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:	PF-06939999
Protocol Number:	C3851001
Dates of Study:	14 March 2019 to 27 April 2022
Title of this Study:	A Dose Escalation Study of PF-06939999 in Participants With Advanced or Metastatic Solid Tumors [A Phase 1 Study to Evaluate the Safety, Pharmacokinetics, and Pharmacodynamics of Escalating Doses of PF-06939999 (PRMT5 Inhibitor) in Participants With Advanced or Metastatic Non-Small Cell Lung Cancer, Head and Neck Squamous Cell Carcinoma, Esophageal Cancer, Endometrial Cancer, Cervical Cancer and Bladder Cancer]
Date(s) of this Report:	17 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 are advanced or metastatic solid tumors?

Cancer is the name for a group of diseases in which abnormal cells divide without control. Most types of cancer cause solid tumors to form, which are masses of these abnormal cells. Cancer that is unlikely to be cured or controlled with treatment is known as advanced cancer. Cancer that has spread from the part of the body where it started to other parts of the body is known as metastatic cancer.

What is PF-06939999?

PF-06939999 was an investigational drug that was being studied for the treatment of certain advanced or metastatic solid tumor cancers. An investigational drug is one that has not been approved for use outside of research studies. PF-06939999 was given as tablets that were taken by mouth daily, in 28-day "treatment cycles".

What was the purpose of this study?

The main purpose of this study was to learn more about the safety of PF-06939999, to determine the recommended dose of PF-06939999 to study further, and to evaluate the early signs of clinical benefit/possible effectiveness of PF-06939999.

Researchers wanted to know:

What medical problems did participants have?

Did participants have any abnormal lab test results?

During Part 1, did participants have any "dose-limiting toxicities"?

During Part 2, how many participants with non-small cell lung cancer, bladder cancer, or head and neck squamous cell carcinoma who received PF-06939999 had a reduction in tumor size?

"Dose-limiting toxicities" (DLTs) are certain medical problems caused by taking PF-06939999 which require the patient to lower the dose or stop taking the medicine (permanently or temporarily).

What happened during the study?

How was the study done?

Researchers studied a group of participants to learn more about the safety and the possible effectiveness of PF-06939999, and to determine the recommended dose of PF-06939999 to study further.

Part 1

This part of the study included 28 participants with non-small cell lung cancer, head and neck squamous cell carcinoma, esophageal cancer, endometrial cancer, cervical cancer, or bladder cancer. Participants received increasing doses of PF-06939999, starting at 0.5 milligrams (mg) once per day, to help determine the recommended dose to study further. Part 1 participants were assigned to "cohorts" (smaller groups) of about 3 participants. So, the first cohort received 0.5 mg once per day, the second cohort received 0.5 mg twice per day, the third cohort received 1 mg once per day, and so on. The study doctors monitored the participants for DLTs. If participants

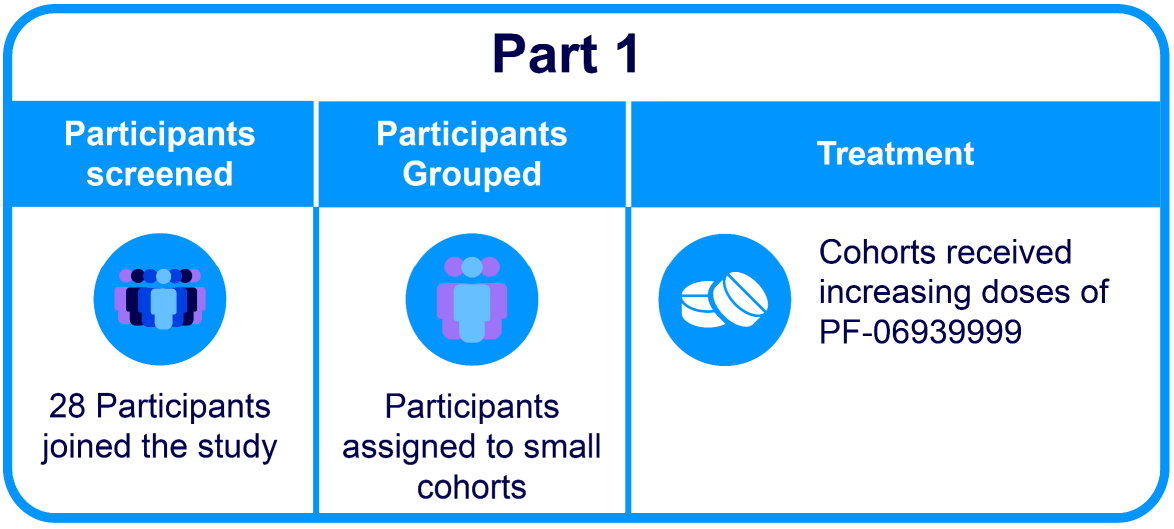
from a cohort had too many DLTs, PF-06939999 doses would not be increased any further.

