NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the safety of VOB560 with MIK665 in people with certain blood cancers

Thank you!

Thank you to the participants who took part in the clinical trial for certain **blood cancers**: **non-Hodgkin lymphoma (NHL)**; **multiple myeloma (MM)** and **acute myeloid leukemia (AML)**. Every participant helped the researchers learn more about the trial drugs **VOB560** with **MIK665**.

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: CVOB560A12101

Novartis drug studied: VOB560 and **MIK665**

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 safety of **VOB560** with **MIK665** in people with certain **relapsed** or **refractory blood cancers**. Cancer that came back after treatment is called relapsed. If the cancer cells did not shrink or stop growing after treatment, it is called refractory.

The **blood cancers** studied in this trial were:

- **Non-Hodgkin lymphoma (NHL). NHL** is a blood cancer that starts in a type of white blood cell called lymphocytes. White blood cells are immune cells that help the body to fight infections. In **NHL**, the lymphocytes grow abnormally and can form tumors throughout the body.
- **Acute myeloid leukemia (AML). AML** is a cancer of the blood and bone marrow. Bone marrow is where new healthy blood cells are produced. **AML** starts in the bone marrow and prevents the production of healthy blood cells. These cancer cells can enter the bloodstream and spread to different parts of the body.
- **Multiple myeloma (MM). MM** is a blood cancer that affects plasma cells in the bone marrow. Plasma cells are a type of white blood cells. When plasma cells become cancerous, they do not function properly.

Researchers were trying to look for a treatment that could help participants with **relapsed** or **refractory blood cancers**.

Sometimes, more than one drug may be used for treating **relapsed** or **refractory blood cancers**. In this trial, researchers were trying to look at the safety of combination of two drugs **VOB560** and **MIK665**.

VOB560 and **MIK665** are drugs that each block a different protein. These proteins help cancer cells to survive. **VOB560** targets a protein called BCL2, and **MIK665** targets a protein called MCL1. Researchers believe that blocking these proteins may kill the cancer cells and help treat certain types of **blood cancer**.

This trial was the first time that **VOB560** with **MIK665** was given to people. Therefore, the researchers had to test increasing doses of **VOB560** with **MIK665** in different groups of participants to find the best doses for further trial.

The researchers also needed to carefully check all the medical problems that happened during the trial and identify any that could cause changes in dosing. This is what researchers call a dose escalation trial, which is the first step in testing a trial drug.

However, the trial stopped early, and the best doses could not be found.

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

- What were the best doses of **VOB560** with **MIK665** for participants to receive?
- 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 July 2024. The participants were in the trial for about 2 and a half years.

This trial was done in 2 parts:

- **Part 1:** A small number of participants were given increasing doses of **VOB560** with **MIK665** to help researchers find the best doses to use in Part 2.
- **Part 2:** Researchers planned to give the best doses of **VOB560** with **MIK665** identified in Part 1 to more participants in order to learn about the effects of **VOB560** with **MIK665** on certain **blood cancers**.

However, in April 2023, Novartis decided to stop the trial early due to business reasons. The decision was not due to any safety concerns. Part 2 did not start and some parts of Part 1 were also stopped early. Hence, the best doses could not be found.

Who was in this trial?

37 participants with **AML**, **NHL**, and **MM** received treatment in this trial – 21 men and 16 women. Participants' ages ranged from 25 to 88 years. Their average age was 60 years.

The number of participants by race is shown below.

