NOVARTIS

Clinical Trial
Results Summary

A clinical trial to learn more about the effects of MBG453 in combination with standard treatment in people with medium to very high-risk myelodysplastic syndrome

Thank you!

Thank you to the participants who took part in the clinical trial for **myelodysplastic syndrome**. 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: CMBG453B12201

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 more about the effects of **MBG453** in combination with standard treatment in people with **medium to very high-risk myelodysplastic syndrome (MDS)**. To find this out, researchers compared the effects of **MBG453** to **placebo**.

MDS is a group of conditions in which the bone marrow does not produce enough healthy blood cells. The common symptoms of **MDS** include weakness, shortness of breath, pale skin, bleeding, being more likely to get infections, and red or purple spots on the skin.
People with **medium-risk MDS** usually have fewer symptoms than those with **high or very high-risk MDS**. The risk level shows how likely the disease is to worsen or cause other life-threatening problems.

In some cases, **MDS** might progress to acute myeloid leukemia, a more aggressive form of blood and bone marrow cancer.

Bone marrow is found in the center of some bones and is where blood cells are made.

MBG453 also called sabatolimab, is the trial drug, and works by blocking a protein called TIM-3, present on the surface of some white blood cells and cancer cells. This process activates the immune system to attack cancer cells.

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

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

In this trial, participants received **azacitidine** or **decitabine**, as **standard treatment** in combination with either **MBG453** or **placebo**. These are approved medicines for **MDS** and are commonly used in care. These medicines work by blocking the growth of cancer cells.

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

- How many participants had **complete remission** after treatment with **MBG453** or **placebo** in combination with the **standard treatment**?
  - In this trial, a participant was considered to have **complete remission** when:
    - The bone marrow has less than or equal to 5% of immature (not fully developed) blood cells
    - The blood has normal levels of hemoglobin, platelets, and neutrophils (a type of white blood cell)
- How long did participants live without their **MDS** getting worse or coming back after treatment with **MBG453** or **placebo** in combination with the **standard treatment**? This is also called **progression-free survival**.
- 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 June 2019 and ended early in January 2024. It was planned that participants would continue the trial treatment for as long as it was beneficial, unless the trial was terminated by the sponsor or consent was withdrawn.

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

Who was in this trial?

127 participants with **MDS** were enrolled in this trial – 86 men and 41 women. Participants' ages ranged from 18 to 89 years. Their average age was 72 years.
Of the 127 participants enrolled, 125 participants received trial treatments (2 participants did not receive treatment as 1 participant withdrew consent, and 1 participant died before starting the treatment).

The number of participants by race is shown below.

Race

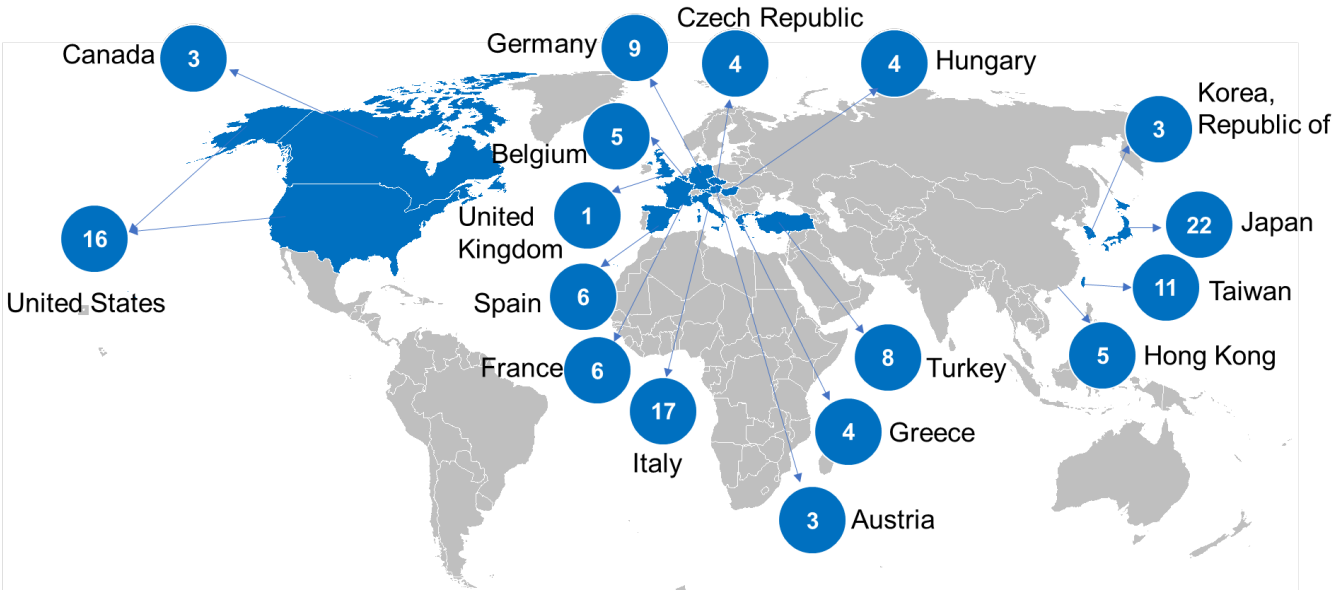
- 77 White
- 4 Asian
- 1 Black or African American
- 7 Unknown

