CLINICAL TRIAL RESULTS

Sponsor: Pfizer, Inc.

Medicine Studied: PF-06291874

Protocol Number: B4801011

Dates of Trial: 19 August 2014 to 19 March 2015

Title of this Trial: A clinical trial to find out if PF-06291874 is safe and tolerated by patients with type 2 diabetes mellitus

[A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Parallel Group Trial to Assess the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Multiple Oral Doses of PF-06291874 Given as Monotherapy to Adults With Type 2 Diabetes Mellitus]

Date of this Report: 07 July 2017

- 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.

This summary of results represents a single trial only.

WHY WAS THIS STUDY DONE?

Type 2 diabetes mellitus (T2DM) is a disease where the body does not make insulin or does not respond properly to the insulin in the blood. Over time, T2DM can cause higher than normal levels of sugar in the blood (hyperglycemia) which can have a negative impact on the health of people with T2DM. People with T2DM are more likely to develop problems with their kidneys, heart, eyes, and nerves.

PF-06291874 was the medicine tested in this study. It works by lowering the level of sugar in your blood. It does this by causing glucagon to be less effective in your body. Glucagon is a naturally produced substance in your body. One of the main functions of glucagon is to help the body produce more sugar when it is needed.

Researchers did this study to look for a new way to treat patients with T2DM. PF-06291874 comes in a tablet that is taken by mouth. The medicine may help lower blood sugar levels by preventing glucagon from having its full effect of raising levels of sugar in the blood. For this study, researchers wanted to answer the question: Is PF-06291874 safe and tolerated by patients with T2DM?

WHAT HAPPENED DURING THE STUDY?

Researchers wanted to find out if PF-06291874 was safe and tolerated by comparing patients who took different doses of the study medicine to patients who took a placebo. A placebo does not have any medicine in it, but looks just like the medicine being tested. Researchers use a placebo to see if the study medicine is safe and works better than not taking anything.

In the study, patients were put into 1 of 5 treatment groups by chance alone, like the flip of a coin. This is known as a "randomized" study. In 4 groups the patients received PF-06291874 and in 1 group they received a placebo. Patients in the 4 groups that received PF-06291874 were given the study medicine at different doses, depending on which group they were put (randomized) into. Randomization is done to make the groups more similar for characteristics like age, sex, etc. Making the groups more similar makes comparing the groups more fair.

The study included patients who met the study requirements for characteristics such as age and weight. Some of the other study requirements were:

- Patients had blood tests that showed their HbA1c levels were within the right levels (HbA1c stands for glycosylated hemoglobin, and the HbA1c blood test measures how well controlled the patient's blood sugar is)
- Patients were willing to stop taking any other oral antidiabetic drugs (OADs) while participating in the study
- Patients were willing to self-test (finger stick) for blood sugar levels during the study
- Females had to no longer be able to have children (for example, they had been through menopause or had undergone a hysterectomy; hysterectomy is a surgery to remove the womb)

Patients were evaluated (screened) to make sure they met all the requirements to be in the study. The study doctor confirmed if a patient qualified for the study. Then, qualified patients took different steps depending if they were taking OADs or not:

- If qualified patients were taking an OAD:
  - They were asked to stop taking the OAD for the rest of their participation in the study. The first 4 weeks of not taking the OAD was called the washout period. During the washout period, patients visited the study doctor once for a brief check-up. After the first 3 weeks of the washout period, patients continued to the next step.
- If qualified patients were <u>not</u> taking an OAD:
  - They continued to the next step.

The next step for all patients was the run-in period. At that time, all patients took placebo for 7 days. This part of the study was "single-blinded". This means that the patients did not know who was given which treatment, but the study doctor did know.

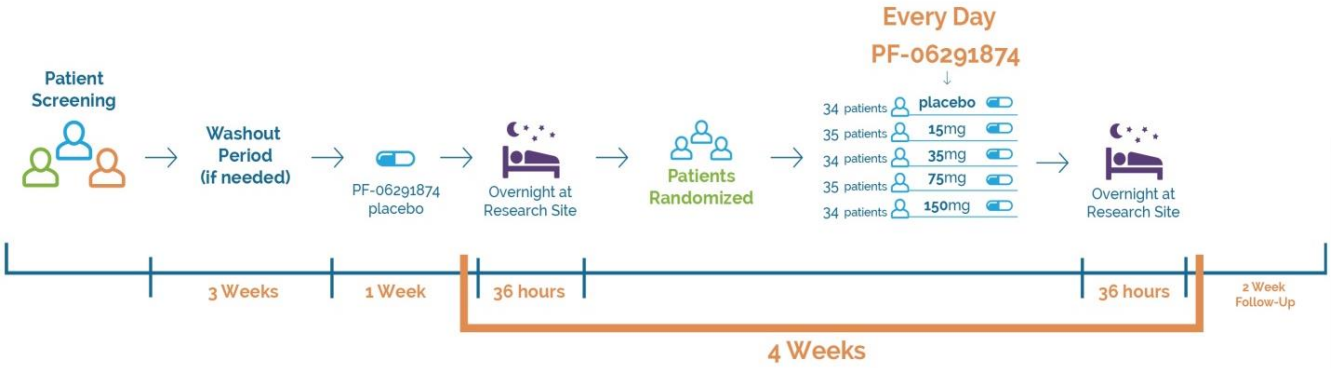
After the run-in period, patients went to the research site to begin their first of two 36-hour stays. During this first stay, patients underwent testing to find out what their starting values were for substances in their body like blood sugar and HbA1c before they started study medicine. These starting values before patients take study medicine are known as "baseline" values. After the baseline tests finished, patients began taking the study medicine based on which treatment group they were randomized. This part of the study was "double-blinded". This means the patients and study doctors did not know who was given which treatment during this part of the study. Researchers use "double-blinded" studies to make sure that the results of the study are not influenced in any way.

