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: Xeljanz® (tofacitinib)

Protocol Number: A3921091

Dates of Trial: 20 January 2014 to 18 December 2015

Title of this Trial: Efficacy and Safety of Tofacitinib in Psoriatic Arthritis: Comparator Study

[A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study of the Efficacy and Safety of 2 Doses of Tofacitinib (CP-690,550) or Adalimumab in Subjects With Active Psoriatic Arthritis]

Date of this Report: 16 January 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?

Psoriatic arthritis (also known as "PsA") is a disease that can cause pain and swelling (inflammation) in or around the joints, tendon areas, fingers, toes, and back, and is often combined with itchy, scaly rashes on the skin. These problems are because the immune system, whose job is to attack foreign invaders like viruses and other germs, mistakenly attacks other parts of the body instead.

If PsA inflammation is left untreated, joints, tendon areas, fingers, and toes may become painful or swollen; skin rashes may occur; and people may become extremely tired. There is no cure for PsA at this time, but common treatments for PsA include medicines that control pain, reduce inflammation, and prevent the immune system from attacking the joints.

Tofacitinib is a medicine that may reduce the activity of the immune system. It is an oral (taken by mouth) medication used to treat adults with PsA. In this study, researchers wanted to learn more about the use of tofacitinib in people who had not been helped by conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) like methotrexate, which were being used to treat PsA.

Researchers did this study to find out if tofactinib, when compared to placebo, in patients on background therapy of csDMARD, reduced PsA symptoms and improved a patient's ability to perform physical activities (improved physical functioning). Researchers wanted to answer this question:

- Does tofacitinib help reduce pain, inflammation, and other symptoms caused by PsA in patients that were not helped by other drugs (csDMARDs) previously being used to treat PsA?

WHAT HAPPENED DURING THE STUDY?

This study compared 5 groups of patients to find out if patients who took tofacitinib had an improvement in PsA symptoms and physical functioning, compared to patients who took placebo. A placebo does not have any medicine in it, but looks just like the medicine being tested. Using a placebo helps researchers learn if the study

drug works better than no treatment at all. In this study, all patients (including those taking placebo) received 1 csDMARD as background therapy; thus, patients taking placebo did take some medicine in this study. Background therapy is the standard treatment routinely used to treat a disease or condition.

In this study, some patients were given adalimumab, which is a medication that is used to treat PsA. Adalimumab is a biologic DMARD (bDMARD) and has been shown to reduce pain and inflammation in patients with PsA.

Researchers also wanted to find out if patients who took adalimumab, an active control, had an improvement in the same symptoms and functioning compared to patients who took placebo. An active control is a drug that is already being used to treat patients with the disease being studied. In this study, the active control was tested against placebo to see if the standard treatment available to patients worked better than no treatment at all.

This study included adult men and women who:

- Had active psoriatic arthritis for more than 6 months;
- Had active plaque psoriasis (skin lesions) that had been diagnosed or confirmed by a doctor;
- Had 3 or more swollen joints and 3 or more tender (painful to the touch) joints;
- Were not helped by at least 1 csDMARD (like methotrexate) for the treatment of psoriatic arthritis.

All patients were taking a medication to treat their PsA that was prescribed by their doctors before they entered the study. At the start of the study, these patients continued to take the prescribed medication and were also assigned by chance alone to receive some combination of tofacitinib, placebo, or adalimumab in 1 of 5 different orders (treatment sequences). 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 trial was also "double-blinded". This means that patients 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.

