Clinical Study Results

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 medication 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 (PF-06946860)
Protocol Number:	C3651009
Dates of Study:	17 November 2020 to 30 March 2022
Title of this Study:	Study to Assess the Safety and Tolerability of Repeated Doses of an Investigational New Drug in Patients With Cancer and Cachexia [A Phase 1B, 12-Week, Open-Label Study to Assess the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics Following Repeated Subcutaneous Administrations of PF-06946860 in Patients With Cancer and Cachexia]
Date(s) of this Report:	09 January 2023

– 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. If you have any questions about the study or the results, please contact the doctor or staff at your study site.

Why was this study done?

What is cancer cachexia?

Cachexia (kak-ex-ee-a) is a "wasting" disorder that causes extreme weight loss, muscle wasting and loss of appetite. Cachexia often happens in people who are very sick with a chronic (long-term) illness or serious disease. People with late-stage cancer often develop cachexia.

The participants in this study had late-stage lung cancer, pancreatic cancer or colorectal cancer (involving the large intestine or rectum), and also had cachexia.

What is growth differentiation factor 15 (GDF-15)?

Researchers have identified certain proteins found in the blood that are at increased levels in several types of chronic diseases such as cancer. These types of proteins are also referred to as "biomarkers". In this study, the researchers were interested in a biomarker called GDF-15 because it may be responsible for some of the main effects of cachexia, including loss of appetite, muscle wasting and weight loss.

What is ponsegromab?

Ponsegromab (pon-se-gro-mab) (PF-06946860) is an investigational drug that is being studied for the treatment of cachexia in cancer patients. 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. Researchers think that by blocking GDF-15, ponsegromab may promote appetite and increase body weight in participants with cancer and cachexia.

What was the purpose of this study?

The main purpose of this study was to learn if ponsegromab was safe to take for adult participants with late-stage cancer and cachexia.

Researchers wanted to know:

- **How safe and well tolerated was ponsegromab?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

Researchers tested ponsegromab on a group of study participants. The researchers did this to learn about the safety and tolerability of ponsegromab.

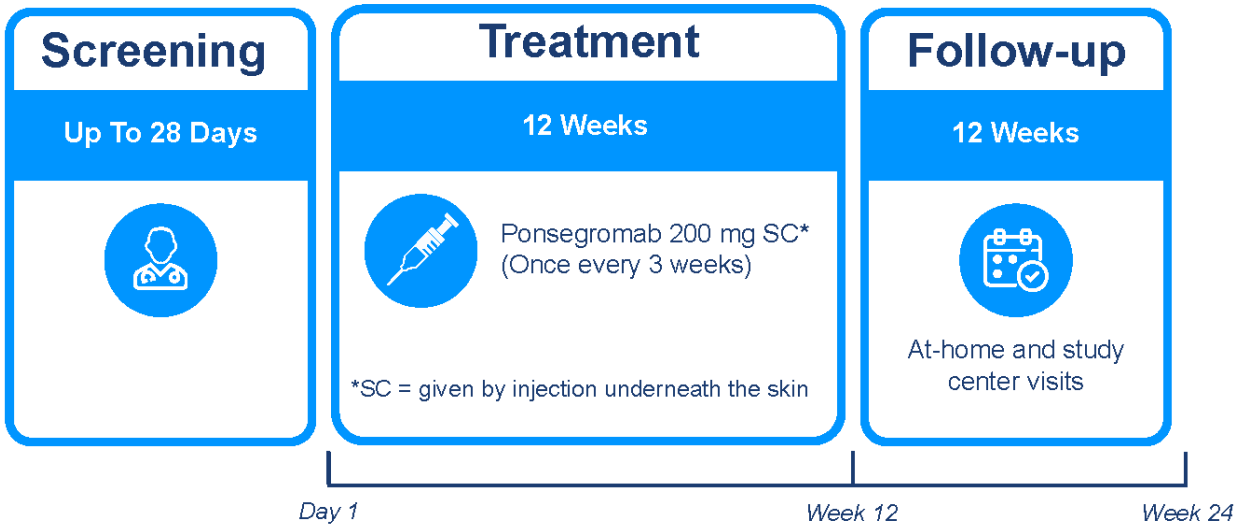
First, a study doctor checked each participant to make sure they were able to join the study. This is known as the screening period. During the 12-week treatment period, participants were given injections of 200 mg ponsegromab once every 3 weeks. Each participant received ponsegromab up to a total of 5 times. The participants were then followed by researchers for 12 weeks (follow-up period) to see how they did after their study treatment ended. Throughout the study, participants also continued with their current course of anti-cancer treatment.

Researchers took samples of blood and urine from participants during the study. Researchers also checked the participants' health during the study and asked them how they were feeling.

A total of 10 participants joined the study and were treated with ponsegromab. One additional participant was enrolled into the study but left the study before receiving any treatment.

The study plan is shown in Figure 1.

