NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about MBG453, ACZ885 and NIS793, either alone or in combination, in people with lower-risk myelodysplastic

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 drugs **MBG453**, also called sabatolimab, **ACZ885**, also called canakinumab, and **NIS793**, also called nisevokitug.

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: CMBG453E12101

Novartis drug studied: **MBG453** (sabatolimab), **ACZ885** (canakinumab), and **NIS793** (nisevokitug)

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 find out the recommended doses of **MBG453**, **ACZ885**, and **NIS793** given alone, and of **MBG453** in combination with **ACZ885** or **NIS793**, in people with **lower-risk myelodysplastic syndrome**. However, the combination of **MBG453** with **NIS793** was not tested.

Myelodysplastic syndrome (MDS) is a group of conditions where blood cells that form 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). People with **lower-risk MDS** generally have fewer symptoms compared to those with high-risk **MDS**. The risk levels also indicate how likely it is that the disease will worsen to acute myeloid leukemia or other life-threatening complications.

The risk level of **MDS** is determined using a scale. Lower-risk **MDS** is classified as "**very low**," "**low**," or "**intermediate risk**" if less than 10% of the blood cells in the bone marrow are immature.

The following drugs are being studied to treat **MDS** and to stop **MDS** from getting worse.

MBG453, is currently being studied for treating **MDS**. It works by blocking a protein called TIM-3 present on the surface of some white blood cells and cancer cells. This process may activate the immune system and reduce the growth of cancer cells.

ACZ885 is currently approved for other indications and is also being studied for treating **MDS**. It targets and blocks a protein called interleukin-1β (IL-1β), which plays a role in cancer growth.

NIS793, also being studied for treating **MDS,** is a drug created to block a protein called transforming growth factor beta (TGF-β), which is involved in various processes that help tumors grow.

Trial drug
MBG453, also called **sabatolimab**
Pronounced as
saba-To-li-mab

ACZ885, also called **canakinumab**
Pronounced as
kana-KI-nu-mab

NIS793, also called **nisevokitug**
Pronounced as
nee-say-voh-ki-tug

In this trial researchers used a recommended dose of **MBG453**, **ACZ885**, and **NIS793** that had been found previously. A recommended dose is the best dose found to be beneficial while minimizing the risk of medical problems for participants.

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

- Were the recommended doses of **MBG453**, **ACZ885**, and **NIS793** alone, and **MBG453** in combination with **ACZ885**, confirmed for participants with lower-risk MDS?
- 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 June 2021 and ended in April 2024. It was planned that participants would continue treatment until their **MDS** got worse or until the occurrence of any unacceptable adverse event. However, the longest period participants stayed in this trial was 1 year and 10 months.

The trial was designed to have 2 parts:

- In **Part 1**, participants received fixed doses of **MBG453**, **ACZ885**, or **NIS793** alone, or received **MBG453** in combination with **ACZ885**.
- **Part 2** was planned to further study the drugs alone or the selected combination of drugs in a larger group of participants. However, **Part 2** did not start because the trial ended earlier than planned due to business decisions.

When the trial ended, researchers created a report of the trial results. This summary is based on that report.

Who was in this trial?

33 participants with **MDS** received treatment in this trial – 22 men and 11 women. Participants' ages ranged from 35 to 85 years. Their average age was 70 years. The number of participants by race is shown below.