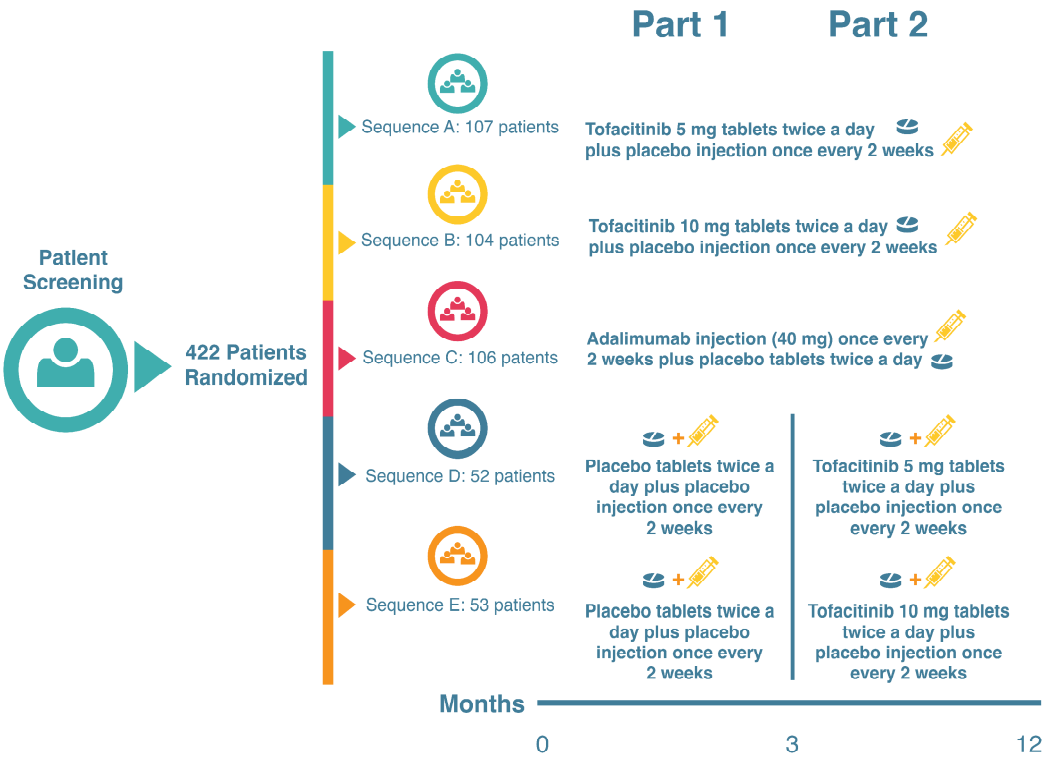
The study had two parts: Part 1, which lasted for 3 months; and Part 2, which lasted for 9 months. Some patients received the same treatment in both parts of the study, but some patients received a different treatment in Part 2 than they received in Part 1. Patients were randomized to receive some combination of tofacitinib, placebo, or adalimumab in 1 of 5 different sequences:

Medicines Given in Each Treatment Sequence

Treatment Sequence	Part 1 (3 months)	Part 2 (9 months)
A	Tofacitinib 5 milligrams (mg) tablets twice a day (BID) plus placebo injection once every 2 weeks	Same as Part 1
B	Tofacitinib 10 mg tablets BID plus placebo injection once every 2 weeks	Same as Part 1
C	Adalimumab injection (40 mg) once every 2 weeks plus placebo tablets BID	Same as Part 1
D	Placebo tablets BID plus placebo injection once every 2 weeks	Tofacitinib 5 mg BID plus placebo injection once every 2 weeks
E	Placebo tablets BID plus placebo injection once every 2 weeks	Tofacitinib 10 mg BID plus placebo injection once every 2 weeks

All patients were required to receive 1 csDMARD (like methotrexate) during the study.

Patients were checked (screened) to make sure they were a good fit for the study. A total of 422 patients who met all the study requirements were randomized to receive tofacitinib, placebo, or adalimumab in 1 of 5 different treatment sequences.



While patients were only in the study for 12 months, the entire study took about 2 years to complete. The Sponsor ran this study at 94 locations in Australia, Canada, Mexico, Russian Federation, Taiwan, the United Kingdom, the United States, and throughout Europe. It began on 20 January 2014 and ended on 18 December 2015. A total of 225 women (53%) and 197 men (47%) participated. All patients were between the ages of 18 and 81 years.