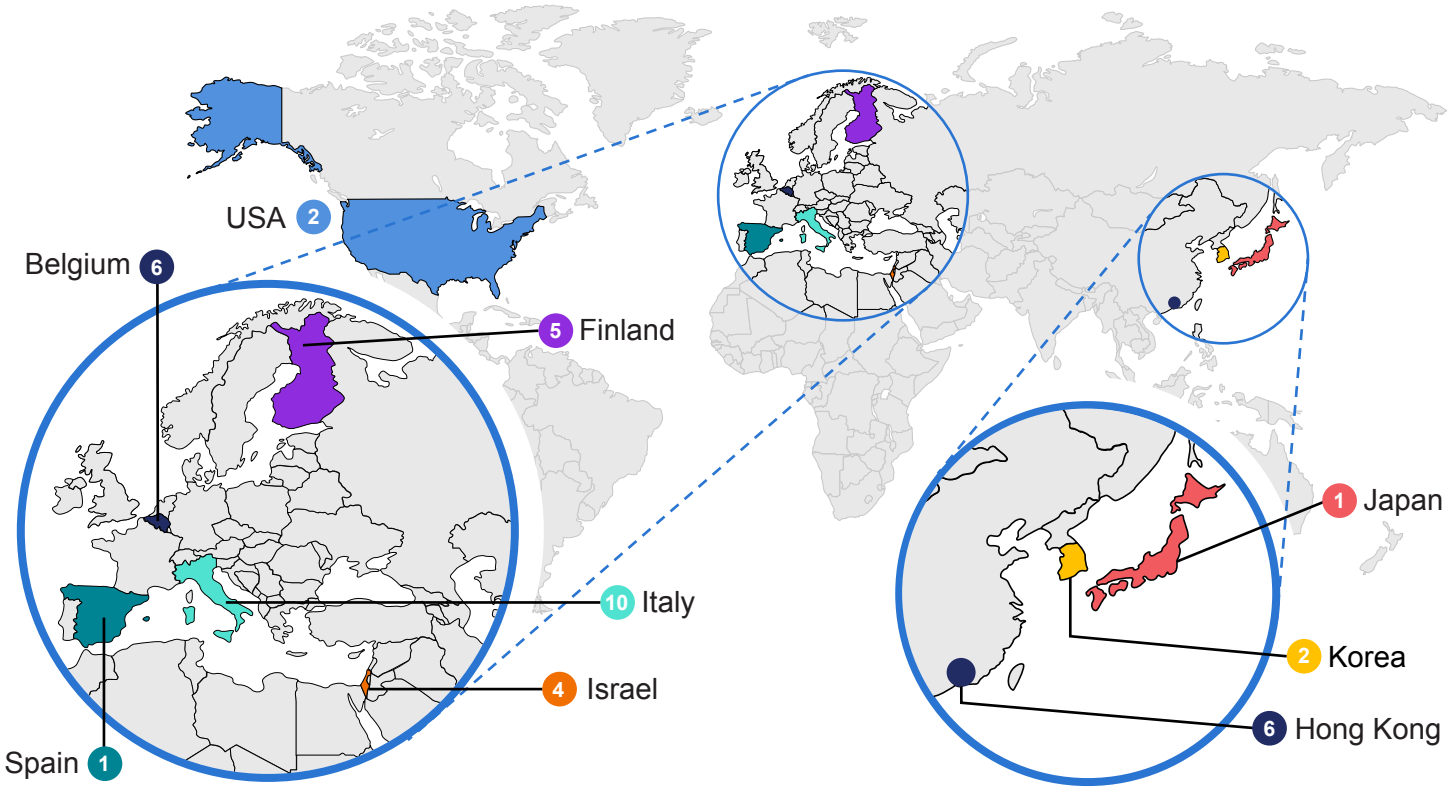
Race

28 White	9 Asian

Adult participants could take part in this trial if they:

- had **NHL**, **AML**, or **MM** that came back, did not respond to or qualify for available treatments,
- were able to walk, capable of self-care with some assistance, and could be out of bed for more than half of their waking hours, and
- were able to undergo bone marrow tests.

37 participants from 9 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:

VOB560 and **MIK665**, were given at either a dose of 25 milligrams (mg) or 50 mg, in different combinations to different groups of participants, as a drip into the vein.

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

The participants received the treatment once every week during a 3-week treatment cycle. All participants received both **VOB560** and **MIK665**, one after the other with a gap of 30 minutes between.

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

The participants could continue trial treatment as long as they were benefiting from it.

What happened during this trial?

Before treatment — 3 weeks

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

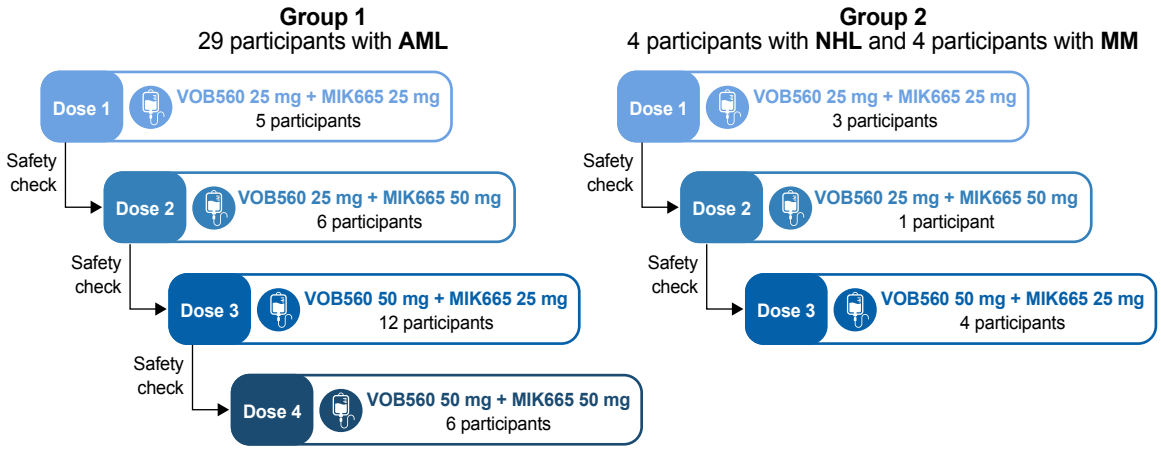
During treatment — For under 2 and a half years

37 participants received treatment.

