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-06821497
Protocol Number:	C2321005
Dates of Study:	17 March 2023 to 20 June 2023
Title of this Study:	A Study to Understand the Effect of Tablet Formulation and Food on PF-06821497 in Healthy Adult Participants. [A Phase 1, Randomized, Open-Label, 3-Period, Crossover, Single-Dose, 2-Part Study in Healthy Participants to Investigate the Effect of Tablet Formulation and Food on the Relative Bioavailability of PF-06821497]
Date(s) of this Report:	11 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 chemotherapy-naïve metastatic castration-resistant prostate cancer?

Prostate cancer is the name for cancer that starts in the prostate, which is a small, walnut-sized gland that lies at the base of the bladder in men and is part of the male reproductive system. Prostate cancer is a common cancer in men, and it is often a slow-growing cancer with few symptoms.

What is PF-06821497?

PF-06821497 is an investigational drug being studied to treat people with a certain type of prostate cancer. "Investigational" means that the drug has not been approved by the United States (U.S.) Food and Drug Administration (FDA). This study medication will be given in the tablet form.

What was the purpose of this study?

The main purpose of this study was to measure and compare how much of the study medication was there in the plasma after taking a single 250 mg dose of the Formulation 1 (material sparing tablet [MST]) tablet and the Formulation 2 (wet granulation [WG]) tablet under fasting conditions (nothing to eat or drink except water for at least 10 hours). This study also looked at how the study medication was tolerated, if there were significant side effects, and how a low-fat, low-calorie meal and a high-fat, high-calorie meal had an effect on the amount of study medication in plasma after taking a single 1,250 mg dose of the WG tablet formulation compared with taking it under fasting conditions.

Researchers wanted to know:

- **How did the tablet formulation of PF-06821497 act in the body of healthy adult participants?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

This was an “open-label” study. This means researchers and participants knew what study medication each participant was receiving.

Researchers tested the tablet formulation of PF-06821497 on a group of healthy participants to learn how PF-06821497 was handled by the body.

All participants were “screened” to see if they would qualify to be in the study. Participants who qualified to be in the study were admitted to the Research Unit the day before dosing (Day -1). Participants were required to stay in the Research Unit for up to 13 nights. The study involved 3 dosing periods during 1 continuous admission. There were at least 5 days between each dose of study medication.

This study consisted of 2 parts. In Part 1, participants were dosed under fasting conditions and in Part 2, participants were dosed fasted and with food (Figure 1). Participants took part only in one part of the study.

Part 1 (Dosing under fasting conditions [following an overnight fast of at least 10 hours]):

- Treatment A: Single oral (by mouth) 250 mg dose of the Formulation 1 given as a single tablet.
- Treatment B: Single oral 250 mg dose of the Formulation 2 given as a single tablet.
- Treatment C: Single oral 250 mg dose of the Formulation 3 (larger particle size) given as a single tablet.

Part 2 (Food effect dosing):

- Treatment D: Single, oral 1,250 mg dose of the Formulation 2 given as five 250 mg tablets under fasting conditions.
- Treatment E: Single oral 1,250 mg dose of the Formulation 2 given as five 250 mg tablets with a low-fat meal.
- Treatment F: Single oral 1,250 mg dose of the Formulation 2 given as five 250 mg tablets with a high-fat meal.