The participants could take part in this trial if they:

- were 18 years of age or older
- had a confirmed diagnosis of very high, high, or medium-risk **MDS**
- were not eligible for a **stem cell transplant** or high-dose chemotherapy at the start of the trial
- were fully active, were able to manage self-care or walk and do light work

A **stem cell transplant** is a procedure that involves transferring blood cells from the bone marrow of a healthy person to people with some disease who may require treatment.

127 participants from 17 countries were enrolled in this trial. 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**. Researchers used a computer to randomly assign participants to receive either MBG453 or a placebo, both given with standard treatment.

Participants received **MBG453** at a dose of 400 milligrams (mg) as an infusion into a vein over 30 minutes, on Day 8 and Day 22 of each treatment cycle.

Participants received **placebo** as an infusion into a vein over 30 minutes, on Day 8 and Day 22 of each treatment cycle.

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

Trial doctors selected the **standard treatment** **as per local practice.**

Participants received one of the following **standard treatments** in combination with either **MBG453** or **placebo**:

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

Decitabine at a dose of 20 **mg/m^2*** as an infusion into a vein on Days 1 to 5 of each 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 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 the trial?

Before treatment

Up to 1 month

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

During treatment

Until the participants left the trial, or the trial stopped

125 participants received one of the below treatments:

Group 1

MBG453 with **standard treatment**: **64** participants

Group 2

Placebo with **standard treatment**: **61** participants

Participants could continue trial treatments as long as they were benefiting from it.

After treatment

Up to 5 months

Trial staff checked participants' general health and for any medical problems for up to 30 days after their last dose of **placebo**, or 5 months after their last dose of **MBG453**.

What were the main results of this trial?

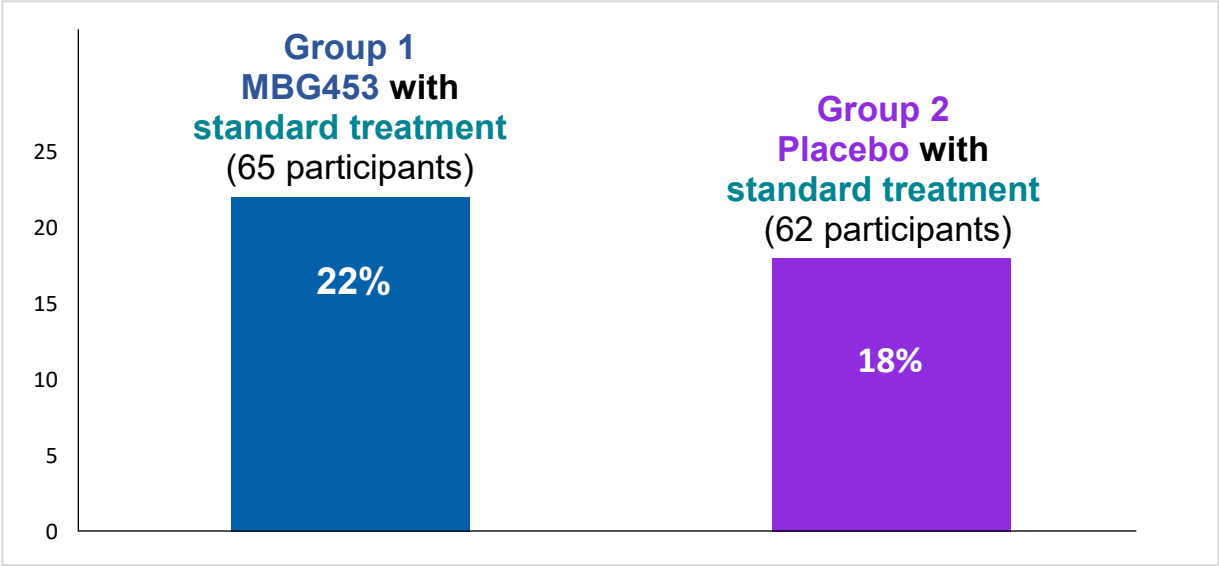
How many participants had complete remission after treatment with MBG453 or placebo in combination with standard treatment?

