

# Plain Language Clinical Study Summary

This summary reports the results of only one study. Researchers must look at the results of many types of studies to understand if a study medicine works, how it works, and if it is safe to prescribe to patients. The results of this study might be different than the results of other studies that the researchers review.

**Sponsor:** Pfizer Inc.

**Medicine(s) Studied:** Ponegromab

**Protocol Number:** C3651003

**Dates of Study:** 21 November 2022 to 23 April 2025

**Title of this Study:** Study of the Efficacy and Safety of Ponegromab in Patients With Cancer, Cachexia and Elevated GDF-15 (PROACC-1)

[A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study to Investigate the Efficacy, Safety and Tolerability of Ponegromab in Patients With Cancer, Cachexia, and Elevated Concentrations of GDF-15, Followed by An Optional Open-Label Treatment Period (PROACC-1)]

**Date(s) of this Report:** 27 March 2026



## – Thank You –

If you participated in this study, Pfizer, the Sponsor, would like to thank you for your participation.

This summary will describe the study results. Do you have any questions about the study or the results? If so, please contact the doctor or staff at your study site.



# Why was this study done?

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## What is cancer?

Cancer is when cells in the body grow without control. The type of cancer depends on which cells have grown out of control. Cancer can stop parts of the body from working properly. It can lead to serious and sometimes incurable illness. The participants in this study had one of 3 types of cancer. Some had a type of lung cancer called “non-small cell” lung cancer. Some had pancreatic cancer (the pancreas is an organ in the body). Some had colorectal cancer, which is a cancer that starts in the large bowel and can involve the rectum, the lowest part of the gut.

## What is cachexia?

Cachexia is muscle wasting with significant weight loss. Cachexia can happen to people with cancer and can cause them to lose a lot of muscle and fat.

## What is GDF-15?

Researchers have identified certain proteins found in the blood that are at increased levels in several types of chronic disease. These types of proteins are also referred to as “biomarkers”. In this study, the researchers were interested in a biomarker called Growth Differentiation Factor 15 (GDF-15). GDF-15 is a protein produced when the body is under stress, especially from inflammation, low oxygen levels, and/or tissue damage. For people with cancer, increased levels of GDF-15 may be involved in cachexia.

## What is ponesegromab?

Ponesegromab (pon-se-gro-mab) is an investigational drug. Investigational means that ponesegromab has not been approved for general use at the time of this study.

Ponsegromab binds to and blocks GDF-15 in the blood stream. Researchers think that by blocking GDF-15, ponsegromab may help improve cachexia.

In this study, ponsegromab was given as an injection under the skin. This is known as a “subcutaneous” (SC) injection.

### **What was the purpose of this study?**

The main purpose of this study was to investigate the effect of ponsegromab on body weight in participants with cancer, cachexia, and increased levels of GDF-15 in their blood.

To do this, researchers compared body weight at the start of the study and at Week 12, in Part A of the study. They compared the results for participants who were given different dose levels of ponsegromab to those who were given placebo. A placebo looks like the study medication but does not have any medicine in it.

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### **Researchers wanted to know:**

- **What effect did low, medium, and high doses of ponsegromab have on participants’ body weight after 12 weeks of treatment, compared to placebo?**

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In Part B of the study, researchers also looked at the body weight results after a longer period of treatment. These Part B body weight results were not the main purpose of this study and are not included in this report. The full scientific report of this study is available online as described on the last page of this report.

# What happened during the study?

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## How was the study done?

First, a study doctor checked each participant to make sure they were able to join the study. This is known as screening.

There were 2 parts to this study, Part A and Part B. Screening was up to 28 days before Part A treatment.

Researchers then assigned participants to one of 4 groups for Part A of the study:

- Placebo.
- Low dose (100 mg) ponesimomab.
- Medium dose (200 mg) ponesimomab.
- High dose (400 mg) ponesimomab.

Participants were assigned to the groups by chance alone.

In Part A, the treatment period was 12 weeks and the follow-up was up to Week 16. A total of 3 doses of ponesimomab or placebo were given. Each dose was given 4 weeks apart - at the start of the study (Week 0), at Week 4, and at Week 8. Each dose was given as 2 injections. Participants and researchers did not know which participant was given which dose level, or whether they were given ponesimomab or placebo. This is called being “double-blind”.

