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-06804103
Protocol Number:	C0541001
Dates of Study:	01 November 2017 to 31 August 2021
Title of this Study:	PF-06804103 Dose Escalation in HER2 Positive and Negative Solid Tumors [A Phase 1 Dose Escalation Study Evaluating the Safety and Tolerability of PF-06804103 in Patients With Human Epidermal Growth Factor Receptor 2 (HER2) Positive and Negative Solid Tumors]
Date(s) of this Report:	15 July 2022

– 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 HER2-positive, HER2-negative, and HER2-low 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. Breast cancer is cancer that begins in the breast. Gastric cancer is cancer that begins in the stomach.

Some people with cancer have high levels of a certain protein receptor on the surface of their cancer cells. This protein is called HER2 (human epidermal growth factor receptor 2). A cell with too many HER2 receptors is stimulated to grow and multiply too fast and can become a cancer. When people with cancer have too much of this protein their cancer is called "HER2-positive". When people with cancer do not have too much of this protein their cancer is called "HER2-negative". Some people with cancer are considered to have "HER2-low" cancer, which means that their cancer is HER2-positive, but with lower amounts of HER2.

What is PF-06804103?

PF-06804103 is an investigational drug that was being studied for the treatment of HER2-positive breast and gastric cancers. An investigational drug is one that has not been approved for use outside of research studies. PF-06804103 is given as an IV (intravenous; through a needle in the vein) on Day 1 of 21-day or 28-day "treatment cycles".

What was the purpose of this study?

The main purposes of this study were to learn more about the safety and about the possible effectiveness of PF-06804103, and to determine the recommended dose of PF-06804103 to study further.

Researchers wanted to know:

What medical problems did participants have?

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

During Part 2, how many participants had a reduction in tumor size?

During Part 2, how long did it take for cancer to get worse?

During Part 2, how long did participants survive without cancer getting worse?

During Part 2, how long did PF-06804103 continue to help cancer?

"Dose-limiting toxicities" (DLTs) are certain medical problems caused by taking PF-06804103 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-06804103, and to determine the recommended dose of PF-06804103 to study further.

Participants included in the study:

- Were examined by a study doctor and determined to be appropriate to participate
- Were adults

- Men could join Part 1A of the study; other parts of this study enrolled women only
- Had breast cancer that was estrogen-receptor or progesterone-receptor positive (meaning that hormones stimulate the growth of the tumor); Part 1A also enrolled participants with gastric cancer
- Had cancer that was HER2-positive or HER2-low assessed by a diagnostic test
- Had cancer that either did not adequately improve with standard treatments, returned after initially improving with standard treatments, or for which no standard treatments were available
- Had cancer that was considered to be advanced (unlikely to be cured), or that had spread to other parts of the body beyond the breast or stomach

Part 1A

This part of the study included men and women with breast cancer or stomach cancer. Participants received increasing doses of PF-06804103, starting with 0.15 milligrams (mg) per kilogram (kg) of body weight every 3 weeks, to help determine the recommended dose to study further. Part 1A participants were assigned to "cohorts" (smaller groups) of about 2 to 4 participants. So, the first cohort received 0.15 mg/kg, the second cohort received 0.5 mg/kg, and so on. The study doctors monitored the participants for DLTs. If participants from a cohort had too many DLTs, PF-06804103 doses would not be increased any further.

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

Cohort/Dose Level	PF-06804103 Dose
1 (Starting Dose)	0.15
2	0.5
3	1.2
4	2.0
5	3.0
6	4.0
7	5.0

Part 1B

This part of the study included 2 women with breast cancer. Participants received 2 mg/kg PF-06804103. Additionally, participants in Part 1B received 125 mg palbociclib by mouth every day for 3 weeks and 2.5 mg letrozole by mouth every day for 4 weeks (standard treatments for breast cancer).

Part 2A

This part of the study included 46 women with breast cancer. Participants were randomly assigned (like the flip of a coin) to receive either PF-06804103 4 mg/kg every 3 weeks or PF-06804103 3 mg/kg every 3 weeks.

