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-07081532
Protocol Number:	C3991002
Dates of Study:	16 March 2020 to 14 July 2021
Title of this Study:	A Phase 1 Study to Assess the Safety, Tolerability, and Pharmacokinetics of Multiple Escalating Oral Doses of PF-07081532 in Adults With Type 2 Diabetes Mellitus [A Phase 1, Randomized, Double-Blind, Sponsor-Open, Placebo-Controlled Study to Assess the Safety, Tolerability, and Pharmacokinetics of Multiple Escalating Oral Doses of PF-07081532 in Adult Participants With Type 2 Diabetes Mellitus]
Date(s) of this Report:	10 July 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 Type 2 diabetes mellitus?

Type 2 diabetes mellitus (T2DM) is a disease which, over time, can cause higher than normal levels of sugar in the blood (hyperglycemia) and this can harm the health of people with T2DM.

Insulin is a hormone that lowers the level of sugar in the blood and glucagon is a substance which helps the body produce more sugar when it is needed. With T2DM, the body does not release enough insulin into the blood and can have too much glucagon in the blood. This can lead to high levels of sugar in the blood. If your blood sugar increases and remains high over a long period of time, this can lead to harmful effects such as heart problems, kidney disease, eye disorders and poor circulation in your limbs. That is why it is important to keep your blood sugar levels within a healthy range.

What is PF-07081532?

PF-07081532 is an experimental medicine that is taken as a tablet by mouth and is not yet approved for use by health authorities. PF-07081532 is type of medicine known as a "glucagon-like peptide 1 receptor agonist" and is intended to keep blood sugar at healthy levels. These medicines work by increasing the amount of insulin released and lowering the amount of glucagon released into the blood. They also slow down the digestion of food and increase the feeling of fullness after eating. PF-07081532 may help in lowering blood sugar levels and body weight if taken along with appropriate diet and exercise.

What was the purpose of this study?

Researchers wanted to see if different doses of PF-07081532 were safe when given to people with T2DM and people with obesity without diabetes. This report describes what happened during the study, what the results of the study are, and how participants can learn more about the study.

Researchers wanted to know:

- **Were different doses of PF-07081532 safe in participants with T2DM and participants with obesity?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

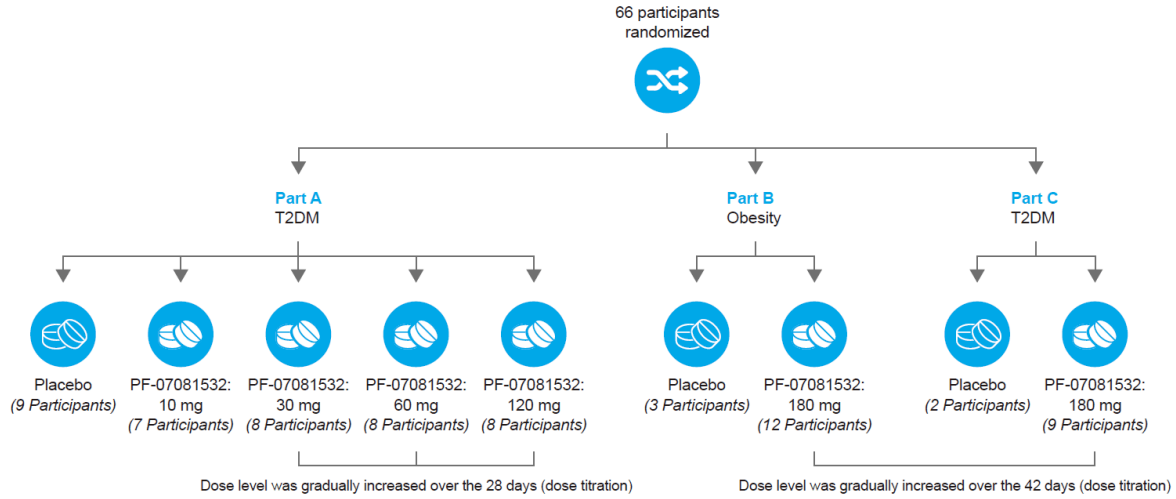
In this study, participants were given either PF-07081532 or a placebo. A placebo does not have any medicine in it but looks just like the medicine being tested. Researchers measured the effect of PF-07081532 by comparing side effects and other safety measurements of participants who took different doses of the study medicine to participants who took a placebo. The participants and researchers did not know who took different doses of PF-07081532 and who took the placebo. This is known as a "double-blinded" study. Researchers use "double-blinded" studies to make sure that the results of the study are not influenced in any way. Participants were assigned to each group by chance alone, like the flip of a coin. This is known as a "randomized" study. Randomization is done to make the groups more similar for characteristics like age and sex.

