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 study participants. 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-06865571 (DGAT2i) (Ervogastat),
PF-05221304 (ACCi) (Clesacostat)

Protocol Number: C3711005

Dates of Study: 10 August 2020 to 28 April 2022

Title of this Study: Study of Pharmacodynamics and Safety of DGAT2i and ACCi Coadministered in Participants With Sponsor-defined Presumed Non Alcoholic Steatohepatitis

[A Phase 2a, 2-Part, Randomized, Double-Blind, Double-Dummy Placebo-Controlled, Parallel-Group (Sponsor Open) Study to Assess Pharmacodynamics and Safety of PF-06865571 (DGAT2i) Coadministered With PF-05221304 (ACCi) in Adult Participants With Presumed Nonalcoholic Steatohepatitis (NASH)]

Date(s) of this Report: 17 February 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 is Nonalcoholic Steatohepatitis (NASH)?

The liver is the largest organ inside the body. It plays an important role in breaking down food, storing energy, and removing waste and toxic materials from the body. A healthy liver also stores a small amount of fat. Liver damage or disease can be caused by heavy alcohol drinking. It can also be damaged when high levels of fat build up in the liver.

Non-alcoholic Steatohepatitis (also known as NASH) is a condition of fat build up in the liver, which can lead to stiffness or hardening of the liver (known as fibrosis). Most often, NASH is driven by fat build up in the liver of a person who is not a heavy alcohol drinker. People with NASH have liver cell damage in addition to fat in the liver. Patients who have NASH have an increased risk of severe liver damage and death.

What are ervogastat and clesacostat?

Ervogastat and clesacostat are 2 investigational medicines being studied for the treatment of NASH. In other studies, ervogastat is being tested separately and together with clesacostat.

What was the purpose of this study?

The purpose of this study was to determine how different doses of ervogastat affects the fat in the liver when taken with clesacostat. Researchers compared the effects to those of a placebo. A placebo does not have any medicine in it, but it looks just like the study medicine.

In this study, researchers used a tool called Magnetic Resonance Imaging using Proton Density Fat Fraction (MRI-PDFF) to determine the amount of fat in the liver.

Researchers wanted to know:

- **How did different doses of ervogastat when taken with clesacostat change the amount of fat in the liver compared to placebo?**
- **What medical problems did participants have during the study?**

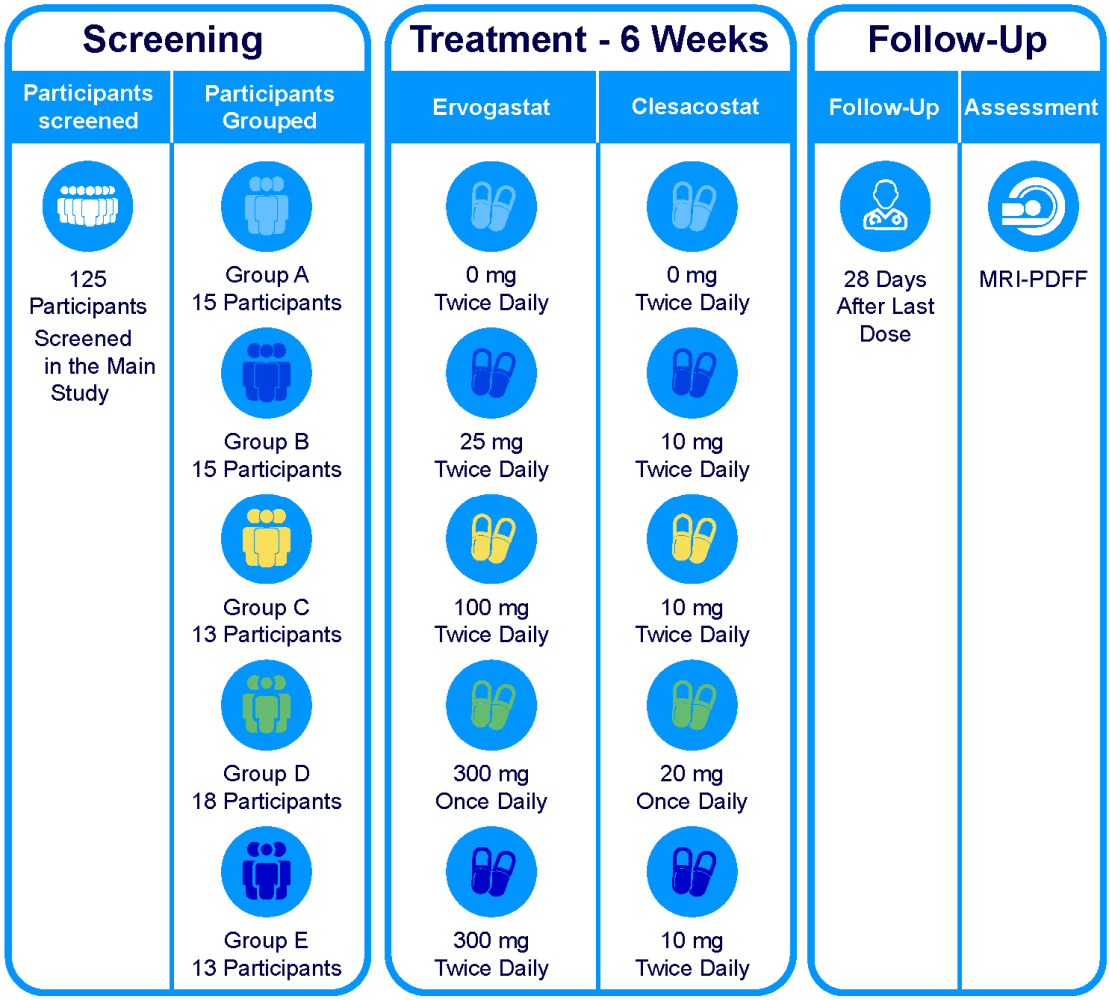
What happened during the study?

