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 Studied: PF-07209960

Protocol Number: C4011001

Dates of Study: 16 December 2020 to 26 May 2023

Title of this Study: A Study to Test the Safety and Tolerability of PF-07209960 in Advanced or Metastatic Solid Tumors

[A Phase 1 Dose Escalation and Expansion Study to Evaluate Safety, Tolerability, Pharmacokinetic, Pharmacodynamic, and Anti-Tumor Activity of PF-07209960 in Participants With Advanced or Metastatic Solid Tumors]

Date of this Report: 25 March 2024

– 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 or metastatic solid tumor?

Solid tumor cancers are cancers of any of the body organs or tissues. Common solid tumors are breast, prostate, lung, and colorectal (part of the intestines) cancers. Others include bladder, kidney, head, and neck, pancreas, and ovary cancers. When a cancer has grown and spread from the organ or tissue where it originally started to other parts of the body, the cancer becomes more difficult to cure and it is called “advanced or metastatic”.

The study included participants who had one of the following types of locally advanced or metastatic solid tumor cancers as defined below:

- Non-small cell lung cancer (NSCLC) is a most common type of lung cancer.
- Renal cell cancer (RCC) also known as kidney cancer.
- Squamous cell carcinoma of the head and neck (SCCHN) is a cancer that originates in the squamous cells, which are flat cells that line the outer layer of the skin and the mouth, nose, and throat.
- Ovarian cancer (OvCa) is a cancer that originates in the ovary (female reproductive organ).
- Microsatellite stable (MSS) colorectal cancer (CRC) is a cancer that starts in the colon (part of the large intestine) or the rectum (last part of the large intestine), with the small pieces of repeating DNA unchanged in the tumor.

What is PF-07209960?

The study drug (PF-07209960) is an investigational cancer medicine and is not approved for use in any country for any disease or condition. This was the first time PF-07209960 was given to people. PF-07209960 is administered as an injection under the skin (subcutaneous or SC).

PF-07209960 is an antibody that works by targeting a specific protein called as programmed death-1 (PD-1). Antibodies are proteins made by body's immune (defense) system. PD-1 is found at higher levels on immune cells such as T cells that are also normally present in tumors.

A cytokine is a protein that enables the cells of the body to signal to each other, turning their function on or off. Interleukin (IL) is a type of cytokine that signals between immune cells fighting infections and tumors. There are many interleukins, each with a specific function. The interleukin in this study named IL-15 is attached to the study drug which activates T cells to divide and attack cancer cells. It is thought that PF-07209960 may help the immune system to fight cancer.

What was the purpose of this study?

The main purpose of this study was to learn about the safety and tolerability of PF-07209960 in participants with locally advanced or metastatic solid tumors. "Tolerability" refers to how well participants can tolerate receiving the study medication.

Researchers wanted to determine the recommended dose of the study medication. This will help them decide what dose to give to people in future studies.

Researchers wanted to know:

- **How safe and well tolerated was PF-07209960?**
- **Did participants receiving PF-07209960 have dose-limiting toxicities?**
- **What medical problems did participants have during the study?**

"Dose-limiting toxicities" (DLTs) are pre-defined medical problems that are severe and may have been caused by taking the study treatment. DLTs may require the participant to modify taking the treatment (permanently discontinue or withhold temporarily). Researchers collect information on DLTs to help determine the recommended dose of a study medication.

What happened during the study?

How was the study done?

This study was a non-randomized, "open-label" study, which means all participants received the study medicine, and the researchers and participants knew about the medicine the participants received. The study was initially planned to be conducted in 2 parts: Part 1 Dose Escalation and Part 2 Dose Expansion. During Part 1 of the study, the Sponsor decided to stop enrolling more participants in the study and not to start Part 2 of the study.

