NOVARTIS

## Clinical Trial Results Summary

# A clinical trial to learn more about the effects of VPM087 in combination with standard treatment in people with metastatic cancer

# Thank you!

Thank you to the participants who took part in the clinical trial for **metastatic colorectal**, **gastroesophageal**, **and renal cancer**. Every participant helped the researchers learn more about the trial drug **VPM087**, also called **gevokizumab**.

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:** CVPM087A2101

**Novartis drug studied:** **VPM087**, also called **gevokizumab**

**Sponsor:** Novartis

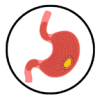
If you were a participant and have any questions about the results, please talk to the doctor or staff at the trial site.

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 effects of **VPM087** when given with **standard anti-cancer treatment** for people with **metastatic cancer**. **Metastatic** means the cancer has spread to other parts of the body from where it started. In this trial, people with the following types of **metastatic cancer** were included:

**Metastatic colorectal cancer** (**mCRC**): **mCRC** is a cancer that starts in the colon or rectum.



**Metastatic gastroesophageal cancer** (**mGEC**): **mGEC** is a cancer that starts in the stomach, esophagus (tube that connects the throat and stomach), or in the area where the stomach and esophagus meet.

**Metastatic renal cell carcinoma** (**mRCC**): **mRCC** is a cancer that starts in the kidneys.

**VPM087,** also called **gevokizumab**, is a trial drug created to block a protein called interlukin-1 beta (IL-1β). This is a protein involved in inflammation in the body which can cause the growth and spread of cancer cells. **VMP087** is expected to reduce the inflammation, therefore helping in treating cancer.

**Trial drug**
**VPM087** also called **gevokizumab**
**Pronounced as**
je-vo-KIZ-oo-mab

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

- What was the change in inflammation levels in the body after the first dose of **VPM087**?
- What was the best dose of **VPM087** for the participants to receive along with the **standard anti-cancer treatment**?
- For how long were participants alive without their cancer getting worse after starting treatment?
- What medical problems, also called adverse events, happened during this trial?

  **Adverse events** reported are any sign or symptom that participants had during this trial. Adverse events **may** or **may not** be caused by treatments in the trial.

# How long was this trial?

The trial began in May 2019 and ended in February 2025. The participants could take part in the trial for as long as they were benefiting from the treatment. The participants started the trial on different dates.

This trial was designed to have 3 parts:

- **Part 1a** (**up to 2 weeks**): Participants with **mCRC** were given different doses of **VPM087** only, to find the dose that could lower inflammation in the body the most.
- **Part 1b** (**up to 6 weeks**): Participants with **mCRC**, **mGEC**, and **mRCC** were given different doses of **VPM087** along with their **standard anti-cancer treatment** to help researchers find the best dose to be used in **part 2**.
- **Part 2** (**as long as participants were benefiting from the treatment**): Participants with **mCRC** and **mGEC** were given the best identified dose of **VPM087** along with their **standard anti-cancer treatment** to learn more about the effects of **VPM087**.

At the end of this trial, Novartis created a report of the trial results. This summary is based on that report.

# Who was in this trial?

166 participants with **metastatic cancer** received treatment in this trial. Participants were grouped as follows based on their cancer type and prior treatment:

- **Group A**: mCRC with no prior anti-cancer treatment
- **Group B**: mCRC with one prior anti-cancer treatment
- **Group C**: mGEC with one prior anti-cancer treatment
- **Group D**: mRCC with one or two prior anti-cancer treatments

The table below shows the number of participants by sex and age:

| | Group A | Group B | Group C | Group D |
|---|---|---|---|---|
| **Male** | 41 | 35 | 20 | 6 |
| **Female** | 30 | 27 | 6 | 1 |
| **Age range** | 27-81 years | 23-78 years | 25-81 years | 53-88 years |
| **Average age** | 58 years | 59 years | 60 years | 74 years |