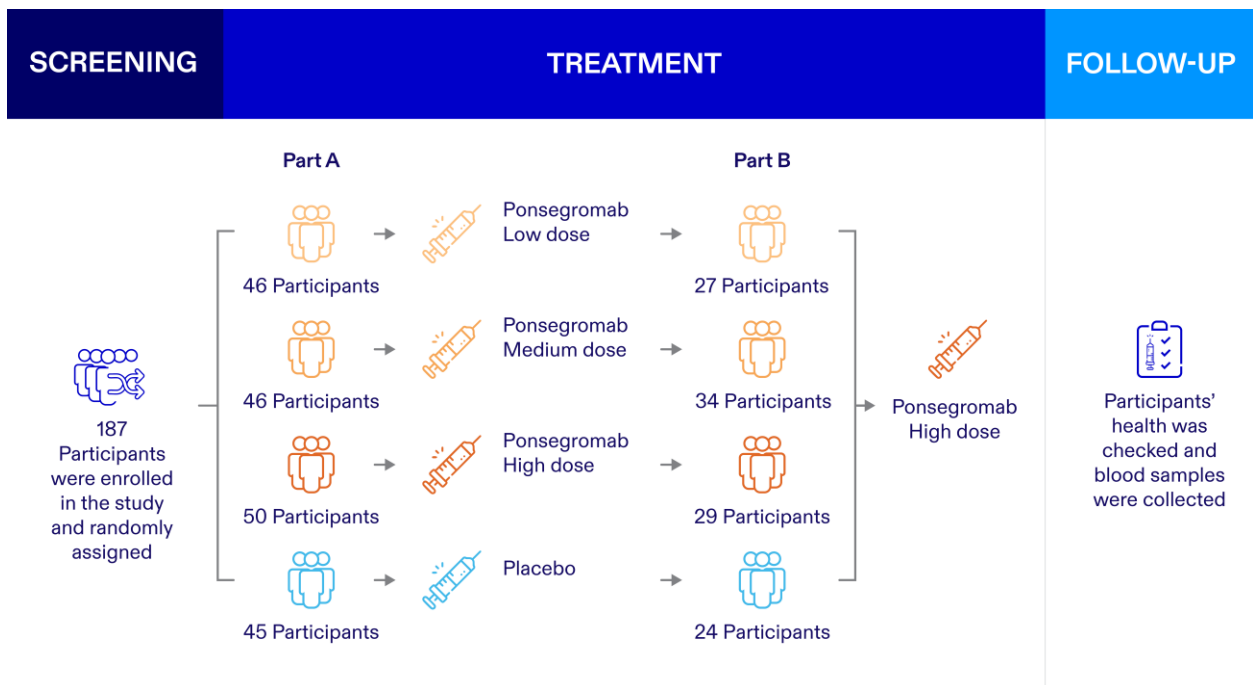
Participants who completed their treatment in Part A were given the option to continue into Part B. In Part B, all participants were to be given high dose (400 mg) ponesimomab every 4 weeks for up to 1 year. Part B did not include a placebo. Participants who chose to take part in Part B received their first dose of Part B at the last study visit of Part A (Week 12). Participants and researchers

knew what treatment the participants were being given in Part B. This is called being “open-label”.

Participants who did not take part in Part B were followed up for Part A until Week 16. Participants who took part in Part B were followed up for around 8 weeks after their last dose of ponesegromab.

Figure 1 below shows how the study was done.

**Figure 1. Study plan**



### Where did this study take place?

The Sponsor ran this study at 62 locations in 11 countries in North America, Europe, Asia, and Australia.

## When did this study take place?

It began 21 November 2022 and ended 23 April 2025.

## Who participated in this study?

The study included adult participants who had non-small cell lung cancer, pancreatic cancer, or colorectal cancer. All participants had cachexia and increased levels of GDF-15 in their blood.

Doctors use stages to describe how much a cancer has spread. Stage 4 cancer means that the cancer has spread from where it started to distant parts of the body.

