Plain Language Clinical Study

Summary

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 medicine 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-07293893

Protocol Number: C5171001

Dates of Study: 09 August 2023 to 22 March 2024

Title of this Study: A Study to Learn About the Study Medicine PF-07293893 at Different Dose Levels 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, and Pharmacokinetics of Single Ascending Oral Doses of PF-07293893 Administered to Healthy Adult Participants]

Date of this Report: 05 March 2025

Pfizer

– 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. Do you have any questions about the study or the results? If so, 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 how much blood is pumped out of the left side of the heart each time it beats. Heart Failure with Preserved Ejection Fraction (HFpEF) is a type of heart failure that occurs when the muscle in the left side of the heart stiffens and is less able to relax. This stiffness creates pressure inside the heart leading to a range of symptoms including breathing difficulties, tiredness, and inflammation.

What is PF-07293893?

The study medicine, PF-07293893 is being developed to help treat people with heart failure. It works by activating a specific protein called adenosine monophosphate-activated protein kinase (AMPKγ3) which is found only in skeletal muscle tissue. AMPKγ3 acts like an energy sensor and becomes activated when a cell is low in nutrients, such as after exercise or during stress. Once activated, AMPKγ3 triggers changes to produce energy that the muscle cell can use.

In this study, PF-07293893 was taken by mouth. Two (2) formulations of PF-07293893 were prepared and given to the study participants as shown below:

- PF-07293893 spray dried dispersion (SDD): In SDD, the drug is mixed with a special substance (like large molecule) and then sprayed into a hot chamber. The heat evaporates the liquid, leaving behind tiny particles of the drug evenly dispersed in the large molecule. This helps the drug dissolve better in the body, making it work more effectively.

- PF-07293893 crystalline (CRYS): In CRYS, the drug is prepared in a way where the molecules are arranged in a very orderly and repeated pattern,

like a well-organized grid. This orderly structure helps the drug to be stable and makes it easier for the body to absorb.

What was the purpose of this study?

The main purpose of this study was to learn about the safety of single increasing doses of PF-07293893 when given to healthy adult participants.

In this study some participants also 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:

How safe were increasing doses of PF 07293893 in healthy adult participants?

What happened during the study?

How was the study done?

Researchers tested different doses of PF-07293893 on healthy adult participants to learn about the safety of PF-07293893.

The study had 3 groups, Group A, Group B, and Group C. Each group was planned to have up to 4 treatment periods. Participants received single doses of PF-07293893, or placebo, on Day 1 of each period.

Participants received from 10 milligrams (mg) to 1500 mg of PF-07293893 or placebo in the sequences shown in Figure 1. They were assigned to each group by chance alone. There were at least 7 days between each period.

Group A participants received doses from 10 mg to 300 mg or placebo.

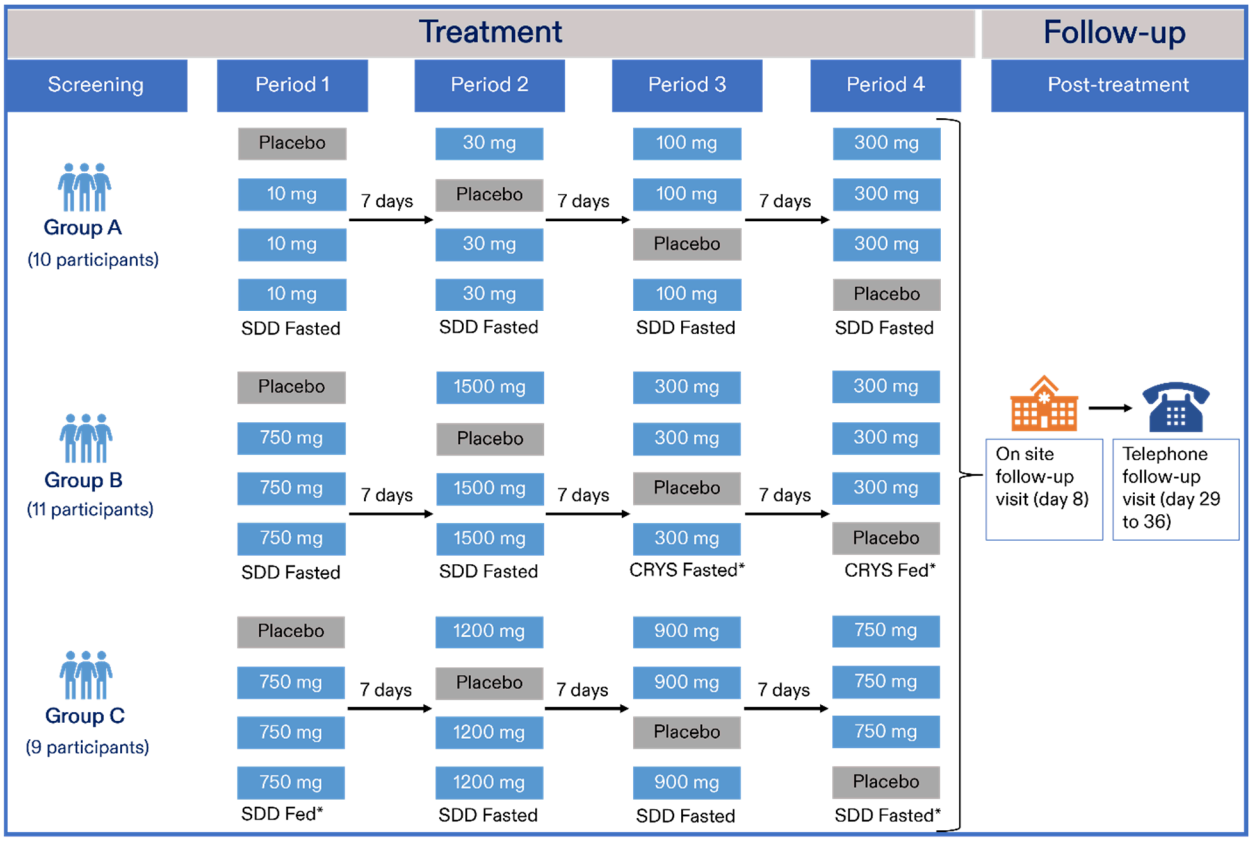
Group B participants received doses from 300 mg to 1500 mg or placebo.