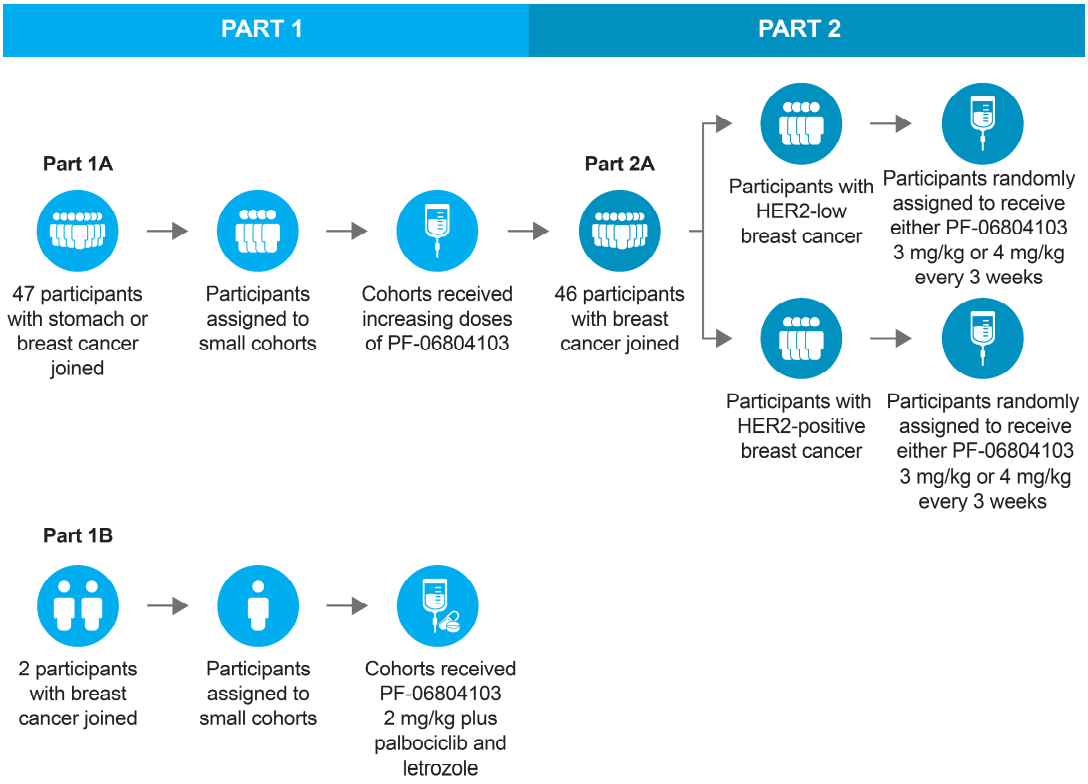
It was also planned to have a Part 2B, but the study was stopped before any participants were treated in that part of the study.

Depending on the part of the study they were in, participants were expected to attend visits at the study center as follows:

- Treatment Cycle 1: Days 1, 4, 8, 15
- Treatment Cycles 2 and 3: Days, 1, 8, 15
- Treatment Cycle 4: Days 1, 4, 8, 15
- Treatment Cycles 5 and Later: Days, 1, 8, 15
- Participants were also expected to attend an end-of-treatment visit and a follow-up visit about 1 month later.

Study participants had the option to receive acetaminophen and diphenhydramine about ½ hour to 2 hours before their PF-06804103, to help prevent possible adverse reactions. 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 the study.



Where did this study take place?

The study was conducted at 36 locations in Australia, Italy, Russia, Spain, South Korea, and the United States.

When did this study take place?

It began 01 November 2017 and ended 31 August 2021.

Who participated in this study?

A total of 95 participants joined this study: 47 participants in Part 1A, 46 participants in Part 2A, and 2 participants in Part 1B.

- A total of 77 women (81%) and 18 men (19%) participated
- All participants were between the ages of 32 and 77 years

Participants could be treated as long as they continued to benefit from PF-06804103, or until the study ended. Of the 95 participants who started the study, 93 (98%) entered the follow-up phase of the study and 56 participants (59%) completed the follow-up phase of the study.

A total of 37 participants (39%) did not finish the follow-up phase because:

- they withdrew from the study: 19 participants (20%)
- they were lost to follow-up (could not be contacted by study staff): 5 participants (5%)
- they passed away: 5 participants (5%)
- the sponsor ended the study: 4 participants (4%)
- other reason: 4 participants (4%)

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 almost 4 years to complete. The Sponsor decided to end the study in August 2021. This decision was made for business reasons and was not due to any safety concerns about PF-06804103. 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.

All 95 participants (100%) in this study had a medical problem, and 89 participants (94%) had a medical problem that was considered to be related to the study treatment. A total of 39 (41%) participants stopped taking study treatment because of medical problems. The table 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 Tables 1 and 2.

Instructions for Understanding Tables 1 and 2.

- 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 95 participants treated with PF-06804103 reported each medical problem. Next to this number is the percentage of the 95 participants treated with PF-06804103 who reported the medical problem.
- Using these instructions, you can see that 43 (45%) participants reported hair loss.

Table 1. Commonly reported medical problems by study participants	
Medical Problem	**PF-06804103 (95 Participants)**
Hair loss	43 out of 95 participants (45%)
Feeling tired	39 out of 95 participants (41%)
Numbness, pain, or weakness in hands or feet caused by nerve damage	31 out of 95 participants (33%)
Muscle pain	30 out of 95 participants (32%)
Constipation	29 out of 95 participants (31%)
Rash	29 out of 95 participants (31%)

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

During Part 1A, 4 out of 47 (9%) participants had DLTs:

- 1 participant in the PF-06804103 3 mg/kg cohort had joint pain and nerve pain
- 1 participant in the PF-06804103 3 mg/kg cohort had musculoskeletal (muscles, bones, and joints) pain
- 1 participant in the PF-06804103 4 mg/kg cohort had decreased ability of the heart to pump blood

- 1 participant in the PF-06804103 4 mg/kg cohort had muscle pain, joint pain, and tiredness

Based on these results, the researchers selected 4 mg/kg as the recommended dose to study further, with flexibility to reduce to a lower dose (such as 3 mg/kg), if needed.