There were 2 participant populations enrolled in this study: participants with T2DM, and participants with obesity without diabetes. The study was conducted in 3 parts: Part A, Part B, and Part C. Participants in each part were given either PF-07081532 or placebo. Each group started at 10 mg of PF-07081532, which increased after a set number of days until a target dose was reached.

- In Part A, 4 groups of participants with T2DM received PF-07081532 or placebo once a day for 28 days. The target doses for the 4 groups in Part A were 10 mg, 30 mg, 60 mg, and 120 mg.
- In Part B, 1 group of participants with obesity (without diabetes) received PF-07081532 or placebo once a day for 42 days. The target dose for this group was 180 mg.
- In Part C, 1 group of participants with T2DM received PF-07081532 or placebo once a day for 42 days. The target dose for this group was 180 mg.

After the Screening visit, participants began an in-patient stay at a study clinic and took PF-07081532 or placebo once a day from Day 1 to Day 28 (Part A) or Day 1 to Day 42 (Parts B and C). Participants stayed at the clinic until after the last dose of study medication and came back for a follow-up visit 7-14 days after taking their last dose of PF-07081532 or placebo.

The study design is shown in the graphic below.



To find out if PF-07081532 was safe, the study doctors used different tests and assessments, such as testing blood and urine samples throughout the study. Participants also had their heart rate, blood pressure, and electrical activity of the heart

(by electrocardiogram [ECG] test) monitored. Researchers also checked the participants' health during the study and asked them how they were feeling.

Researchers then compared the results of participants taking different doses of the study medication to the results of participants taking placebo.

Where did this study take place?

The Sponsor ran this study at 2 locations in the United States.

When did this study take place?

It began 16 March 2020 and ended 14 July 2021.

Who participated in this study?

The study included adult participants with T2DM and adult participants with obesity without diabetes who met certain criteria for things such as type of diabetes and body mass index (BMI). Participants with T2DM had blood sugar that was not under control with standard treatment with metformin, an approved medicine prescribed to them by their doctor.

- A total of 35 men participated
- A total of 31 women participated
- All participants were required to be between the ages of 18 and 70

Of the 66 participants who started the study, 61 finished blinded treatment. Of the 5 participants who did not finish the study, 3 stopped because of treatment-related side effects given below:

- 1 participant with T2DM experienced nausea (a feeling of sickness in the stomach), and left the study after receiving PF-07081532 for 13 days up to a dose of 40 mg

- 1 participant with T2DM experienced hypoglycemia (low blood sugar level), and left the study after receiving PF-07081532 for 5 days up to a dose of 40 mg
- 1 participant with obesity felt upper abdominal pain (pain in upper belly), and stopped taking study drug after receiving PF-07081532 for 31 days up to a dose of 150 mg.

2 participants (1 in T2DM and 1 in placebo) did not finish the study for other reasons.

How long did the study last?

Study participants were in the study for approximately 10 weeks (Part A), 12 weeks (Part B and Part C) including the Screening visit and on-site follow-up visit. The entire study took about 16 months to complete.

When the study ended in July 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?

Were doses of PF-07081532 safe in participants with T2DM and participants with obesity?

Yes, doses of PF-07081532 from 10 mg to 180 mg given once a day were found to be safe.

There were no harmful trends in the results of any of the safety tests done as part of the study (this included laboratory tests on blood and urine, blood pressure, pulse rate and ECG parameters). This means that the results of these tests did not appear to be meaningfully different with increasing PF-07081532 doses or placebo.

Based on these results, comparing PF-07081532 to placebo, the researchers have decided that the results are not likely the result of chance.

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 medication might have on a participant.

44 out of 51 (86%) participants with T2DM and 14 out of 15 (93%) participants with obesity had at least 1 medical problem. A total of 3 participants left the study because of medical problems. The most common medical problems – those reported by more than 5% of the total number 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 in decreasing order.
- The **2nd - 7th** column tells how many of the 66 participants taking the PF-07081532 or placebo reported each medical problem. Next to this

number is the percentage of the participants taking the PF-07081532 or placebo who reported the medical problem.

- For example, using these instructions, you can see that a total of 26 out of the 52 (50%) participants taking PF-07081532 and a total of 4 out of the 14 (29%) participants taking a placebo reported nausea. Using these instructions, you can see that nausea was reported by 19 out of the 40 (48%) participants with T2DM taking PF 07081532 and 3 out of the 11 (27%) participants with T2DM taking placebo.