Group C participants received doses from 750 mg to 1200 mg or placebo.

The dosing occurred in the fasted state for all treatment periods, except for Group B and Group C which included a treatment period where the impact of food (fed state) on CRYS and SDD PF-07293893 was tested.

The study participants and researchers did not know who took PF-07293893 and who took placebo. This is known as a "blinded" study.

Figure 1: Study design



n= Number of participants I SDD= Spray dried dispersion I CRYS= Crystalline formulation

*The participants taking placebo in Group B, Periods 3 and 4 (CRYS 300 mg Fasted and Fed) were the same, and similarly were participants in Group C, Periods 1 and 4 (SDD 750 mg Fed and Fasted).

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

Where did this study take place?

The Sponsor ran this study at 1 location in Belgium.

When did this study take place?

It began on 09 August 2023 and ended on 22 March 2024.

Who participated in this study?

The study included healthy participants with a body mass index (a measure of body weight in relation to height) of 16 to 30.5 kilograms per square meter (kg/m2) and weighing more than 50 kg.

- A total of 30 men participated.
- All participants were between the ages of 20 and 65 years inclusive.

Of the 30 participants who started the study, 23 finished the study.

Seven (7) did not finish the study due to:

- a medical problem,
- no longer meeting the inclusion criteria, or
- other reason.

How long did the study last?

Study participants were in the study for up to 14 weeks. The entire study took about 7 months to complete.

When the study ended in March 2024, 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 were increasing doses of PF-07293893 in healthy adult participants?

In this study, researchers looked at the safety of PF-07293893 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 (detailed below in the safety section).
- Abnormalities in laboratory test results, vital signs (blood pressure, heart rate, and body temperature), and electrocardiogram (ECG). An ECG is a test that looks at how well the heart is working. There were no meaningful changes in the results from these tests.

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 medicine might have on a participant.

Twenty-five (25) out of 30 (83%) participants in this study had at least 1 medical problem. The most frequently reported medical problems were headache, feeling sick, and reaction at the site where tiny sensor was applied to monitor heart activity. For participants who received SDD in fasting condition, the frequency of headache generally increased at higher dose levels (more than or equal to 750 mg). A total of 3 participants left the study because of medical problems. The most common medical problems – those reported by more than 5% 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 5% of participants are listed.
- The **2nd** column tells how many of the 30 participants taking PF-07293893 and placebo reported each medical problem. Next to

this number is the percentage of the 30 participants taking PF-07293893 and placebo who reported the medical problem.

- Using these instructions, you can see that 14 out of the 30 (47%) participants taking PF-07293893 and placebo reported headache.

Table 1. Commonly reported medical problems by study participants

Medical Problem	Total (PF-07293893 and placebo) (30 Participants)
Headache	14 out of 30 participants (47%)
Feeling sick	4 out of 30 participants (13%)
Reaction at the site where tiny sensor was applied to monitor heart activity	4 out of 30 participants (13%)
Bruise at the needle insertion site for laboratory tests	2 out of 30 participants (7%)
Collection of blood under the skin	2 out of 30 participants (7%)
Flu-like symptoms	2 out of 30 participants (7%)
Inflammation of the nose and throat	2 out of 30 participants (7%)
Sleepiness	2 out of 30 participants (7%)

Table 1. Commonly reported medical problems by study participants	
Medical Problem	**Total (PF-07293893 and placebo) (30 Participants)**
Tiredness	2 out of 30 participants (7%)
Weakness	2 out of 30 participants (7%)

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.

No participants had serious medical problems.

No participants 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 **C5171001**

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

www.clinicaltrials.gov	Use the study identifier **NCT05907395**
www.euclinicaltrials.eu	Use the study identifier **2023-504921-37-00**

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!

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