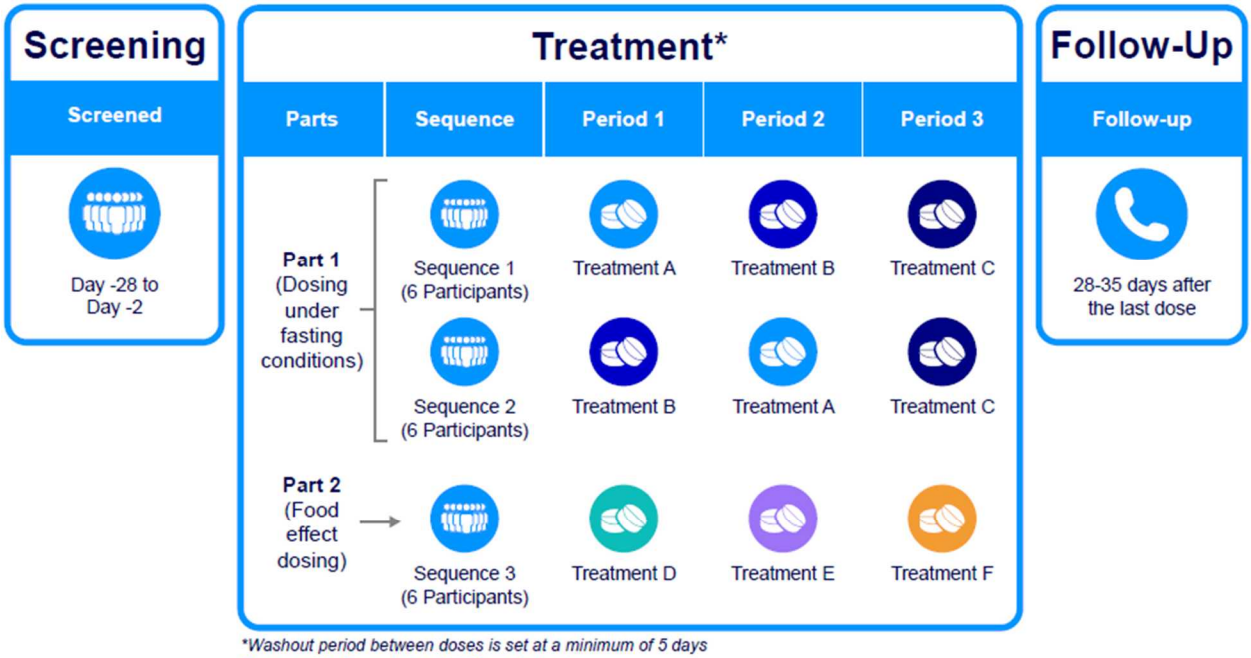
On Day 1 of each period, participants received a single dose of the study medication. Participants fasted overnight (nothing to eat or drink except water) for at least 10 hours before dosing or eating breakfast.

Study treatment sequence and assignment to fasting or food effect dosing were randomly assigned like pulling a number out of a hat.

Each treatment consisted of a single dose of PF-06821497. The treatments differ by tablet formulation and/or whether the medicine is to be given with food or without food conditions.

Researchers took samples of plasma from participants during the study and measured the amount of study medication. Researchers also checked the participants' health during the study and asked them how they were feeling.

Figure 1: Study Design



*Washout period between doses is set at a minimum of 5 days
Treatment A: Formulation 1 (250 mg fasted).
Treatment B: Formulation 2 (250 mg fasted).
Treatment C: Formulation 3 (250 mg fasted).
Treatment D: Formulation 2 (1250 mg fasted).
Treatment E: Formulation 2 (1250 mg fed: Low-fat meal).
Treatment F: Formulation 2 (1250 mg fed: High-fat meal).

Where did this study take place?

The Sponsor ran this study at 1 location in the United States.

When did this study take place?

It began on 17 March 2023 and ended on 20 June 2023.

Who participated in this study?

The study included 18 healthy participants (12 participants in Part 1 and 6 participants in Part 2) who met the inclusion/exclusion criteria for things such as age and weight.

- A total of 7 men (6 in Part 1 and 1 in Part 2) participated.
- A total of 11 women (6 in Part 1 and 5 in Part 2) participated.
- All participants were between the ages of 26 and 75.

Of the 18 participants who started the study, all participants in Part 1 finished the study. One (1) participant of PF-06821497 Formulation 2 1250 mg fed low-fat group in Part 2 left from study due to medical problem after period 2.

How long did the study last?

Study participants were in each part of the study for up to 10 weeks. The entire study took approximately 3 months to complete.

When the study ended in June 2023, 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?

How did different formulations of PF-06821497 act in the body?

To answer this question, the researchers compared the plasma samples of participants from Period 1, Period 2, and Period 3.

What was the amount of PF-06821497 in the plasma after the participants took Formulation 1 and Formulation 2 of PF-06821497?