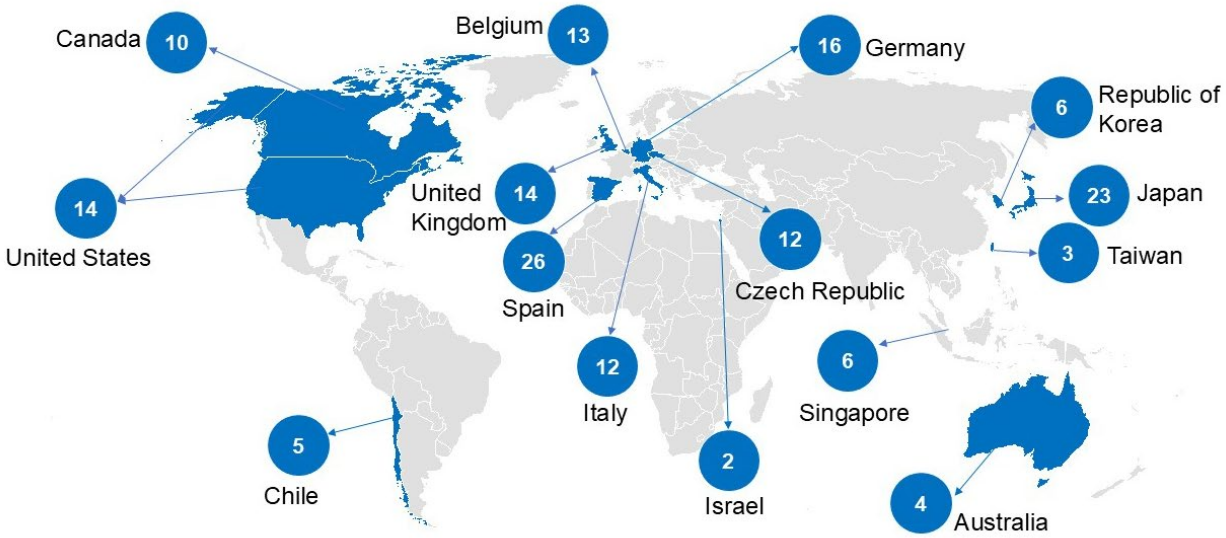
The table below shows the number of participants by race:

| Race | Group A | Group B | Group C | Group D |
|---|---|---|---|---|
| **Asian** | 17 | 18 | 3 | 6 |
| **Black or African American** | 1 | 1 | 0 | 0 |
| **Native Hawaiian or Other Pacific Islander** | 2 | 0 | 0 | 0 |
| **White** | 51 | 43 | 23 | 1 |

The participants could take part in this trial if they:

- were more than 18 years of age
- had any of the following:
  - **mCRC** with no prior anti-cancer treatment
  - **mCRC** or **mGEC** with one prior anti-cancer treatment
  - **mRCC** with one or two prior anti-cancer treatments
- were either fully active or at least able to do light activities

166 participants from 15 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 **28-day cycles**. A cycle is a treatment period that is repeated.

The treatments in this trial were:

**VPM087**: Participants received **VPM087** as a drip into a vein on the first day of each cycle. This trial looked at 3 different doses of **VPM087**:

- **30 mg**
- **60 mg**
- **120 mg**

Researchers used a computer to randomly assign participants to one of the 3 doses of **VPM087**.

**Standard anti-cancer treatment**: Participants received one or more of the following approved anti-cancer treatments based on their cancer. These treatments were given according to their locally approved treatment schedule.

- **Bevacizumab**
- **Modified FOLFOX6** (fluorouracil, folinic acid, and oxaliplatin)
- **FOLFIRI** (fluorouracil, folinic acid, and irinotecan)
- **Ramucirumab**
- **Paclitaxel**
- **Cabozantinib**

The participants, researchers, and trial staff knew that all participants received **VPM087**.

# 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

As long as participants were benefiting from the treatment

The trial had 3 parts:

**Part 1a (up to 2 weeks)**

39 participants from **group A** and 26 participants from **group B** were divided equally to receive either **30 mg**, **60 mg** or **120 mg** dose of **VPM087** only.
1 participant in **group B** stopped treatment after **part 1a** and did not continue into **part 1b**.

**Part 1b (up to 6 weeks)**

39 participants from **group A** and 25 participants from **group B** continued with the same **VPM087** doses as previously assigned in **part 1a**.
Additionally, 6 participants in **group C** and 7 participants in **group D** were enrolled and received only **120 mg** dose of **VPM087**.
All the participants also received their **standard anti-cancer treatment**.

Researchers identified **120 mg** as the best dose of **VPM087**, during **part 1b**.

**Part 2 (as long as participants were benefiting from the treatment)**

All participants in **groups A**, **B**, and **C** received the **120 mg** dose of **VPM087** along with the **standard anti-cancer treatment**.

Some more participants were also enrolled in each group within **part 2** of the study as an expansion.

## After treatment

Up to 3 months

Trial staff checked participants' general health and for any medical problems for up to 3 months 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 was the change in inflammation levels in the body after the first dose of VPM087?

Researchers found the change in inflammation levels was similar across different doses of **VPM087**.

To answer this question, researchers checked the levels of **C-reactive protein** in the blood of **mCRC** participants before and after 2 weeks of receiving **VPM087** only during **part 1a** of the trial.

Researchers calculated the change in **C-reactive protein levels**. The table below shows the results for **group A** and **group B** combined at different doses.