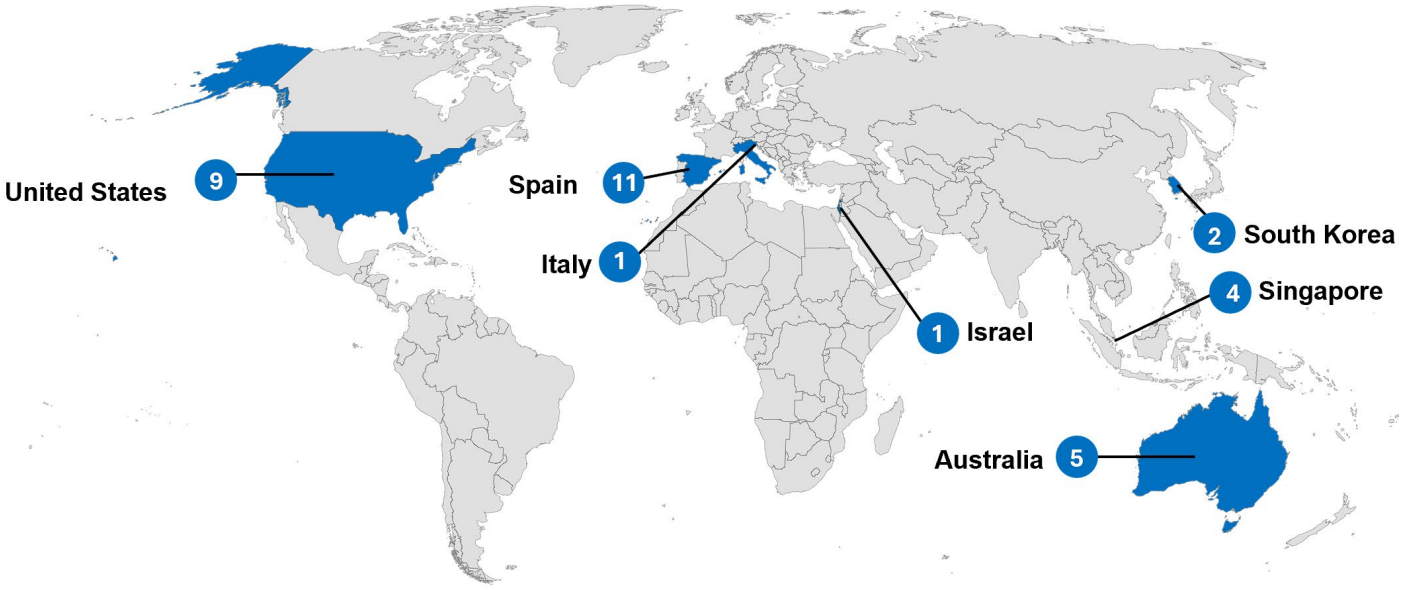
Race

6	Asian
27	White

The participants could take part in this trial if they:

- were at least 18 years of age
- were diagnosed with **very low, low,** or **intermediate-risk MDS** and had low counts of red blood cells, neutrophils (a type of white blood cell), and/or platelets
- did not improve with standard treatments, like lenalidomide, or could not take the standard treatments

33 participants from 7 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**:

MBG453: Participants received 800 milligrams (mg) of **MBG453** once every 4 weeks as an infusion into a vein.

ACZ885: Participants received 250 mg of **ACZ885** once every 4 weeks as an injection under the skin.

NIS793: Participants received 1400 mg of **NIS793** once every 3 weeks as an infusion into a vein.

What is a cycle?

A cycle is a treatment period that is repeated. In this trial, a **cycle** was a 3-week or 4-week period during which participants received trial treatments. A cycle could be repeated as long as the disease did not grow or spread further and the trial doctor approved of the participant's continuation in the trial.

All participants received **MBG453**, **ACZ885**, or **NIS793** alone, or received **MBG453** in combination with **ACZ885**, during the trial. The participants, researchers, and trial staff knew what treatment the participants were receiving.

What happened during this trial?

Before treatment

Up to 1 month

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

During treatment

Up to 1 year and 5 months

Participants received **MBG453**, **ACZ885**, or **NIS793** alone, or received **MBG453** in combination with **ACZ885**, during the trial. Participants were assigned to the following groups:

Group	Treatment
Group 1 17 participants	**MBG453** 800 mg every 4 weeks
Group 2 6 participants	**ACZ885** 250 mg every 4 weeks
Group 3 8 participants	**NIS793** 1400 mg every 3 weeks
Group 4 2 participants	**MBG453** + **ACZ885** 800 mg + 250 mg every 4 weeks

After treatment

Up to 5 months

After the last dose of a participant's trial treatment, trial staff checked their general health and monitored for any medical problems for:

- about 4 months for **Group 2** participants
- 5 months for **Group 1**, **Group 3**, and **Group 4** participants

What were the main results of this trial?

Were the recommended doses of MBG453, ACZ885, and NIS793 alone, and MBG453 in combination with ACZ885, confirmed for participants with lower-risk MDS?

Researchers confirmed the following doses of **MBG453**, **ACZ885**, and **NIS793** alone, and **MBG453** in combination with **ACZ885**, for participants with **lower-risk MDS**:

- **MBG453**: 800 mg every 4 weeks
- **ACZ885**: 250 mg every 4 weeks
- **NIS793**: 1400 mg every 3 weeks

To learn about this, researchers closely monitored the participants' health and recorded the number of participants who had**:**

- any **dose-limiting toxicities** (**DLTs**) during their first 2 treatment cycles
- to have their dose of the trial drug lowered or paused during treatment

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

The table below shows the number of participants who had DLTs and the number of participants who had to receive a lowered dose of the trial drug during treatment.

	Group 1 MBG453	Group 2 ACZ885	Group 3 NIS793	Group 4 MBG453 + ACZ885
DLT	1 of 17 6%	0 of 6	1 of 6 17%	0 of 1
Lowered dose	1 of 17 6%	1 of 6 17%	3 of 8 38%	0 of 2

Note: The number of participants included in the DLT results differed from the total number of participants. Researchers only included participants who had available results during the first 2 treatment cycles.

No participant had their treatment paused during the trial.

