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-06650833

Protocol Number: B7921005

Dates of Trial: 10 November 2016 to 15 August 2018

Title of this Trial: Effect of 12 Weeks of Treatment with PF-06650833 on Rheumatoid Arthritis [A 12 Week Randomized, Double-Blind, Double Dummy, Parallel Group, Active and Placebo-Controlled, Multicenter Study to Assess the Efficacy and Safety Profile of PF-06650833 in Subjects With Active Rheumatoid Arthritis With an Inadequate Response to Methotrexate]

Date of this Report: 25 March 2020

– 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?

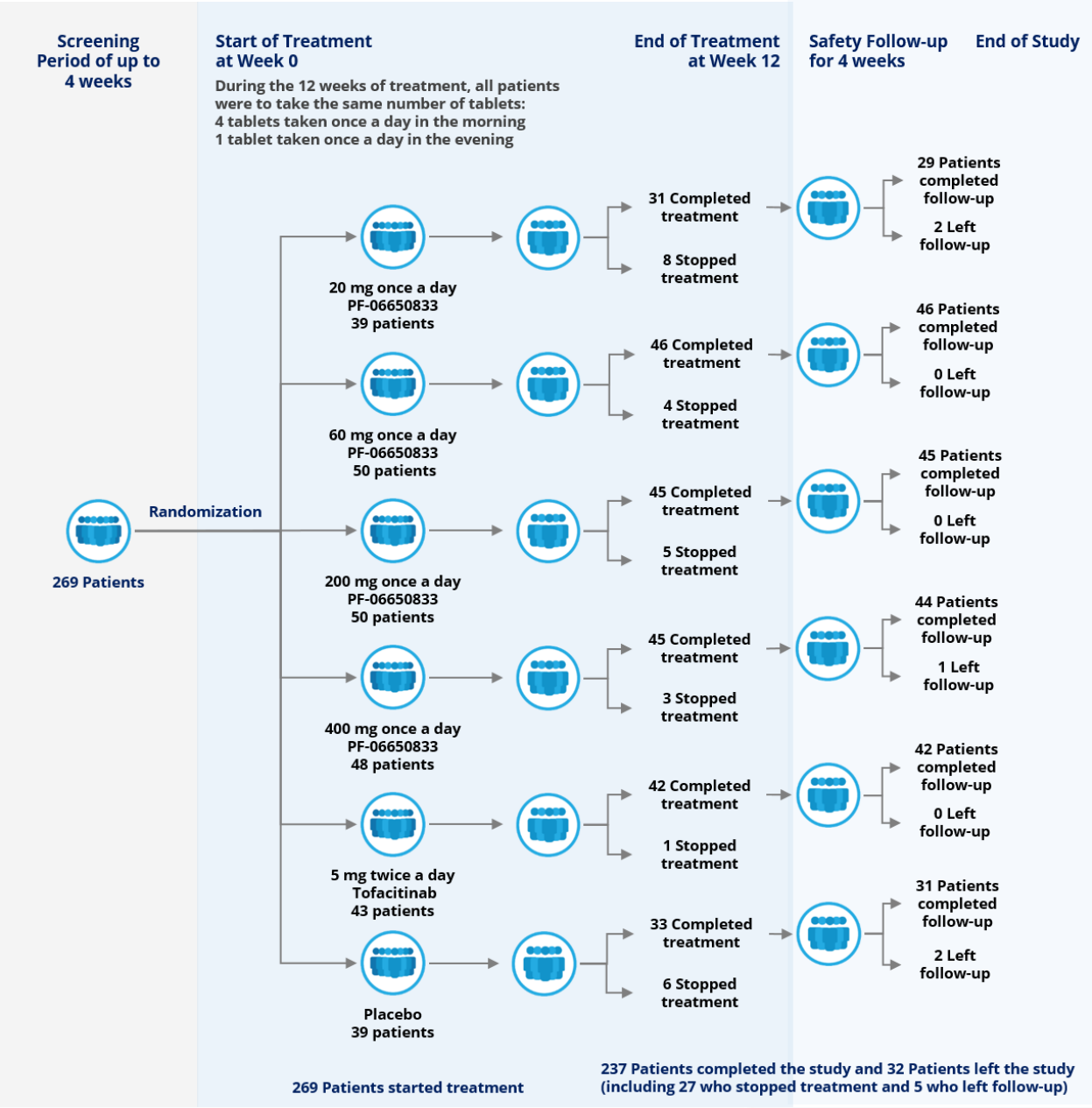
Rheumatoid arthritis, or "RA", is a disease that causes swelling, pain, and stiffness in the joints. RA is an "autoimmune disease", which means that patients with RA have an overactive immune system that mistakenly attacks healthy parts of the body, such as the joints. RA can cause permanent damage to the joints if it goes untreated, so researchers are looking for new treatment options for RA.

