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-07328948
Protocol Number:	C4921001
Dates of Study:	17 October 2022 to 03 May 2023
Title of this Study:	A study to determine the safety and tolerability of PF-07328948 in healthy adult participants [A Phase 1, Randomized, Double-Blind, Sponsor-Open, Placebo-Controlled, 4-Period, Crossover, First-in-Human Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Single Ascending Oral Doses of PF-07328948 Administered to Healthy Adult Participants]
Date(s) of this Report:	27 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 Heart Failure With Preserved Ejection Fraction?

Ejection Fraction is a measure of how much blood is pumped out of the left side of the heart each time it beats. Heart Failure with Preserved Ejection Fraction is a type of heart failure where the heart's pumping function, measured by the ejection fraction, is normal, or almost normal. However, despite a normal ejection fraction, the heart does not fill properly with blood because of stiff heart muscle in this condition.

What is PF-07328948?

PF-07328948 has not been approved for use outside of a research study. When the heart is not functioning properly, there is a build-up of certain types of molecules which are thought to reduce heart function. Removing the build-up of these molecules is prevented by a protein called branched chain ketoacid dehydrogenase kinase (BDK). PF-07328948 may help the heart function better by blocking BDK.

What was the purpose of this study?

The main purpose of this study was to evaluate the safety and tolerability of increasing doses of PF-07328948 when given to healthy adult participants.

In this study some participants took PF-07328948, and some took placebo. A placebo does not have any medicine in it, but it looks just like the study medicine. This study did not test if the drug helps to improve heart failure.

Researchers wanted to know:

- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

Researchers tested increasing doses of PF-07328948 on healthy participants to determine the safety and tolerability of PF-07328948.

This study consisted of 3 Cohorts (participant groups). Each Cohort was planned to have up to 4 periods. Participants received increasing doses of PF-07328948 or placebo, in these periods.

Participants in the 3 Cohorts received from 10 mg to 1500 mg of PF-07328948 or placebo in the sequence as shown in the Figure 1. There were 7 days in between the periods.

Cohort 1 participants received doses from 10 mg to 300 mg or placebo. There was a safety event in the 4th period in a participant that received placebo (described below).

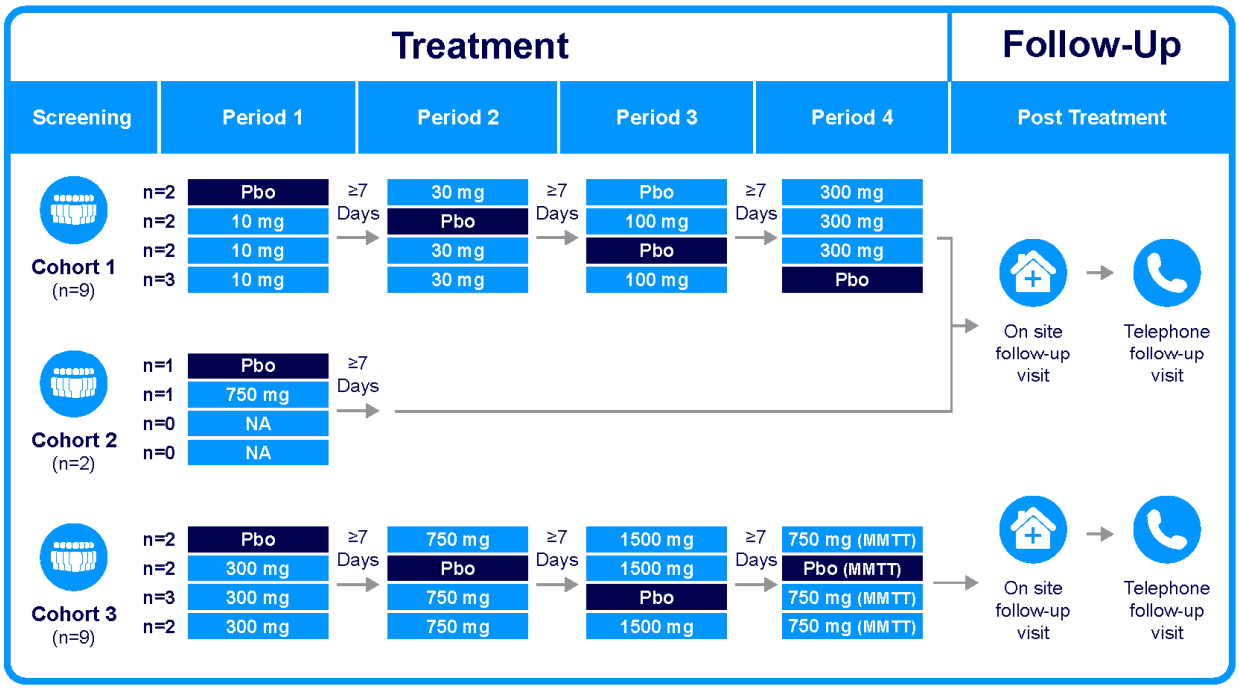
Cohort 2 participants received 750 mg or placebo. This cohort was ended early, during the 1st period, due to a safety event reported during the follow-up period in Cohort 1 Period 4.

