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Clinical Trial Results Summary

A clinical trial to learn about the safety of PHE885 in people with multiple myeloma

Thank you!

Thank you to the participants who took part in the clinical trial for **multiple myeloma**. Every participant helped to learn more about the trial drug **PHE885**, also called **durcabtagene autoleucel**.

Novartis sponsored this trial. We believe 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: CADPT07A12101

Novartis drug studied: **PHE885**, also called **durcabtagene autoleucel**

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 **PHE885** and identify the recommended dose that can be given to people with **multiple myeloma**. This trial was the first time that **PHE885** was given to people.

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.

PHE885 is a type of treatment called chimeric antigen receptor (CAR) T-cell therapy. CAR T-cell therapy uses a person's own **T-cells** (another type of white blood cell) which are taken from the blood and modified in the laboratory to find and fight cancer cells. These are then put back into the body.

Trial drug
PHE885 also called
durcabtagene autoleucel
Pronounced as
dur-KAB-tuh-jeen
aw-to-LOO-sel

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

- What was the recommended dose of **PHE885** for participants to receive in this trial?
- 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 July 2020 and ended in April 2025. In January 2024, the trial was paused to look into a safety concern in participants with newly diagnosed multiple myeloma. In August 2024, due to business reasons, a decision was made to end the trial earlier than planned.

This trial was designed to have 2 parts:

- During **Part A**, participants received increasing doses of **PHE885** to find the recommended doses for further use.
- It was planned that **Part B** would further study the recommended doses of **PHE885**, which were determined in **Part A**. However, the trial was stopped earlier than planned before **Part B** could be completed.

Who was in this trial?

Part A: 55 participants with **multiple myeloma** received treatment in **Part A** - 28 males and 27 females. Participants' ages ranged from 43 to 81 years.

The table below shows the number of participants by race.

Race					
42	White	10	Black or African American	3	Unknown

Part B: 25 participants with **multiple myeloma** received treatment in **Part B** - 17 males and 8 females. Participants' ages ranged from 43 to 79 years.

The table below shows the number of participants by race.

Race					
19	White	5	Asian	1	Unknown

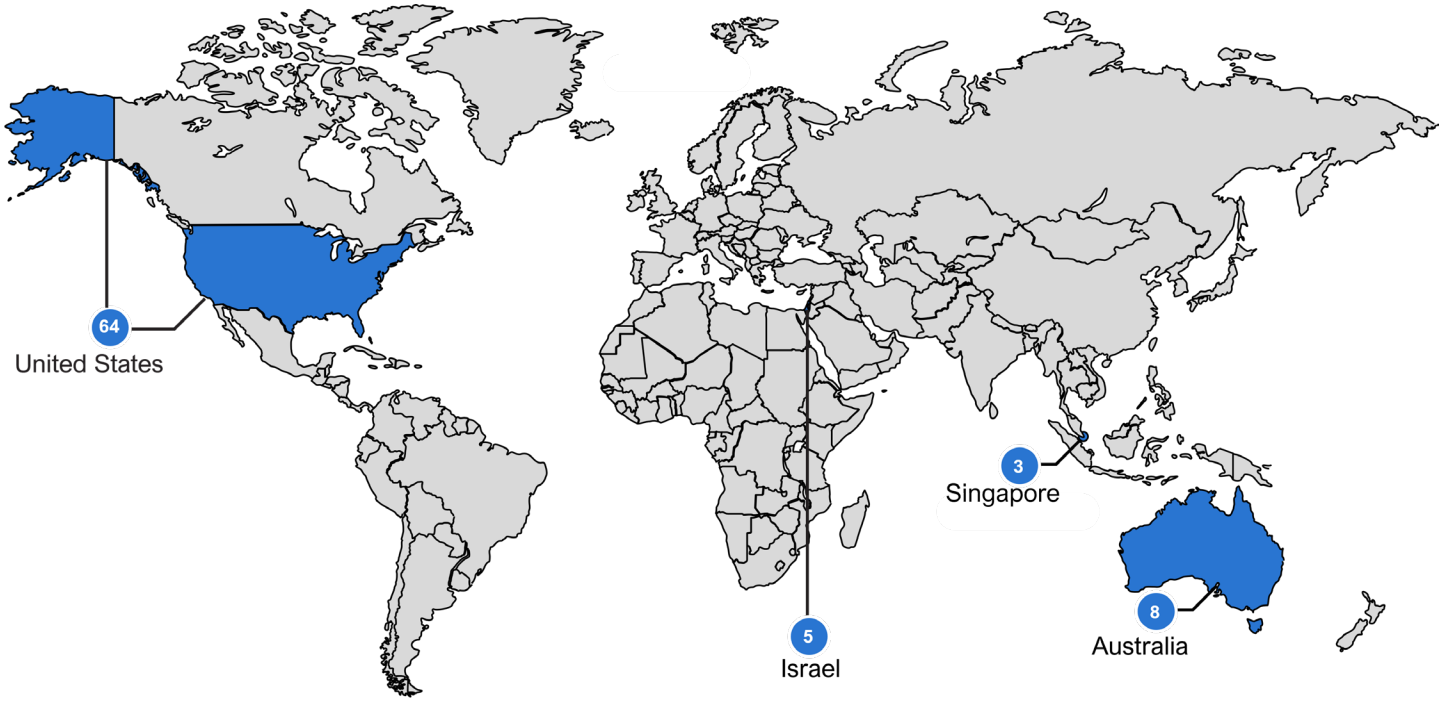
The participants could take part in this trial if they:

