the trial doctors think that it could be related to the trial treatment
- is too severe to continue giving that specific dose

	MBG453 400 mg + Azacitidine + Venetoclax 4 participants	MBG453 800 mg + Azacitidine + Venetoclax 11 participants
DLT	0	**1 of 11** **9%**  The participant had **inflammation of the heart muscle** (myocarditis)

How many participants had complete remission at least one year after treatment with 800 mg MBG453 in combination with azacitidine and venetoclax?

The trial was originally planned to evaluate results after participants had completed at least 12 treatment cycles (approximately one year). However, this was not possible because the trial ended early. Instead the available data was used to estimate the complete remission rate in participants, who received any number of treatment cycles with 800 mg of **MBG453** in combination with **azacitidine** and **venetoclax**.

To answer this, researchers planned to conduct various tests, such as bone marrow biopsy (examining small pieces of tissue from the bone marrow under a microscope) and blood tests.

In this trial, a participant was considered to have **complete remission** when the signs and symptoms of their disease had disappeared, and their blood tests showed the disease was under control. This included:

- the bone marrow had less than 5% of immature (not fully developed) blood cells
- the blood had normal levels of neutrophils (a type of white blood cell) and platelets
- there were no immature cells in the blood
- there were no signs of the disease outside the bone marrow, such as in the brain or soft tissues

Although the results were not available for all participants, they were available for participants who received any number of treatment cycles.

40 out of 85 participants (47%) who received any number of treatment cycles with 800 mg of **MBG453** in combination with **azacitidine** and **venetoclax** had complete remission after treatment. However, the researchers concluded that this result was not considered meaningful because the complete remission rate of 47% did not meet the criteria that were pre-specified in the clinical trial protocol. The researchers defined these criteria before the trial began to determine whether the treatment was successful.

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 1 month after the last dose of **MBG453**.

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 90 participants had adverse events including serious and other adverse events.

- 71 out of 90 participants had adverse events that were considered serious
- 12 participants left the trial due to an adverse event
- 12 participants died

The researchers concluded there were no new or unexpected safety concerns for **MBG453** in this trial.

How many participants had adverse events?

Participants who	MBG453 400 mg + Azacitidine + Venetoclax 5 participants	MBG453 800 mg + Azacitidine + Venetoclax 85 participants
Had at least 1 **adverse event** including serious and other	**5 of 5** 100%	**85 of 85** 100%
Had at least 1 **serious adverse event**	**4 of 5** 80%	**67 of 85** 79%
Left the trial due to an adverse event	**1 of 5** 20%	**11 of 85** 13%
Died	**1 of 5** 20%	**11 of 85** 13%

What serious adverse events did the participants have?

71 participants had serious adverse events.

The table below shows the most common serious adverse events.

	MBG453 400 mg + Azacitidine + Venetoclax 5 participants	MBG453 800 mg + Azacitidine + Venetoclax 85 participants
Low white blood cells with fever Febrile neutropenia	**3 of 5** 60%	**30 of 85** 35%
Lung infection Pneumonia	**1 of 5** 20%	**8 of 85** 9%
Fever Pyrexia	**0**	**13 of 85** 15%
COVID-19	**0**	**5 of 85** 6%
Severe complication of an infection Sepsis	**0**	**4 of 85** 5%

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

The table below shows the most common other adverse events.

	MBG453 400 mg + Azacitidine + Venetoclax 5 participants	MBG453 800 mg + Azacitidine + Venetoclax 85 participants
Constipation	**3 of 5** 60%	**48 of 85** 57%
Nausea	**3 of 5** 60%	**32 of 85** 38%
Decreased number of platelets Platelet count decreased	**3 of 5** 60%	**29 of 85** 34%
Low neutrophils Neutrophil count decreased	**3 of 5** 60%	**22 of 85** 26%
Itching Pruritus	**3 of 5** 60%	**20 of 85** 24%
Injection site reaction	**3 of 5** 60%	**7 of 85** 8%

What was learned from this trial?

The sponsor decided to stop studying **MBG453** earlier than planned. This was because the results from another **MBG453** trial did not show the expected effects in participants with another disease, called **myelodysplastic syndrome (MDS)**.

Researchers found that:

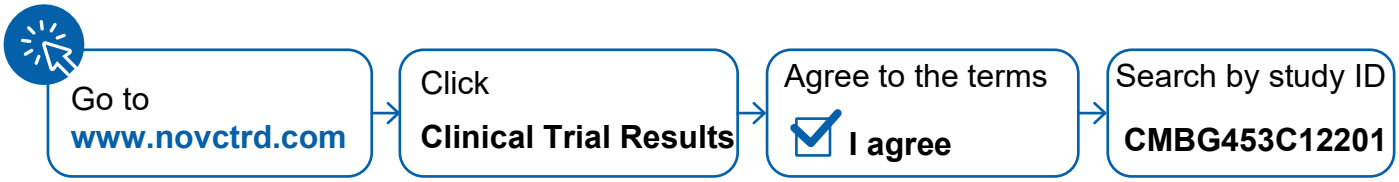
- 800 mg of **MBG453** was the best dose to be combined with **azacitidine** and **venetoclax** in participants with **unfit AML**.
- However, they could only learn limited information about the effects of 800 mg of **MBG453** in combination with **azacitidine** and **venetoclax** in these participants.
- There were no new or unexpected safety concerns with the use of **MBG453** in combination with **azacitidine** and **venetoclax** in this trial.

When this summary was written, participants who were still benefiting from treatment were given the option to join the **CMBG453B12206B** trial to continue receiving the same treatment (roll-over trial).

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 the following websites:

- **www.clinicaltrials.gov** - search using the number **NCT04150029**
- **clinicaltrialsregister.eu/** - search using the number **2019-000439-14**

Other trials of **MBG453** may appear on the public websites above. When there, search for **MBG453** or sabatolimab.

Full clinical trial title: A phase II multi-center, single arm, safety and efficacy study of MBG453 in combination with azacitidine and venetoclax for the treatment of Acute Myeloid Leukemia (AML) in adult patients unfit for chemotherapy

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