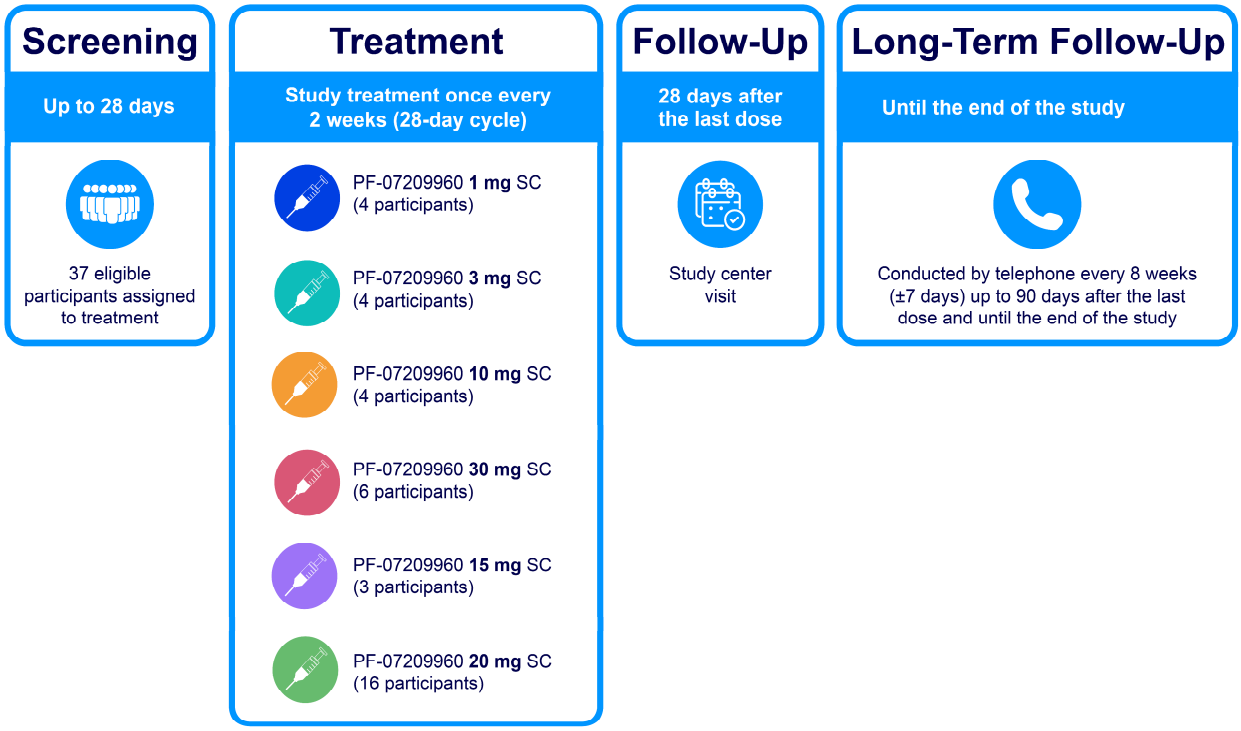
In Part 1, researchers tested increasing doses of PF-07209960 injected subcutaneously. All participants were "screened" to see if they qualify for the study. Participants who qualified for treatment after screening entered the Treatment Phase. Participants received the study medication every 2 weeks (on Day 1 and Day 15) in "cycles". One cycle is 28 days (4 weeks) in duration. Participants were continuously treated until their

cancer got worse, they experienced unacceptable medical problems, or they decided to stop taking part, whichever occurred first.

About a month (28 days) after their last dose, participants had a safety Follow-Up visit to check their health and medical problems if any. After the 1-month follow-up, participants were contacted by telephone every 8 weeks (±7 days) to assess safety up to 90 days after the last dose and for survival until the end of the study. This was called “Long-Term-Follow-Up” (LTFUP) or “Survival Follow-Up”.

Participants were assigned to receive single increasing doses of SC PF-07209960 starting from the lowest dose of 1 mg as shown in Figure 1 on the next page. The safety and tolerability of PF-07209960 was assessed at each dose level. The dose was increased or decreased for the next group of participants based on participants’ tolerability and the number of DLTs. PF-07209960 30 mg SC dose was the highest dose level that was tested in the study.

Figure 1. Study design for Part 1



In addition to clinical tests and safety laboratory tests, researchers took samples of blood and urine from participants during the study and measured the amount of study medication in the blood. Researchers also checked the participants' health during the study and asked them how they were feeling.

Researchers then compared the results of participants who received different doses of PF-07209960. They did this to see if medical problems experienced during the study could be related to the study medication or something else.

Where did this study take place?

The study took place across 7 study centers in the United States.

When did this study take place?

It began on 16 December 2020 and ended on 26 May 2023.

Who participated in this study?

