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: Tofacitinib

Protocol Number: A3921120

Dates of Trial: 7 June 2018 to 20 August 2020

Title of this Trial: Efficacy and Safety of Tofacitinib in Patients With Active Ankylosing Spondylitis (AS)

[A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Study of the Efficacy and Safety of Tofacitinib in Subjects With Active Ankylosing Spondylitis (AS)]

Date of this Report: 29 January 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?

Ankylosing spondylitis (AS) is a disease that can cause pain and swelling (inflammation) in the joints around the spine. This is because the immune system, whose job is to attack foreign invaders like viruses and other germs, mistakenly attacks the joints instead.

Patients with AS may have pain and stiffness in the lower back, buttocks, or neck, along with mild fever and fatigue. There is no cure for AS at this time, but common treatments for AS include medicines that control pain, reduce inflammation, and prevent the immune system from attacking the joints.

Tofacitinib is an oral (taken by mouth) medicine that may reduce the activity of the immune system. It is being studied as a possible treatment for adults with AS, but is not approved for this use outside of research studies like this one. In this study, researchers wanted to learn more about the use of tofacitinib in people who had not been helped by or could not tolerate other drugs for AS, including non-steroidal anti-inflammatory drugs (NSAIDs) and/or tumor necrosis factor (TNF) inhibitors.

Researchers did this study to find out if tofacitinib, when compared to placebo, reduced AS symptoms and improved a patient's ability to perform physical activities (improved physical functioning). Researchers wanted to answer this question:

- Does tofacitinib 5 mg given twice per day improve pain, inflammation, and physical functioning in patients with AS who were not helped by other drugs, compared to placebo?

WHAT HAPPENED DURING THE STUDY?

This study compared 2 groups of patients to find out if patients who took tofacitinib 5 mg twice per day had an improvement in AS 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.

This study included adult men and women who:

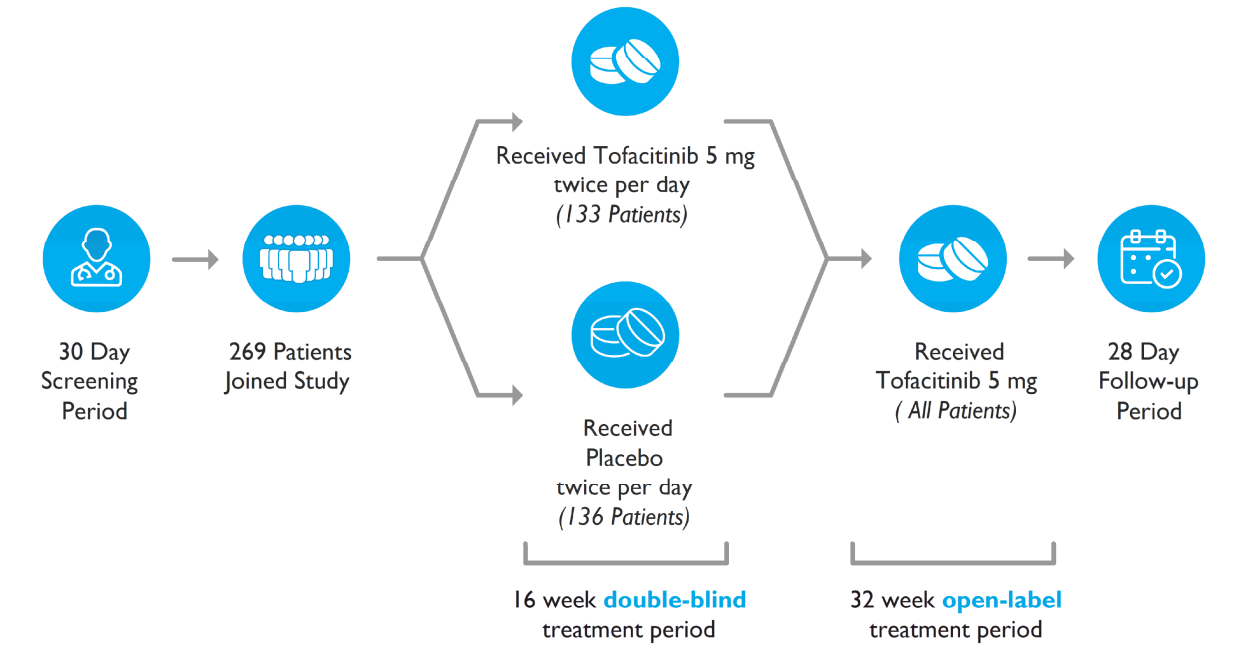
- Had AS that was confirmed by X-ray
- Were not helped by or could not tolerate treatment with NSAIDs, or treatment with both NSAIDs and TNF inhibitors