Part 1 (Dosing Under Fasting Conditions):

- The estimated total amount of PF-06821497 in the plasma ([Area under curve from time zero extrapolated to infinite time] AUC_{inf}) from when participants took single 250 mg dose of the Formulation 1 and the Formulation 2 under fasting conditions were 3302 and 3375 ng•hr/mL (nanogram hours per milliliter) respectively (Figure 2). The ng•hr/mL is a unit used to measure the total amount of drug over time in the plasma (Figure 2).

- The highest amount of PF-06821497 in the plasma ([Maximum observed concentration] C_{max}) after participants took single 250 mg dose of the Formulation 1 and the Formulation 2 under fasting conditions were 862.6 and 1023 ng/mL (nanograms per milliliter) respectively (Figure 2). The amount of drug in the plasma was measured in nanograms per milliliter, also called ng/mL (Figure 2).

Part 2 (Food Effect Dosing):

- The estimated total amount of PF-06821497 in the plasma (AUC_{inf}) from when participants took single 1250 mg of the Formulation 2 under fasting conditions, low-fat or low-calorie diet, and high-fat or high calorie diet was 11220, 22810, and 25690 ng•hr/mL respectively (Figure 3).

- The highest amount of PF-06821497 in the plasma (C_{max}) after participants took single 1250 mg of the Formulation 2 under fasting conditions, low-fat or low-calorie diet, and high-fat or high calorie diet were 2699, 7685, and 8905 ng/mL respectively (Figure 3).

Figure 2: Total amount of PF-06821497 in the plasma and highest amount of PF-06821497 in the plasma in Part 1

