CLINICAL TRIAL 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 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(s) Studied: PF-05221304

Protocol Number: C1171002

Dates of Trial: 22 August 2017 to 27 March 2019

Title of this Trial: Study that looked at the effect of different doses of PF-05221304 on the amount of fat in the liver

[A Phase 2a, Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging, Parallel Group Study to Evaluate Safety, Tolerability, and Pharmacodynamics of PF-05221304 Administered Daily for 16-Weeks to Adult Subjects With Nonalcoholic Fatty Liver Disease]

Date(s) of this Report: 19 April 2021

– Thank You –

Pfizer, the Sponsor, would like to thank you for your participation in this clinical trial and provide you a summary of results representing everyone who participated. If you have any questions about the study or results, please contact the doctor or staff at your study site.

WHY WAS THIS STUDY DONE?

Nonalcoholic fatty liver disease (NAFLD) is a condition where there is a high amount of fat in the liver in people who drink few alcoholic drinks or do not drink alcoholic drinks. The liver is an organ in the body that cleans the blood. If not treated, NAFLD can cause damage to the liver and develop into a more serious condition called nonalcoholic steatohepatitis (NASH). In NASH, the liver contains a high amount of fat, is "inflamed" or swollen, and/or scarred. This condition may be described as a 'stiff liver'. If not treated, NASH can worsen and, in some people, the liver may stop working and a liver transplant could be needed.

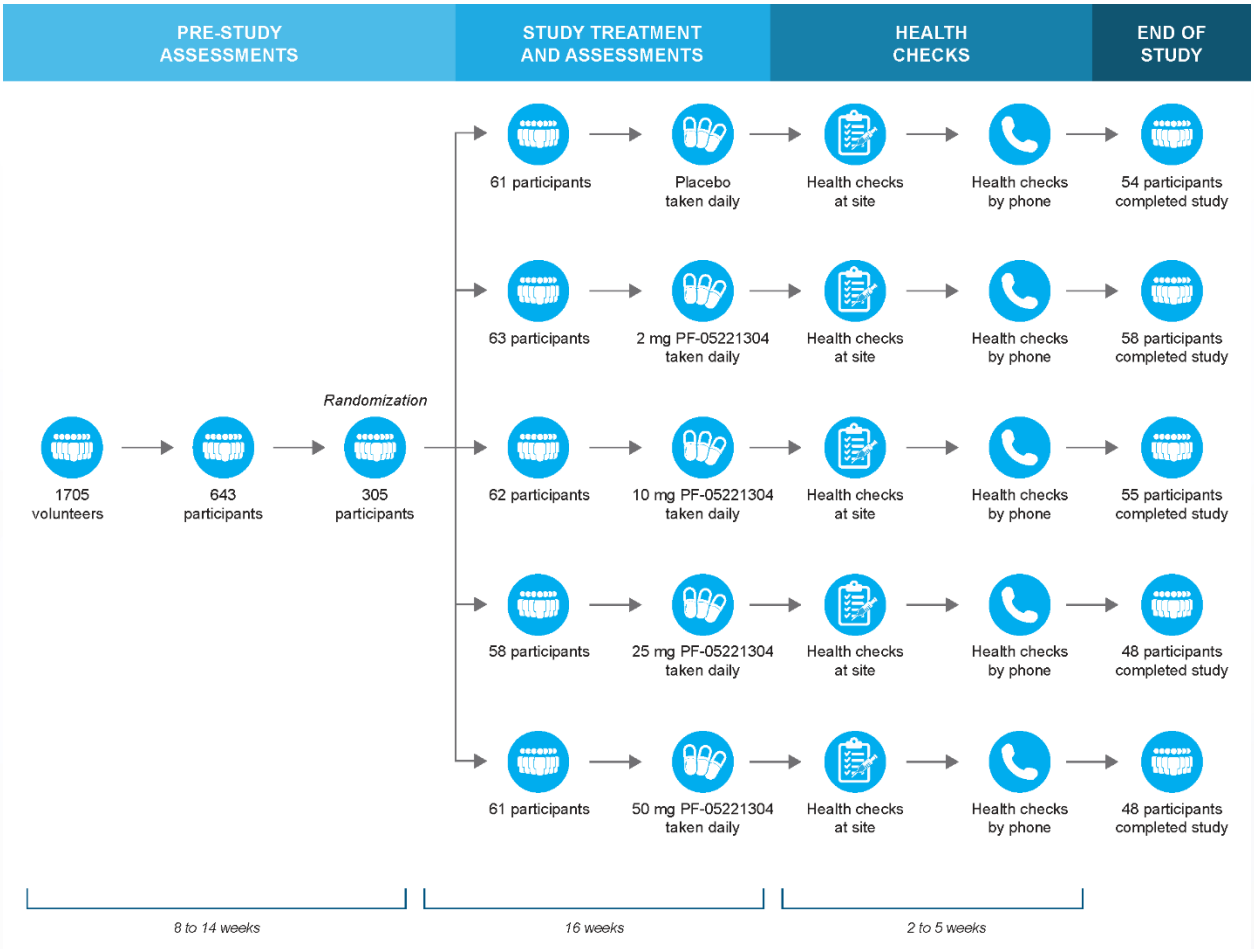
PF-05221304 is a new investigational drug that is being studied to see if it could be used in the future to treat people with NASH. An investigational drug is one that is not approved for sale in this country where the clinical study is taking place. This study looked at different doses (or amounts) of PF-05221304 to see what happens to the amount of fat in the liver after treatment. This study should help decide what dose of PF-05221304 could be used in future clinical studies in NASH.