The study included participants who were 18 years or older and who had advanced or metastatic solid tumors.

A total of 37 participants participated in the study, including 20 men and 17 women.

- Of the 37 participants who took part in the study, 26 participants had CRC, 1 participant had NSCLC, 4 participants had OvCa, and 6 participants had RCC.
- All participants were between the ages of 31 and 88 years.

All 37 participants discontinued the study treatment due to the following reasons:

- Worsening of cancer (22 participants [59.5%])
- Participants left before the study was over by their choice (7 participants [18.9%])
- A doctor decided it was best for a participant to stop being in the study (4 participants [10.8%])
- Death (2 participants [5.4%])
- Overall health deterioration (2 participants [5.4%])

Sixteen of the 37 (43.2%) participants entered the 1 month follow-up. Nine participants completed and 6 participants discontinued the follow-up due to death, lost to follow-up, and by their own choice (2 participants each). One participant did not complete the follow-up due to being in hospice and this participant died during the LTFUP. Nineteen of the 37 (51.4%) participants

entered the LTFUP, and 16 participants discontinued. The main reasons for discontinuation were death (10 participants) and early study termination (5 participants).

How long did the study last?

Participants stayed in the study for a median duration of 1.41 months, ranging from 0.0-13.6 months. The entire study took around 2 years 5 months and 10 days to complete.

The study was closed (terminated) by the Sponsor in June 2022, and stopped recruiting participants into the study but continued to follow-up participants for safety until May 2023

When the study ended in May 2023, 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 PF-07209960?

The researchers assessed the safety and tolerability of PF-07209960 by looking at the medical problems participants had during the study. They also looked at the results of certain laboratory tests. Researchers recorded Grade 3, 4, and 5 medical problems reported during the study as defined below:

- Grade 3 medical problems are considered as the events to be severe or medically significant by the study doctors.
- Grade 4 medical problems are those considered as ‘life-threatening’ (could harm their health) and require urgent intervention by the study doctors.

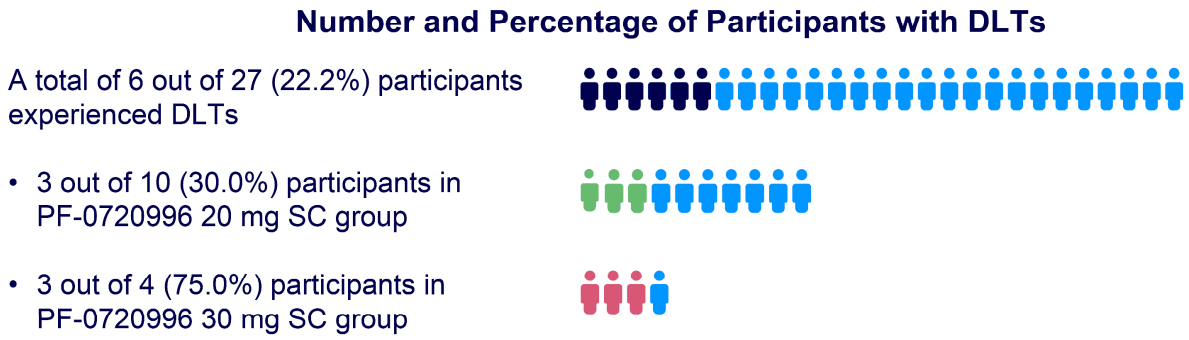
- Grade 5 medical problems are those that result in death.

Medical problems throughout the whole of the study are discussed in full in the next section of this document.

Did participants receiving PF-07209960 have any DLTs?

Twenty-seven out of 37 participants who received PF-07209960 were considered evaluable for DLTs in their first treatment cycle (Cycle 1). Six out of 27 (22.2%) participants had DLTs (as shown in Figure 2).

Figure 2. Number of Participants with DLTs



Three participants who received PF-07209960 20 mg SC had DLTs:

- One participant had Grade 3 cytokine release syndrome (CRS). CRS is an immune response causing fever, vomiting, shortness of breath, headache, and low blood pressure.
- One participant had acute (sudden or short-term) kidney injury.
- One participant had Grade 3 injection site pain. All the 3 events of DLTs were resolved during the study.