Patients were checked (screened) to make sure they were a good fit for the study. Patients who were a good fit were assigned by chance alone to receive either tofacitinib or placebo for 16 weeks. 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 part of the trial was also "double-blinded". This means that patients and doctors did not know who was given which treatment. This was done to make sure that the trial results were not influenced in any way.

After 16 weeks of double-blinded treatment, all patients were switched to "open-label" treatment with tofacitinib for 32 weeks. Open-label means that both the doctors and patients knew which treatment they received. Finally, patients were expected to complete a 28-day follow-up period after they finish study treatment.

The figure below shows what happened during the study.



Patients were expected to be in the study for about 56 weeks total. The Sponsor ran this study at 95 locations in Asia, Australia, Europe, and North America. It began on 7 June 2018 and ended on 20 August 2020. A total of 224 men (83%) and 45 women (17%) participated. All patients were between the ages of 20 and 70 years.

Of the 269 patients who started the study and received treatment, 252 (94%) completed it. A total of 17 patients (6%) left the study early by their choice or because a doctor decided it was best for them to stop the study.

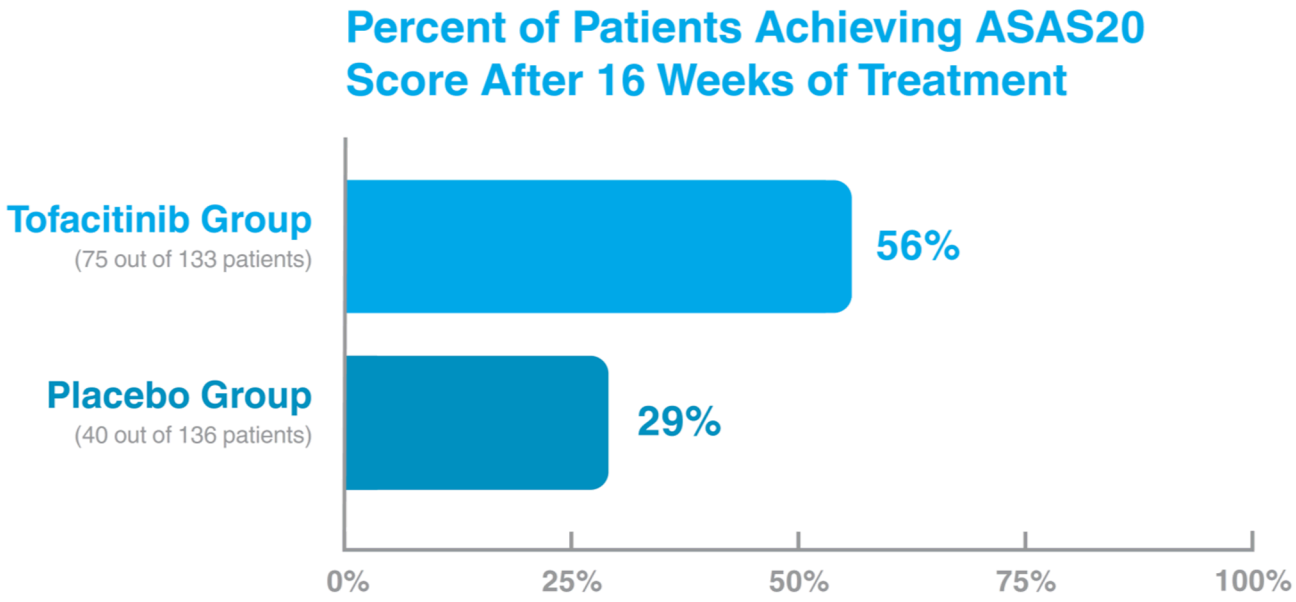
When the study ended in August 2020, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

WHAT WERE THE RESULTS OF THE STUDY?