The chart below shows the doses that were to be tested in Part 1.

Cohort/Dose Level	PF-06939999 Dose
1 (Starting Dose)	0.5 mg once per day
2	0.5 mg twice per day
3	1 mg twice per day
4	2 mg twice per day
5	4 mg twice per day
6	6 mg once per day
7	6 mg twice per day
8	8 mg once per day

Participants were to attend a screening visit, 6 visits during their first 28-day treatment cycle, 2 visits during each subsequent cycle, an end-of-treatment visit, and a safety follow-up visit about 1 month after end of treatment.

The figure below shows what happened during Part 1.



Part 2

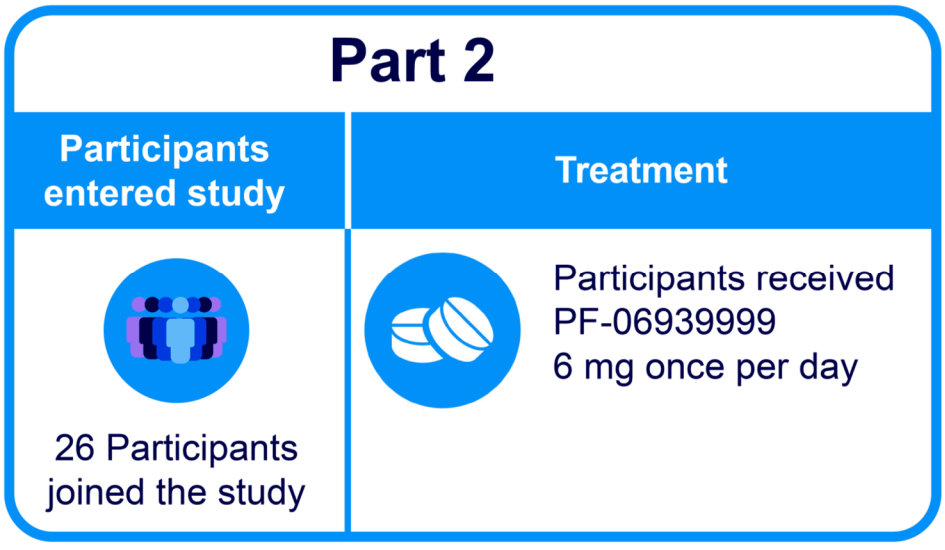
This part of the study included 26 participants with non-small cell lung cancer, bladder cancer, or head and neck squamous cell carcinoma. Participants were treated with 6 mg PF-06939999, once per day. Participants were assigned to the following cohorts:

- 2A: 14 participants with non-small cell lung cancer
- 2B: 2 participants with bladder cancer
- 2C: 10 participants with head and neck squamous cell carcinoma

Participants were to attend a screening visit, 6 visits during their first 28-day treatment cycle, 2 visits during each subsequent cycle, an end-of-treatment visit, and a safety follow-up visit about 1 month after end of treatment. After the follow-up visit, they were also contacted by phone every 12 weeks until the study ended, to determine survival status.

This was an open-label study, which means that the participants, researchers, and study doctors knew which treatments the participants received.

The figure below shows what happened during Part 2.



Where did this study take place?

The study was conducted at 10 locations in the United States.

When did this study take place?

It began 14 March 2019 and ended 27 April 2022.

Who participated in this study?

