NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of MBG453 in combination with azacitidine and venetoclax in people with high or 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: CMBG453B12203

Drug studied: MBG453 also known as 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.

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 azacitidine and venetoclax in people with **high or very high-risk myelodysplastic syndrome (MDS).**

Myelodysplastic syndrome is a group of conditions where the blood cells formed in the bone marrow do not mature or become healthy. Bone marrow is found in the center of some bones and is where blood cells are made. The symptoms of **MDS** include weakness, shortness of breath, pale skin, bleeding, being more prone to infections, and red or purple spots on the skin. In some cases, MDS might progress to acute myeloid leukemia (blood and bone marrow cancer).

MBG453 is currently being studied for **intermediate, high, or very high-risk MDS**, and blood and bone marrow cancer. It 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 and reduces the growth of cancer cells.

Trial drug
MBG453 also called sabatolimab

Pronounced as
Saba-To-li-mab

The trial purpose was to answer these main questions:

- Was **MBG453** in combination with azacitidine and venetoclax safe to be received in participants with high or very high-risk MDS?
- How many participants had a complete disappearance of MDS symptoms, also called complete remission, after treatment with **MBG453** in combination with azacitidine and venetoclax?
- What adverse events did the participants have during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial.

How long was this trial?

This trial began in May 2021 and ended in May 2023. It was planned for the participants to be in the trial for about 3 years after receiving the trial treatment.

This trial was planned to have 2 parts. However, the trial ended early because the researchers decided to change the development strategy for **MBG453**. This decision was not based on any safety concerns. Therefore, only Part 1 of the trial was completed.

Who was in this trial?

20 participants with MDS received treatment in this trial. Participants' ages ranged from 45 to 82 years. Their average age was 69 years.

The number of participants by gender and race are shown below.

Gender

16 **Men**	4 **Women**

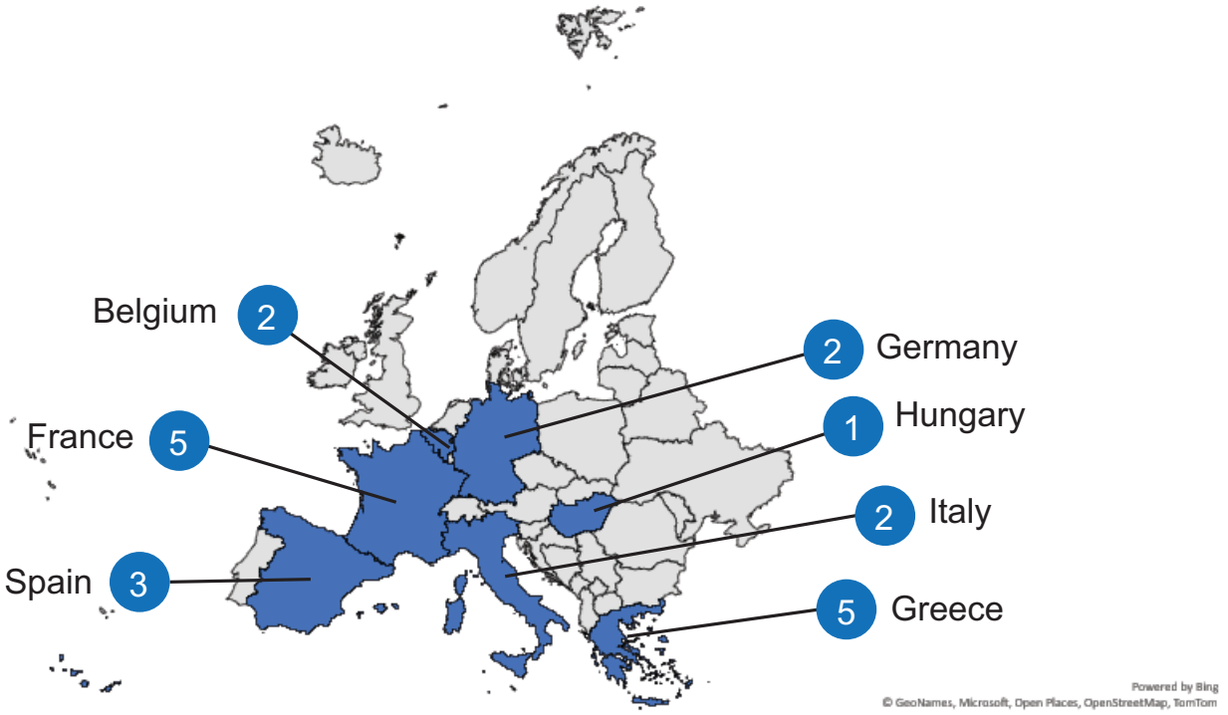
Race

30 **Men**	2 **Unknown**

The participants could take part in this trial if they:

- were at least 18 years of age
- had confirmed diagnosis of high or very high-risk MDS
- were at least able to walk, manage self-care, and be out of bed for more than 50% of waking hours
- were not eligible for treatment requiring transfer of blood cells from the bone marrow of a healthy person (also called stem cell transplant) or high-dose chemotherapy at the start of the trial

20 participants from 7 countries received treatment. This map of Europe 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**. Each treatment **cycle** lasted 28 days.