Patients were to be treated for 12 months. Of the 422 patients who started the study, 373 (88%) finished the whole study. A total of 49 patients (12%) left before the study was over by their choice or because a doctor decided it was best for them to stop the study.

When the study ended in December 2015, the Sponsor began reviewing the study results. The Sponsor then created a report of the results. This is a summary of that report.

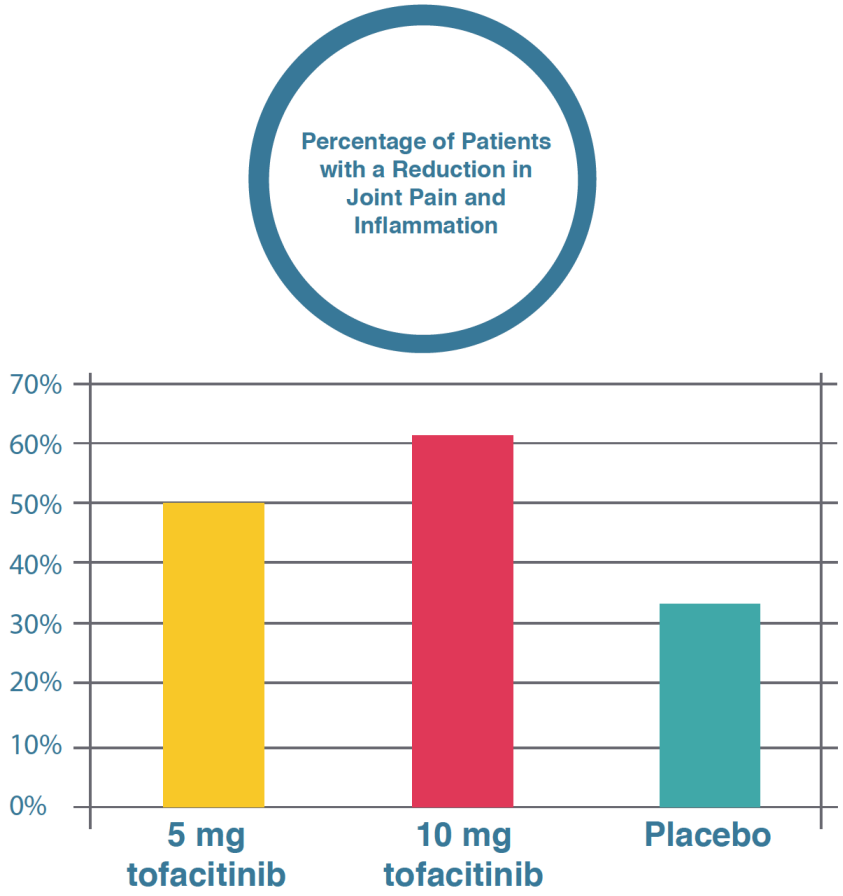
WHAT WERE THE RESULTS OF THE STUDY?

Does tofacitinib reduce joint pain and inflammation in patients who were not helped by csDMARDs (like methotrexate)?

Yes. In this study, tofacitinib reduced joint pain and inflammation in patients who were not helped by csDMARDs.

Researchers looked at the percentage of patients (number of patients out of 100) in each treatment group who had at least a 20% reduction in the number of joints that were tender/painful and swollen (inflamed) after 3 months of taking study drug. They compared the number of tender/painful and swollen joints that patients had at the end of the 3 months of treatment to the number of tender/painful and swollen joints that patients had before they started the study, to see if tofacitinib reduced pain and inflammation.

More patients in both tofacitinib groups (5 mg and 10 mg) had less joint pain and inflammation at the end of 3 months of treatment than patients in the placebo group. Half of the patients taking 5 mg tofacitinib (50%; 5 out of every 10 patients) and over half of the patients taking 10 mg tofacitinib (61%; 6 out of every 10 patients) had less pain and inflammation than they had before they started treatment. One-third (33%) of the patients taking placebo had a reduction in joint pain and inflammation compared to their pain and inflammation before treatment.



Does tofacitinib improve a patient's ability to complete activities of daily living?

