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-06835919

Protocol Number: C1061011

Dates of Study: 18 July 2019 to 30 March 2021

Title of this Study: A Double-blind Study to Assess 2 Doses of an Investigational Product for 16 Weeks in Participants With Non-alcoholic Fatty Liver Disease and Type 2 Diabetes Mellitus

[A Phase 2a, Randomized, Double-Blind, Placebo-Controlled, 3-Arm, Parallel Group Study to Evaluate Safety, Tolerability and Pharmacodynamics of PF-06835919 Administered Daily for 16 Weeks in Adults With Non-Alcoholic Fatty Liver Disease and Type 2 Diabetes Mellitus on Metformin]

Date(s) of this Report: 14 June 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 is non-alcoholic fatty liver disease with type 2 diabetes mellitus?

Non-alcoholic fatty liver disease (NAFLD) is a condition where too much fat is stored in the liver and where those affected drink little to no alcohol. NAFLD may worsen into a condition called non-alcoholic steatohepatitis (NASH). NASH develops when excess fat contributes to increased inflammation and liver cell death. NASH is associated with increased risk of death, scarring and failure of the liver, and liver cancers.

Conditions that increase the risk of NAFLD and NASH to develop include being overweight, type 2 diabetes mellitus (T2DM), high blood pressure, and high levels of cholesterol and fats in the blood. Participants with T2DM are of special interest and included in this study.

What is PF-06835919?

PF-06835919 was the drug investigated in this study in participants who have T2DM and may have NAFLD. PF-06835919 reduces the activity of an enzyme called ketohexokinase (KHK). KHK speeds up the change of fruit sugar (fructose) to energy used by the body and increases fat production in the liver. Fructose increases the risk of too much fat in the liver. PF-06835919 was used as a treatment to lower the activity of KHK, reduce liver fat, reduce HbA1c, and prevent the development of NASH. PF-06835919 is an investigational drug because it is not approved for use in this country.

What were the purposes of this study?

The primary purposes of the study were to compare the effects of PF-06835919 at 2 doses (150 mg and 300 mg) compared with a placebo to find out if PF-06835919 helps reduce liver fat and hemoglobin A1C (HbA1c). The amount of HbA1c in the blood shows the average amount of glucose (a type of sugar) over the past 3 months.

This study looked at the efficacy, safety, and tolerability of 2 doses of PF-06835919 over a 16-week period. Specifically, researchers wanted to know if PF-06835919 reduced liver fat and HbA1c at 16 weeks compared to placebo (efficacy). Safety means that any medical problems that happened were studied. Tolerability means whether a medical problem interfered with a participant's usual activities.

Researchers wanted to know:

Did PF-06835919 reduce the fat in the liver and HbA1c in the blood compared to a placebo?

What happened during the study?

How was the study done?

This study lasted about 24 weeks and was in 3 parts: a screening period, a treatment period, and a follow-up period.

The screening period lasted up to 3 weeks and included:

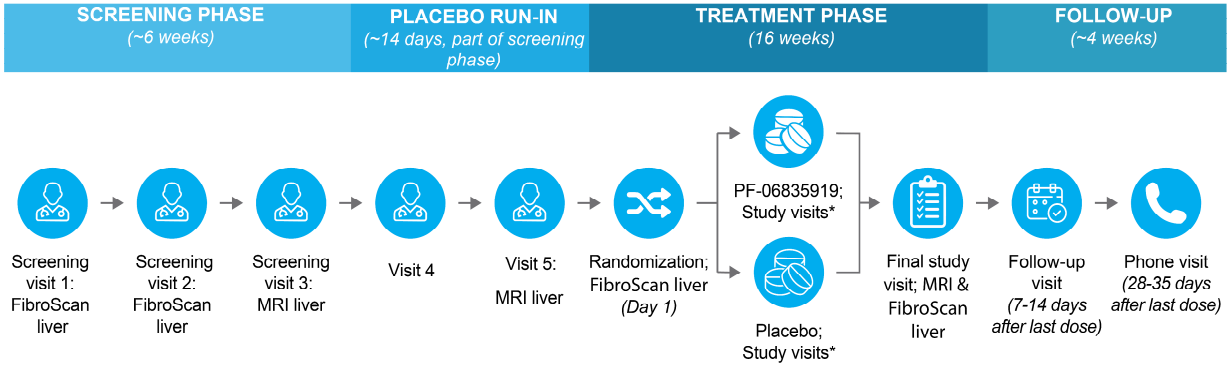
- Scans of the liver to test for fat and stiffness
- Magnetic resonance imaging (MRI) of the liver to measure fat content in the liver
- A period of taking a placebo for 14 days to make sure participants were comfortable taking a study drug.