Most participants had Stage 4 cancer at the start of the study. A higher percentage of participants in the high dose ponesegromab group had Stage 4 cancer at the start of the study than in the medium ponesegromab dose group, and fewer still in the placebo and low dose ponesegromab groups.

Figure 2 shows what happened to the participants who took part in Part A of the study.

**Figure 2. What happened to the participants who took part in Part A of the study**

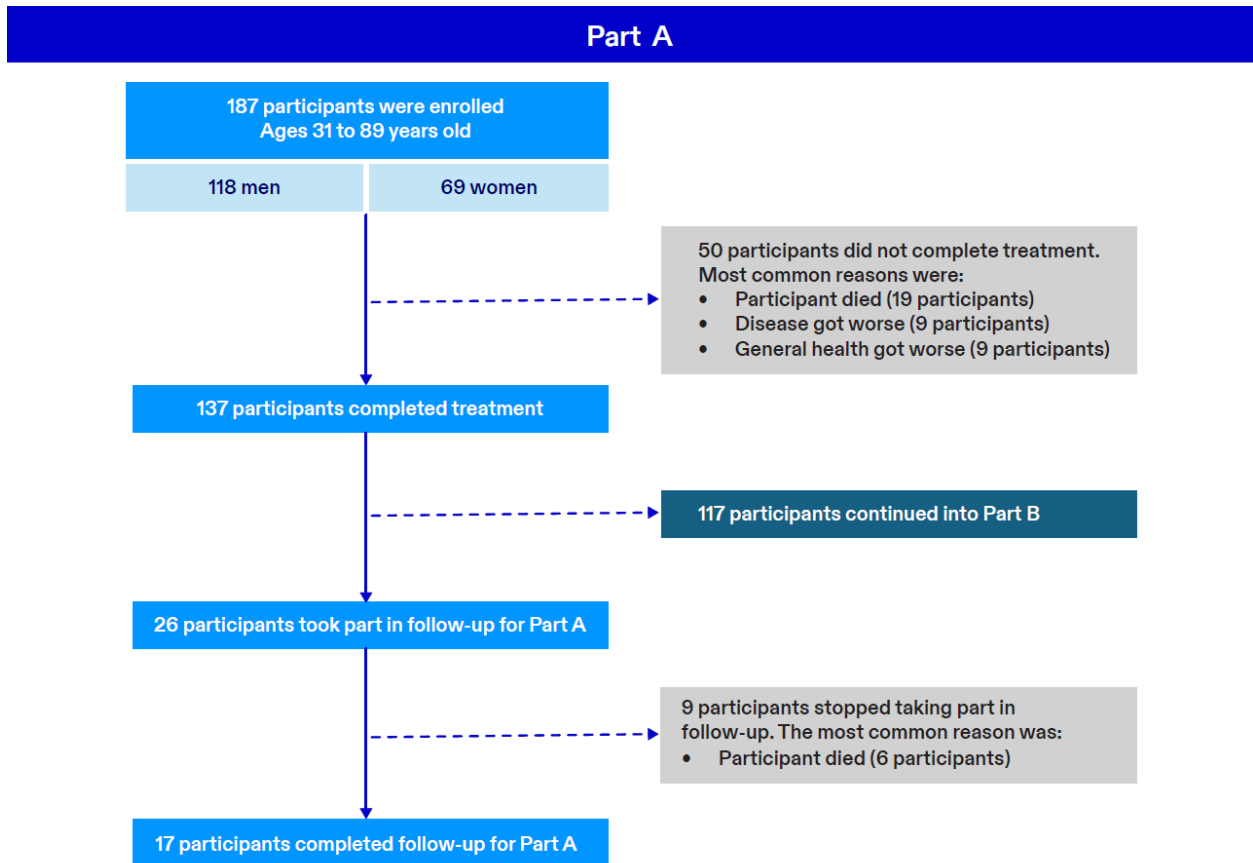
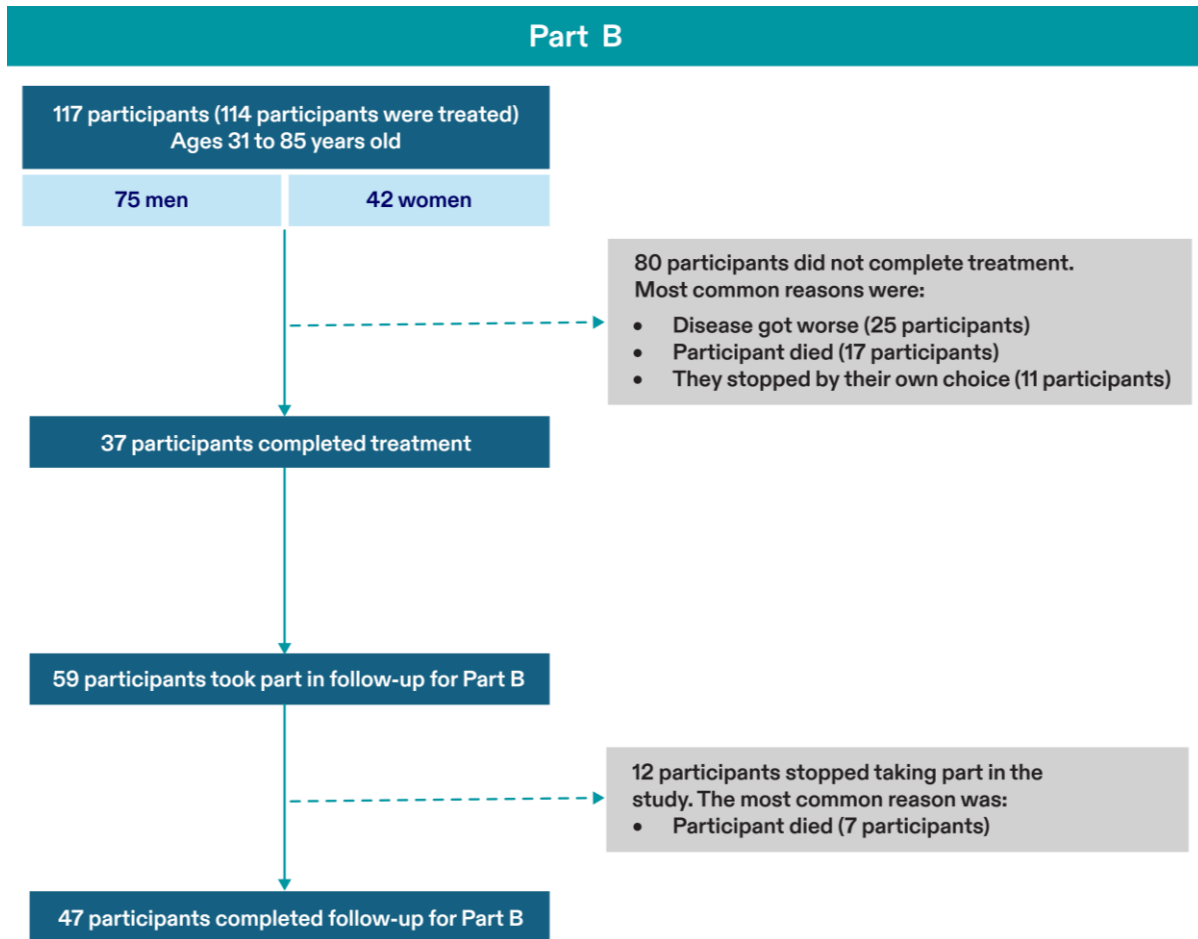