Cohort 3 participants received doses from 300 mg to 1500 mg or placebo, including a period where the impact of high-protein mixed meal (MMTT) was tested.

This was a “double-blind” study, which means the participants and the investigators did not know who took the study medication and who took placebo.

Researchers checked the participants’ health periodically during the study and asked them how they were feeling and collected blood samples for laboratory tests.

Figure 1. How was the study done?



n = Number of Participants | Pbo = Placebo

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 17 October 2022 and ended 03 May 2023

Who participated in this study?

The study included healthy participants who met the inclusion/exclusion criteria for things such as age and weight.

- A total of 17 men participated
- A total of 3 women participated
- All participants were between the ages of 20 and 60 years

Of the 20 participants who started the study 15 finished the double-blind treatment phase and 5 did not finish the double-blind treatment phase.

- 2 participants discontinued due to unwanted medical problems
- 2 participants discontinued due to early termination of Cohort 2
- 1 participant discontinued by their own choice

How long did the study last?

Each participant was in the study for up to 14 weeks. The entire study took about 7 months to complete.

When the study ended in May 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 safe and well tolerated was PF-07328948?

In this study, researchers looked at the safety and tolerability of PF-07328948 when given in increasing doses. Researchers did this by looking at medical problems that participants had during the study.

Researchers were specifically interested in seeing if participants had the following:

- Any unwanted medical problems
- Abnormalities in laboratory tests, vital signs, and electrocardiograms (ECG). (ECG is a test that looks at how well the heart is working).

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.

Twelve out of 20 (60.0%) participants in this study had at least 1 medical problem. A total of 2 participants left the study because of medical problems. One participant temporarily discontinued due to an upper respiratory tract infection. The most common medical problems reported by the 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 the participants are listed.
- The **2nd** column tells how many of the 13 participants taking placebo reported each medical problem. Next to this number is the percentage of the 13 participants taking the study medication who reported the medical problem.
- The **3rd** column tells how many of the 2 participants taking placebo with mixed meal reported each medical problem. Next to this number is the percentage of the 2 participants taking placebo with mixed meal who reported the medical problem.
- The **4th** column tells how many of the 6 participants taking 10 mg of PF-07328948 reported each medical problem. Next to this number is the percentage of the 6 participants taking the study medication who reported the medical problem.
- The **5th** column tells how many of the 5 participants taking 30 mg of PF-07328948 reported each medical problem. Next to this number is the percentage of the 5 participants taking the study medication who reported the medical problem.
- Using these instructions, you can see that 1 out of 6 (16.7%) participants taking 10 mg of PF-07328948 reported constipation. None of the participants who took placebo,

placebo with mixed meal, or 30 mg of PF-07328948 reported constipation.

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 the participants are listed.
- The **2nd** column tells how many of the 5 participants taking 100 mg of PF-07328948 reported each medical problem. Next to this number is the percentage of the 5 participants taking the study medication who reported the medical problem.
- The **3rd** column tells how many of the 12 participants taking 300 mg of PF-07328948 reported each medical problem. Next to this number is the percentage of the 12 participants taking the study medication who reported the medical problem.
- The **4th** column tells how many of the 7 participants taking 750 mg of PF-07328948 reported each medical problem. Next to this number is the percentage of the 7 participants taking the study medication who reported the medical problem.
- The **5th** column tells how many of the 5 participants taking 750 mg of PF-07328948 with mixed meal reported each medical problem. Next to this number is the percentage of the 5 participants taking the study medication with mixed meal who reported the medical problem.
- The **6th** column tells how many of the 6 participants taking 1500 mg of PF-07328948 reported each medical problem. Next to this number is the percentage of the 6 participants

taking the study medication who reported the medical problem.