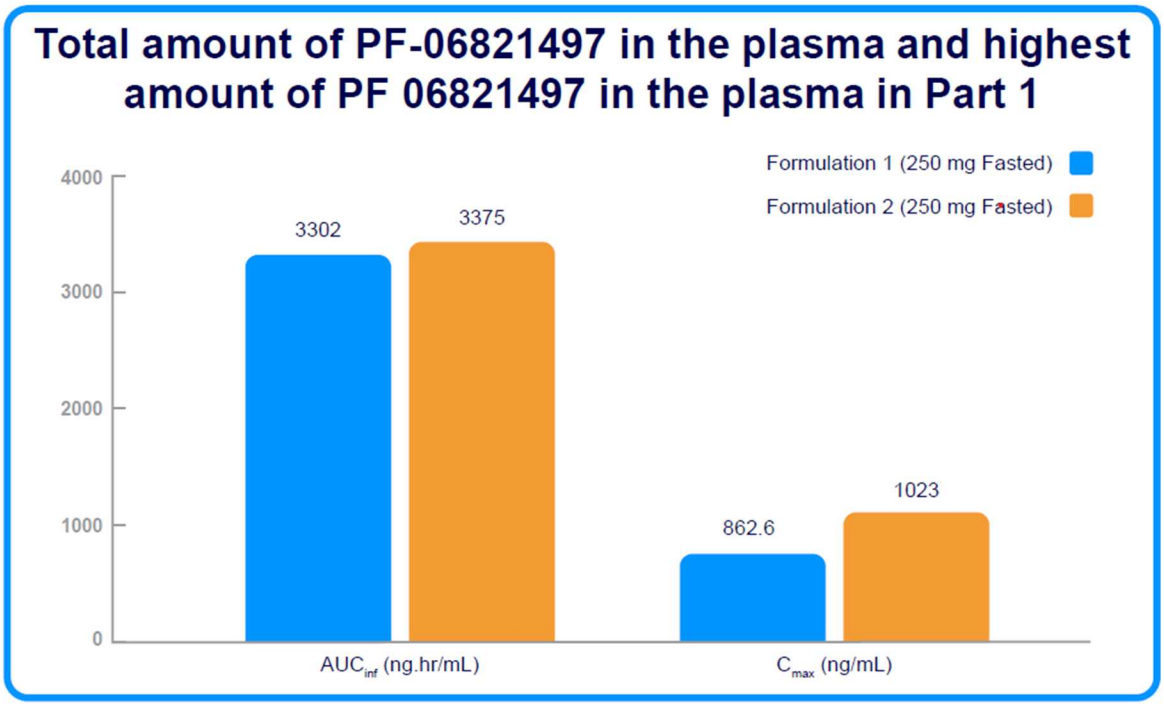
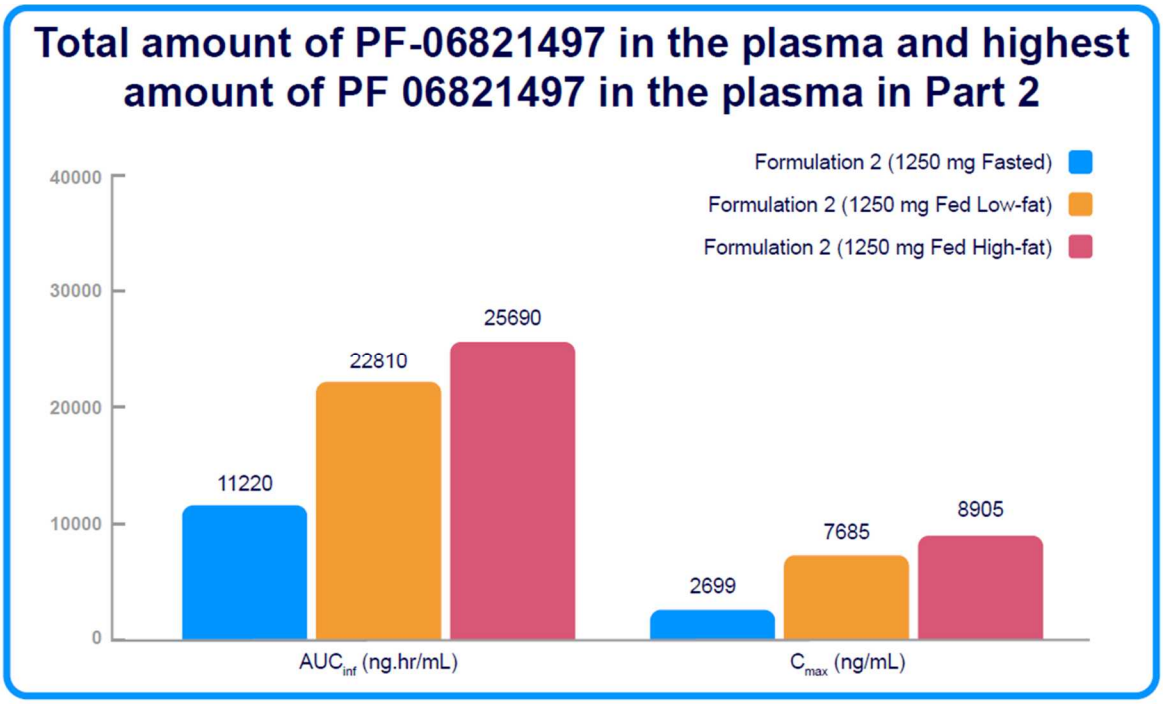


Figure 3: Total amount of PF-06821497 in the plasma and highest amount of PF-06821497 in the plasma in Part 2



Based on the results, the study medication behaves similarly in the body and the formulations 1 and 2 are comparable. The study medication may act differently in the body depending on the fasted or the fed conditions at 1250 mg dose. These differences could have been due to chance.

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 unknown 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.

Eight (8) out of 12 (66.7%) and 4 out of 6 (66.7%) participants in this study had at least 1 medical problem during Part 1 and Part 2 of the study, respectively. One (1) participant left the study because of medical problem of Alanine aminotransferase (ALT) liver test increased. The most common medical problems – those reported by at least 1 participant – 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 at least 1 participant are listed.
- The **2nd** column tells how many of the 12 participants taking PF-06821497 (Formulation 1) Fasted group reported each medical problem in Part 1 of the study. Next to this number is the percentage of the 12 participants taking the study medication who reported the medical problem.
- The **3rd** column tells how many of the 12 participants taking PF-06821497 (Formulation 2) Fasted group reported each medical problem in Part 1 of the study. Next to this number is the percentage of the 12 participants taking PF-06821497 who reported the medical problem.
- The **4th** column tells how many of the 12 participants taking PF-06821497 (Formulation 3) Fasted group reported each medical problem in Part 1 of the study. Next to this number is the percentage of the 12 participants taking PF-06821497 who reported the medical problem.
- Using these instructions, you can see that 1 out of the 12 (8.3%) participants taking the study medication (Formulation 3) reported abdominal pain in Part 1 of the study.

