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: A3921288

Dates of Trial: 16 November 2017 to 20 February 2020

Title of this Trial: A Study of Tofacitinib in Patients With Ulcerative Colitis in Stable Remission

[A Phase 3b/4, Multi-Center, Double-Blind, Randomized, Parallel Group Study of Tofacitinib (CP-690,550) in Subjects With Ulcerative Colitis in Stable Remission]

Date(s) of this Report: 23 March 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?

Ulcerative colitis ("UC") is a long-term inflammatory bowel disease that causes inflammation (swelling) and ulcers (sores) in the digestive tract. UC affects the mucosa (inner lining) of the large intestine (colon) and rectum. Patients with UC experience occasional periods of increased inflammation, known as flares. Flares are characterized by diarrhea (loose stools) and presence of blood in the stools, as well as sense of urgency. Flares are followed by periods of remission (time with no symptoms) that vary in length from weeks to years.

There is no known cure for UC. Treatment can greatly reduce signs and symptoms of UC and can even lead to long-term remission. However, there are few treatment options for patients with moderately to severely active UC. Medication is the most common treatment for UC. Tofacitinib is a medicine that works to reduce the activity of the immune system. 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 UC that did not respond well to other medications.

Researchers have continued to study tofacitinib to find out more about its safety and how well it works. In one study, researchers saw that participants with UC who took either 5 mg or 10 mg of tofacitinib twice a day were more likely to stay in remission compared to participants who took placebo. However, a formal study to compare a reduced dose of tofacitinib (5 mg twice a day) to the standard dose (10 mg twice a day) of tofacitinib had not been done.

In this study, researchers wanted to find out if participants with UC who were in stable remission (ongoing time with no symptoms) would stay in remission if the dose of the treatment was reduced from 10 mg of tofacitinib twice a day to 5 mg of tofacitinib twice a day. Researchers wanted to answer the question:

- What difference did switching from 10 mg of tofacitinib twice a day to 5 mg of tofacitinib twice a day have on the percent of participants in remission after 6 months compared to staying on 10 mg of tofacitinib twice a day?

Researchers also wanted to learn more about the safety of tofacitinib in participants

who switched from 10 mg of tofacitinib twice a day to 5 mg of tofacitinib twice a day compared to participants who continued to take 10 mg of tofacitinib twice a day. They monitored participants for any medical problems that happened while they were taking tofacitinib.

The results for the primary endpoint (percent of participants in remission after 6 months) as well as safety results for participants from the start of the study until February 2020 (27 months) are summarized here.

WHAT HAPPENED DURING THE STUDY?

This study compared 2 groups of participants with UC to find out how many participants who were in stable remission and switched from taking 10 mg tofacitinib twice a day to 5 mg tofacitinib twice a day would be in remission 6 months later compared to participants who continued to take 10 mg tofacitinib twice a day.The study included participants who:

- Were participating in another study of tofacitinib (Study A3921139),
- Had been taking 10 mg tofacitinib twice a day for at least 2 years in a row,
- Were in stable remission for UC on 10 mg tofacitinib twice a day for 6 months prior to beginning this study, and
- Had not been taking any oral corticosteroids for their UC for at least 4 weeks prior to beginning this study.

Participants were put into 1 of 2 treatment groups by chance alone. 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 participants and doctors did not know who was given which dose of tofacitinib. This was done to make sure that the trial results were not influenced in any way.

Each participant in the study took 2 pills twice a day by mouth:

- **5 mg tofacitinib group:** one 5 mg tofacitinib tablet and one placebo tablet twice a day (70 out of 140 participants in the study).
- **10 mg tofacitinib group:** two 5 mg tofacitinib tablets twice a day (70 out of 140 participants in the study).

A placebo does not have any medicine in it, but it looks just like the study medicine. The pills for the investigational medicine looked exactly the same as the pills for the placebo. This made it so that participants did not know to which study group they were assigned.