14 participants (22%) in **Group 1** who received **MBG453** and 11 participants (18%) in **Group 2** who received the **placebo** had complete remission of **MDS** after treatment. The researchers concluded that the difference between the 2 groups was not meaningful.

A participant was considered to have **complete remission** when:

- The bone marrow has less than or equal to 5% of immature blood cells
- The blood has normal levels of hemoglobin, platelets, and neutrophils (a type of white blood cell)

Percentage (number) of participants who had complete remission



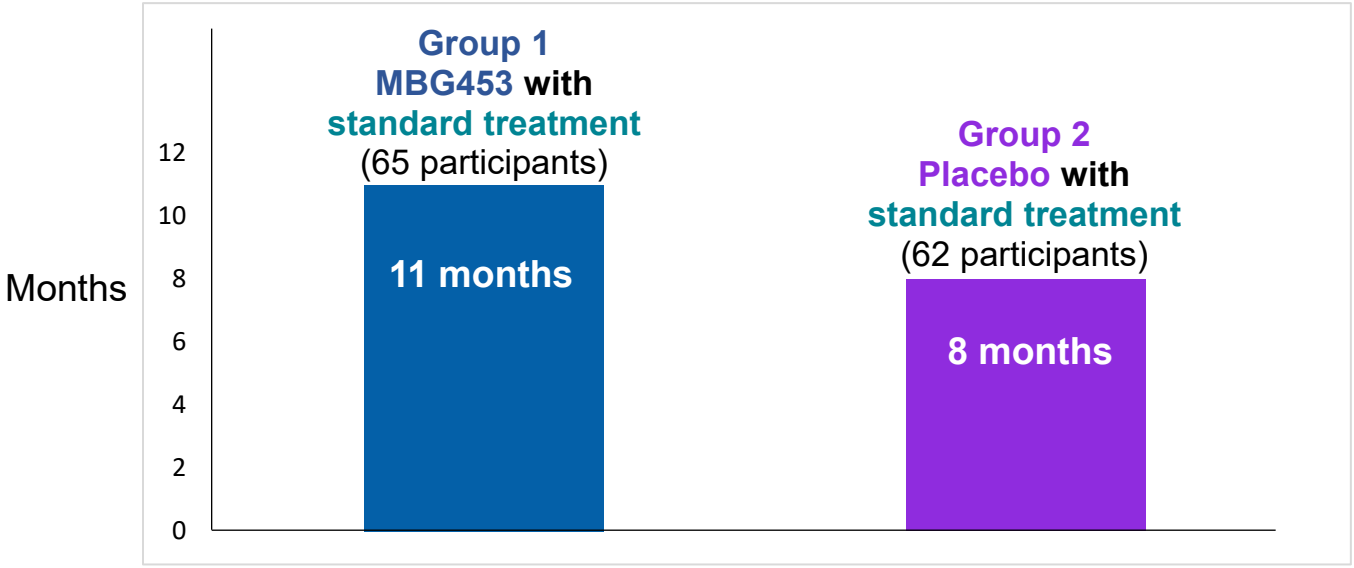
The results are shown for all participants who were enrolled in this trial regardless of whether they received treatment.

How long did participants live without their MDS getting worse or coming back after treatment with MBG453 or the placebo in combination with standard treatment? This is also called progression-free survival.

In **Group 1**, participants who received **MBG453** lived on average for more than 11 months without their disease getting worse or coming back.
In **Group 2**, participants who received the **placebo** lived on average for more than 8 months without their disease getting worse or coming back.
The researchers concluded that the difference between the 2 groups was not meaningful.

To answer this question, researchers did bone marrow tests to assess the evolution of the **MDS** disease and checked participants' general health. This helped them find the length of time from the start of the trial until their **MDS** worsened or came back, in any treatment group.

Average time (in months) from the start of the trial until participant's MDS worsened or came back



The results are shown for all participants who were enrolled in this trial regardless of whether they received 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 30 days after the last dose of trial 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.

The results were included for all participants who received at least one dose of trial treatment. In **Group 1**, 2 participants received only **standard treatment**, so they were recorded in **Group 2**. As a result, the results were available for 62 participants in **Group 1** and 63 participants in **Group 2**.

Almost all the participants (124 of 125) had adverse events, including serious and non-serious.