Patients in this study were treated with PF-06650833, which is an "investigational drug". This means it is not approved for use in people with RA and is a new type of drug that is being studied for the treatment of RA. Some of the patients in this study were also treated with tofacitinib. This is a medicine that works to reduce the activity of the immune system in people with RA. It is an oral (taken by mouth) medication that has been approved, and is available by prescription, to treat adults with active, moderate to severe RA that did not respond well to medications known as disease-modifying anti-rheumatic drugs (DMARDs) like methotrexate.

Researchers did this study to see if taking PF-06650833 helped with the symptoms of RA by reducing inflammation.

WHAT HAPPENED DURING THE STUDY?

This study compared 6 groups of patients to find out if PF-06650833 given at 4 different doses works to treat RA compared to patients taking a "placebo" or a comparator medicine of tofacitinib (see Figure and Table). A placebo does not have any medicine in it, but looks just like the medicine. The patients and the doctors did not know who was given which treatment/medicine and at what dose in this study. This is known as a "double-blinded" study. This was done to make sure that the trial results were not influenced in any way. Volunteers were assigned to each group by chance alone. This is known as a "randomized study". This is done to make the groups more similar, which makes comparing the groups more fair.


Screening Period of up to 4 weeks
Start of Treatment at Week 0
During the 12 weeks of treatment, all patients were to take the same number of tablets:
4 tablets taken once a day in the morning
1 tablet taken once a day in the evening
End of Treatment at Week 12
Safety Follow-up for 4 weeks
End of Study
269 Patients
Randomization
20 mg once a day PF-06650833 39 patients
31 Completed treatment
8 Stopped treatment
29 Patients completed follow-up
2 Left follow-up
60 mg once a day PF-06650833 50 patients
46 Completed treatment
4 Stopped treatment
46 Patients completed follow-up
0 Left follow-up
200 mg once a day PF-06650833 50 patients
45 Completed treatment
5 Stopped treatment
45 Patients completed follow-up
0 Left follow-up
400 mg once a day PF-06650833 48 patients
45 Completed treatment
3 Stopped treatment
44 Patients completed follow-up
1 Left follow-up
5 mg twice a day Tofacitinab 43 patients
42 Completed treatment
1 Stopped treatment
42 Patients completed follow-up
0 Left follow-up
Placebo 39 patients
33 Completed treatment
6 Stopped treatment
31 Patients completed follow-up
2 Left follow-up
269 Patients started treatment
237 Patients completed the study and 32 Patients left the study (including 27 who stopped treatment and 5 who left follow-up)

Description of Treatment Groups

Treatment Group	Timing of the Blinded Study Medication	
	4 tablets[a] in the morning for 12 weeks	**1 tablet[a] in the evening for 12 weeks**
20 mg PF-06650833	1 x 20 mg PF-06650833 tablet and 3 x placebo tablets	1 x placebo tablet
60 mg PF-06650833	3 x 20 mg PF-06650833 tablets and 1 x placebo tablets	1 x placebo tablet
200 mg PF-06650833	2 x 100 mg PF-06650833 tablets and 2 x placebo tablets	1 x placebo tablet
400 mg PF-06650833	4 x 100 mg PF-06650833 tablets	1 x placebo tablet
10 mg tofacitinib	1 x 5 mg tofacitinib tablet and 3 x placebo tablets	1 x 5 mg tofacitinib tablet
Placebo	4 x placebo tablets	1 x placebo tablet

[a] All tablets were identical in appearance.

The study included adult patients with moderate to severe active RA. All the patients in this study were already taking methotrexate, but still had active RA symptoms. In addition to methotrexate, the patient could have been previously treated with an anti-tumor necrosis factor (anti-TNF). This is a particular kind of treatment that specifically "inhibits" the activity of chemicals in the body known as TNFs. Inhibits means that activity of a chemical is slowed down, reduced, or stopped. Anti-TNF treatment is used in RA to help control the disease and reduce pain and disability. The anti-TNF treatment could have been stopped because of safety concerns, if it did not seem to give sufficient help to the patient, or if the patient was not able to obtain the treatment due to access problems.