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 38 out of 95 (40%) participants had serious medical problems, and 19 (20%) participants had serious medical problems that were considered to be related to study treatment. The table below shows the most common serious medical problems—those occurring in 2 or more participants—that happened during the study.

Table 2. Commonly reported serious medical problems by study participants	
Serious Medical Problem	**PF-06804103 (95 Participants)**
Blockage of bowel	6 out of 95 participants (6%)
Kidney failure	2 out of 95 participants (2%)
Deep infection of the skin (cellulitis)	2 out of 95 participants (2%)
Decreased appetite	2 out of 95 participants (2%)
Muscle pain	2 out of 95 participants (2%)
Rash with pus-filled bumps	2 out of 95 participants (2%)

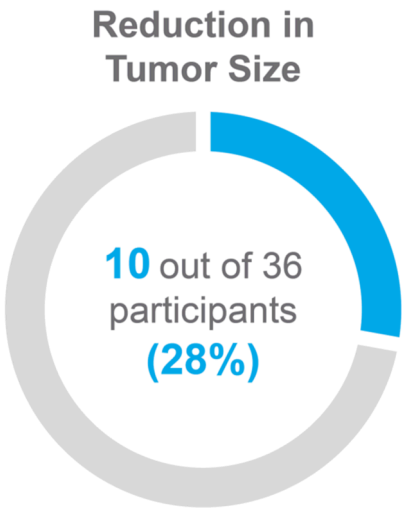
Eight participants (8%) died during this study. These deaths were due to worsening cancer and were not considered to be related to study treatment.

What were the results of the study?

During Part 2, how many participants had a reduction in tumor size?

In Part 2A, 10 out of 36 (28%) participants had a reduction in tumor size (meaning their tumors got smaller).

The figure below shows this result.



During Part 2, how long did it take for cancer to get worse?

During Part 2A, there were 16 participants whose cancer worsened during the study. Among these participants, the median amount of time that it took cancer to get worse was about 5.5 months. Median means the middle amount. So, cancer worsened before 5.5 months for half of these participants, and after 5.5 months for half of these participants.

During Part 2, how long did participants survive without cancer getting worse?

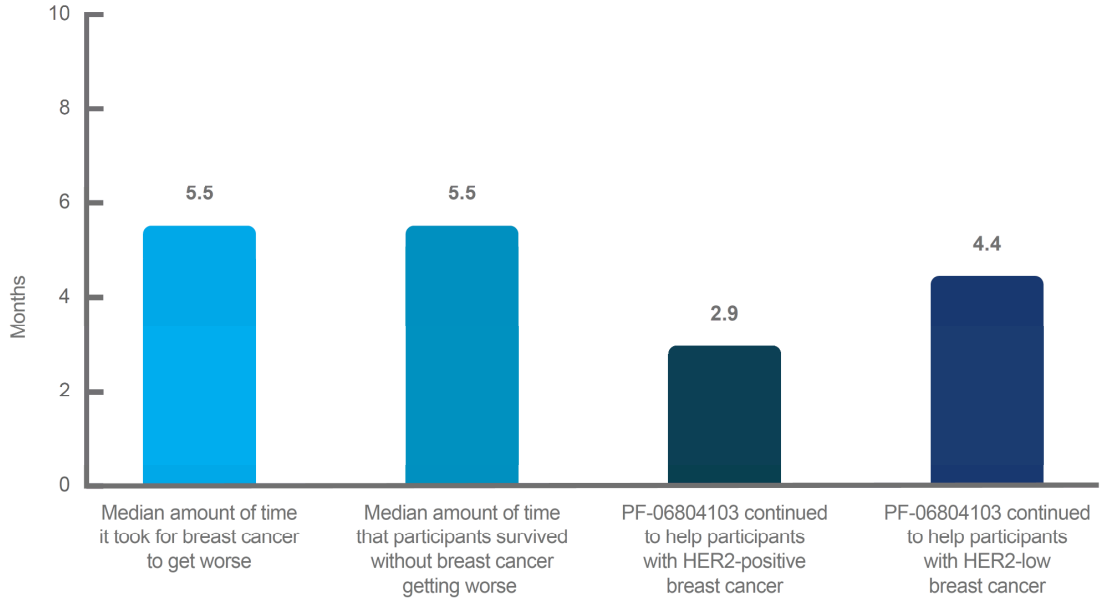
The median amount of time that participants in Part 2A survived without cancer getting worse was about 5.5 months. So, half of these participants survived without cancer getting worse for longer than 5.5 months, and half of these participants survived without cancer getting worse for less than 5.5 months.

During Part 2, how long did PF-06804103 continue to help cancer?

In Part 2A, the median amount of time that PF-06804103 continued to help two participants with HER2-positive breast cancer was 2.9 months. The median

amount of time that PF-06804103 continued to help two participants with HER2-low breast cancer was 4.4 months.

The figure below shows these results.



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.

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.clinicaltrials.gov Use the study identifier **NCT03284723**

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!