The treatment period lasted for 16 weeks. Participants were randomized (assigned by an equal chance) to one of 2 treatment doses of PF-06835919 tablets taken by mouth or a placebo tablet taken by mouth. A total of 164 participants were given one of the following during the treatment period:

- 55 participants: PF-06835919 150 mg

- 55 participants: PF-06835919 300 mg
- 54 participants: Placebo

The follow-up period lasted up to 35 days. Participants were seen in person at a study clinic 7 days to 14 days after their last dose. Participants received a phone call between 28 days to 35 days after their last dose.



*Participants attended study visits on weeks 2, 4, 8, 12, 14, & 16

Researchers tested PF-06835919 on 2 groups of study participants to find out if PF-06835919 lowered the amount of fat in liver cells and lowered HbA1c in the blood. Researchers then compared the results of study participants taking the study medication to the results of study participants taking a placebo. A placebo does not have any medicine in it, but it looks just like the study medication.

The study participants and researchers did not know who took PF-06835919 and who took the placebo. This is known as a "double-blinded" study. Study participants were assigned to each group by chance alone (randomization).

The trial was completed even with the COVID-19 pandemic, and the primary objectives of the study were successfully evaluated. The impact of the pandemic enrollment pause was limited, as sites were able to recruit and enroll quickly once sites were allowed to restart.

Where did this study take place?

The Sponsor ran this study at 58 locations in 2 countries in North America, specifically in Canada and the United States.

When did this study take place?

It began 18 July 2019 and ended 30 March 2021.

Who participated in this study?

Requirements for being in the study included:

- Male or female participants aged between 18 years and 70 years
- Participants with T2DM taking greater than or equal to 500 mg/day metformin alone for at least 8 weeks prior screening visit 1
- Liver fat content greater than or equal to 8% at screening visit 3 on MRI

Conditions that kept participants out of the study included:

- Type 1 diabetes mellitus
- Complications from diabetes (kidney or nerve complications)

Participants included:

- A total of 71 (43%; 43 out of 100) men participated
- A total of 93 (57%; 57 out of 100) women participated
- All participants were between the ages of 21 years and 71 years

Participants were to be treated until Week 16. Of the 164 participants who started the study, 145 (88%; 88 out of 100) finished the treatment period.

A total of 19 participants out of 164 (12%; 12 out of 100) discontinued the double-blind treatment:

- 9 (16%; 16 out of 100) participants in the PF-06835919 150 mg group
- 6 (11%; 11 out of 100) participants in the PF-06835919 300 mg group
- 4 (7%; 7 out of 100) participants in the placebo group

19 participants out of 164 (12%; 12 out of 100) did not finish the treatment period because:

- 7 participants (4%; 4 out of 100) stopped treatment because of their choice
- 4 participants (2%; 2 out of 100) stopped treatment because of medical problems
- 4 participants (2%; 2 out of 100) stopped treatment because of other reasons
- 3 participants (2%; 2 out of 100) stopped treatment because of problems with study procedures
- 1 participant (1%; 1 out of 100) stopped treatment because they were lost to follow-up

How long did the study last?

Study participants were in the study for about 24 weeks. The entire study took around 1 year and 8 months to complete.

Due to the COVID-19 pandemic, enrollment in the trial was paused temporarily in all sites between 24 March 2020 and 26 May 2020, and then restarted.

When the study ended in March 2021 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?

Did PF-06835919 reduce the fat in the liver and HbA1c in the blood compared to a placebo?

Both PF-06835919 dose groups (300 mg and 150 mg doses) showed greater reductions in whole liver fat and HbA1c compared to placebo at Week 16. For the results for whole liver fat, the researchers believe the difference was due to the study drug, PF-06835919, (statistically significant) and not due to chance. For the HbA1c results, the researchers could not determine if the results were due to the study drug, PF-06835919, or due to chance (not statistically significant).