- Were at least 18 years of age
- Were fully active and able to walk or carry out light activities
- Had **multiple myeloma** that had come back and/or not responded to standard treatment (**Part A**)
- Had newly diagnosed **multiple myeloma** and recently received 4 to 6 **cycles** of **standard induction treatment** (**Part B**) and showed improvement

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

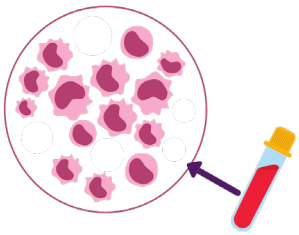
Standard induction treatment is the first set of treatments given after diagnosis of cancer to reduce or control the cancer before further treatment.

Across **Part A** and **Part B**, 80 participants from 4 countries received treatment. The map below shows the number of participants who received treatment in each country.



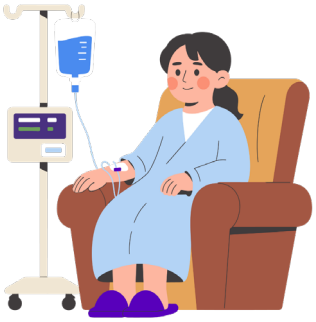
What treatment did the participants receive?

All participants received **PHE885**. To make **PHE885**, researchers:



Took the participants' blood and collected T-cells

Modified the T-cells in a laboratory so they could find and fight cancer cells



Gave the modified T-cells to the participants as an infusion into a vein

The participants, researchers, and trial staff knew that all participants received **PHE885**.

What happened during the trial?

Before treatment

About 1 month

The trial staff checked the participants' health and **multiple myeloma** to make sure the participants could be in this trial.

- Participants' blood was filtered using a machine process called apheresis to collect T-cells. These cells were modified in a lab to make each participant's **PHE885** infusion. This could take up to 4 weeks. During this time, participants could receive their regular treatment for cancer if needed.
- Between 2 and 8 days before **PHE885** treatment, participants also received chemotherapy. Chemotherapy was given before **PHE885** treatment to lower the number of existing T-cells in the body. This helped to make space for the **PHE885** T-cells and helped them grow and work better.

During treatment

1 day

The trial was done in two parts:

Part A: Trial doctors tested increasing dose levels of **PHE885** in small groups of participants. Each dose level was given to a separate group of participants. After the first group received their assigned dose, the trial doctors waited 28 days to check for any safety concerns before starting treatment in the next group. At the end of **Part A**, two dose levels (Dose 3 and 4) were selected for further testing in **Part B**.

Part A (55 participants)				
PHE885	**Dose 1**	**Dose 2**	**Dose 3**	**Dose 4**
Number of participants	4	13	20	18

Part B: Participants were randomly assigned to receive one of the two doses of **PHE885**.

Part B (25 participants)		
PHE885	**Dose 3**	**Dose 4**
Number of participants	13	12

After treatment

Up to 2 years

Participants returned to the hospital for up to 2 years after receiving **PHE885** or were contacted by phone every 6 months if hospital visits were no longer possible.

After this trial finished, participants could choose to enter another trial (CCTL019A2205B) in which they would be monitored for any medical problems for up to 15 years from treatment.

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

What were the main results of this trial?

What was the recommended dose of PHE885 for participants to receive in this trial?

As the trial ended earlier than planned, the researchers could not identify the recommended dose of **PHE885**.

Researchers closely monitored participants' health and recorded any **dose-limiting toxicities** (**DLTs**) that occurred during the first 28 days after 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

Part A

The most common **DLTs** observed in the participants were:

- **Low number of white blood cells called neutrophils** (neutropenia)
- **Number of neutrophils (a type of white blood cell) goes down in the blood** (neutrophil count decreased)
- **Amount of a protein called lipase in the blood goes up** (lipase increased)
- **An impact on the brain or nerves leading to headache, confusion, loss of consciousness, difficulty speaking, changes in mental status, or possibly even seizure** (neurotoxicity)

Part B

The most common **DLTs** observed in the participants were:

- **Serious immune reaction causing widespread inflammation** (immune effector cell-associated HLH-like syndrome, IEC-HS)
- **Rare but serious immune system overreaction** (haemophagocytic lymphohistiocytosis)
- **Low number of white blood cells called neutrophils** (neutropenia)
- **Number of neutrophils (a type of white blood cell) goes down in the blood** (neutrophil count decreased)
- **Low number of platelets** (thrombocytopenia)
- **Number of platelets goes down in the blood** (platelet count decreased)

In **Parts A** and **B**, some participants had more than one **DLT**.

