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: Ponsegromab

Protocol Number: C3651011

Dates of Study: 22 November 2023 to 20 February 2025

Title of this Study: A Study of Ponsegromab in People With Heart Failure – Cohort B Results

[A Phase 2, Double-Blind, Randomized, Placebo-Controlled, 4-Arm Study to Investigate Symptoms, Function, Health-Related Quality of Life and Safety With Repeated Subcutaneous Administration of Ponsegromab Versus Placebo in Adult Participants with Heart Failure]

Date(s) of this Report: 18 February 2026

Pfizer

– 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?

What is heart failure?

The heart is like a pump that sends blood all around the body. This blood carries oxygen, which the body needs to do all of its daily work. Heart failure happens when the heart does not pump blood as well as it should. This can be because the heart becomes weaker or because it is too stiff to work properly. Symptoms of heart failure include shortness of breath, swollen feet and legs, fainting or feeling light-headed, a build-up of fluid around the lungs, and tiredness.

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. In heart failure, GDF-15 can act as a warning signal. Researchers and doctors can measure the amount of GDF-15 in the blood and use this to check how well the heart is working.

What is ponsegromab?

Ponsegromab (pon-se-gro-mab) is an investigational drug that is being studied for the treatment of heart failure and high levels of GDF-15. Investigational means that ponsegromab has not been approved for general use. In this study, ponsegromab was given as an injection under the skin; this is known as "subcutaneous" (SC).

Ponsegromab binds to and blocks GDF-15 in the bloodstream. Researchers think that by blocking GDF-15, ponsegromab may help improve heart failure symptoms.

What was the purpose of this study?

In this study, adult participants with heart failure and high levels of GDF-15 were included in either the Main Study (Cohort A) or in Cohort B. A cohort is a word used to describe a group of participants who are included in a larger clinical study.

- This document only describes the safety results for Cohort B as this was the main purpose of this part of the study.
- The study stopped early because ponsegromab was not working well in participants with heart failure and high levels of GDF-15.

Researchers wanted to know:

- **What was the safety and tolerability of ponsegromab?**

What happened during the study?

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 a screening period.

Researchers gave the 3 groups of participants in Cohort B one of the following doses of ponsegromab once every 4 weeks:

- Low dose (100 mg)
- Medium dose (200 mg)
- High dose (300 mg)

The study participants and researchers knew who was given the different doses of ponsegromab in Cohort B. This is known as an 'open-label' study. Study participants were assigned to each group by chance alone.

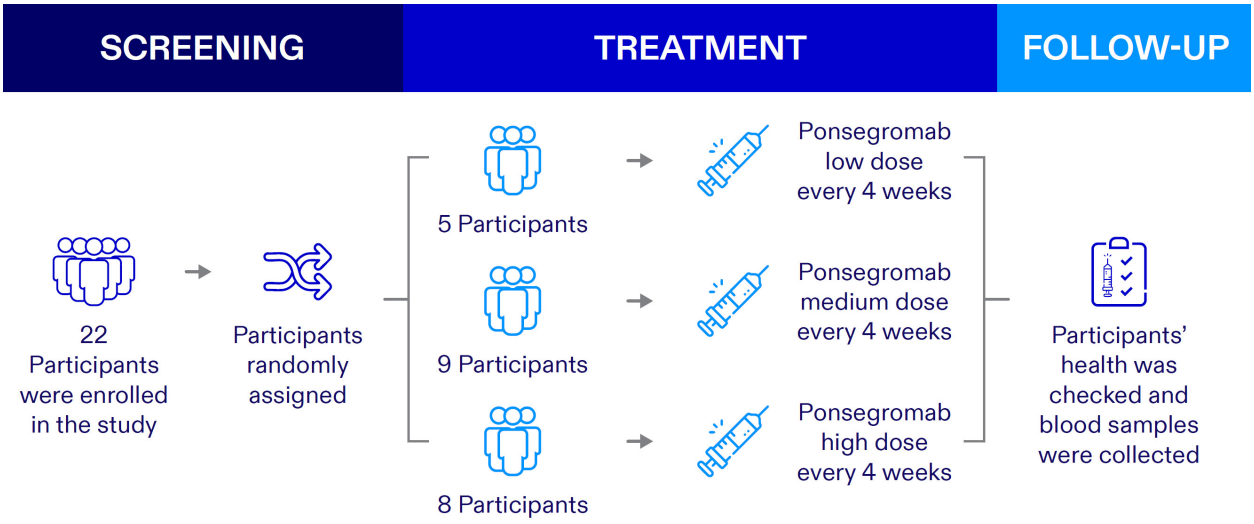
Participants visited the study site every 4 weeks for treatment. Each participant was given a total of 4 treatments. The last treatment was given at Week 12.

During the study, the researchers took blood samples from participants. This was done to measure the amount of study medicine in the participant's blood and for safety blood tests. Participants were asked about their health. This was done during treatment and follow-up.

Researchers then compared the results from study participants given the different doses of ponsegromab.

Figure 1 shows a diagram of what happened in the Cohort B part of the study.

Figure 1. Study diagram for Cohort B



The screening period was 8 weeks, the treatment period was 12 weeks, and the follow-up was 10 weeks.
During treatment and follow-up, the researchers took blood samples from participants and asked them about their health.

Where did this study take place?