Table 1. Commonly reported medical problems by study participants

Medical Problem	Part A + C (51 Participants with T2DM)		Part B (15 Participants with Obesity)		Total (66 Participants with T2DM + Obesity)	
	PF-07081532	Placebo	PF-07081532	Placebo	PF-07081532	Placebo
Feeling of sickness in the stomach (Nausea)	19 out of 40 participants (48%)	3 out of 11 participants (27%)	7 out of 12 participants (58%)	1 out of 3 participants (33%)	26 out of 52 participants (50%)	4 out of 14 participants (29%)
Loose bowel movement (Diarrhoea)	13 out of 40 participants (33%)	2 out of 11 participants (18%)	5 out of 12 participants (42%)	1 out of 3 participants (33%)	18 out of 52 participants (35%)	3 out of 14 participants (21%)
Decreased number of or difficulty making bowel movements (Constipation)	10 out of 40 participants (25%)	3 out of 11 participants (27%)	6 out of 12 participants (50%)	2 out of 3 participants (67%)	16 out of 52 participants (31%)	5 out of 14 participants (36%)
Headache	12 out of 40 participants (30%)	2 out of 11 participants (18%)	2 out of 12 participants (17%)	1 out of 3 participants (33%)	14 out of 52 participants (27%)	3 out of 14 participants (21%)
Low blood sugar (Hypoglycaemia)	8 out of 40 participants (20%)	0 out of 11 participants (0%)	6 out of 12 participants (50%)	0 out of 3 participants (0%)	14 out of 52 participants (27%)	0 out of 14 participants (0%)

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Medical Problem	Part A + C (51 Participants with T2DM)		Part B (15 Participants with Obesity)		Total (66 Participants with T2DM + Obesity)	
	PF-07081532	Placebo	PF-07081532	Placebo	PF-07081532	Placebo
Decreased appetite	9 out of 40 participants (23%)	0 out of 11 participants (0%)	4 out of 12 participants (33%)	1 out of 3 participants (33%)	13 out of 52 participants (25%)	1 out of 14 participants (7%)
Vomiting	9 out of 40 participants (23%)	1 out of 11 participants (9%)	3 out of 12 participants (25%)	1 out of 3 participants (33%)	12 out of 52 participants (23%)	2 out of 14 participants (14%)
Feeling fullness (Early satiety)	9 out of 40 participants (23%)	0 out of 11 participants (0%)	2 out of 12 participants (17%)	0 out of 3 participants (0%)	11 out of 52 participants (21%)	0 out of 14 participants (0%)
Swelling in belly (Abdominal distension)	5 out of 40 participants (13%)	0 out of 11 participants (0%)	5 out of 12 participants (42%)	1 out of 3 participants (33%)	10 out of 52 participants (19%)	1 out of 14 participants (7%)
Indigestion, trouble digesting food with discomfort after meals (Dyspepsia)	8 out of 40 participants (20%)	1 out of 11 participants (9%)	0 out of 12 participants (0%)	0 out of 3 participants (0%)	8 out of 52 participants (15%)	1 out of 14 participants (7%)

Table 1. Commonly reported medical problems by study participants

Medical Problem	Part A + C (51 Participants with T2DM)		Part B (15 Participants with Obesity)		Total (66 Participants with T2DM + Obesity)	
	PF-07081532	Placebo	PF-07081532	Placebo	PF-07081532	Placebo
Dizziness	6 out of 40 participants (15%)	3 out of 11 participants (27%)	0 out of 12 participants (0%)	0 out of 3 participants (0%)	6 out of 52 participants (12%)	3 out of 14 participants (21%)
Pain in belly (Abdominal pain)	4 out of 40 participants (10%)	0 out of 11 participants (0%)	2 out of 12 participants (17%)	0 out of 3 participants (0%)	6 out of 52 participants (12%)	0 out of 14 participants (0%)
Acid reflux (Gastrooesophageal reflux disease)	0 out of 40 participants (0%)	0 out of 11 participants (0%)	5 out of 12 participants (42%)	1 out of 3 participants (33%)	5 out of 52 participants (10%)	1 out of 14 participants (7%)
Burping (Eructation)	2 out of 40 participants (5%)	0 out of 11 participants (0%)	2 out of 12 participants (17%)	0 out of 3 participants (0%)	4 out of 52 participants (8%)	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.

1 participant (1 out of 66 total participants) had serious medical problems.

- 1 participant with T2DM in the PF-07081532 30 mg group had obstructive pancreatitis.

Study doctors believed the serious medical problem reported by the participant might be related to study medication. However, after final review, the serious medical problem was not thought to be related to the study drug by the sponsor. There were no deaths 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:

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

www.clinicaltrials.gov	Use the study identifier NCT04305587
www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number C3991002

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!