Yes, patients had an easier time completing daily activities after taking tofacitinib.

Researchers asked patients how difficult it was to complete daily living activities, such as dressing and grooming, getting up, eating, walking, and bathing. They used a questionnaire that asked patients to rate their level of difficulty completing an activity on a scale ranging from "no difficulty completing activity" (a score of 0) to "unable to complete activity" (a score of 3). Researchers then compared the patients' responses after taking tofacitinib or placebo to their responses before they started study treatment.

On average, patients who took tofacitinib (5 mg and 10 mg) had a greater improvement in how easy it was to complete daily activities than patients taking placebo. At the end of 3 months of treatment, the questionnaire score (amount of difficulty completing activities) decreased by an average of 0.35 (out of 3) for patients who took tofacitinib 5 mg twice daily, 0.40 (out of 3) for patients who took tofacitinib 10 mg twice daily, and 0.18 (out of 3) for patients who took placebo.

Based on these results, the researchers have decided that the results are /are not likely the result of chance. Tofacitinib may be an option for treating patients with PsA who were not previously helped by csDMARDs.

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.

175 out of 422 patients (41%) in this study had at least 1 medical problem. A total of 17 patients (4%) left the study because of medical problems. The most common medical problems are listed on the next page.

Most Common Medical Problems (Reported by More Than 5% of Patients)

Medical Problem	Tofacitinib 5 mg (107 Patients Treated)	Tofacitinib 10 mg (104 Patients Treated)	Adalimumab (106 Patients Treated)	Placebo, then Tofacitinib 5 mg (52 Patients Treated	Placebo, then Tofacitinib 10 mg (53 Patients Treated)
Stomach pain	1 (1%)	1 (1%)	2 (2%)	0	3 (6%)
Nausea	3 (3%)	4 (4%)	6 (6%)	0	1 (2%)
Common cold	8 (7%)	12 (12%)	11 (10%)	4 (8%)	4 (8%)
Sore throat	5 (5%)	6 (6%)	7 (7%)	0	3 (6%)
Upper respiratory tract infection	10 (9%)	11 (11%)	8 (8%)	5 (10%)	5 (9%)
Urinary tract infection	2 (2%)	4 (4%)	4 (4%)	1 (2%)	4 (8%)
Alanine aminotransferase increased	3 (3%)	3 (3%)	8 (8%)	3 (6%)	1 (2%)
Aspartate aminotransferase increased	0	1 (1%)	7 (7%)	1 (2%)	1 (2%)
Blood creatine phosphokinase increased	5 (5%)	5 (5%)	3 (3%)	1 (2%)	5 (9%)
Spinal (back) pain	2 (2%)	1 (1%)	3 (3%)	3 (6%)	0
Headache	5 (5%)	11 (11%)	7 (7%)	2 (4%)	4 (8%)

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

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

28 patients (7%) had serious medical problems. Eight (8) patients (7%) in the tofacitinib 5 mg group, 4 patients (4%) in the tofacitinib 10 mg group, 9 patients (8%) in the adalimumab group, 3 patients (6%) in the placebo→tofacitinib 5 mg group, and 4 patients (8%) in the placebo→tofacitinib 10 mg group had at least 1 serious medical problem. A total of 2 patients (less than 1%) had an injury to the joint, and the other serious medical problems happened in 1 patient each.

One (1) patient (1%) in the tofacitinib 10 mg group and 2 patients (4%) in the placebo→tofacitinib 5 mg group had a serious medical problem that study doctors and the Sponsor determined was related to tofacitinib. One (1) patient (1%) in the tofacitinib 5 mg group had a serious medical problem that the study doctor said was related to tofacitinib, but the Sponsor said was unrelated. One (1) patient (2%) in the placebo→tofacitinib 5 mg group died during the study. The study doctors and Sponsor determined that the death was not related to the study medicines.

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 **NCT01877668**
www.clinicaltrialsregister.eu	Use the study identifier **2011-003668-55**
www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number **A3921091**

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients. Further clinical trials with tofacitinib are planned.

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!