WHAT HAPPENED DURING THE STUDY?

This study compared 5 groups of participants to find out if participants taking PF-05221304 had a reduced amount of fat in the liver compared to participants taking a placebo. A placebo does not have any medicine in it, but it looks just like the study medicine.

The study included participants who had a high amount of fat in their liver that was not related to alcohol consumption, and who were overweight. The participants and researchers did not know who took PF-05221304 and who took the placebo. This is known as a "blinded" study. Participants were put into 1 of 5 groups by chance alone. This is known as a "randomized" study. This is done to make the groups more similar. Reducing differences between the groups (like age or the number of men and women), makes the groups more even to compare.

This study was also "double-blinded". This means that participants and doctors did not know who was given which treatment/medicine. This was done to make sure that the trial results were not influenced in any way.



While participants were only in the study for 16 weeks, or approximately 4 months, the entire study took 19 months, or just over a year and a half to complete. The Sponsor ran this study at 76 locations in 6 countries in Europe, the Middle East, North America, and Asia-Pacific. It began on 22 August 2017 and ended on 27 March 2019. A total of 134 men and 171 women participated. All participants were between the ages of 19 and 70 years.

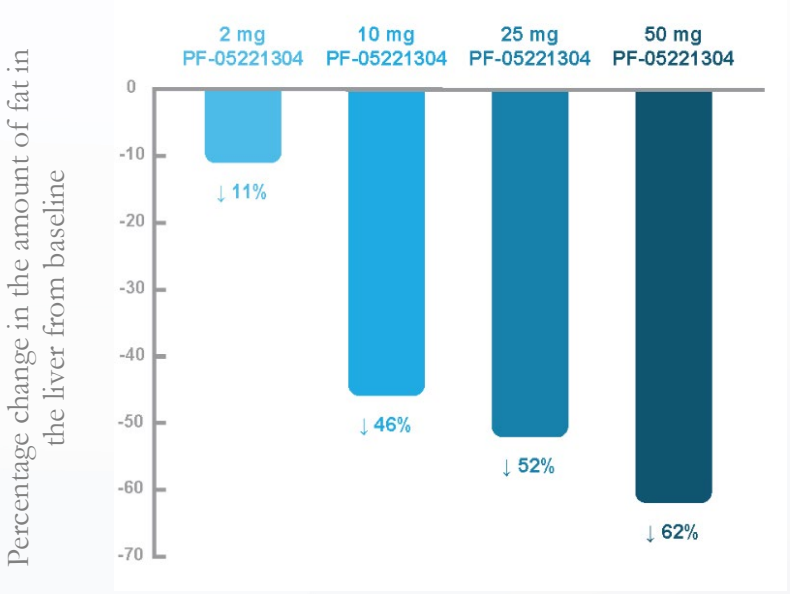
Participants were to be treated for 16 weeks or approximately 4 months. Of the 1705 volunteers who were assessed, 643 entered the main study, 305 participants were randomized and started treatment, and 263 finished the study. There were 42 participants who started treatment but did not finish the study. These participants

left before the study was over by their choice or a doctor decided it was best for the participant to stop being in the study.

When the study ended in March 2019, 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?

What happens to the amount of fat in the liver after participants are given different doses of PF-05221304 for 16 weeks compared to placebo treatment? The graphic below shows how the amount of fat in the liver changed after 16 weeks of treatment with PF-05221304 compared with placebo. After 16 weeks of treatment, the amount of fat in the liver was reduced by between 11% and 62% depending on the dose of PF-05221304. The reductions in the amount of fat in the liver seen with 10 mg, 25 mg, and 50 mg PF-05221304 was over 40% and the researchers have determined that these results are not likely the result of chance.



This does not mean that everyone in this study had these results. Other studies may produce different results, as well. These are just some of the main findings of the study, and more information may be available at the websites listed at the end of this summary.

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 the side effects of an experimental drug might be.

Approximately two-thirds of the 305 participants who were treated in this study had at least 1 medical problem. A total of 22 participants left the study because of medical problems. There were 13 participants who had their dose of PF-05221304 reduced or stopped treatment temporarily because of medical problems. The most common medical problems are listed in the following table.