Figure 3 shows what happened to the participants who took part in Part B of the study.

**Figure 3. What happened to the participants who took part in Part B of the study**



## How long did the study last?

Study participants were in the study for around 20 weeks (around 5 months) if they participated in Part A only. Participants were in the study for up to around 76 weeks (around 18 months) if they participated in both Part A and Part B. The entire study took around 2 years and 5 months to complete.

When the study ended in April 2025, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

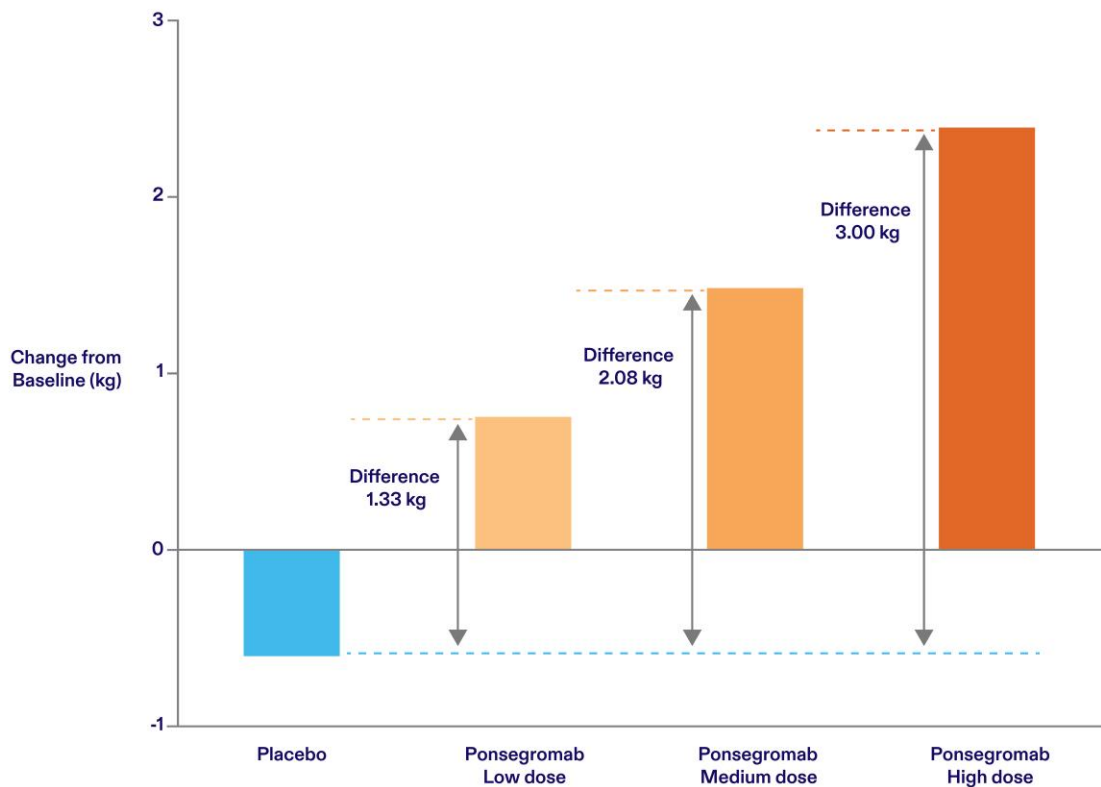
## What were the results of the study?

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### **What effect did low, medium, and high doses of ponesegromab have on participants' body weight after 12 weeks of treatment, compared to placebo?**

On average, after 12 weeks of treatment, participants who were given placebo had lost weight and participants who were given ponesegromab had gained weight. The results are shown in Figure 4 below.

**Figure 4. Average change in body weight after 12 weeks of treatment**



Based on these results, the researchers have decided that the results are not likely the result of chance. The study medication may help participants with cancer, cachexia, and increased GDF-15 levels with their weight. These differences could have been due to chance.

This does not mean that everyone in this study had these results. This is a summary of just some of the main results of this study. Other studies may have different results.

## What medical problems did participants have during the study?

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The researchers recorded any medical problems the participants had during the study. Participants could have had medical problems for reasons not related to the study (for example, caused by an underlying disease or by chance). Or, medical problems could also have been caused by a study treatment or by another medicine the participant was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many treatment groups in many studies, doctors try to understand what effects a study medicine might have on a participant.

### Part A

A total of 136 out of 187 participants (72.7%) in Part A of this study had at least 1 medical problem after starting treatment. A total of 30 participants (16.0%) left Part A of the study because of medical problems. The most common medical problems – those reported by 7% or more of participants overall in Part A – are described below.

Below are instructions on how to read Table 1. Table 2 can be read in a similar way.