During the entire study, participants are to come to the study site 17 times over 42 months and have their UC assessed. At 4 of these visits, participants are to have a lower endoscopy (flexible sigmoidoscopy/colonoscopy) to look for swelling or unusual changes to the lining of their colon. A lower endoscopy uses a tiny camera on the end of a thin, flexible tube that is inserted into the anus to view the inside of the rectum and most of the colon.

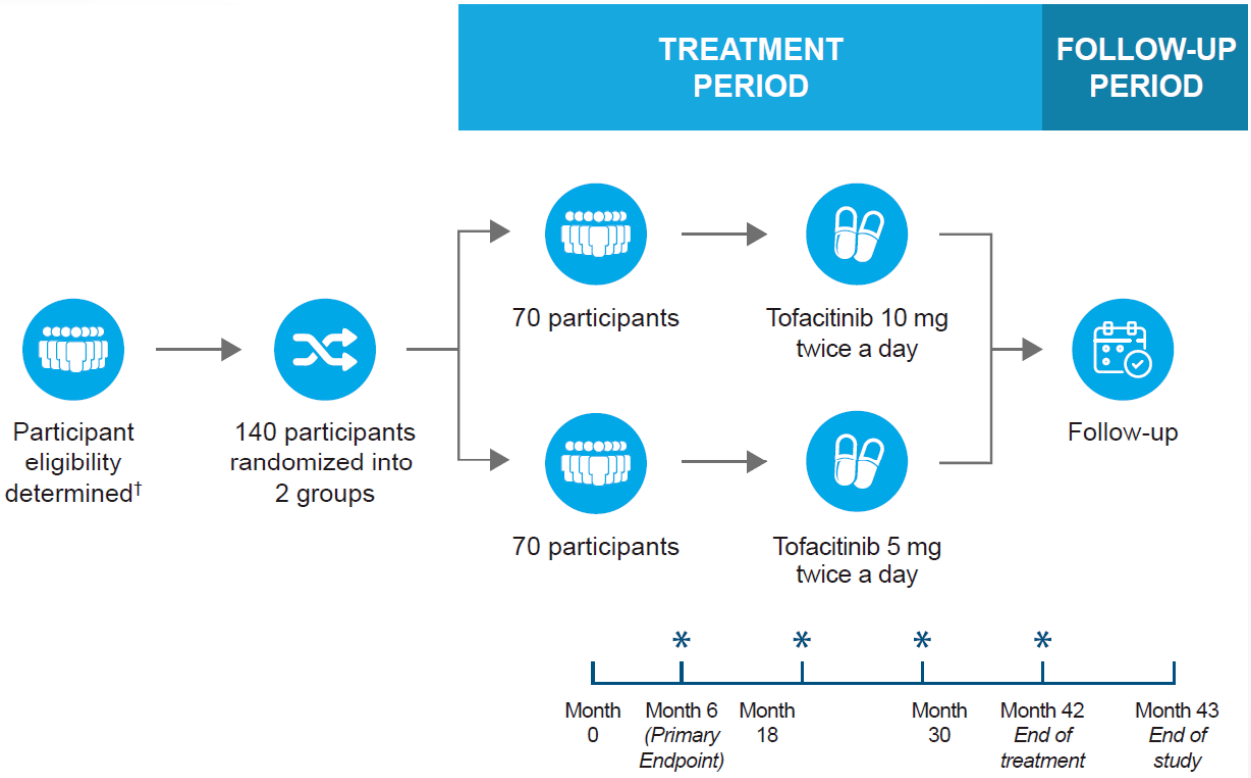
The participant's UC disease activity was measured using a modified Mayo score. The modified Mayo score rates the activity of UC based on 3 categories. Each category is graded from 0 to 3, with 3 being the most severe. The 3 categories are:

- Stool frequency (how many bowel movements per day?)
- Rectal bleeding (is blood seen in the stool?)
- Endoscopy results (how does the lining of the colon look?)

The scores from each of the 3 categories were added together to give the modified Mayo score. The modified Mayo score rates the disease activity of UC on a scale from 0 to 9. Participants who had a score of 0 or 1 for the endoscopy results, a stool frequency score of 0 or 1, and a score of 0 for rectal bleeding were said to be in remission. Any participant who experienced a worsening of their UC disease activity (flares) was allowed to have their dose adjusted during the study.