How was the study done?

This study compared 4 groups of participants diagnosed with NASH to find out what effect taking different doses of ervogastat along with affixed daily dose of clesacostat had on fat content in the liver compared to a group of participants taking placebo.

Participants were to take either ervogastat at doses of 25 mg, 100 mg, or 300 mg twice daily along with 10 mg of clesacostat twice daily or matching placebos daily for 6 weeks as shown in Figure 1. Study also included a group of participants who received ervogastat 300 mg once daily with 20 mg once daily of clesacostat.

Figure 1. How Was the Study Done?



Note: During the 6 weeks treatment period, Group D participants who took Ervogastat 300 mg once daily/Clesacostat 20 mg once daily received placebo as their second (evening) dose.

Researchers took images of the liver from participants during the study and measured the amount of fat in the liver. The amount of fat in the liver of each participant was measured using a series of pictures called MRI-PDFF. These pictures were taken at the beginning of the study on Day 1 and at the end of the treatment period at 6 weeks. The difference in the amount of fat in the liver between Day 1 and 6 weeks

was determined for each participant. These numbers were combined for all participants in each treatment group and an average change in amount of liver fat was determined. for each of the treatment groups.

Researchers then compared the average change in the amount of fat in the liver of participants taking different doses of ervogastat and clesacostat to the results of participants taking placebo.

Placebo was given to participants to help researchers try to understand if medical problems participants had during the study could be related to the study medication or related to something else.

Researchers also checked the participants' health during the study and asked them how they were feeling.

The participants and researchers did not know who took study medication and who took the placebo. This is known as a "blinded" study. Participants were assigned to each group by chance alone.

Where did this study take place?

The Sponsor ran this study at 16 locations in Canada and United States.

When did this study take place?

The study began 10 Aug 2020 and ended 28 Apr 2022.

Who participated in this study?

In this study, 75 participants who met the inclusion/exclusion criteria for age, condition type, severity, prior treatments, etc. were allocated to one of the 5 treatment groups. One participant was randomized but not treated and therefore 74 participants started the study. Of these:

- A total of 40 men participated
- A total of 34 women participated

- All participants were between the ages of 25 and 75 years

Of the 74 participants who started the study, 69 participants finished the study. 5 did not finish the study because of medical problems, work schedule conflicts, and declining to complete the study.

4 participants left before the study was over by their choice.

How long did the study last?

Study participants were in the treatment phase of the study for 6 weeks. The entire study took 1 year and 8 months to complete.