#### Instructions for Understanding Table 1.

- The **1st** row of the table shows the groups in Part A of the study and the number of participants in each group.
- The blue and white rows in Table 1 show individual medical problems that were commonly reported by 7% or more of participants overall in Part A.

- The **1st** column of Table 1 tells how many of the 45 participants who were given placebo reported each medical problem. Below the number is the percentage of the 45 participants who were given placebo and reported the medical problem.
- The **2nd** column of Table 1 tells how many of the 142 participants who were given ponesegromab at any dose reported each medical problem. This ponesegromab group includes participants who were given low, medium, and high doses of ponesegromab. Below the number is the percentage of the 142 participants who were given ponesegromab at any dose and reported the medical problem.
- The **3rd** column of Table 1 tells how many of the 46 participants who were given the low dose of ponesegromab reported each medical problem. Below the number is the percentage of the 46 participants who were given the low dose of ponesegromab and reported the medical problem.
- The **4th** column of Table 1 tells how many of the 46 participants who were given the medium dose of ponesegromab reported each medical problem. Below the number is the percentage of the 46 participants who were given the medium dose of ponesegromab and reported the medical problem.
- The **5th** column of Table 1 tells how many of the 50 participants who were given the high dose of ponesegromab reported each medical problem. Below the number is the percentage of the 50 participants who were given the high dose of ponesegromab and reported the medical problem.
- Using these instructions, you can see that 8 out of the 45 participants (17.8%) who were given placebo reported diarrhea (loose stools).

**Table 1. Commonly reported medical problems by study participants in Part A**

<b>Placebo (45 Participants)</b>	<b>Ponsegromab at Any Dose (142 Participants)</b>	<b>Ponsegromab Low Dose (46 Participants)</b>	<b>Ponsegromab Medium Dose (46 Participants)</b>	<b>Ponsegromab High Dose (50 Participants)</b>
<b>Diarrhea (loose stools)</b>				
8 out of 45 participants (17.8%)	12 out of 142 participants (8.5%)	3 out of 46 participants (6.5%)	4 out of 46 participants (8.7%)	5 out of 50 participants (10.0%)
<b>Feeling about to be sick (nausea)</b>				
7 out of 45 participants (15.6%)	6 out of 142 participants (4.2%)	1 out of 46 participants (2.2%)	1 out of 46 participants (2.2%)	4 out of 50 participants (8.0%)
<b>Vomiting</b>				
6 out of 45 participants (13.3%)	7 out of 142 participants (4.9%)	2 out of 46 participants (4.3%)	3 out of 46 participants (6.5%)	2 out of 50 participants (4.0%)
<b>Fever</b>				
3 out of 45 participants (6.7%)	10 out of 142 participants (7.0%)	0 participants	5 out of 46 participants (10.9%)	5 out of 50 participants (10.0%)

**Table 1. Commonly reported medical problems by study participants in Part A**

<b>Placebo (45 Participants)</b>	<b>Ponsegromab at Any Dose (142 Participants)</b>	<b>Ponsegromab Low Dose (46 Participants)</b>	<b>Ponsegromab Medium Dose (46 Participants)</b>	<b>Ponsegromab High Dose (50 Participants)</b>
<b>Low blood potassium</b>				
4 out of 45 participants (8.9%)	12 out of 142 participants (8.5%)	6 out of 46 participants (13.0%)	0 participants	6 out of 50 participants (12.0%)
<b>Low red blood cell count</b>				
5 out of 45 participants (11.1%)	12 out of 142 participants (8.5%)	4 out of 46 participants (8.7%)	4 out of 46 participants (8.7%)	4 out of 50 participants (8.0%)

## Part B

A total of 96 out of 114 (84.2%) treated participants in Part B of the study had at least 1 medical problem. A total of 30 participants (26.3%) left Part B of the study because of medical problems. The most common medical problems – those reported by 7% or more of participants overall in Part B – are described below.