In addition to study medication (PF-06650833 plus placebo or tofacitinib plus placebo), patients could take their normal treatments for RA including methotrexate, non-steroidal anti-inflammatory drugs (NSAIDs), cyclooxygenase (COX)-2 inhibitors, some types of opioid and/or acetaminophen (paracetamol) for pain relief and/or a low dose of oral corticosteroids like prednisone.

While each patient was only in the study for 20 weeks, the entire study took 21 months to complete. The Sponsor ran this study at 103 locations in 19 countries in Asia, Europe, Central America, North America, and Oceania. It began on 10 November 2016 and ended on 15 August 2018. 59 men and 210 women participated. All patients were between the ages of 19 and 73 years.

Patients were to be treated for 12 weeks. Of the 269 patients who started the study, 237 finished the study (e.g., 12 weeks of treatment plus 4 weeks of follow up). During the follow-up period, patients were not given treatment but were only monitored for possible safety events. There were 32 patients who left before the study was over by their choice or a doctor decided it was best for a patient to stop the study. Of these 32 patients, 27 patients did not complete the 12 weeks of treatment and 5 patients completed the 12 weeks of treatment, but did not completed the 4 weeks of follow-up.

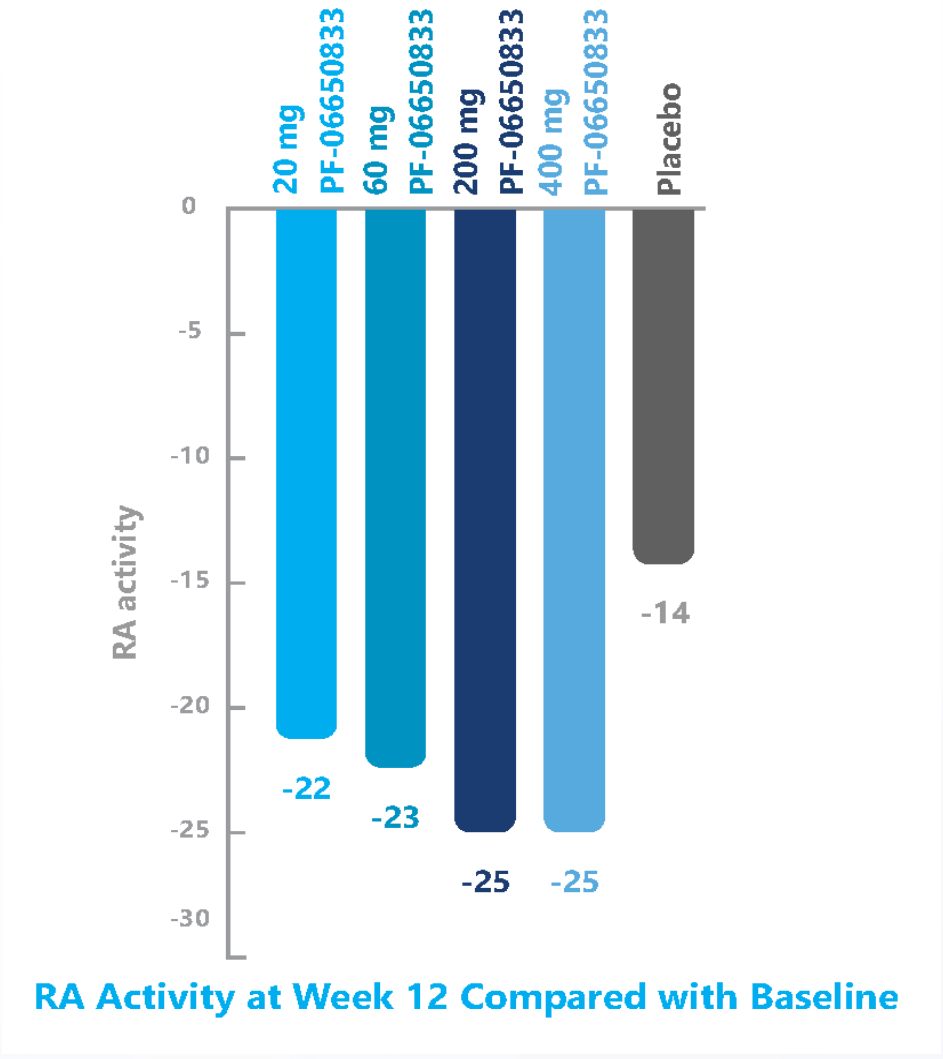
When the study ended in August 2018, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

WHAT WERE THE RESULTS OF THE STUDY?