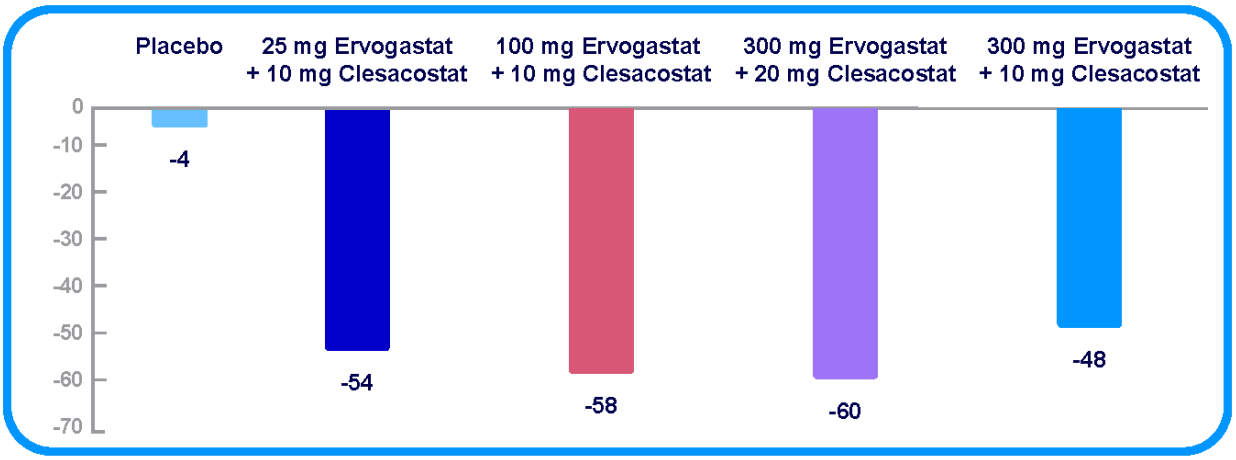
When the study ended in April 2022, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

What were the results of the study?

How did different doses of ervogastat when taken with clesacostat change the amount of fat in the liver compared to placebo?

In this study, participants who took a combination of Ervogastat and Clesacostat had a decrease in the amount of fat in their liver at the end of the treatment period of 6-weeks. Participants in Group B (25 mg Ervogastat and 10 mg clesacostat twice daily) had 54% reduction, in Group C (100 mg Ervogastat and 10 mg clesacostat twice daily) had 58% reduction, in Group D (300 mg Ervogastat and 20 mg clesacostat once daily) had 60% reduction, in Group E (300 mg Ervogastat and 10 mg clesacostat twice daily) had 48% reduction and those who took placebo had a 4% reduction in liver fat as shown in Figure 2.

Figure 2. Percent Change in the Amount of Fat in the Liver from Initial Assessment To Week 6



Based on these results, the researchers have decided that the changes in liver fat recorded during the study are not likely the result of chance. The combination of ervogastat and clesacostat may help lower liver fat levels in patients with NASH.

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 medication might have on a participant.

24 out of 75 (32%) participants in this study had at least 1 medical problem. 1 participant left the study because of medical problems. All medical problems – reported by at least 2 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 at least 2 participants are listed.
- The **2nd** column tells how many of the 15 participants in Group A reported each medical problem. Next to this number is the percentage of the 15 participants in Group A who reported the medical problem.
- The **3rd** column tells how many of the 15 participants in Group B reported each medical problem. Next to this number is the percentage of the 15 participants in Group B who reported the medical problem.
- The **4th** column tells how many of the 13 participants in Group C reported each medical problem. Next to this number is the percentage of the 13 participants in Group C who reported the medical problem.
- The **5th** column tells how many of the 18 participants in Group D reported each medical problem. Next to this number is the percentage of the 18 participants in Group D who reported the medical problem.
- The **6th** column tells how many of the 14 participants in Group E reported each medical problem. Next to this number is the percentage of the 14 participants in Group E who reported the medical problem.
- Using these instructions, you can see that 1 out of the 15 (7%) participants in Group A reported diarrhea. A total of 0 out of the 15 (0%) participants in Group B, 0 out of the 13 (0%) participants in Group C, 2 out of the 18 (11%) participants in Group D, and 1 out of the 14 (7%) participants in Group E reported diarrhoea.

Table .Commonly reported medical problems by study participants					
Medical Problem	Group A 15 Participants	Group B 15 Participants	Group C 13 Participants	Group D 18 Participants	Group E 14 Participants
Diarrhea	**1 out of 15 participants (7%)**	**0 out of 15 participants (0%)**	**0 out of 13 participants (0%)**	**2 out of 18 participants (11%)**	**1 out of 14 participants (7%)**
Alanine Aminotransferase Liver Test Increased	**0 out of 15 participants (0%)**	**1 out of 15 participants (7%)**	**0 out of 13 participants (0%)**	**1 out of 18 participants (6%)**	**0 out of 14 participants (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.

No participants in the study had serious medical problems.

There were no deaths among participants in 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:

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

www.clinicaltrials.gov
www.pfizer.com/research/research_clinical_trials/trial_results

Use the study identifier **NCT04399538**
Use the protocol number C3711005

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!