Three participants who received PF-07209960 30 mg SC had DLTs:

- One participant had 3 episodes of fatigue (worsened from Grade 2 [moderate] on study Day 5 to Grade 4 on study Day 8). All episodes of fatigue were resolved.
- One participant had Grade 3 rash which was not resolved during the study.
- Another participant had 2 episodes of Grade 3 rash (2nd episode of rash was not resolved) and Grade 3 inflamed mucosal lining which was not resolved during the study.

Did participants in the study have any Grade 3, 4 or 5 medical problems due to the study treatment?

Overall, 23 out of 37 (62.2%) participants had maximum Grade 3 or 4 medical problems and 6 out of 37 (16.2%) participants had maximum Grade 5 medical problems in the study.

- Twelve out of 37 (32.4%) participants had Grade 3 medical problems related to the study treatment. Five participants (13.5%) reported anemia (low red blood cell count) which was the most common Grade 3 medical problem.
- Four out of 37 (10.8%) participants had Grade 4 medical problems related to the study treatment. Medical problems of fatigue, decreased neutrophil (type of white blood cells [WBCs]) count, decreased lymphocyte (type of WBCs), and low blood sodium were reported in 1 participant (2.7%) each.
- No participants had Grade 5 medical problems that were related to the study treatment.

Did participants receiving PF-07209960 have any medically important abnormal laboratory tests?

Abnormal laboratory values reported in at least 10% of participants during the study were decreased lymphocyte (WBCs) count (29 participants [78.4%]), anemia (7 participants [18.9%]), and low blood sodium (5 participants [13.5%]). These events were medical problems of Grade 3 or more.

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.

Thirty-six out of 37 (97.3%) participants in this study had at least 1 medical problem. A total of 5 participants (13.5%) left the study because of medical problems. The most common medical problems – those reported by more than 20% of participants – are described below.

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 more than 20% of participants are listed.
- The **2nd** column tells how many of the 37 participants taking PF-07209960 reported each medical problem. Next to this number is the percentage of the 37 participants taking PF-07209960 who reported the medical problem.
- Using these instructions, you can see that 17 out of the 37 (45.9%) participants taking the study medication reported CRS.

Table 1. Commonly reported medical problems reported by more than 20% of study participants

Medical Problem	PF-07209960 (37 Participants)
CRS	17 out of 37 participants (45.9%)
Fatigue	15 out of 37 participants (40.5%)
Fever	13 out of 37 participants (35.1%)
Nausea	12 out of 37 participants (32.4%)

Table 1. Commonly reported medical problems reported by more than 20% of study participants	
Medical Problem	**PF-07209960 (37 Participants)**
Rash	12 out of 37 participants (32.4%)
Swelling where the injection was given	11 out of 37 participants (29.7%)
Anemia	10 out of 37 participants (27.0%)
Shortness of breath	10 out of 37 participants (27.0%)
Cough	9 out of 37 participants (24.3%)
Diarrhea	9 out of 37 participants (24.3%)
Not feeling hungry	8 out of 37 participants (21.6%)

Researchers monitored specifically for CRS which was a medical problem of special interest for the study because of the effect PF-07209960 has on the immune system.

A total of 17 participants (45.9%) experienced CRS. The median time that CRS occurred was around 3 days after study treatment, and generally resolved by about 6 days. Some participants experienced quicker or later onset of CRS and took shorter or longer to resolve. All CRS events were resolved during the study period.

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 26 out of 37 (70.3%) participants in this study had serious medical problems. The most common serious medical problems reported in more than 10% of participants include:

- CRS (11 participants [29.7%])
- Worsening of cancer, fever, and rash (in 4 participants [10.8%] each)

A total of 13 out of 37 (35.1%) participants had serious medical problems which were considered related to the study treatment. The most common events reported in more than 10% of participants were CRS (11 participants [29.7%]) and rash (4 participants [10.8%]).

A total of 17 participants died during the study. Eight participants died while in the treatment period of the study, either due to disease under the study (5 participants), cardiac arrest (1 participant), severe bleeding behind the lining of the belly (1 participant), or unknown reason (1 participant). Nine participants died during the follow-up period, due to disease under the study (1 participant) or mostly for unknown reasons (8 participants).

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 C4011001

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

www.clinicaltrials.gov	Use the study identifier **NCT04628780**
www.clinicaltrialsregister.eu	Use the study identifier 2021-004587-10

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!