Out of 33 participants who received their assigned treatment, 31 were included in the analysis for DLTs. The observed DLTs were:

- **Chest discomfort** in 1 out of 17 participants in **Group 1**
- **A reaction at the infusion site** in 1 out of 6 participants in **Group 3**

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:

- 4 months after the last treatment for **Group 2** participants
- 5 months after the last treatment for **Group 1**, **Group 3**, and **Group 4** participants

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.

- Almost all the participants (32 of 33) had adverse events.
- 8 participants had adverse events that were considered serious.
- No participant died.
- 1 participant left the trial due to an adverse event.
- Researchers concluded there were no new safety concerns for **MBG453**, **ACZ885** or **NIS793** in this trial.

How many participants had adverse events?

	Group 1 MBG453 17 participants	Group 2 ACZ885 6 participants	Group 3 NIS793 8 participants	Group 4 MBG453 + ACZ885 2 participants
Had at least 1 **serious adverse event**	3 of 17 18%	3 of 6 50%	1 of 8 13%	1 of 2 50%
Had at least 1 **other** (not including serious) **adverse event**	16 of 17 94%	6 of 6 100%	8 of 8 100%	1 of 2 50%
Left the trial due to an adverse event	1 of 17 6%	0	0	0

What serious adverse events did the participants have?

8 participants had serious adverse events. None of the participants died during the trial.

The table below shows the serious adverse events that happened during this trial.

	Group 1 MBG453 17 participants	Group 2 ACZ885 6 participants	Group 3 NIS793 8 participants	Group 4 MBG453 + ACZ885 2 participants
Low red blood cell count Anemia	0	2 of 6 33%	0	0
Constipation	1 of 17 6%	0	0	0

	Group 1 MBG453 17 participants	Group 2 ACZ885 6 participants	Group 3 NIS793 8 participants	Group 4 MBG453 + ACZ885 2 participants
Bleeding from stomach or intestines Gastrointestinal hemorrhage	0	0	1 of 8 13%	0
Chest pain	1 of 17 6%	0	0	0
A bacterial skin infection Cellulitis	1 of 17 6%	0	0	0
Lung infection Pneumonia	1 of 17 6%	0	0	1 of 2 50%
Bleeding under the skull Subdural hematoma	1 of 17 6%	0	0	0
Shortness of breath Dyspnoea	0	1 of 6 17%	0	0

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

32 participants had other adverse events. The table below shows the 5 most common other adverse events:

	Group 1 MBG453 17 participants	Group 2 ACZ885 6 participants	Group 3 NIS793 8 participants	Group 4 MBG453 + ACZ885 2 participants
Low red blood cell count Anemia	4 of 17 24%	4 of 6 67%	2 of 8 25%	1 of 2 50%
Feeling tired Fatigue	3 of 17 18%	0	1 of 8 13%	1 of 2 50%
Rapid, strong, or irregular heartbeat Palpitations	1 of 17 6%	0	0	1 of 2 50%
Inflammation of the eyelids Blepharitis	0	0	0	1 of 2 50%
Vitamin B deficiency Folate deficiency	0	0	1 of 8 13%	1 of 2 50%

What was learned from this trial?

Researchers confirmed the recommended doses of **MBG453**, **ACZ885**, and **NIS793** alone, and the combination of **MBG453** with **ACZ885**, in people with lower-risk **myelodysplastic syndrome**.

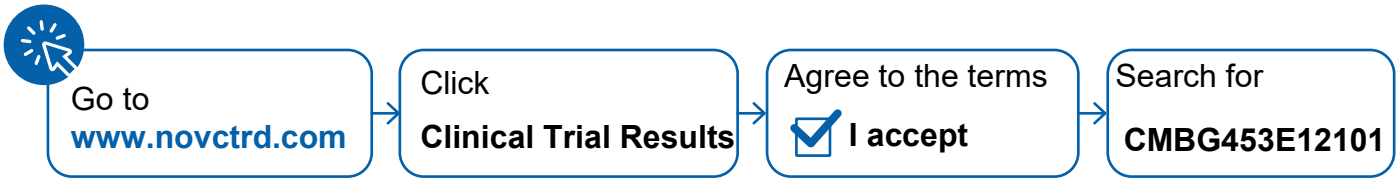
- The researchers concluded there were no new safety concerns for **MBG453**, **ACZ885** or **NIS793** in this trial.
- This trial ended earlier than planned due to business reasons.

When this summary was written, Novartis had no plans for future studies with **MBG453**, **ACZ885**, and **NIS793** in people with **lower-risk myelodysplastic syndrome**.

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 this website:

- clinicaltrials.gov – search using the number **NCT04810611**

Other trials of **MBG453**, **ACZ885**, and **NIS793** may appear on the public website above. When there, search for **MBG453** or sabatolimab, **NIS793** or nisevokitug, or **ACZ885** or canakinumab.

Full clinical trial title: A Phase Ib, multicenter, open-label platform study of select drug combinations in adult patients with lower risk (very low, low, or intermediate risk) myelodysplastic syndrome

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