**C-reactive protein** levels increase in the blood in response to any inflammation or injury in the body.

**Change in C-reactive protein levels at different doses of VPM087**

| | 30 mg<br>22 participants | 60 mg<br>22 participants | 120 mg<br>21 participants |
|---|---|---|---|
| **Change in C-reactive protein levels** | 0.3 ⇧<br>(Slight increase) | -0.1 ⇩<br>(Slight decrease) | 0.0<br>(No Change) |

Changes in C-reactive protein levels were similar across the doses.

## What was the best dose of VPM087 for the participants to receive along with the standard anti-cancer treatment?

Researchers found the **120 mg** dose of **VPM087** as the best dose for the participants to receive when given along with the **standard anti-cancer treatment**.

To answer this question, researchers closely monitored the participants' health and recorded the number of participants who had **dose-limiting toxicities** (**DLTs**) during **part 1b** of the trial.

In this trial, researchers monitored DLTs during the first 6 weeks of treatment for **group A** and **group B** and during the first 4 weeks of treatment for **group C** and **group D**.

**DLTs** are medical problems that:

- the trial doctors think could be related to the trial treatment
- lead to a pause in, or lowering of the dose of treatment

No DLTs were observed in participants in **group A** and **group B**.

**1 of 6** participants (**17%**) in **group C** had a DLT of **decreased number of neutrophils**, **a type of white blood cell** (neutrophil count decreased).

**1 of 7** participants (**14%**) in **group D** had a DLT of **low blood sodium levels** (hyponatraemia).

Based on these results and the change in C-reactive protein levels, researchers chose **120 mg** of **VPM087** as the dose to use for **part 2**.

## For how long were participants alive without their cancer getting worse after starting treatment?

Researchers found that participants lived without their cancer getting worse for up to **15 months** in **group A**, **13 months** in **group B**, and **4 months** in **group C** after starting treatment with **VPM087** along with the **standard anti-cancer treatment**.

To answer this question, researchers assessed participants' cancers using imaging scans at different time points during **parts 1b and 2** of the trial. For each participant, they recorded the period from the start of the treatment to the worsening of their cancer or death from any cause, also called **progression-free survival (PFS)**.

The tables below show the **median PFS** in months for participants after starting treatment with **VPM087** along with the **standard anti-cancer treatment**. The **median PFS** is the length of time from the start of the trial until half of the participants had their cancer get worse, which means tumors grew in size, new tumors appeared, or they died due to any cause.

| Group A | 30 mg Dose<br>13 participants | 60 mg Dose<br>13 participants | 120 mg Dose<br>45 participants |
|---|---|---|---|
| **Median PFS** | 9 months | 15 months | 11 months |

| Group B | 30 mg Dose<br>8 participants | 60 mg Dose<br>9 participants | 120 mg Dose<br>44 participants |
|---|---|---|---|
| **Median PFS** | 7 months | 13 months | 7 months |

| Group C | 120 mg Dose<br>26 participants |
|---|---|
| **Median PFS** | 4 months |

# 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 do this even if they think the adverse events are not related to the trial treatments.

Researchers need results from many trials to decide if a drug or treatment causes an adverse event.

This section is a summary of the adverse events that happened from the day participants started the trial treatment until 3 months after the 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, requires hospital care, or results in death

Treatments in the trial **may** or **may not** cause adverse events.

All the participants (166 of 166) had adverse events, including serious and other (not including serious) adverse events.

- Adverse events that were considered **serious** were reported in:
  - 27 of 71 participants (38%) in **group A**,
  - 20 of 62 participants (32%) in **group B**,
  - 13 of 26 participants (50%) in **group C**, and
  - 7 of 7 participants (100%) in **group D**

- Participants who died due to any cause, including **metastatic cancer** were:
  - 51 of 71 participants (72%) in **group A**,
  - 48 of 62 participants (77%) in **group B**,
  - 21 of 26 participants (81%) in **group C**, and
  - 3 of 7 participants (43%) in **group D**

The researchers concluded there were no new or unexpected safety concerns for **VPM087** in this trial.

## What serious adverse events did the participants have?

### Group A

27 participants had serious adverse events.

The most common serious adverse events reported were:

- **Fever** (pyrexia) in 7 of 71 participants (10%)
- **Bleeding in the intestine** (lower gastrointestinal haemorrhage) in 3 of 71 participants (4%)
- **COVID-19** in 3 of 71 participants (4%)
- **Diarrhea** in 2 of 71 participants (3%)
- **Stomach pain** (Abdominal pain upper) in 2 of 71 participants (3%)

### Group B

20 participants had serious adverse events.