To find out if PF-06291874 was safe and tolerated, the study doctors used different tests and assessments, such as testing the patient's blood and urine samples throughout the study. Researchers wanted to measure how much PF-06291874 was in the patient's body after taking the study medicine, and also measure how much sugar was in the patient's blood at different times before and after taking the study medicine. Other substances in blood and urine related to diabetes were also measured to better determine how PF-06291874 works. Patients also had their heart rate, blood pressure, and electrical activity of the heart (by electrocardiogram test) monitored.

Patients took the study medicine once a day at the same time each day. They continued taking the study medicine this way for the rest of the time they were in the study. They were given a diary to keep track of what time they took the study medicine. Patients also used a diary to keep track of their blood sugar levels (tested by home monitoring finger stick) and any symptoms of high or low (hypoglycemia) blood sugar they may have experienced.

About 28 days (4 weeks) after starting the study medicine, patients began their second 36-hour stay at the research site. Following this visit, the patients stopped taking the study medication.

Patients went to the research site for their final visit about 10-14 days after the second 36-hour stay. The visit was for a final check-up, and blood and urine samples were taken for testing. Study doctors also talked to patients about restarting any medications that were stopped for the study.



While patients were only in the study for 8 to 11 weeks (around 2 to 4 months) depending if they needed a washout period or not, the entire study took the Sponsor 7 months to complete. The Sponsor ran this study at 16 research sites in the United States. It began on 19 August 2014 and ended 19 March 2015. 172 patients entered into this study. 101 patients were men and 71 patients were women. All patients were between the ages of 18 and 70 when the study started.

Patients were supposed to be treated for 4 weeks. Of the 172 patients who started the study, 166 patients finished the study; 6 patients left before the study was over by their choice or a doctor decided it was best for a patient to stop the study.

When the study ended in March 2015, 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?

Is PF-06291874 safe and tolerated by patients with T2DM?

Yes.

Researchers wanted to see what medical problems the patients had. Patients 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 have been caused by a study treatment, or by another drug the patient 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.

The researchers found out that each group had about the same amount of medical problems. There were slightly more medical problems reported in the groups that received 75 mg or 150 mg of PF-06291874.

Number of Medical Problems Reported During the Study			
Study Medicine Given	**Number of Treated Patients in Group**	**Number of Patients Who Had Medical Problems**	**Number of Medical Problems Reported in the Whole Group**
Placebo	**34**	**11 (32%)**	**16**
PF-06291874 15 mg	**35**	**7 (20%)**	**15**
PF-06291874 35 mg	**34**	**10 (29%)**	**15**
PF-06291874 75 mg	**35**	**11 (31%)**	**20**
PF-06291874 150 mg	**34**	**12 (35%)**	**21**

WHAT MEDICAL PROBLEMS DID PATIENTS HAVE DURING THE STUDY?

When new medicines are being studied, researchers keep track of all medical problems that patients have. A total of 51 out of 172 (about 30%, or 3 out of 10) patients in this study had at least 1 medical problem. One (1) patient left the study due to a medical problem. This patient was in the placebo group and had the medical problem of hyperglycemia. The most common medical problems are listed below.

Most Common Non-Serious Medical Problems (Reported by 3% or More of Patients in the Study)					
Medical Problem	**Placebo** (34 Patients treated)	**PF-06291874 15 mg** (35 Patients treated)	**PF-06291874 35 mg** (34 Patients treated)	**PF-06291874 75 mg** (35 Patients treated)	**PF-06291874 150 mg** (34 Patients treated)
Cold symptoms	**2 (6%)**	**2 (6%)**	**3 (9%)**	**4 (11%)**	**1 (3%)**
Loose stools	**1 (3%)**	**1 (3%)**	**3 (9%)**	**1 (3%)**	**3 (9%)**
Headache	**1 (3%)**	**0 (0%)**	**3 (9%)**	**1 (3%)**	**1 (3%)**

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

A medical problem is considered "serious" when it is life-threatening, causes lasting problems, or needs hospital care.

Only 1 out of the 172 (less than 1%, or less than 1 out of 100) patients had a serious medical problem. The patient with the serious medical problem was in the PF-06291874 75 mg group. The study doctors and the Sponsor decided that the study medicine did not cause the serious medical problem. No patients died during 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.

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

www.clinicaltrials.gov Use the study identifier **NCT02175121**

Findings from this study will be used in other studies to learn whether patients are helped by this drug.

Please remember that researchers look at the results of many studies to find out which medicines work best and are safest 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!