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: C3651010

Dates of Study: 11 May 2021 to 09 August 2022

Title of this Study: Study to Compare the Effects of Repeated Doses of an Investigational New Drug and a Placebo on Appetite in Advanced Cancer and Anorexia

[A 6-Week, Randomized, Double-Blind, Sponsor-Open Study to Assess the Effect of Repeated Subcutaneous Administration of PF-06946860 on Appetite in Participants With Advanced Cancer and Anorexia, Followed by an 18-Week Open-Label Treatment Period]

Date(s) of this Report: 13 April 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 advanced cancer and anorexia?

Cancer occurs when cells in the body divide without control. Advanced (or late-stage) cancer is cancer that has spread to other parts of the body or has come back. It is usually used to describe cancer that cannot be cured.

Anorexia is the loss of appetite or desire to eat. Anorexia often happens in people who are very sick with a chronic (long-term) illness or serious disease. People with late-stage cancer often develop anorexia.

The participants in this study had one of the following types of late-stage cancer: lung, pancreatic, colorectal (involving the large intestine or rectum), prostate, breast, or ovarian. All participants also had anorexia.

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 anorexia in late-stage cancer patients, such as loss of appetite leading to unintended weight loss, tiredness, and reduced mobility.

What is ponsegromab?

Ponsegromab (pon-se-gro-mab) (PF-06946860) is an investigational drug that is being studied for the treatment of anorexia 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 late-stage cancer patients with anorexia.

What was the purpose of this study?

The main purpose of this study was to find out if ponsegromab had an early effect on appetite in adult participants with late-stage cancer and anorexia compared to placebo. A placebo does not have any medicine in it, but it looks like the study medicine.

Researchers wanted to know:

- **Did ponsegromab have an effect on participants' appetite after 4 weeks of treatment compared to placebo?**

What happened during the study?

How was the study done?

Participants were checked by a study doctor to make sure they were able to join the study. This is known as the screening visit, which happened no more than 28 days and no less than 5 days, before each participant joined the study.

Participants then entered Part A of the study and were put into 1 of 2 treatment groups:

- Ponsegromab 200 milligrams (mg) once every 3 weeks by SC injection
- Placebo once every 3 weeks by SC injection

Participants were assigned to each treatment group by chance alone. This is known as a "randomized" study. Part A was "double-blind", which means that participants and doctors did not know who was given ponsegromab and who was given placebo. This was done to make sure that the study results were not influenced in any way. During Part A, participants received a total of 2 doses of study treatment (ponsegromab or placebo).

After the 6-week Part A treatment period, participants had the option to continue into Part B and receive treatment for up to another 18 weeks. In Part B, all participants received ponsegromab 200 mg once every 3 weeks. Part B was "open-label", which means that participants and doctors knew the treatment that was being given in this part of the study. During Part B, participants received up to 7 additional doses of ponsegromab. Overall, participants could receive up to 9 doses of study treatment over 24 weeks for Parts A and B combined. There was also a follow-up visit about 4 weeks after the last dose of study treatment (in either Part A or Part B).

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

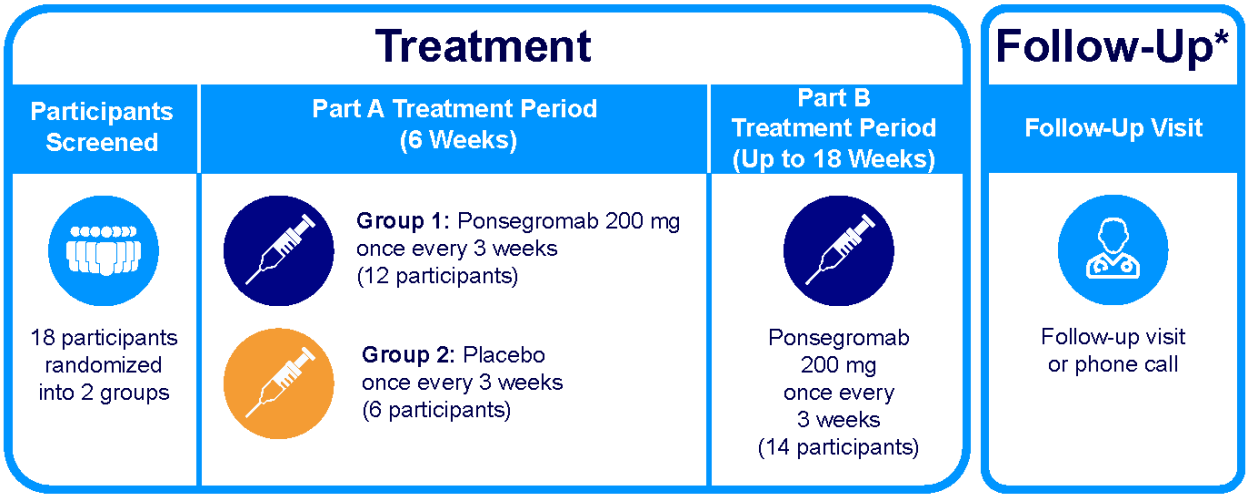
This report summarizes the findings for the "primary endpoint" in the study. The primary endpoint is the main question in a study that researchers want to answer. The primary endpoint in this study looked at appetite scores after participants had taken study treatment for 4 weeks (during Part A).