**Table 2. Commonly reported medical problems by study participants in Part B**

Placebo in Part A Then Ponsegromab High Dose in Part B (24 Participants)	Ponsegromab Low Dose in Part A Then High Dose in Part B (27 Participants)	Ponsegromab Medium Dose in Part A Then High Dose in Part B (34 Participants)	Ponsegromab High Dose in Part A Then High Dose in Part B (29 Participants)
<b>Diarrhea (loose stools)</b>			
9 out of 24 participants (37.5%)	3 out of 27 participants (11.1%)	3 out of 34 participants (8.8%)	3 out of 29 participants (10.3%)
<b>Low red blood cell count</b>			
4 out of 24 participants (16.7%)	6 out of 27 participants (22.2%)	3 out of 34 participants (8.8%)	1 out of 29 participants (3.4%)
<b>Worsening of cancer</b>			
3 out of 24 participants (12.5%)	7 out of 27 participants (25.9%)	2 out of 34 participants (5.9%)	2 out of 29 participants (6.9%)

**Table 2. Commonly reported medical problems by study participants in Part B**

Placebo in Part A Then Ponsegromab High Dose in Part B (24 Participants)	Ponsegromab Low Dose in Part A Then High Dose in Part B (27 Participants)	Ponsegromab Medium Dose in Part A Then High Dose in Part B (34 Participants)	Ponsegromab High Dose in Part A Then High Dose in Part B (29 Participants)
<b>Fever</b>			
4 out of 24 participants (16.7%)	3 out of 27 participants (11.1%)	3 out of 34 participants (8.8%)	3 out of 29 participants (10.3%)
<b>Fatigue (feeling very tired)</b>			
1 out of 24 participants (4.2%)	2 out of 27 participants (7.4%)	5 out of 34 participants (14.7%)	3 out of 29 participants (10.3%)
<b>Constipation</b>			
0 participants	3 out of 27 participants (11.1%)	2 out of 34 participants (5.9%)	5 out of 29 participants (17.2%)
<b>COVID-19 infection</b>			
1 out of 24 participants (4.2%)	4 out of 27 participants (14.8%)	3 out of 34 participants (8.8%)	1 out of 29 participants (3.4%)

**Table 2. Commonly reported medical problems by study participants in Part B**

Placebo in Part A Then Ponsegromab High Dose in Part B (24 Participants)	Ponsegromab Low Dose in Part A Then High Dose in Part B (27 Participants)	Ponsegromab Medium Dose in Part A Then High Dose in Part B (34 Participants)	Ponsegromab High Dose in Part A Then High Dose in Part B (29 Participants)
<b>Low blood potassium</b>			
3 out of 24 participants (12.5%)	2 out of 27 participants (7.4%)	1 out of 34 participants (2.9%)	3 out of 29 participants (10.3%)
<b>Infection of the lung</b>			
3 out of 24 participants (12.5%)	3 out of 27 participants (11.1%)	1 out of 34 participants (2.9%)	2 out of 29 participants (6.9%)

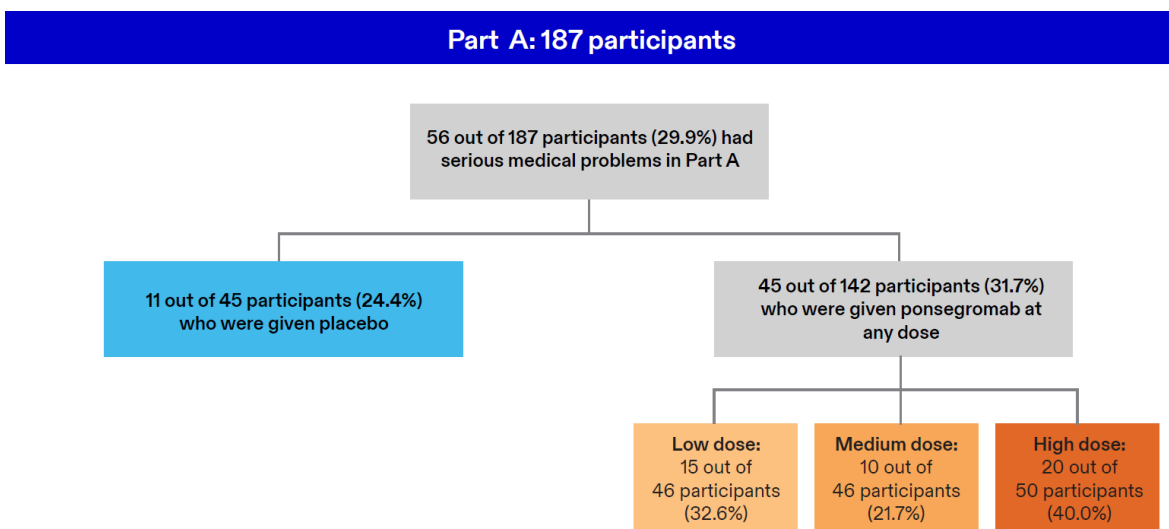
# Did study participants have any serious medical problems?

