NOVARTIS

Clinical Trial
Results Summary

A clinical trial to learn about the safety of WVT078 in people with relapsed and/or refractory multiple myeloma

Thank you!

Thank you to the participants who took part in the clinical trial for **multiple myeloma**. Every participant helped the researchers learn about the trial drug **WVT078**.

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: CWVT078A12101

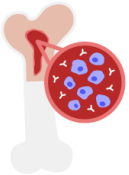
Novartis drug studied: WVT078

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 **WVT078** and how well it is tolerated alone and in combination with **WHG626** for people with **relapsed and/or refractory multiple myeloma.**



Multiple myeloma is a type of blood cancer that primarily affects plasma cells. Plasma cells are white blood cells that help the body fight infection. Cancers that come back after treatment are called **relapsed**. If the cancer did not shrink or stop growing after treatment, it is called **refractory.**

The trial drug, **WVT078,** aims to work by binding to certain proteins on the surface of both cancer cells and immune cells. This helps the immune cells find and attack the cancer cells.

WHG626 is another drug that was studied during this trial in combination with **WVT078**. It helps to keep the proteins on the surface of cancer cells, so **WVT078** can stick to them more easily.

This trial was the first time that **WVT078** was given to people alone and in combination with **WHG626**. Therefore, the researchers had to test increasing doses of **WVT078** alone and in combination with **WHG626** in different groups of participants to find the best dose for further testing.

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.

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

- What was the best dose of **WVT078** alone and in combination with **WHG626** 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 December 2019. It was planned that participants would continue the trial treatment for as long as they continued to benefit from it. However, the sponsor decided to stop the trial earlier than planned in December 2024 due to business reasons. The decision was not due to any safety concerns with **WVT078** or **WHG626**. This trial was designed to have 2 parts:

- **Part 1:** A small number of participants were given increasing doses of **WVT078** alone and in combination with **WHG626** to help researchers find the best doses to use in Part 2. Part 1 lasted about 5 years.
- **Part 2:** Researchers planned to give the best doses identified in Part 1 to more participants in order to learn about the effects of **WVT078** alone and in combination with **WHG626**. However, the trial ended early, and Part 2 was not conducted.

Who was in this trial?

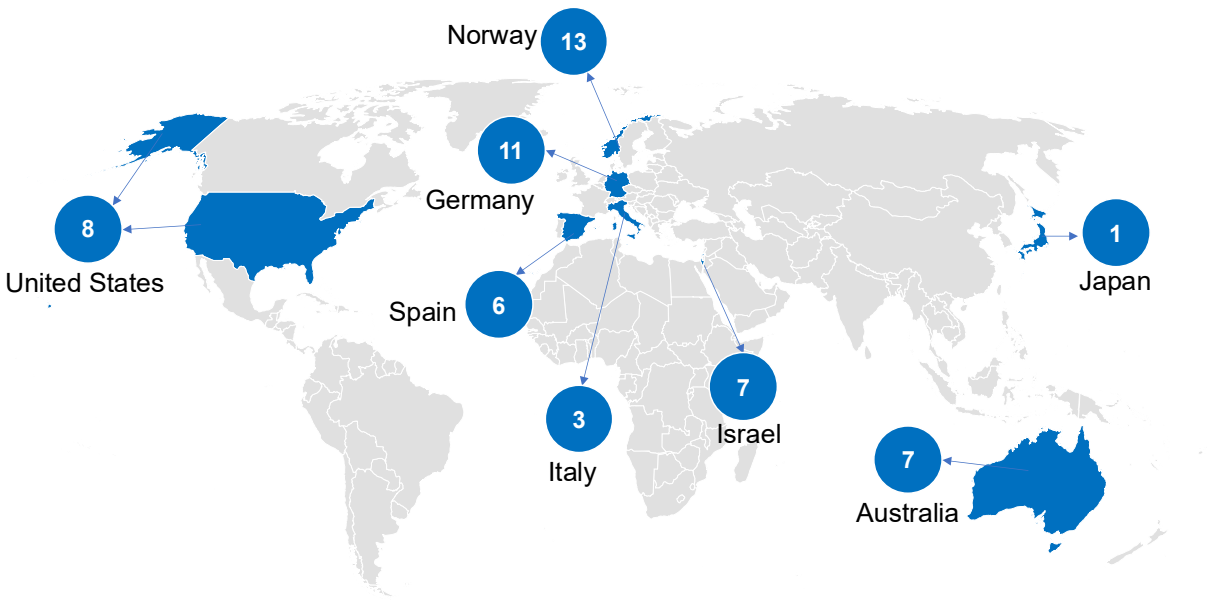
56 participants with multiple myeloma received treatment in this trial – 32 men and 24 women. The participants' ages ranged from 49 to 76 years. Their average age was 64 years.