- Using these instructions, you can see that 1 out of 7 (14.3%) participants taking 750 mg of PF-07328948 reported rapid heartbeat. None of the participants taking 100 mg of PF-07328948, 300 mg of PF-07328948, 750 mg of PF-07328948 with mixed meal or 1500 mg of PF-07328948 reported rapid heartbeat.

Medical problems reported by all 20 participants are reported below. Each column shows the number of participants that received that particular treatment.

Table 1. Reported medical problems by study participants

Medical problem	Placebo (13 participants)	Placebo MMTT (2 participants)	PF-07328948 10 mg (6 participants)	PF-07328948 30 mg (5 participants)
Rapid heartbeat	0	0	0	0
Vision blurred	0	0	0	0
Abdominal pain	0	0	0	0

Table 1. Reported medical problems by study participants				
Medical problem	**Placebo (13 participants)**	**Placebo MMTT (2 participants)**	**PF-07328948 10 mg (6 participants)**	**PF-07328948 30 mg (5 participants)**
Abdominal pain upper	0	0	0	0
Constipation	0	0	1 out of 6 participants (16.7%).	0
Difficulty swallowing	0	0	0	0
Feeling like Vomiting	0	0	0	0
Inflamed red skin at application site	2 out of 13 participants (15.4%)	0	0	0
Chest discomfort	0	0	0	0
Tiredness	0	0	0	0

Table 1. Reported medical problems by study participants				
Medical problem	**Placebo (13 participants)**	**Placebo MMTT (2 participants)**	**PF-07328948 10 mg (6 participants)**	**PF-07328948 30 mg (5 participants)**
Bruise at injection site	0	0	1 out of 6 participants (16.7%)	0
Pain at injection site	0	0	0	0
Seasonal allergy	0	0	0	1 out of 5 participants (20.0%)
Swelling of the sinus tissues	1 out of 13 participants (7.7%)	0	0	0
COVID-19	0	0	1 out of 6 participants (16.7%)	0
Infection of nose and throat (cold)	0	0	0	0

Table 1. Reported medical problems by study participants				
Medical problem	Placebo (13 participants)	Placebo MMTT (2 participants)	PF-07328948 10 mg (6 participants)	PF-07328948 30 mg (5 participants)
Sore throat due to infection	0	0	0	0
Upper respiratory tract infection	0	0	0	1 out of 5 participants (20.0%)
Bruising	1 out of 13 participants (7.7%)	0	0	0
Blood Pressure increased	0	0	0	0
Heart rate increased	0	0	0	0
Joint pain	0	0	0	0

Table 1. Reported medical problems by study participants				
Medical problem	**Placebo (13 participants)**	**Placebo MMTT (2 participants)**	**PF-07328948 10 mg (6 participants)**	**PF-07328948 30 mg (5 participants)**
Pain in the bone or muscles of chest	0	0	0	0
Dizziness with change in position	0	0	0	0
Headache	1 out of 13 participants (7.7%)	0	1 out of 6 participants (16.7%)	0
Nervous system symptoms	1 out of 13 participants (7.7%)	0	0	0
Feeling faint	0	0	0	0
Seizure	1 out of 13 participants (7.7%)	0	0	0

Table 1. Reported medical problems by study participants

Medical problem	Placebo (13 participants)	Placebo MMTT (2 participants)	PF-07328948 10 mg (6 participants)	PF-07328948 30 mg (5 participants)
Itchy skin on contact	0	1 out of 2 participants (50.0%)	0	0
Breaking of the fingernails or toenails	0	0	0	0

Table 2. Reported medical problems by study participants

Medical Problem	PF-07328948 100 mg (5 participants)	PF-07328948 300 mg (12 participants)	PF-07328948 750 mg (7 participants)	PF-07328948 750 mg MMTT (5 participants)	PF-07328948 1500 mg (6 participants)
Rapid heartbeat	0	0	1 out of 7 participants (14.3%)	0	0
Vision blurred	0	0	1 out of 7 participants (14.3%)	0	0