Did 12 weeks of treatment with PF-06650833 reduce RA activity?

RA activity was measured using a "simplified disease activity index", which gives a score for disease activity. This score is based on the number of swollen and tender joints as well as how the patient feels about their RA, what the patient's doctor thinks about the patient's RA, and the amount of a substance known as "C-reactive protein", or CRP, which can be found in a patient's blood. CRP is made by the liver if there is an "inflammatory response". An inflammatory response is the body's reaction to an infection or something the body thinks is foreign. A negative score at Week 12 in the simplified disease activity index compared with "baseline", or the score the patient had just before the start of treatment in this study, means the patient and their doctor thinks that their RA activity has been reduced.

After 12 weeks of treatment, RA activity was reduced in patients who took PF-06650833 compared with patients taking placebo. The average reduction in RA activity with PF-06650833 depended on the dose given, but the score was between 22 and 25 for PF-06650833 compared with a score of 14 for placebo. Based on these results, the researchers have decided that the results are not likely a result of chance. Note: This study was specifically set up to look at the RA activity after PF-06650833 treatment compared with placebo. Therefore RA activity after tofacitinib treatment was not included in the graph below.



RA Activity at Week 12 Compared with Baseline

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 PATIENTS 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.

123 out of 269 patients in this study had at least 1 medical problem. A total of 12 patients (5%, 12 out of 269 patients) left the study because of medical problems. There were 20 patients (7%, 20 out of 269 patients) who stopped taking the study treatment for a short period of time or who had their dose of study treatment reduced during this study. The most common medical problems are listed below.

Most Common Medical Problems (Reported by 2 or More Patients in Any Group)

Medical Problem	PF-06650833 given once a day				Tofacitinib 5 mg given twice a day (43 Patients Treated)	Placebo (39 Patients Treated)
	20 mg (39 Patients Treated)	60 mg (50 Patients Treated)	200 mg (50 Patients Treated)	400 mg (48 Patients Treated)		
Low numbers of red blood cells	0	1 (2%)	0	0	1 (2%)	0
Stomach pain	0	0	1 (2%)	1 (2%)	0	2 (5%)
Upper stomach pain	2 (5%)	0	1 (2%)	0	1 (2%)	0
Loose stools	0	1 (2%)	0	2 (4%)	1 (2%)	0

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Upset stomach	1 (3%)	4 (8%)	2 (4%)	1 (2%)	1 (2%)	0
Feeling hot/high temperature	0	0	0	2 (4%)	0	0
Shingles	1 (3%)	2 (4%)	0	0	0	0
Flu	0	1 (2%)	0	0	2 (5%)	1 (3%)
Common cold	4 (10%)	2 (4%)	1 (2%)	2 (4%)	3 (7%)	2 (5%)
Chest infection	2 (5%)	0	2 (4%)	3 (6%)	2 (5%)	1 (3%)
Alanine amino-transferase increased	0	1 (2%)	2 (4%)	1 (2%)	1 (2%)	2 (5%)
Aspartate amino-transferase increased	0	1 (2%)	2 (4%)	1 (2%)	1 (2%)	1 (3%)
Muscle spasms	0	2 (4%)	0	0	0	
Rheumatoid arthritis	4 (10%)	2 (4%)	1 (2%)	3 (6%)	2 (5%)	2 (5%)
Headache	1 (3%)	3 (6%)	0	1 (2%)	0	2 (5%)

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

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

8 patients (3%, or 8 out of 269 patients) had serious medical problems: 6 patients in the PF-06650833 groups, 1 patient in the tofacitinib group, and 1 patient in the placebo group. The doctors thought that 1 serious medical problem was related to study treatment. This was a report of serious liver injury by a patient in the PF-06650833 20 mg group. All of the other serious medical problems were reported by 1 patient each and none were thought by the doctors to be linked with study treatment. No patients 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.

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

www.clinicaltrials.gov	Use the study identifier **NCT02996500**
www.clinicaltrialsregister.eu	Use the study identifier **2016-002337-30**

Clinical trials with PF-06650833 are ongoing and further trials are planned. 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!