The number of participants by race is shown below.

The participants could take part in this trial if they:

- were at least 18 years of age
- had relapsed and/or refractory multiple myeloma
- had received 2 or more standard treatments and could not receive any other available standard treatments, as confirmed by the trial doctor
- were at least able to walk and do self-care activities

56 participants from 8 countries received the 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:

WVT078: Given as an infusion into a vein, once a week, during the 28-day treatment cycle. This trial looked at **9 different doses** of **WVT078**, from 3 micrograms per kilogram of body weight (mcg/kg) to 250 mcg/kg.

WHG626: Given once daily as a capsule by mouth for the first 2 days of each week during the 28-day treatment cycle. This trial looked at 2 doses—a **low dose** (2 milligrams (mg)) and a **high dose** (4 mg)—of **WHG626**.

A **cycle** is a treatment period that is repeated. In this trial, a cycle was 28 days.

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

What happened during the trial?

Before treatment

Up to a month

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

During treatment

For as long as participants were benefiting from the treatment

Participants were divided into the following 2 groups and assigned different doses of **WVT078** and **WHG626**:

Group 1 (33 participants)									
WVT078	Dose 1 3 mcg/kg	Dose 2 6 mcg/kg	Dose 3 12 mcg/kg	Dose 4 24 mcg/kg	Dose 5 48 mcg/kg	Dose6 64 mcg/kg	Dose 7 96 mcg/kg	Dose 8 192 mcg/kg	Dose 9 250 mcg/kg
Participants	1	2	2	2	4	1	3	14	4

Group 2 (23 participants)				
WVT078 + WHG626	Dose 3 (12 mcg/kg) + Low Dose (2 mg)	Dose 4 (24 mcg/kg) + Low Dose (2 mg)	Dose 5 (48 mcg/kg) + Low Dose (2 mg)	Dose 5 (48 mcg/kg) + High Dose (4 mg)
Participants	5	4	10	4

Researchers checked the safety of each dose or combination before giving the higher dose to the next group of participants.

Changes in doses in **Group 1** and **Group 2** continued while researchers looked for the best doses for participants to receive.

After treatment

Up to 3 months

Trial staff checked participants' general health and for any medical problems, after the participants' last dose of trial treatment, for up to 3 months or until their cancer come back or they start any new cancer treatment.

What were the main results of this trial?

What was the best dose of WVT078 alone and in combination with WHG626 for participants to receive?

The trial ended earlier than planned, and the researchers could not identify the best dose of **WVT078** alone or in combination with **WHG626**.

During the trial, researchers closely monitored the participants' health and recorded the number of participants who had:

- any **dose-limiting toxicities (DLTs)** during their first treatment cycle
- their dose of the trial drug **lowered**, **paused** or **stopped** during treatment due to any reason

DLTs are medical problems that
- the trial doctors think **could be related** to the trial treatment.
- are serious enough to preventing increasing the dose.

DLTs

Results were available for 49 out of 56 participants who completed the first treatment cycle and had available results to report.

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

	Group 1								
WVT078	**Dose 1**	**Dose 2**	**Dose 3**	**Dose 4**	**Dose 5**	**Dose 6**	**Dose 7**	**Dose 8**	**Dose 9**
Total Participants	1	2	1	2	4	1	3	12	3
Participants with DLTs	0	0	0	0	0	1 of 1 100%	0	1 of 12 8%	0

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

- **Lung infection** (Pneumonia)
- **A strong immune reaction leading to widespread inflammation in the body** (Cytokine release syndrome)

The table below shows how many participants had DLTs in **Group 2**.

	Group 2			
WVT078 + WHG626	**Dose 3 + Low Dose**	**Dose 4 + Low Dose**	**Dose 5 + Low Dose**	**Dose 5 + High Dose**
Total participants	**3**	**4**	**9**	**4**
Participants with DLTs	0	1 of 4 25%	2 of 9 22%	2 of 4 50%

The **DLTs** observed in **Group 2** were:

- **A low number of white blood cells called neutrophils** (Neutropenia)
- **A serious complication of an infection caused by a bacterium** (Pneumococcal sepsis)
- **Increased blood levels of a liver enzyme called alanine aminotransferase** (Alanine aminotransferase increased)
- **Increased blood levels of a liver enzyme called aspartate aminotransferase** (Aspartate aminotransferase increased)
- **Increased blood levels of a protein called lipase** (Lipase increased)
- **Low number of platelets** (Thrombocytopenia)
- **Lung infection** (Pneumonia)
- **Pain due to tumor** (Tumor pain)

Some participants in **Group 2** have had more than one **DLT**.