Table 1. Commonly reported medical problems by study participants (Part 1)			
Medical Problem	**Part 1 PF-06821497**		
	Formulation 1 250 mg Fasted (12 Participants)	**Formulation 2 250 mg Fasted (12 Participants)**	**Formulation 3 250 mg Fasted (12 Participants)**
Abdominal pain	0	0	1 out of 12 participants (8.3%)
Abnormal urine odour	0	1 out of 12 participants (8.3%)	0
Back pain	0	1 out of 12 participants (8.3%)	0
Constipation	0	1 out of 12 participants (8.3%)	0
Disturbance in attention	1 out of 12 participants (8.3%)	1 out of 12 participants (8.3%)	0
Headache	2 out of 12 participants (16.7%)	1 out of 12 participants (8.3%)	0

Nausea	0	1 out of 12 participants (8.3%)	0
Losing a toenail or fingernail because of an injury (Nail avulsion)	1 out of 12 participants (8.3%)	0	0
Narrowing of blood vessels at the site of injury (Vessel puncture site pain)	0	1 out of 12 participants (8.3%)	1 out of 12 participants (8.3%)
Neck Pain	1 out of 12 participants (8.3%)	0	0
Vessel puncture site bruise	1 out of 12 participants (8.3%)	0	0

Below are instructions on how to read Table 2.

Instructions for Understanding Table 2.

- The **1st** column of Table 2 lists medical problems that were commonly reported during the study. All medical problems reported by at least 1 participant are listed.
- The **2nd** column tells how many of the 6 participants taking PF-06821497 (Formulation 2) in fasted group reported each medical problem in Part 2 of the study. Next to this number is the percentage of the 6 participants taking the study medication who reported the medical problem.
- The **3rd** column tells how many of the 6 participants taking PF-06821497 (Formulation 2) in fed low-fat group reported each medical problem in Part 2 of the study. Next to this number is the percentage of the 6 participants taking PF-06821497 who reported the medical problem.
- The 4th column tells how many of the 5 participants taking PF-06821497 (Formulation 2) in fed high-fat group reported each medical problem in Part 2 of the study. Next to this number is the percentage of the 5 participants taking PF-06821497 who reported the medical problem.
- Using these instructions, you can see that 1 out of the 6 (16.7%) participants taking study medication (Formulation 2) in fed low-fat group reported abdominal discomfort in Part 2 of the study.

Table 2. Commonly reported medical problems by study participants (Part 2)			
Medical Problem	**Part 2 PF-06821497**		
	Formulation 2 1250 mg Fasted (6 Participants)	**Formulation 2 1250 mg Fed Low-fat (6 Participants)**	**Formulation 2 1250 mg Fed High-fat (5 Participants)**
Abdominal discomfort	0	1 out of 6 participants (16.7%)	0
Blood clotting disorders	1 out of 6 participants (16.7%)	0	0
Eyelid pain	0	1 out of 6 participants (16.7%)	0
Fall	0	0	1 out of 5 participants (20.0%)

Headache	0	0	1 out of 5 participants (20.0%)
Muscle spasms	0	1 out of 6 participants (16.7%)	0
Muscle aches and pain (myalgia)	0	1 out of 6 participants (16.7%)	0
Narrowing of blood vessels at the site of injury (Vessel puncture site pain)	0	1 out of 6 participants (16.7%)	0
Raised red bump on the skin (rash macular)	1 out of 6 participants (16.7%)	0	0
Sign of liver damage (ALT increased)	1 out of 6 participants (16.7%)	0	0
Wrist fracture	0	0	1 out of 5 participants (20.0%)

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.

There were no participants in Part 1 of the study who had serious medical problems. One (1) out of 5 participants (20.0%) in Part 2 of the study had a serious medical problem of wrist fracture which was not related to the study medication.

No participant died during the study.

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 C2321005

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

www.clinicaltrials.gov	Use the study identifier **NCT05767905**

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!