The researchers grouped the participants based on their type of blood cancer.

- **Group 1** included 29 participants with **AML**.
- **Group 2** included 4 participants with **NHL** and 4 participants with **MM**.

Participants received 1 of the below combinations of **VOB560** with **MIK665**, once every week during each 3-week treatment cycle:



Participants in the Dose 1 group received the lowest doses of **VOB560** and **MIK665**. After participants completed 1 treatment cycle and safety checks, the next group of participants received the next dose level. Changes in dose continued until researchers found the best doses for participants to receive.

However, as this trial ended early, only 4 dose combinations were tested in **Group 1** and 3 dose combinations in **Group 2**.

After treatment — 1 month

Trial staff checked participants' general health and for any medical problems for up to 1 month after participants' last dose of trial treatment.

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

What were the main results of this trial?

What were the best doses of VOB560 with MIK665 for participants to receive?

As the trial stopped earlier than planned, the researchers could not find the best doses for **VOB560** with **MIK665** for participants to receive.

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 treatment cycle
- to have their dose of the trial drug lowered or paused during treatment

The tables below show the number of participants who had DLTs and the number of participants who had to pause or reduce their dose of trial drugs during the treatment period.

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

DLTs

In **Group 1**, results were available for 26 out of the 29 participants. This is because not all required tests were performed for 3 participants. The researchers observed that 5 out of 26 participants (19%) had DLTs.

The table below shows how many participants had DLTs in **Group 1**.

VOB560 with MIK665

	25 mg + 25 mg 4 participants	25 mg + 50 mg 6 participants	50 mg + 25 mg 11 participants	50 mg + 50 mg 5 participants
Participants who had DLTs	1 of 4 25%	1 of 6 17%	1 of 11 9%	2 of 5 40%

The DLTs observed in **Group 1** were:

- a type of reaction to cancer treatment that can occur in people with **AML**, which can cause symptoms like fever, cough, low blood pressure, weight gain, swelling, or kidney failure (differentiation syndrome),
- decrease in the blood pumped out of the heart with each beat (ejection fraction decreased),
- muscle cramps (muscle spasms),
- inflammation of the heart muscle and protective membrane (myopericarditis),
- a condition where rapid break down of cancer cells can affect the function of the heart, kidney and muscles (tumor lysis syndrome).

In **Group 2**, researchers observed no DLTs.

Dose of the trial drug lowered or paused during treatment

The table below shows how many participants in **Group 1** had to lower or pause their dose of either **VOB560** or **MIK665**.

VOB560 with **MIK665**

Participants who	25 mg + 25 mg 5 participants	25 mg + 50 mg 6 participants	50 mg + 25 mg 12 participants	50 mg + 50 mg 6 participants
lowered their dose of **VOB560**	0 of 5 0%	0 of 6 0%	2 of 12 17%	1 of 6 17%
paused their dose of **VOB560**	1 of 5 20%	0 of 6 0%	4 of 12 33%	1 of 6 17%
lowered their dose of **MIK665**	0 of 5 0%	0 of 6 0%	0 of 12 0%	0 of 6 0%
paused their dose of **MIK665**	1 of 5 20%	0 of 6 0%	4 of 12 33%	1 of 6 17%

The table below shows how many participants in **Group 2** had to lower or pause their dose of either **VOB560** or **MIK665.**

VOB560 with **MIK665**

Participants who	25 mg + 25 mg 3 participants	25 mg + 50 mg 1 participant	50 mg + 25 mg 4 participants
lowered their dose of **VOB560**	0 of 3 0%	0 of 1 0%	0 of 4 0%
paused their dose of **VOB560**	1 of 3 33%	0 of 1 0%	1 of 4 25%
lowered their dose of **MIK665**	0 of 3 0%	0 of 1 0%	0 of 4 0%
paused their dose of **MIK665**	1 of 3 33%	0 of 1 0%	1 of 4 25%

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 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.

Group 1: 28 out of 29 participants (97%) had adverse events.

- 18 out of 29 participants had adverse events that were considered serious.
- 3 out of 29 participants left the trial due to an adverse event.
- 8 out of 29 participants died due to any cause, including participants who died from their underlying cancer.

Group 2: All participants (8 out of 8) had adverse events.

- No participants had adverse events that were considered serious.
- No participants left the trial due to an adverse event.
- No participants died.

The researchers concluded there were no new safety concerns for **VOB560** with **MIK665** in this trial.