Dose of the trial drug was lowered, paused or stopped during treatment

The table below shows how many participants had to have their dose of the trial drug **lowered** or **paused** due to any medical problem or **stopped** due to any reason during treatment in **Group 1**.

	Group 1								
WVT078	**Dose 1**	**Dose 2**	**Dose 3**	**Dose 4**	**Dose 5**	**Dose 6**	**Dose 7**	**Dose 8**	**Dose 9**
Total Participants	1	2	2	2	4	1	3	14	4
Had at least 1 dose of **WVT078** lowered	0	0	0	0	1 of 4 25%	1 of 1 100%	0	2 of 14 14%	2 of 4 50%
Had at least 1 dose of **WVT078** paused	0	0	0	1 of 2 50%	1 of 4 25%	0	1 of 3 33%	5 of 14 36%	3 of 4 75%
Had to stop **WVT078** due to any reason	1 of 1 100%	2 of 2 100%	2 of 2 100%	2 of 2 100%	4 of 4 100%	1 of 1 100%	3 of 3 100%	14 of 14 100%	4 of 4 100%

The table below shows how many participants had to have their dose of the trial drug **lowered** or **paused** due to any medical problem or **stopped** due to any reason during treatment in **Group 2**.

	Group 2			
WVT078 + WHG626	**Dose 3 + Low Dose**	**Dose 4 + Low Dose**	**Dose 5 + Low Dose**	**Dose 5 + High Dose**
Total participants	5	4	10	4
Had at least 1 dose of **WVT078** lowered	0	0	3 of 10 30%	2 of 4 50%
Had at least 1 dose of **WVT078** paused	1 of 5 20%	0	5 of 10 50%	4 of 4 100%
Had at least 1 dose of **WHG626** lowered	0	0	1 of 10 10%	4 of 4 100%
Had at least 1 dose of **WHG626** paused	2 of 5 40%	1 of 4 25%	6 of 10 60%	4 of 4 100%
Had to stop **WVT078** or **WHG626** due to any reason	5 of 5 100%	4 of 4 100%	10 of 10 100%	4 of 4 100%

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 3 months 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: All the participants (33 of 33) had adverse events.

- 19 participants had adverse events that were considered serious.
- 2 participants left the trial due to an adverse event.
- 3 participants died.

Group 2: All the participants (23 of 23) had adverse events.

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

The researchers concluded there were no unexpected safety concerns for **WVT078** alone or in combination with **WHG626** in this trial.

How many participants had adverse events?

	Group 1								
WVT078	**Dose 1**	**Dose 2**	**Dose 3**	**Dose 4**	**Dose 5**	**Dose 6**	**Dose 7**	**Dose 8**	**Dose 9**
Total participants	1	2	2	2	4	1	3	14	4
Had at least 1 **serious adverse event**	0	0	2 of 2 100%	2 of 2 100%	0	1 of 1 100%	0	10 of 14 71%	4 of 4 100%
Left the trial due to an adverse event	0	0	0	0	0	0	0	1 of 14 7%	1 of 4 25%
Died due to any cause	0	0	0	0	0	0	0	3 of 14 21%	0

	Group 2			
WVT078 + WHG626	**Dose 3 + Low Dose**	**Dose 4 + Low Dose**	**Dose 5 + Low Dose**	**Dose 5 + High Dose**
Total participants	5	4	10	4
Had at least 1 **serious adverse event**	2 of 5 40%	4 of 4 100%	7 of 10 70%	4 of 4 100%
Left the trial due to an adverse event	0	0	2 of 10 20%	0
Died due to any cause	3 of 5 60%	2 of 4 50%	1 of 10 10%	0

What serious adverse events did the participants have?

The table below shows the most common serious adverse events that happened during the trial. Additional serious adverse events happened in fewer participants.