This report summarizes the findings for the primary endpoint in this study. The primary endpoint is the main question in a study that researchers want to answer. In some studies, like this one, results for the primary endpoint are studied while participants are still taking part in the rest of the study. In this study, the primary endpoint was studied ("primary analysis") after all participants had been on the study for 6 months. The percentage of participants in remission after taking tofacitinib for 6 months was calculated for participants in the 5 mg and 10 mg tofacitinib groups. The percentage of participants in remission after 6 months was compared between the 2 groups.

The figure below shows what is to happen during the entire study.



†Results from an endoscopy (flexible sigmoidoscopy/colonoscopy) performed in another study (Study A3921139) were used to determine if a participant from that study was eligible to enroll in this study. This endoscopy must have been performed no more than 6 months before a participant was enrolled in this study.

*Endoscopy (flexible sigmoidoscopy/colonoscopy) performed.

The Sponsor is running this study at 69 locations in 20 countries in Europe, North America, Asia, Africa, and Oceania. The primary endpoint of the study whose results are reported here began 16 November 2017 and ended 20 February 2020; the rest of

the study is ongoing. Ninety-two (92) men and 48 women participated. All participants were between the ages of 21 and 81. Results for the rest of the study will be reported when all participants have completed the entire study.

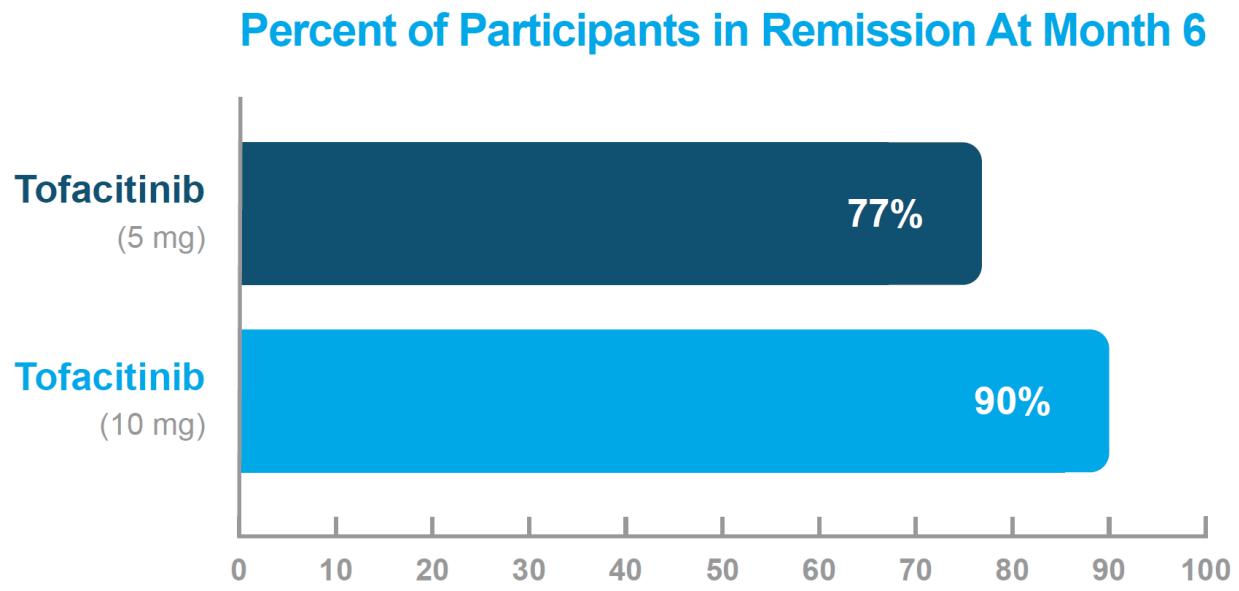
Participants were to be treated for 42 months, with the primary analysis occurring after all participants had taken tofacitinib for 6 months. Of the 140 participants who started the study, 115 finished the first 6 month part of the study. Twenty-five (25) participants did not finish the first 6 month portion of the study; of these, 2 participants from the 5 mg group did not finish because their UC worsened and 1 participant from the 5 mg group did not finish because their UC worsened and 1 participant from the 5 mg group did not finish due to pregnancy. Twenty-two (22) participants left before the first 6 month part of the study was over by their choice or a doctor decided it was best for a participant to stop being in the study.