- 81 participants had adverse events that were considered serious.
- 17 participants left the trial due to an adverse event.
- 18 participants died.

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

How many participants had adverse events?

Participants who:	Group 1 MBG453 62 participants	Group 2 Placebo 63 participants
Had at least 1 adverse event	**61 of 62** 98%	**63 of 63** 100%
Had at least 1 serious adverse event	**38 of 62** 61%	**43 of 63** 68%
Left the trial due to an adverse event	**7 of 62** 11%	**10 of 63** 16%

Participants who:	Group 1 MBG453 62 participants	Group 2 Placebo 63 participants
Died	5 of 62 8%	13 of 63 21%

What serious adverse events did the participants have?

81 participants had serious adverse events.

The table below shows the most common serious adverse events.

	Group 1 MBG453 62 participants	Group 2 Placebo 63 participants
Fever with a low number of neutrophils, a type of white blood cell that helps the body fight infections Febrile neutropenia	16 of 62 26%	14 of 63 22%
Fever Pyrexia	1 of 62 2%	9 of 63 14%
Lung infection Pneumonia	9 of 62 15%	11 of 63 17%
Serious complication of an infection Sepsis	4 of 62 6%	8 of 63 13%
Serious complication of an infection causing very low blood pressure Septic shock	2 of 62 3%	4 of 63 6%

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

The table below shows the most common other adverse events.

	Group 1 MBG453 62 participants	Group 2 Placebo 63 participants
Constipation	**29 of 62** 47%	**26 of 63** 41%
Decreased number of neutrophils, a type of white blood cell that helps the body fight infections* Neutrophil count decreased	**14 of 62** 23%	**23 of 63** 37%
Decreased number of platelets, cells that help blood to clot* Platelet count decreased	**12 of 62** 19%	**19 of 63** 30%
Diarrhea	**27 of 62** 44%	**15 of 63** 24%
Feeling sick Nausea	**15 of 62** 24%	**19 of 63** 30%
Fever Pyrexia	**17 of 62** 27%	**13 of 63** 21%
Low number of neutrophils* Neutropenia	**25 of 62** 40%	**20 of 63** 32%
Low number of platelets* Thrombocytopenia	**20 of 62** 32%	**13 of 63** 21%
Low number of red blood cells Anemia	**22 of 62** 35%	**32 of 63** 51%
White blood cell count decreased	**13 of 62** 21%	**17 of 63** 27%

*"Decreased number of neutrophils" and "low number of neutrophils" refer to the same medical problem. Similarly, "decreased number of platelets" and "low number of platelets" also mean the same thing. These terms were recorded differently for some participants, but they describe the same condition.

What was learned from this trial?

The sponsor decided to stop studying **MBG453** earlier than planned. This was because the results from this trial and another **MBG453** trial did not show the expected effects in people with **MDS**.

Researchers found that:

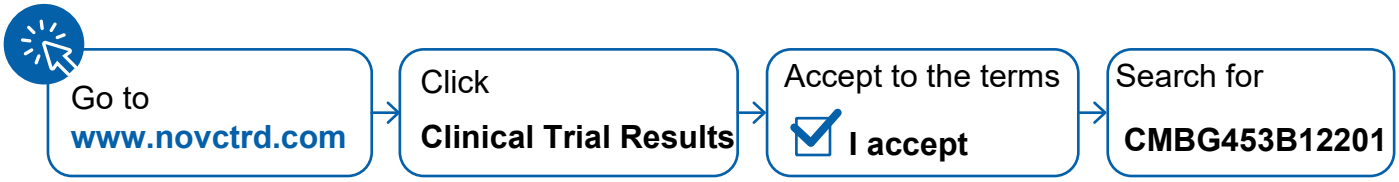
- Participants who received **MBG453** and those who received **placebo** had similar results. Both groups had participants who experienced complete remission.
- On average, participants who received **MBG453** lived more than 11 months without their disease getting worse or coming back, compared to more than 8 months for those who received **placebo**. However, researchers concluded that the difference between the 2 groups was not meaningful.
- Researchers did not find any new safety concerns with the use of **MBG453** in combination with **standard treatment** in this trial.

When this summary was written, the trial **CMBG453B12206B** was ongoing to learn more about the safety of **MBG453** in people who received it in past trials.

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 **NCT03946670**
- clinicaltrialsregister.eu/ - search using the number **2018-004479-11**

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

Full clinical trial title: A randomized, double-blind, placebo-controlled phase II multi-center study of intravenous MBG453 added to hypomethylating agents in adult subjects with intermediate, high or very high risk myelodysplastic syndrome (MDS) as per IPSS-R criteria

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