A medical problem is considered “serious” when it is life-threatening, needs hospital care, or causes lasting problems.

## Part A

Figure 5 shows a summary of the participants that reported serious medical problems in Part A.

**Figure 5. Summary of the participants that reported serious medical problems in Part A**



Two (2) of these serious medical problems in Part A were believed to be potentially related to the study treatment:

- Abdominal pain, for a participant who was given the low dose of ponesgromab.
- Shortness of breath, for a participant who was given the medium dose of ponesgromab.

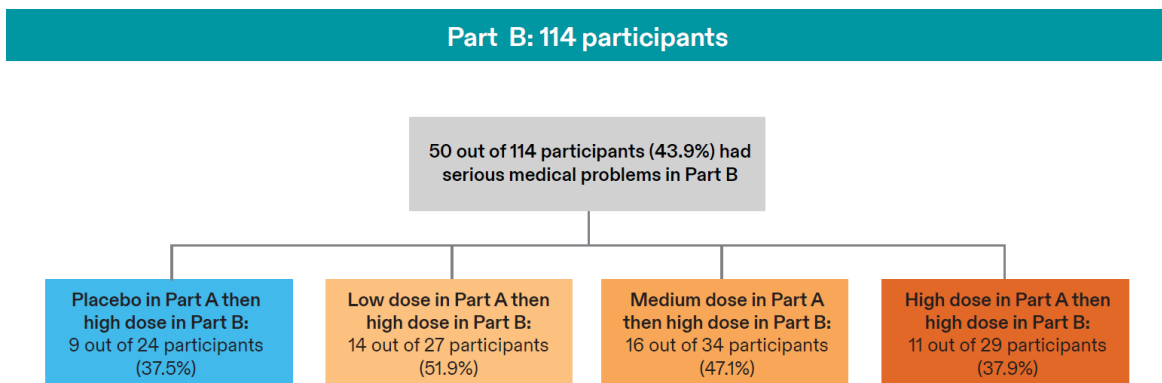
All other serious medical problems in Part A were believed to be not related to the study treatment.

Twenty-six (26) out of 187 participants (13.9%) died during Part A of the study. None of these deaths were believed to be related to the study treatment. Most of these deaths were believed to be due to the participants' illness.

## Part B

Figure 6 shows a summary of the participants that reported serious medical problems in Part B.

**Figure 6. Summary of the participants that reported serious medical problems in Part B**



None of these serious medical problems were believed to be related to the study treatment.

Twenty-three (23) out of 114 treated participants (20.2%) died during Part B of the study. None of these deaths were believed to be related to the study treatment. Most of these deaths were believed to be due to the participants' illness.

## Where can I learn more about this study?

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If you have questions about the results of your study, please speak with the doctor or staff at your study site.

For more details on your study protocol, please visit:

[www.pfizer.com/research/  
research\\_clinical\\_trials/trial\\_results](http://www.pfizer.com/research/research_clinical_trials/trial_results) Use the protocol number  
**C3651003**

The full scientific report of this study is available online at:

[www.clinicaltrials.gov](http://www.clinicaltrials.gov) Use the study identifier  
**NCT05546476**

<https://euclinicaltrials.eu> Use the study identifier  
**2023-510446-24-00**

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients.

Again, if you participated in this study,  
**thank you** for volunteering.  
We do research to try to find the  
best ways to help patients, and you helped  
us to do that!