Most Common Medical Problems (Reported by 5 or More Participants Across All Groups)					
Medical Problem	PF-05221304 (244 Participants Treated)[a]				Placebo (61 Participants Treated)
	2 mg	10 mg	25 mg	50 mg	
Headache	3 (5%)	3 (5%)	7 (12%)	4 (7%)	8 (13%)
Increased amounts of triglycerides (a certain type of fat or lipid) in blood[b]	1 (2%)	6 (10%)	4 (7%)	10 (16%)	2 (3%)
Loose stools (diarrhea)	3 (5%)	8 (13%)	2 (3%)	4 (7%)	3 (5%)
Nose, sinus, or throat infection (cold)	6 (10%)	4 (7%)	3 (5%)	2 (3%)	2 (3%)
Nausea	0	3 (5%)	5 (9%)	4 (7%)	3 (5%)
Feeling dizzy	3 (5%)	1 (2%)	3 (5%)	3 (5%)	4 (7%)
Tiredness	3 (5%)	2 (3%)	2 (3%)	2 (3%)	5 (8%)
Urinary tract infection (infection of the kidneys, bladder, or urethra)	1 (2%)	2 (3%)	5 (9%)	4 (7%)	1 (2%)
Arm or leg pain	3 (5%)	4 (7%)	2 (3%)	1 (2%)	2 (3%)
Common cold	0	3 (5%)	3 (5%)	2 (3%)	2 (3%)

Most Common Medical Problems (Reported by 5 or More Participants Across All Groups)					
Medical Problem	PF-05221304 (244 Participants Treated)[a]				Placebo (61 Participants Treated)
	2 mg	10 mg	25 mg	50 mg	
Pain in the upper part of the abdomen	0	1 (2%)	6 (10%)	1 (2%)	1 (2%)
Pain in the joints	1 (2%)	3 (5%)	4 (7%)	0	1 (2%)
Muscle spasm	0	2 (3%)	1 (2%)	0	4 (7%)
Itching	2 (3%)	0	3 (5%)	1 (2%)	1 (2%)
Abdominal pain	1 (2%)	0	1 (2%)	2 (3%)	2 (3%)
Increased amount of triglycerides (a certain type of fat or lipid) in blood[b]	0	1 (2%)	3 (5%)	2 (3%)	0
Not being able to pass stool (constipation)	1 (2%)	2 (3%)	1 (2%)	2 (3%)	0
Influenza	2 (3%)	0	1 (2%)	0	3 (5%)
Swelling in the arms and/or legs	2 (3%)	0	2 (3%)	1 (2%)	1 (2%)
Infection in the sinuses	1 (2%)	3 (5%)	0	1 (2%)	0

a The 244 participants treated included 63 with 2 mg, 62 with 10 mg, 58 with 25 mg, and 61 with 50 mg PF-05221304.

b In clinical studies, increased amounts of triglycerides (a certain type of fat or lipid) in the blood may be reported using different terminology that has the same meaning such as hypertriglyceridemia or blood triglycerides increased'.

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

A medical problem is considered "serious" when it is life-threatening, needs hospital care, or causes lasting problems. These serious medical problems could be related to the study treatment, because of disease, or due to other factors that have nothing to do with the study treatment.

There were 16 participants (approximately 1%, or 16 out of 1705 participants) who had serious medical problems after starting the pre-study assessments. This included 13 serious medical problems in 10 participants that occurred before randomization. This was therefore before treatment with PF-05221304 or placebo (and seen in approximately 1%, or 10 out of 1705 participants). This included 1 participant who passed away. There were 9 serious medical problems in 6 participants that occurred after randomization in participants who received treatment with PF-05221304 or placebo (2%, or 6 out of the 305 participants who were treated). None of the participants left the study completely because of these serious medical problems. There was 1 participant who had 2 serious medical problems that meant their study treatment was stopped temporarily. The researchers did not think that any of these serious medical problems were related to the treatment the participants had been given. All 6 participants recovered from these serious medical problems.

Serious Medical Problems (Reported After Starting Treatment with Study Drug)		
Serious Medical Problem	**PF-05221304 (244 Participants Treated)**	**Placebo (61 Participants Treated)**
Heart attack[a]	**1**	**0**
Severe chest infection (pneumonia)[a]	**1**	**0**
Broken rib[b]	**1**	**0**
Infection of the nose, throat, and upper airways[b]	**1**	**0**
Angina unstable	**1**	**0**
Worsened condition[c]	**1**	**0**
Heart not pumping blood properly[c]	**1**	**0**
Asthma	**1**	**0**
Pain from kidney stones	**1**	**0**

a A single participant reported the serious medical problems of heart attack and severe chest infection (pneumonia).

b A single participant reported the serious medical problems of broken rib and the infection of the nose, throat, and upper airways and this participant temporarily stopped their study medication because of these serious medical problems.

c A single participant reported the serious medical problems of worsening condition and the heart not pumping blood properly.

There was 1 death during this study and this participant passed away before receiving treatment with PF-05221304 or placebo.

There were 15 participants who stopped treatment with either PF-05221304 or placebo because of laboratory test results. This was because they had higher than normal levels of a certain type of fat or lipid (triglycerides) in their blood or their liver function test results were not normal.

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.

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

www.clinicaltrials.gov	Use the study identifier **NCT03248882**
www.clinicaltrialsregister.eu	Use the study identifier **2017-001156-55**

Findings from this trial will be used in other studies to compare this drug with other treatments for NASH. Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients.

Again, **thank you** for volunteering. We do research to try to find the best ways to help patients, and you helped us to do that!