Figure 1. Study Plan



Where did this study take place?

The Sponsor ran this study at 13 locations in the United States of America.

When did this study take place?

It began 17 November 2020 and ended 30 March 2022.

Who participated in this study?

The study included adult participants with cachexia, increased levels of GDF-15 in their blood, and late-stage lung cancer, pancreatic cancer or colorectal cancer.

- A total of 7 men participated
- A total of 3 women participated
- All participants were between the ages of 47 and 81

Of the 10 participants who joined the study and started the treatment period, 8 participants completed the treatment. Two (2) participants stopped taking the treatment because their health status got worse.

Of the 8 participants who started the follow-up period, 7 participants completed the follow-up period. One participant stopped being in the study during the follow-up period because they passed away.

How long did the study last?

Study participants were in the study for up to 24 weeks. The entire study took about 1 year and 4 months to complete.

When the study ended in March 2022, the Sponsor reviewed 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?

How safe and well tolerated was ponsegromab?

In this study, the researchers assessed the safety and tolerability of ponsegromab when given at a dose of 200 mg once every 3 weeks for a period of 12 weeks. The researchers did this by looking at the medical problems that participants had during the study. They also looked at the results of laboratory tests, blood pressure, pulse rate, and electrocardiogram (ECG) tests. An ECG is a machine that looks at how well the heart is working when it pumps blood around the body.

What was the result of laboratory tests after participants had taken ponsegromab for 12 weeks?

- There were 8 participants assessed for laboratory tests during the study. Of these, all 8 participants had abnormal laboratory test results. Abnormal laboratory test results considered as medical problems were reported in 5 of the 8 participants. The researchers did not think any of these medical problems were related to ponsegromab.

What was the result of the blood pressure and pulse rate tests after participants had taken ponsegromab for 12 weeks?

- There were 9 participants assessed for blood pressure and pulse rate tests during the study. Of these, 3 participants had abnormal blood pressure increases. Blood pressure increases considered as medical problems were reported in 2 of the 3 participants. The researchers did not think either of these medical problems were related to ponsegromab.
- None of the participants had abnormal pulse rate tests, but 1 of the 9 participants was reported to have a rapid heart rate which was considered as a medical problem. The researchers did not think the rapid heart rate was related to ponsegromab.

What was the result of the ECG tests after participants had taken ponsegromab for 12 weeks?

- There were 8 participants assessed for ECG tests during the study. Of these, 2 participants had abnormal ECG results. Abnormal ECG result considered as a medical problem was reported in 1 of the 2 participants. The researchers did not think the abnormal ECG result was related to ponsegromab.

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?

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 medication might have on a participant.

All 10 participants (100%) in this study had at least 1 medical problem. One (10%) participant left the study because of medical problems. Table 1 shows the most common medical problems (those reported by 2 or more participants).

Below are instructions on how to read Table 1.

Instructions for Understanding Table 1.

- The **1st** column of Table 1 lists medical problems that were commonly reported during the study. It lists all medical problems reported by 2 or more participants.
- The **2nd** column tells how many of the 10 participants taking ponsegromab were reported to have each medical problem. Next to this number is the percentage of the 10 participants taking ponsegromab who reported the medical problem.
- Using these instructions, you can see that 5 out of the 10 participants (50%) taking ponsegromab were reported to have low numbers of red blood cells.

Table 1. Most common medical problems in the study

Medical Problem	Ponsegromab (10 Participants)
Low numbers of red blood cells	5 out of 10 participants (50%)
Diarrhoea	5 out of 10 participants (50%)
Feeling like about to vomit (nausea)	4 out of 10 participants (40%)

Feeling very tired	4 out of 10 participants (40%)
Watering eye (increased tears)	2 out of 10 participants (20%)
Stomach pain	2 out of 10 participants (20%)
Vomiting	2 out of 10 participants (20%)
Fall	2 out of 10 participants (20%)
Low numbers of white blood cells	2 out of 10 participants (20%)
Low numbers of platelets in the blood	2 out of 10 participants (20%)
Loss of water from the body (dehydration)	2 out of 10 participants (20%)
Low levels of potassium in the blood	2 out of 10 participants (20%)
Dizziness	2 out of 10 participants (20%)
Trouble sleeping (insomnia)	2 out of 10 participants (20%)
High blood pressure	2 out of 10 participants (20%)

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.

Four (4) participants (40%) had at least 1 serious medical problem during the study. These were reported in the 12-week treatment period in 2 participants and in the 12-week follow-up period in another 2 participants. All serious medical problems were reported in only 1 participant each. None of these serious medical problems were considered to be related to ponsegromab.

There was 1 participant who passed away during the study; this happened during the follow-up period. This death was due to the participant's cancer and was not considered to be related to ponsegromab.

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.

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

www.clinicaltrials.gov
Use the study identifier **NCT04299048**

www.pfizer.com/research/research_clinical_trials/trial_results
Use the protocol number **C3651009**

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!