Table 2. Reported medical problems by study participants

Medical Problem	PF-07328948 100 mg (5 participants)	PF-07328948 300 mg (12 participants)	PF-07328948 750 mg (7 participants)	PF-07328948 750 mg MMTT (5 participants)	PF-07328948 1500 mg (6 participants)
Abdominal pain	0	0	0	0	1 out of 6 participants (16.7%)
Abdominal pain upper	0	1 out of 12 participants (8.3%)	0	0	0
Constipation	0	0	0	0	0
Difficulty swallowing	0	1 out of 12 participants (8.3%)	0	0	0
Felling like vomiting	0	1 out of 12 participants (8.3%)	0	0	0
Inflamed skin at application site	0	0	0	0	0

Table 2. Reported medical problems by study participants

Medical Problem	PF-07328948 100 mg (5 participants)	PF-07328948 300 mg (12 participants)	PF-07328948 750 mg (7 participants)	PF-07328948 750 mg MMTT (5 participants)	PF-07328948 1500 mg (6 participants)
Chest discomfort	0	0	1 out of 7 participants (14.3%)	0	0
Tiredness	0	1 out of 12 participant (8.3%	0	0	0
Bruise at injection site	0	0	0	0	0
Pain at injection site	0	1 out of 12 participants (8.3%)	0	0	0
Seasonal allergy	0	0	0	0	0
Swelling of the sinus tissues	0	0	0	0	0
COVID-19	0	0	0	0	0

Table 2. Reported medical problems by study participants

Medical Problem	PF-07328948 100 mg (5 participants)	PF-07328948 300 mg (12 participants)	PF-07328948 750 mg (7 participants)	PF-07328948 750 mg MMTT (5 participants)	PF-07328948 1500 mg (6 participants)
Infection of nose and throat (cold)	0	0	1 out of 7 participants (14.3%)	0	0
Sore throat due to infection	1 out of 5 participants (20.0%)	0	0	0	0
Upper respiratory tract infection	0	0	0	0	0
Bruising	0	0	0	0	0
Blood Pressure increased	0	1 out of 12 participants (8.3%)	0	0	0

Table 2. Reported medical problems by study participants

Medical Problem	PF-07328948 100 mg (5 participants)	PF-07328948 300 mg (12 participants)	PF-07328948 750 mg (7 participants)	PF-07328948 750 mg MMTT (5 participants)	PF-07328948 1500 mg (6 participants)
Heart rate increased	0	1 out of 12 participants (8.3%)	0	0	0
Joint pain	0	1 out of 12 participants (8.3%)	0	0	0
Pain in the bone or muscles of chest	0	0	1 out of 7 participants (14.3%)	1 out of 5 participants (20.0%)	0
Dizziness with change in position	0	0	1 out of 7 participants (14.3%)	0	0
Headache	0	2 out of 12 participants (16.7%)	0	0	0

Table 2. Reported medical problems by study participants

Medical Problem	PF-07328948 100 mg (5 participants)	PF-07328948 300 mg (12 participants)	PF-07328948 750 mg (7 participants)	PF-07328948 750 mg MMTT (5 participants)	PF-07328948 1500 mg (6 participants)
Nervous system symptoms	0	0	0	0	0
Feeling faint	0	0	0	0	1 out of 6 participants (16.7%)
Seizure	0	0	0	0	0
Itchy skin on contact	0	0	0	0	0
Separation of nail from nail bed	0	0	1 out of 7 participants (14.3%)	0	0

What were the results of the laboratory tests after participants received PF-07328948 or placebo?

Laboratory abnormalities that were reported in >1 participant in any treatment group are shown below.

- No participants in the placebo groups had laboratory test abnormalities.
- 2 participants who took PF-07328948 had white blood cell counts above normal.
- 2 participants who took PF-07328948 had ketones (chemicals released when your body breaks down fat) in their urine.
- None of the laboratory test abnormalities were considered clinically significant.

What were the results of the ECG tests after participants received PF-07328948 or placebo?

- None of the participants who took PF-07328948 had any clinically significant changes in ECG tests.

What were the results of the blood pressure checks after participants received PF-07328948 or placebo?

- 1 participant who took PF-07328948 had an increase in blood pressure and heart rate which returned to normal by Study Day 4.
- 1 participant who took PF-07328948 experienced a feeling of fainting (presyncope).

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.

1 participant in Cohort 1 experienced a serious medical problem of seizure (abnormal electric activity in the brain) after taking placebo.

No deaths were reported in this 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 C4921001

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

www.clinicaltrials.gov	Use the study identifier **NCT05654181**

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!