	Group 1								
WVT078	**Dose 1**	**Dose 2**	**Dose 3**	**Dose 4**	**Dose 5**	**Dose 6**	**Dose 7**	**Dose 8**	**Dose 9**
Total participants	1	2	2	2	4	1	3	14	4
A strong immune reaction leading to widespread inflammation in the body Cytokine release syndrome	0	0	0	1 of 2 50%	0	0	0	3 of 14 21%	1 of 4 25%
An irregular and unusually fast heart rate Atrial fibrillation	0	0	1 of 2 50%	0	0	0	0	0	1 of 4 25%
Fever while having a low number of white blood cells Febrile neutropenia	0	0	0	0	0	0	0	1 of 14 7%	1 of 4 25%
Lung infection Pneumonia	0	0	0	0	0	1 of 1 100%	0	0	1 of 4 25%
Lung infection caused by a specific fungus Pneumocystis jirovecii pneumonia	0	0	0	0	0	0	0	1 of 14 7%	1 of 4 25%
Sudden kidney damage Acute kidney injury	0	0	0	0	0	0	0	1 of 14 7%	1 of 4 25%

WVT078 + WHG626	Group 2			
	Dose 3 + Low Dose	Dose 4 + Low Dose	Dose 5 + Low Dose	Dose 5 + High Dose
Total participants	5	4	10	4
A strong immune reaction leading to widespread inflammation in the body Cytokine release syndrome	0	1 of 4 25%	3 of 10 30%	1 of 4 25%
Lung infection Pneumonia	0	3 of 4 75%	1 of 10 10%	0
Infusion-related reaction	1 of 5 20%	2 of 4 50%	0	0

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

The table below shows the most common other (not including serious) adverse events. Additional other adverse events happened in fewer participants.

	Group 1								
WVT078	**Dose 1**	**Dose 2**	**Dose 3**	**Dose 4**	**Dose 5**	**Dose 6**	**Dose 7**	**Dose 8**	**Dose 9**
Total participants	1	2	2	2	4	1	3	14	4
A strong immune reaction leading to widespread inflammation in the body Cytokine release syndrome	0	0	0	1 of 2 50%	4 of 4 100%	1 of 1 100%	1 of 3 33%	10 of 14 71%	3 of 4 75%
Fever Pyrexia	0	0	1 of 2 50%	2 of 2 100%	1 of 4 25%	1 of 1 100%	2 of 3 67%	8 of 14 57%	3 of 4 75%
Low number of red blood cells Anaemia	0	0	2 of 2 100%	0	1 of 4 25%	1 of 1 100%	1 of 3 33%	8 of 14 57%	2 of 4 50%
Low number of platelets Thrombocytopenia	0	0	1 of 2 50%	0	1 of 4 25%	1 of 1 100%	1 of 3 33%	7 of 14 50%	2 of 4 50%
Low number of neutrophils Neutropenia	0	0	0	1 of 2 50%	1 of 4 25%	0	0	6 of 14 43%	4 of 4 100%
Increased blood levels of a liver enzyme called aspartate aminotransferase Aspartate aminotransferase increased	0	0	0	0	1 of 4 25%	1 of 1 100%	1 of 3 33%	6 of 14 43%	3 of 4 75%

WVT078 + WHG626	Group 2			
	Dose 3 + Low Dose	Dose 4 + Low Dose	Dose 5 + Low Dose	Dose 5 + High Dose
Total Participants	5	4	10	4
A strong immune reaction leading to widespread inflammation in the body Cytokine release syndrome	2 of 5 40%	1 of 4 25%	5 of 10 50%	4 of 4 100%
Low number of neutrophils Neutropenia	1 of 5 20%	1 of 4 25%	7 of 10 70%	3 of 4 75%
Low number of platelets Thrombocytopenia	2 of 5 40%	3 of 4 75%	4 of 10 40%	3 of 4 75%
Fever Pyrexia	2 of 5 40%	1 of 4 25%	6 of 10 60%	2 of 4 50%
Low number of red blood cells Anaemia	3 of 5 60%	2 of 4 50%	3 of 10 30%	2 of 4 50%

What was learned from this trial?

Researchers learned about the safety and tolerability of **WVT078** alone and in combination with **WHG626** in people with refractory and/or relapsed multiple myeloma.

- This trial ended earlier than planned due to business reasons, and the researchers could not identify the best dose of **WVT078** alone or in combination with **WHG626**.
- The researchers concluded that there were no unexpected safety concerns for **WVT078** or **WHG626** in this trial.

When this summary was written, the sponsor had no plans for future trials of **WVT078** in people with refractory and/or relapsed multiple myeloma.

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:

Go to **www.novctrd.com** → Click **Clinical Trial Results** → Agree to the terms ☑ **I agree** → Search by study ID **CWVT078A12101**

For more information about this trial, go to any of the following websites:

- www.clinicaltrials.gov– search using the number **NCT04123418**
- clinicaltrialsregister.eu/ctr-search/search - search using the number **2019-001743-48**

Other trials of **WVT078** may appear on the public websites above. When there, search for **WVT078** or **WHG626**.

Full clinical trial title: A phase I, open-label, multicenter, study of WVT078 in subjects with relapsed and/or refractory multiple myeloma

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