At various times during the study, participants were asked to complete a questionnaire to rate their appetite over the past 7 days. Participants could score their appetite from 0 (no appetite) to 10 (very good appetite). Researchers then compared the results of participants given ponsegromab to the results of participants given placebo.

This report also summarizes medical problems that participants had during the study. Medical problems were assessed over the full 24 weeks of treatment and during a 4-week follow-up period after stopping the study treatment (Parts A and B).

Figure 1 on the next page shows what happened during the entire study.

Figure 1. Study Design



* Follow-up:
Participants continuing to Part B had follow-up done about 4 weeks after last dose of study treatment in Part B.
Participants not continuing to Part B had follow-up done about 4 weeks after last dose of study treatment in Part A.

Where did this study take place?

The Sponsor ran this study at 16 locations in Canada and the United States.

When did this study take place?

This study began on 11 May 2021 and ended on 09 August 2022 after the Sponsor decided to stop the study early. This decision was made for business reasons and was not due to any safety concerns about ponsegromab.

Who participated in this study?

The study included adult participants with late-stage cancer and anorexia, and with increased levels of GDF-15 in their blood.

- A total of 11 men participated
- A total of 7 women participated
- All participants were between the ages of 58 and 88 years

Of the 18 participants who started the Part A treatment period, 14 participants completed treatment in Part A and continued to Part B. Four (4) participants stopped study treatment in Part A for the following reasons: because they passed away (2 participants), by their own choice (1 participant), or a doctor decided it was best for a participant to stop treatment (1 participant).

Of the 14 participants who started the Part B treatment period, 7 participants completed treatment in Part B. Seven (7) participants stopped study treatment in Part B for the following reasons: because they passed away (3 participants), by their own choice (1 participant), a doctor decided it was best for a participant to stop treatment (1 participant), due to a medical problem (1 participant), or due to another unspecified reason (1 participant).

How long did the study last?

Study participants were treated for up to 24 weeks: 6 weeks for Part A and up to 18 weeks for the optional Part B. As noted earlier, the study was stopped early by the Sponsor for business reasons and not due to any safety concerns about ponsegromab. It was planned to enrol about 40 participants overall but due to stopping the study early, a total of 18 participants were enrolled. The entire study lasted about 1 year and 3 months.

When the study ended in August 2022, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

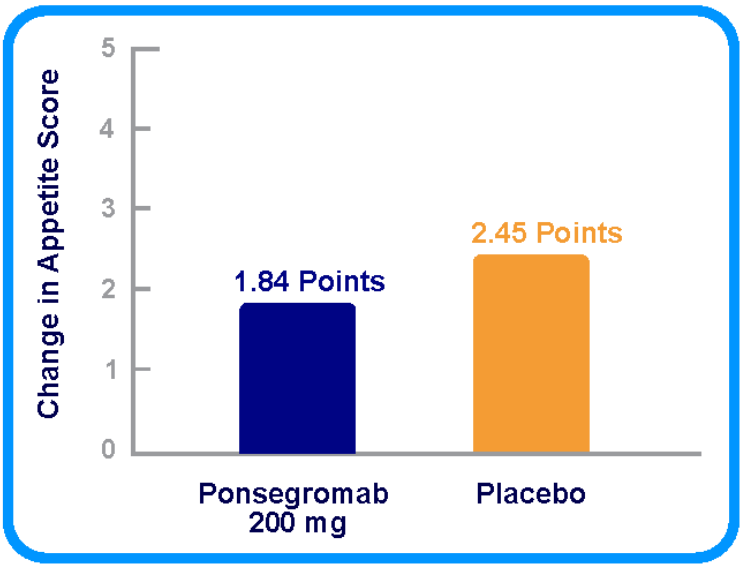
What were the results of the study?