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 2 years after receiving **PHE885**.

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.

Part A: All the participants (55 of 55) had adverse events, including serious and other adverse events.

- 35 participants had serious adverse events.

Part B: All the participants (25 of 25) had adverse events, including serious and other adverse events.

- 20 participants had serious adverse events.

29 participants in total died due to any cause during this trial.

What adverse events did the participants have?

Part A

The most common adverse events that happened in the participants were:

- **Serious immune reaction that may cause fever, nausea, headache, rash, dizziness, and difficulty breathing** (cytokine release syndrome)
- **Low red blood cell count** (anaemia)
- **Low number of white blood cells called neutrophils** (neutropenia)
- **Number of neutrophils (a type of white blood cell) goes down in the blood** (neutrophil count decreased)
- **Fever** (pyrexia)
- **Low blood pressure** (hypotension)

Part B

The most common adverse events that happened in the participants were:

- **Serious immune reaction that may cause fever, nausea, headache, rash, dizziness, and difficulty breathing** (cytokine release syndrome)
- **Low number of white blood cells called neutrophils** (neutropenia)
- **Number of neutrophils (a type of white blood cell) goes down in the blood** (neutrophil count decreased)
- **Low red blood cell count** (anaemia)
- **Low number of platelets** (thrombocytopenia)
- **Number of platelets goes down in the blood** (platelet count decreased)
- **Diarrhea**
- **Serious immune reaction causing widespread inflammation** (immune effector cell-associated HLH-like syndrome, IEC-HS)
- **Rare but serious immune system overreaction** (haemophagocytic lymphohistiocytosis)

What serious adverse events did the participants have?

Part A

The most common serious adverse events that happened in the participants were:

- **Serious immune reaction that may cause fever, nausea, headache, rash, dizziness, and difficulty breathing** (cytokine release syndrome)
- **Lung infection** (pneumonia)
- **Common cold virus infection** (rhinovirus infection)
- **Bone marrow disorder where the body does not make enough healthy blood cells** (myelodysplastic syndrome)
- **Shortness of breath** (dyspnoea)
- **Fever** (pyrexia)

Part B

The most common serious adverse events that happened in the participants were:

- **Serious immune reaction causing widespread inflammation** (immune effector cell-associated HLH-like syndrome, IEC-HS)
- **Rare but serious immune system overreaction** (haemophagocytic lymphohistiocytosis)
- **Fever with a low number of white blood cells called neutrophils** (febrile neutropenia)
- **Low number of white blood cells called neutrophils** (neutropenia)
- **Number of neutrophils (a type of white blood cell) goes down in the blood** (neutrophil count decreased)
- **Lung infection** (pneumonia)
- **Low number of platelets** (thrombocytopenia)
- **Bloodstream infection caused by bacteria** (enterococcal bacteremia)
- **Serious complication of an infection causing dangerously low blood pressure** (septic shock)

What was learned from this trial?

Researchers learned about the safety of **PHE885** and planned to identify the recommended dose that could be given to people with **multiple myeloma**. During **Part B** of the trial, a safety concern was identified in participants with newly diagnosed **multiple myeloma**, but this was not seen in **Part A** in participants who had **multiple myeloma** that had come back and/or not responded to standard treatment. After reviewing all the information, including safety and other factors, the trial ended earlier than planned following a business decision. As a result, a recommended dose of **PHE885** could not be confirmed.

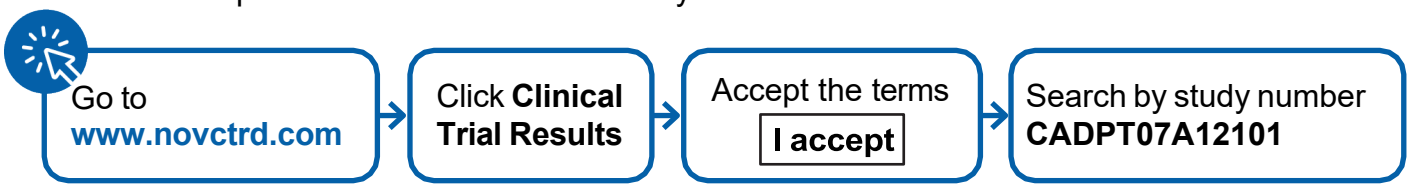
When this summary was written, Novartis had no plans for future trials of **PHE885** in people with **multiple myeloma**.

After this trial finished, participants could choose to enter another trial (CCTL019A2205B) in which they would be monitored for any medical problems for up to 15 years from **PHE885** treatment.

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 this website:

- clinicaltrials.gov – search using the number **NCT04318327**

Other trials of **PHE885** may appear on the public websites above. When there, search for **PHE885** or **durcabtagene autoleucel**.

Full clinical trial title: Phase I, open label, study of B-cell Maturation Antigen (BCMA)-directed CAR-T cells in adult patients with multiple myeloma

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