Does tofacitinib 5 mg given twice per day improve pain, inflammation, and physical functioning in patients with AS who were not helped by other drugs, compared to placebo?

To answer this question, researchers used a scoring tool called the "ASAS20" to look at 4 areas: spine pain, inflammation, physical functioning, and the patient's own opinion on how they thought they were doing. To achieve an ASAS20 score, the patients needed at least a 20% improvement in at least 3 of these areas, without worsening of more than 20% in the remaining area. The researchers compared the percentage of patients (number of patients out of 100) in each treatment group (tofacitinib or placebo) who achieved ASAS20 at the end of the 16-week double-blind treatment period.

In this study, 75 out of 133 patients (56%) who received tofacitinib during the 16-week double-blind treatment period achieved an ASAS20 score. 40 out of 136 patients (29%) who received placebo during the 16-week double-blind treatment period achieved an ASAS20 score. The figure below shows these results.



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

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.

The researchers looked at medical problems that happened during the first 48 weeks of the study.

196 out of 269 patients (73%) in this study had at least 1 medical problem, including 103 out of 133 patients (77%) who received tofacitinib and 93 out of 136 patients (68%) who received placebo for 16 weeks and switched to open-label tofacitinib. A total of 1 patient (less than 1%) left the study because of medical problems. The most common medical problems are listed in the table below.

Most Common Medical Problems (Reported by At Least 5% of Patients in Either Group)

Medical Problem	Tofacitinib (133 Patients Treated)	Placebo (16 Weeks) Then Tofacitinib (136 Patients Treated)
Infection of the nose, throat, and upper airways	21 (16%)	18 (13%)
Common cold	11 (8%)	17 (13%)
Diarrhea	10 (8%)	8 (6%)
Increased liver enzyme, which may indicate liver damage (alanine aminotransferase)	8 (6%)	2 (1%)
Protein in urine	8 (6%)	4 (3%)
Headache	5 (4%)	7 (5%)
Joint pain	2 (2%)	9 (7%)
Upper abdominal pain	2 (2%)	7 (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.

During the 48-week period, 9 out of 269 patients (3%) had serious medical problems. 7 patients out of 133 (5%) who received tofacitinib and 2 patients out of 136 (2%) who received placebo for 16 weeks and switched to tofacitinib had at least 1 serious medical problem. No patients died during this study. The serious medical problems are listed in the table below.

Serious Medical Problem	Tofacitinib (133 Patients Treated)	Placebo (16 Weeks) Then Tofacitinib (136 Patients Treated)
Hearing loss	1 (1%)	0 (0%)
Bands of scar tissue in abdomen	1 (1%)	0 (0%)
Worsening of medical condition	0 (0%)	1 (1%)
Inflammation of membranes surrounding brain and spinal cord	1 (1%)	0 (0%)
Broken rib	1 (1%)	0 (0%)
Broken spinal bone	0 (0%)	1 (1%)
Migraine headache	1 (1%)	0 (0%)
Kidney stone	1 (1%)	0 (0%)

Collapsed lung	**1 (1%)**	**0 (0%)**
Air trapped in tissue under skin	**1 (1%)**	**0 (0%)**
Build-up of cholesterol in gallbladder	**1 (1%)**	**0 (0%)**
Arthritis of spine	**0 (0%)**	**1 (1%)**

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:

www.clinicaltrials.gov	Use the study identifier **NCT03502616**
www.clinicaltrialsregister.eu	Use the study identifier **2018-000226-58**

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!