Participants included in the study:

- Were examined by a study doctor and determined to be appropriate to participate
- Were adults
- Had the following types of cancer: non-small cell lung cancer, head and neck squamous cell carcinoma, esophageal cancer, endometrial cancer, cervical cancer, or bladder cancer
- Had cancer that was considered to be advanced or metastatic

A total of 54 participants joined this study: 28 participants in Part 1 and 26 participants in Part 2.

- A total of 23 women (43%) and 31 men (57%) participated
- All participants were between the ages of 32 and 84 years, with an average age of 63

Participants could be treated as long as they continued to benefit from PF-06939999 for up to 2 years, or until the study ended. All 54 participants discontinued study treatment; the main reason for discontinuing treatment was worsening cancer. A total of 35 (65%) participants discontinued the follow-up phase of the study. The main reasons were discontinuing follow-up were:

- they passed away: 13 participants (24%)
- they withdrew from the study: 6 participants (11%)

- study doctor's decision: 5 participants (9%)
- sponsor ended the study: 1 participant (2%)
- other reason: 10 participants (19%)

How long did the study last?

The amount of time that participants were in the study varied depending on how they responded to study treatment. The entire study took a little more than 3 years to complete. The Sponsor decided to end the study in April 2022. This decision was made for business reasons and was not due to any safety concerns about PF-06939999.

The Sponsor began reviewing the information collected and created a report of the results. This is a summary of that 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 the 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.

What medical problems did participants have?

All 54 participants (100%) in this study had a medical problem, and 45 participants (83%) had a medical problem that was considered to be related to the study treatment. A total of 5 (9%) participants stopped taking study treatment because of medical problems, and 8 (15%) participants left the study because of medical problems. The table (Table 1) below shows the most common medical problems—those occurring in at least 30% of participants—that happened during the study, some of which resulted in participants having to stop treatment.

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 at least 30% of participants are listed.
- The **2nd** column tells how many of the 54 participants treated with PF-06939999 reported each medical problem. Next to this number is the percentage of the 54 participants treated with PF-06939999 who reported the medical problem.
- Using these instructions, you can see that 24 (44%) participants reported low number of red blood cells.

Table 1. Commonly reported medical problems by study participants	
Medical Problem	**PF-06939999 (54 Participants)**
Low number of red blood cells	24 out of 54 participants (44%)
Feeling tired	23 out of 54 participants (43%)
Nausea	22 out of 54 participants (41%)
Low appetite	17 out of 54 participants (31%)

Did participants have any dose-limiting toxicities (DLTs)?

During Part 1, 4 out of 24 (17%) participants had DLTs:

- 2 participants treated with 6 mg twice per day of PF-06939999 had a low number of platelets in the blood
- 1 participant treated with 8 mg once per day of PF-06939999 had a low number of red blood cells
- 1 participant treated with 6 mg once per day of PF-06939999 had a low number of a type of white blood cell called a neutrophil

Based on these results, the researchers selected 6 mg once per day as the recommended dose of PF-06939999 to study further.

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.

What serious medical problems did participants have?

A total of 22 out of 54 (41%) participants had serious medical problems. The most common serious medical problems were worsening of cancer (6 out of 54 participants; 11%) and lung infection (4 out of 54 participants; 7%).

3 (6%) participants had serious medical problems that were considered to be related to study treatment: 1 participant had an embolism (blood flow to artery blocked by blood clot), 1 participant had a low number of red blood cells, and 1 participant had low number of red blood cells and low number of platelets in the blood.

16 (30%) participants died during this study. These deaths were mainly due to worsening cancer, and none were considered to be related to study treatment.

What were the results of the study?

During Part 2, how many participants with non-small cell lung cancer, bladder cancer, or head and neck squamous cell carcinoma who received PF-06939999 had a reduction in tumor size?

11 out of 21 participants (52%) treated in Part 2 demonstrated good disease control by imaging, including significant tumor size reduction (partial response) and no significant growth of tumor (stable disease). Additionally, 11 out of 23 participants (48%) treated in Part 1 demonstrated good disease control by imaging, including

significant tumor size reduction (partial response) and no significant growth of tumor (stable disease).

This does not mean that everyone in this study had these results. This is a summary of the main results of this study.

Where can I learn more about this study?

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

For more details on your study protocol, please visit:
www.clinicaltrials.gov Use the study identifier **NCT03854227**

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!