At Week 16, the average whole liver fat was reduced by:

- 19% (19 out of 100) for the PF-06835919 300 mg dose
- 17% (17 out of 100) for the PF-06835919 150 mg dose
- 5% (5 out of 100) for the placebo

At Week 16, the average HbA1c was reduced by:

- 0.34% for the PF-06835919 300 mg dose
- 0.17% for the PF-06835919 150 mg dose
- 0.09% for the placebo

This does not mean that everyone in this study had these results. These are just some of the main findings 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 medication might have on a participant.

7 out of 164 (4%; 4 out of 100) participants in this study had at least 1 treatment-related medical problem. Treatment-related medical problems were reported in:

- 4 (7%) participants in the PF-06835919 150 mg group
- 2 (4%) participants in the placebo group
- 1 (2%) participant in the PF-06835919 300 mg group

A total of 2 participants stopped PF-06835919 because of medical problems: 1 participant in the PF-06835919 300 mg group and 1 participant in the PF-06835919 group stopped treatment because of medical problems. Two participants left the study because of medical problems. The most common medical problems – those reported by 2 or more 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 2 or more participants are listed.
- The **2nd** column tells how many of the 55 participants taking PF-06835919 300 mg reported each medical problem. Next to this number is the percentage of participants taking PF-06835919 300 mg who reported the medical problem.
- The **3rd** column tells how many of the 55 participants taking PF- 06835919 150 mg reported each medical problem. Next to this number is the percentage of participants taking PF-06835919 150 mg who reported the medical problem.
- The **4th** column tells how many of the 54 participants taking a placebo reported each medical problem. Next to this number is the percentage of participants taking a placebo who reported the medical problem.
- Using these instructions, you can see that 4 out of the 55 participants (7%) taking PF-06835919 150 mg reported high blood sugar. A total of 0 out of the 54 (0%) participants taking a placebo reported high blood sugar.

Table 1. Commonly reported medical problems by study participants

Medical Problem	PF-06835919 300 mg (55 Participants)	PF-06835919 150 mg (55 Participants)	Placebo (54 Participants)
High blood sugar	0 out of 55 participants (0%)	4 out of 55 participants (7%)	0 out of 54 participants (0%)
Loose Stools	0 out of 55 participants (0%)	3 out of 55 participants (6%)	2 out of 54 participants (4%)
Joint pain	0 out of 55 participants (0%)	3 out of 55 participants (6%)	0 out of 54 participants (0%)
High fat in blood (triglycerides)	0 out of 55 participants (0%)	2 out of 55 participants (4%)	0 out of 54 participants (0%)
Ear, nose, or throat infection	0 out of 55 participants (0%)	2 out of 55 participants (4%)	1 out of 54 participants (2%)
Feeling dizzy	2 out of 55 participants (4%)	0 out of 55 participants (0%)	0 out of 54 participants (0%)
Upper abdominal pain	2 out of 55 participants (4%)	0 out of 55 participants (0%)	0 out of 54 participants (0%)
Urinary tract infection	2 out of 55 participants (4%)	1 out of 55 participants (2%)	0 out of 54 participants (0%)
Abdominal pain	2 out of 55 participants (4%)	1 out of 55 participants (2%)	1 out of 54 participants (2%)
Headache	1 out of 55 participants (2%)	1 out of 55 participants (2%)	3 out of 54 participants (6%)
Low blood sugar	0 out of 55 participants (0%)	1 out of 55 participants (2%)	3 out of 54 participants (6%)

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.

2 participants out of 164 (1%; 1 out of 100) had serious medical problems.

- 1 participant out of 55 participants (2%; 2 out of 100) in the PF-06835919 150 mg group had a serious medical problem of a positive COVID-19 test that was not related to PF-06835919. No participants in the PF- 06835919 300 mg group had a serious medical problem.

- 1 participant out of 54 (2%; 2 out of 100) participants in the placebo group had a serious medical problem of a bleed under the lining of the brain during the screening period. This was not related to PF-06835919.

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:

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

www.clinicaltrials.gov Use the study identifier **NCT03969719**

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for study participants.

Again, if you participated in this study,
thank you for volunteering.
We do research to try to find the
best ways to help study participants, and you
helped us to do that!