The most common serious adverse events reported were:

- **COVID-19** in 3 of 62 participants (5%)
- **Fever** (pyrexia) in 2 of 62 participants (3%)
- **Low fluids in the body** (dehydration) in 2 of 62 participants (3%)
- **Slowing of the intestinal movement** (ileus) in 2 of 62 participants (3%)
- **Toxicity to various agents** in 2 of 62 participants (3%)

### Group C

13 participants had serious adverse events.

The most common serious adverse event reported was:

- **Blockage in the intestine** (intestinal obstruction) in 2 of 26 participants (8%)

### Group D

All 7 participants had serious adverse events.

The most common serious adverse events reported were:

- **Low blood sodium levels** (hyponatraemia) in 2 of 7 participants (29%)
- **Lung infection** (pneumonia) in 2 of 7 participants (29%)

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

### Group A

The most common other adverse events reported were:

- **Tiredness** (fatigue) in 33 of 71 participants (46%)
- **Constipation** in 32 of 71 participants (45%)
- **Decreased ability to move and feel due to nerve damage** (peripheral sensory neuropathy) in 31 of 71 participants (44%)
- **Feeling sick** (nausea) in 28 of 71 participants (39%)
- **Low number of neutrophils, a type of white blood cells** (neutropenia) in 25 of 71 participants (35%)

### Group B

The most common other adverse events reported were:

- **Diarrhea** in 31 of 62 participants (50%)
- **Feeling sick** (nausea) in 31 of 62 participants (50%)
- **Low number of neutrophils, a type of white blood cells** (neutropenia) in 22 of 62 participants (35%)

### Group C

The most common other adverse event reported was:

- **Nosebleed** (epistaxis) in 10 of 26 participants (38%)

### Group D

The most common other adverse events reported were:

- **Abnormal liver function** (hepatic function abnormal) in 5 of 7 participants (71%)
- **Low levels of calcium in blood** (hypocalcaemia) in 5 of 7 participants (71%)
- **Low number of platelets, a type of blood cells** (platelet count decreased) in 4 of 7 participants (57%)
- **High blood pressure** (hypertension) in 4 of 7 participants (57%)
- **Presence of proteins in urine** (proteinuria) in 4 of 7 participants (57%)
- **Underactive thyroid gland** (hypothyroidism) in 4 of 7 participants (57%)
- **Rash and numbness on the palms and soles** (Palmar-plantar erythrodysaesthesia syndrome) in 3 of 7 participants (43%)

# What was learned from this trial?

Researchers learned about the effects of **VPM087** when given along with **standard anti-cancer treatment** in people with **metastatic colorectal**, **gastroesophageal**, **and renal cancer.**

The researchers concluded that:

- The change in inflammation levels was similar across different doses of **VPM087**.
- The **120 mg** dose of **VPM087** was the best dose for the participants to receive along with the **standard anti-cancer treatment**.
- The combination of **VPM087** with **standard anti-cancer treatment** did not show the expected effect on participants with **metastatic colorectal**, **gastroesophageal**, and **renal cancer**.

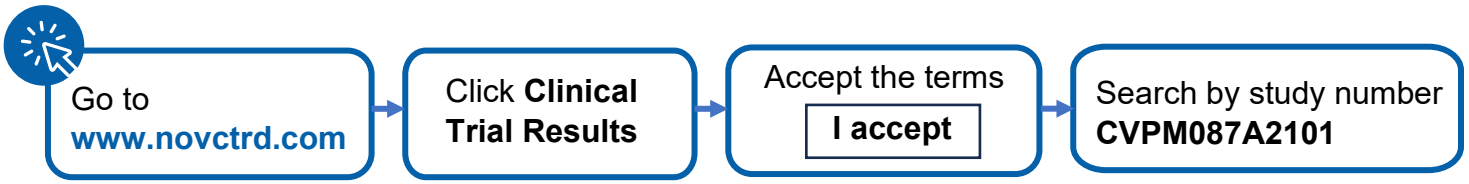
The researchers concluded there were no new or unexpected safety concerns for **VPM087** in this trial.

When this summary was written, Novartis had no plans for future trials of **VPM087** in people with **metastatic cancer**.

# Where can I learn more about this trial?

To learn more about the results and adverse events in this trial, read the scientific summary of the results. It is 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 **NCT03798626**

Other trials of **VPM087** may appear on the public websites above. When there, search for **VPM087** or **gevokizumab**.

**Full clinical trial title:** Phase Ib study of gevokizumab in combination with standard of care anti-cancer therapies in patients with metastatic colorectal cancer, gastroesophageal cancer and renal cell carcinoma.

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