Did ponsegromab have an effect on participants' appetite after 4 weeks of treatment compared to placebo?

To answer this question, the researchers compared each participant's appetite score at Week 4 with their score at the start of the study. A higher appetite score at Week 4 compared with the start of the study indicated an increase in a participant's appetite.

After 4 weeks of treatment, an increase in appetite score was seen for both treatment groups. Figure 2 below shows these results.

Figure 2. Average Change in Appetite Score at Week 4



Participants in the ponsegromab group had an average change in their appetite score of 1.84 points, while participants in the placebo group had an average change of 2.45 points.

Based on these results, the researchers have decided that the difference between the groups could have been due to chance. This means the study results did not show a clear effect of ponsegromab compared to placebo on participants' appetite after 4 weeks of treatment.

These results are based on the 18 participants enrolled in the study. As noted previously, the study was stopped early before the planned number of participants were enrolled.

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 of ponsegromab 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.

Medical problems were assessed over the entire treatment period of up to 24 weeks. In the Part A treatment period, participants could receive either ponsegromab 200 mg or placebo. In the Part B treatment period, all participants received ponsegromab 200 mg.

The treatment groups for the overall study were as follows:

- Ponsegromab → ponsegromab (ponsegromab in both Parts A and B)
- Placebo → ponsegromab (placebo in Part A, then ponsegromab in Part B)

All 18 participants (100%) in this study had at least 1 medical problem. A total of 7 participants (38.9%) left the study because of medical problems. This included 4 participants in the ponsegromab → ponsegromab group and 3 participants in the placebo → ponsegromab group.

Table 1 shows the most common medical problems during the study - those reported by 2 or more participants in total. 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. All medical problems reported by 2 or more participants in total are listed.
- The **2nd** column tells how many of the 12 participants in the ponsegromab → ponsegromab group reported each medical problem. Next to this number is the percentage of the 12 participants in the ponsegromab → ponsegromab group who reported the medical problem.
- The **3rd** column tells how many of the 6 participants in the placebo → ponsegromab group reported each medical problem. Next to this number is the percentage of the 6 participants in the placebo → ponsegromab group who reported the medical problem.
- Using these instructions, you can see that 3 out of the 12 participants (25.0%) in the ponsegromab → ponsegromab group reported infection of the kidney, bladder, or urethra. One (1) out of 6 participants (16.7%) in the placebo → ponsegromab group reported infection of the kidney, bladder, or urethra.

Table 1. Most common medical problems in the study: Parts A and B		
Medical Problem	**Ponsegromab → ponsegromab (12 Participants)**	**Placebo → ponsegromab (6 Participants)**
Infection of the kidney, bladder, or urethra	3 out of 12 participants (25.0%)	1 out of 6 participants (16.7%)
Feeling like about to vomit (nausea)	2 out of 12 participants (16.7%)	1 out of 6 participants (16.7%)
Worsening of cancer	2 out of 12 participants (16.7%)	1 out of 6 participants (16.7%)
Vomiting	2 out of 12 participants (16.7%)	0
Limb swelling	2 out of 12 participants (16.7%)	0
Lack of energy	2 out of 12 participants (16.7%)	0
Lung inflammation	2 out of 12 participants (16.7%)	0
Feeling very tired	1 out of 12 participants (8.3%)	1 out of 6 participants (16.7%)
Nerve damage affecting the feet, legs, arms, or hands	1 out of 12 participants (8.3%)	1 out of 6 participants (16.7%)
Constipation	0	2 out of 6 participants (33.3%)
Fall	0	2 out of 6 participants (33.3%)

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.

Overall, 7 out of 18 participants (38.9%) in the study had serious medical problems.

In Part A:

- 3 participants who received ponsegromab 200 mg had at least 1 serious medical problem.
- 1 participant who received placebo had at least 1 serious medical problem.

In Part B:

- 3 participants who received ponsegromab 200 mg had at least 1 serious medical problem.

Researchers did not believe any of the serious medical problems were related to the study treatment.

A total of 6 participants (33.3%) died during the study. This included 3 participants during Part A (2 participants who received ponsegromab 200 mg and 1 participant who received placebo), and 3 participants during Part B (all who received ponsegromab 200 mg). Half of the deaths (3 out of 6 participants) were due to the participants' cancer getting worse. Researchers did not believe any of the deaths were related to the study treatment.

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 **C3651010**

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

www.clinicaltrials.gov

Use the study identifier **NCT04803305**

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!