MBG453: Participants received MBG453 at a dose of 400 milligrams (mg) or 800 mg as an infusion into a vein, once, on Day 8 of every treatment cycle.

Azacitidine is an approved treatment for MDS.

Participants received azacitidine at a dose of 75 mg/m^2)* as an infusion into a vein or as an injection into a muscle on Days 1 to 7 of every treatment cycle.

Venetoclax is an approved treatment for blood cancer.

Participants took venetoclax at a dose of 400 mg as a tablet by mouth, once daily on Days 1 to 14 of every treatment cycle.

In this trial, a **cycle** is a 28-day treatment period, that can be repeated as needed, and during which participants received **MBG453, azacitidine** and **venetoclax** as an infusion into a vein or as an injection or as a tablet by mouth.

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

In this trial, the participants, trial doctors, or trial staff knew what treatment participants were receiving.

What happened during the trial?

Before treatment — Up to 1 month

Trial doctors checked participants' overall health to ensure they could be in this trial.

During treatment — Up to 13 months

Part 1: Five participants who entered Group 1 received a 400 mg dose of MBG453 on Day 8 of each treatment cycle. They also received azacitidine and venetoclax.

Following a safety review, where no safety concerns were observed for the 400 mg dose in Group 1, 15 new participants were enrolled in Group 2, and they received an 800 mg dose of MBG453.

- **Group 1** (5 participants): **400 mg MBG453** + **azacitidine** + **venetoclax**
- **Group 2** (15 participants): **800 mg MBG453** + **azacitidine** + **venetoclax**

Participants could continue treatment until their MDS got worse or any unacceptable adverse event occurred.

Part 2: This part was not completed because the trial ended early due to change in the development strategy for **MBG453**.

Trial doctors monitored the overall health of the participants throughout the trial.

After treatment — Up to 22 months

Researchers followed up with all participants after they received their last dose.

- **Safety follow-up:** Study doctors checked on participants' health up to 5 months after the last dose of **MBG453**.
- **Long-term follow-up:** Study doctors checked for disease relapse or death until the end of the trial.

What were the main results of this trial?

Was MBG453 in combination with azacitidine and venetoclax safe to be received in participants with high or very high-risk MDS?

Researchers found that MBG453 in combination with azacitidine and venetoclax could be safely given in participants with high or very high-risk MDS.

To answer this question, researchers calculated the number of participants with **DLTs** in each group. The number of DLTs helped researchers decide whether the tested dose of **MBG453** in combination with **azacitidine** and **venetoclax** could be safely given to participants or not. These results were available for 17 participants who met the criteria for treatment utilization and had sufficient safety assessments or experienced a DLT during the first 2 treatment cycles.

Dose limiting toxicities (DLTs) are defined as severe events caused by the drug that led to stopping treatment.

Percentage (number) of participants with DLTs

Group 1 (MBG453 400 mg + azacitidine + venetoclax) (out of 4)	Group 2 (MBG453 800 mg + azacitidine + venetoclax) (out of 13)
0	15% (2 out of 13)

The DLTs that participants had were:

- **low number of platelets in the blood** (thrombocytopenia)
- **bleeding in and around the brain** (intracranial hemorrhage)

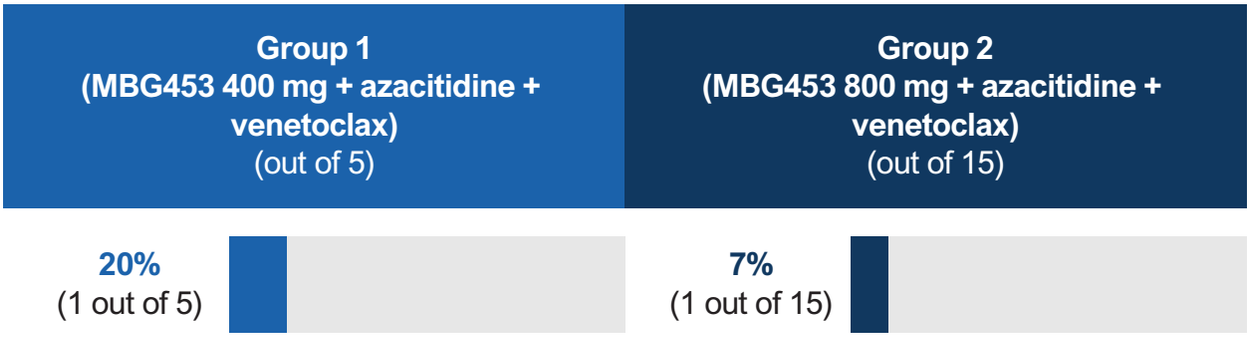
How many participants had a complete disappearance of MDS symptoms, also called complete remission, after treatment with MBG453 in combination with azacitidine and venetoclax?