The Sponsor ran the Cohort B part of the study at 13 locations in North America (8 in the United States and 5 in Canada).

When did this study take place?

Cohort B began 22 November 2023. The study was stopped early by the Sponsor on 27 November 2024 because ponsegromab was not working well in participants with heart failure and high levels of GDF-15. Participants were last seen by the researchers on 20 February 2025.

Who participated in this study?

Cohort B included 22 adult participants who had heart failure and high levels of GDF-15 in their blood.

- A total of 19 men participated.
- A total of 3 women participated.
- All participants were between the ages of 41 years and 85 years.

Of the 22 participants who started treatment in Cohort B, 16 participants (72.7%) finished the treatment phase. There were 6 participants (27.3%) who did not finish the treatment phase. These participants stopped treatment because the Sponsor ended the study early, the participant wanted to stop treatment, or for other reasons.

There were 21 participant (95.5%) who entered the follow-up part of the study. This was after their treatment stopped, either because they completed treatment or they stopped treatment early. Twenty (20) participants (90.9%) completed follow-up and 1 participant (4.5%) did not. This participant died.

How long did the study last?

Study participants were to be in the study for around 30 weeks. Some participants did not complete the full 12 weeks of treatment because the study was stopped early by the Sponsor, as described above.

When the Cohort B part of the study ended in February 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?

Although the researchers looked at other types of results for Cohort B, they were not the main purpose for Cohort B so they are not included in this report.

What medical problems did participants have during the study?

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.

A total of 12 out of 22 participants (54.5%) in this study had at least 1 medical problem after starting treatment. One (1) participant died during the study. This death was considered not related to the study treatment but related to the

participant's illness. The most common medical problems – those reported by 2 or more participants in any group – are described below.

Below are instructions on how to read Table 1.

Instructions for Understanding Table 1.

- The **1st** row of the table shows the groups in the study and the number of participants in each group.
- The blue and white rows in Table 1 show individual medical problems that were reported by 2 or more participants in any group.
- The **1st** column of Table 1 tells how many of the 22 participants who were given ponsegromab at any dose reported each medical problem. This ponsegromab group includes participants who were given the low, medium, and high doses of ponsegromab. Below the number is the percentage of the 22 participants who were given ponsegromab at any dose and reported the medical problem.
- The **2nd** column of Table 1 tells how many of the 5 participants who were given the low dose of ponsegromab reported each medical problem. Below the number is the percentage of the 5 participants who were given the low dose of ponsegromab and reported the medical problem.
- The **3rd** column of Table 1 tells how many of the 9 participants who were given the medium dose of ponsegromab reported each medical problem. Below the number is the percentage of the 9 participants who were given the medium dose of ponsegromab and reported the medical problem.
- The **4th** column of Table 1 tells how many of the 8 participants who were given the high dose of ponsegromab reported each medical

problem. Below the number is the percentage of the 8 participants who were given the high dose of ponsegromab reported the medical problem.

- Using these instructions, you can see that 3 out of the 22 participants (13.6%) in the ponsegromab at any dose group had a sudden injury to their kidneys. This included 1 out of the 9 participants (11.1%) given the medium dose of ponsegromab and 2 out of the 8 participants (25.0%) given the high dose of ponsegromab.

Table 1. Commonly reported medical problems by study participants

Ponsegromab At Any Dose (22 Participants)	Ponsegromab Low Dose (5 Participants)	Ponsegromab Medium Dose (9 Participants)	Ponsegromab High Dose (8 Participants)
Sudden injury to the kidneys			
3 out of 22 participants (13.6%)	0 participants	1 out of 9 participants (11.1%)	2 out of 8 participants (25.0%)
Nose and throat infection			
3 out of 22 participants (13.6%)	1 out of 5 participants (20.0%)	0 participants	2 out of 8 participants (25.0%)
Diarrhea (loose stools)			
2 out of 22 participants (9.1%)	0 participants	0 participants	2 out of 8 participants (25.0%)
Fatigue (feeling very tired)			

Table 1. Commonly reported medical problems by study participants			
2 out of 22 participants (9.1%)	1 out of 5 participants (20.0%)	0 participants	1 out of 8 participants (12.5%)

Laboratory test results and blood pressure and pulse rate measurements were similar across all groups of participants. There were no medically important differences seen.

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.

A total of 3 out of 22 participants (13.6%) had serious medical problems. These serious medical problems were:

- One (1) participant in the medium dose group had high levels of a protein called troponin I in blood samples. High levels of troponin I can be seen when the heart is damaged. This was considered not related to study treatment.
- One (1) participant in the high dose group had cancer of the colon. The colon is part of the intestines or bowel. This participant also had worsening heart failure, an infection of the lungs known as pneumonia, and low levels of red blood cells in blood samples due to blood loss. These events were considered not related to study treatment.

- One (1) participant in the high group had:
    - Diarrhea (loose stools).
    - Low levels of the mineral potassium in blood samples.
    - Sudden injury to the kidneys.
    - Severe blood or fluid loss that caused dangerously low blood pressure.

    This participant died. Although the 4 medical problems above were considered possibly related to study treatment, this death was considered not related to the study treatment but related to the participant's illness.

Where can I learn more about this study?

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	Use the protocol number **C3651011**

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

www.clinicaltrials.gov	Use the study identifier **NCT05492500**
https://euclinicaltrials.eu	Use the study identifier **2023-509747-27-00**

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!

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