How many participants had adverse events?

Group 1: Participants with **AML**

VOB560 with **MIK665**

	25 mg + 25 mg 5 participants	25 mg + 50 mg 6 participants	50 mg + 25 mg 12 participants	50 mg + 50 mg 6 participants
Had at least 1 **serious adverse event**	2 of 5	6 of 6	7 of 12	3 of 6
Had at least 1 **other (not including serious) adverse event**	5 of 5	6 of 6	11 of 12	5 of 6
Left the trial due to an adverse event	0 of 5	1 of 6	2 of 12	0 of 6
Died	2 of 5	3 of 6	3 of 12	0 of 6

Group 2: Participants with **NHL** or **MM**

VOB560 with **MIK665**

	25 mg + 25 mg 3 participants	25 mg + 50 mg 1 participant	50 mg + 25 mg 4 participants
Had at least 1 **serious adverse event**	0 of 3	0 of 1	0 of 4
Had at least 1 **other (not including serious) adverse event**	3 of 3	1 of 1	4 of 4
Left the trial due to an adverse event	0 of 3	0 of 1	0 of 4
Died	0 of 3	0 of 1	0 of 4

What serious adverse events did the participants have?

18 participants had serious adverse events in **Group 1**.

The table below shows the most common serious adverse events in **Group 1**.

VOB560 with **MIK665**

	25 mg + 25 mg 5 participants	25 mg + 50 mg 6 participants	50 mg + 25 mg 12 participants	50 mg + 50 mg 6 participants
COVID-19	0 of 5 0%	0 of 6 0%	3 of 12 25%	0 of 6 0%
Fever with low levels of white blood cells, called neutropenia Febrile neutropenia	0 of 5 0%	2 of 6 33%	1 of 12 8%	1 of 6 17%
Lung infection Pneumonia	0 of 5 0%	2 of 6 33%	0 of 12 0%	0 of 6 0%
A condition where rapid break down of cancer cells can affect the function of the heart, kidney and muscles Tumor lysis syndrome	0 of 5 0%	0 of 6 0%	2 of 12 17%	0 of 6 0%

In **Group 2**, no participant had a serious adverse event.

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

The table below shows the most common other adverse events in **Group 1**.

VOB560 with **MIK665**

	25 mg + 25 mg 5 participants	25 mg + 50 mg 6 participants	50 mg + 25 mg 12 participants	50 mg + 50 mg 6 participants
Possible sign of liver disease Aspartate aminotransferase increased	0 of 5 0%	2 of 6 33%	3 of 12 25%	0 of 6 0%
Diarrhea	3 of 5 60%	2 of 6 33%	3 of 12 25%	2 of 6 33%
Headache	1 of 5 20%	1 of 6 17%	4 of 12 33%	2 of 6 33%
Low levels of potassium in the blood Hypokalemia	2 of 5 40%	2 of 6 33%	4 of 12 33%	3 of 6 50%
Low levels of sodium in the blood Hyponatremia	0 of 5 0%	3 of 6 50%	0 of 12 0%	0 of 6 0%
Feeling sick Nausea	1 of 5 20%	3 of 6 50%	4 of 12 33%	2 of 6 33%
Fever Pyrexia	2 of 5 40%	4 of 6 67%	2 of 12 17%	1 of 6 17%
Vomiting	1 of 5 20%	1 of 6 17%	3 of 12 25%	1 of 6 17%

The table below shows the most common other adverse events in **Group 2**.

VOB560 with **MIK665**

	25 mg + 25 mg 3 participants	25 mg + 50 mg 1 participant	50 mg + 25 mg 4 participants
Low number of red blood cells Anemia	2 of 3 67%	0 of 1 0%	2 of 4 50%

What was learned from this trial?

Researchers learned about the safety of **VOB560** with **MIK665** in people with **relapsed** or **refractory blood cancers**, specifically **acute myeloid leukemia (AML)**; **non-Hodgkin lymphoma (NHL) and multiple myeloma (MM)**.

In April 2023, Novartis ended this trial early due to business reasons. The decision was not due to any safety concerns.

There were no new safety concerns in this trial. As the trial ended early, the researchers could not find the best dose for the combination of **VOB560** with **MIK665** for participants to receive.

When this summary was written, Novartis had no plans for future trials of **VOB560** with **MIK665** in people with **AML**, **NHL**, and **MM**.

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 **NCT04702425**

Other trials of **VOB560** and **MIK665** may appear on the public website above. When there, search for **VOB560** and **MIK665**.

Full clinical trial title: A phase Ib, multicenter study of VOB560 in combination with MIK665 in patients with relapsed/refractory non-Hodgkin lymphoma, relapsed/refractory acute myeloid leukemia, or relapsed/refractory multiple myeloma

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

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