A total of 2 participants, 1 in each group had complete disappearance of MDS symptoms.

Complete disappearance of MDS symptoms or Complete remission means

- less than 5% of the cells in the bone marrow were abnormal
- normal levels of hemoglobin, platelets, and neutrophils (a type of white blood cell)
- no signs of MDS in the bone marrow

Percentage (number) of participants who had complete disappearance of MDS symptoms



What adverse events did the participants have?

Trial doctors keep track of all **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 **up to 5 months** after receiving 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 participants had adverse events. 17 of 20 participants had adverse events that were considered serious. 7 of 20 participants died during the trial. 8 of 20 participants left the trial due to an adverse event. The researchers concluded that there were no new safety concerns for MBG453 for this trial.

How many participants had adverse events?

Participants who:	MBG453 400 mg + azacitidine + venetoclax 5 participants	MBG453 800 mg + azacitidine + venetoclax 15 participants
Had at least 1 serious adverse event	**3 of 5** 60%	**14 of 15** 93%
Had at least 1 other adverse event	**5 of 5** 100%	**15 of 15** 100%
Stopped treatment due to an adverse event	**2 of 5** 40%	**6 of 15** 40%
Died during the trial	**1 of 5** 20%	***6 of 15** 40%

*One death in the **MBG453 800 mg** group occurred during the treatment period.

What serious adverse events did the participants have?

17 out of 20 participants had serious adverse events. The table below shows the most common serious adverse events that happened in **10% or more** participants in either group.

	MBG453 400 mg + azacitidine + venetoclax 5 participants	**MBG453 800 mg + azacitidine + venetoclax** 15 participants
Fever with a low number of neutrophils, a type of white blood cell that helps the body fight infections Febrile Neutropenia	**2 of 5** 40%	**5 of 15** 33%
Fever due to a condition where bone marrow does not make blood cells Febrile bone marrow aplasia	**1 of 5** 20%	**0**
Low number of neutrophils, a type of white blood cell that helps the body fight infections Neutropenia	**1 of 5** 20%	**0**
Low number of platelets, cells that help blood to clot Thrombocytopenia	**1 of 5** 20%	**0**
Low number of red blood cells Anemia	**0**	**2 of 15** 13%
Low number of all types of blood cell Pancytopenia	**1 of 5** 20%	**0**
Lung cancer Lung Adenocarcinoma	**1 of 5** 20%	**0**
Severe immune response to a bacterial infection Bacterial Sepsis	**1 of 5** 20%	**0**
Severe immune response to an infection Sepsis	**1 of 5** 20%	**1 of 15** 7%

What other adverse events did the participants have?

All participants had other adverse events. The table below shows the most common other adverse events that happened in **30% or more** participants in either group.

	MBG453 400 mg + azacitidine + venetoclax 5 participants	**MBG453 800 mg + azacitidine + venetoclax** 15 participants
Constipation	**2 of 5** 40%	**4 of 15** 27%
Diarrhea	**2 of 5** 40%	**2 of 15** 13%
Feeling sick Nausea	**1 of 15** 20%	**6 of 15** 40%
Low number of neutrophils, a type of white blood cell that helps the body fight infections Neutropenia	**3 of 5** 60%	**8 of 15** 53%
Low number of platelets, cells that help blood to clot Thrombocytopenia	**3 of 5** 60%	**7 of 15** 47%
Low number of red blood cells Anemia	**1 of 5** 20%	**7 of 15** 47%

What was learned from this trial?

This trial ended early after only a small number of participants were treated in this trial. Therefore, researchers could only learn limited information about the effects of **MBG453** in combination with **azacitidine** and **venetoclax** in people with high or very high-risk MDS in this trial.

Researchers did not find any new safety concerns with the use of **MBG453** in combination with **azacitidine** and **venetoclax** in this trial compared to what has been reported for participants treated with **azacitidine** and **venetoclax**.

There are currently no follow-up trials planned for the combination of **MBG453**, **azacitidine**, and **venetoclax** in high or very high-risk MDS.

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 **NCT04812548**
- **clinicaltrialsregister.eu/ctr-search/search** search using the number **2020-003669-21**

Full clinical trial title: A single-arm, open-label, Phase II study of sabatolimab in combination with azacitidine and venetoclax in adult participants with high or very high risk myelodysplastic syndrome (MDS) as per IPSS-R criteria

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1-888-669-6682 (US) | +41-61-324 1111 (EU)

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