When data collection for the primary endpoint ended in February 2020, the Sponsor reviewed the information collected for the primary endpoint. The Sponsor then created a report of those results. This is a summary of that report.

WHAT WERE THE RESULTS OF THE STUDY?

What difference did switching from 10 mg of tofacitinib twice a day to 5 mg of tofacitinib twice a day have on the percent of participants in remission after 6 months compared to staying on 10 mg of tofacitinib twice a day?

In this study, more than 75% (3 out of 4) of all participants in the study were in remission after 6 months of taking tofacitinib. More participants in the 10 mg group (90%) were in remission after 6 months of taking tofacitinib compared to participants in the 5 mg group (77%).



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 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 the side effects of an experimental drug might be.

Fifty (50) out of 140 participants in this study had at least 1 medical problem. A total of 9 participants left the study because of medical problems. Of these, 1 participant in the tofacitinib 5 mg group and 1 participant in the tofacitinib 10 mg group left the study due to medical problems which the researchers believed to be related to tofacitinib. The most common medical problems are listed below.

Most Common Medical Problems (Reported by 3 or More Participants in the Study)		
Medical Problem	Tofacitinib 5 mg (70 Participants Treated)	Tofacitinib 10 mg (70 Participants Treated)
Worsening of ulcerative colitis	10 (14%)	9 (13%)
Common cold	6 (9%)	7 (10%)
Nose and throat infection	4 (6%)	4 (6%)
Stomach pain	4 (6%)	3 (4%)
Upset stomach	3 (4%)	3 (4%)
Bronchitis	1 (1%)	5 (7%)
Headache	2 (3%)	3 (4%)
High blood pressure	2 (3%)	3 (4%)
Increased level of a certain protein in the blood (creatine phosphokinase)	1 (1%)	4 (6%)
Cold sores	4 (6%)	0
Muscle pain	3 (4%)	1 (1%)
Leg swelling	2 (3%)	2 (3%)
Shingles	1 (1%)	3 (4%)
Flu	1 (1%)	3 (4%)
Increased level of a certain protein in the stool (fecal calprotectin)	1 (1%)	2 (3%)
Abnormal growth on the lining of the colon	1 (1%)	2 (3%)

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

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

Ten (10) participants (7%) had serious medical problems: 6 participants in the tofacitinib 5 mg group and 4 participants in the tofacitinib 10 mg group. Two (2) of the 6 participants in the tofacitinib 5 mg group had a flare and were allowed to start taking 10 mg of tofacitinib. The serious medical problem for these 2 participants happened after they started taking 10 mg of tofacitinib. No participants died during the study. The serious medical problems reported by participants in the study are shown in the table below. Some participants reported more than 1 serious medical problem.

Serious Medical Problems (Reported by Any Participant)		
Serious Medical Problem	Tofacitinib 5 mg (70 Participants Treated)	Tofacitinib 10 mg (70 Participants Treated)
Low numbers of red blood cells due to low levels of iron	1 (1%)	0
Chest pain	0	1 (1%)
Skin infection	1 (1%)	0
Bladder infection	1 (1%)	0
Injury to the arm or leg	0	1 (1%)
Back pain	0	1 (1%)
Non-cancerous (benign) tumor in the mouth	1 (1%)	0
Skin cancer located on the outside portion of the vagina	1 (1%)	0
Stroke	1 (1%)	0
Breast disorder	1 (1%)	0
Thickening of the lining of the uterus	1 (1%)	0
Blood clot in the lung	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 **NCT03281304**
www.clinicaltrialsregister.eu	Use the study identifier **2017-002274-39**

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

www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number **A3921288**

This clinical trial is ongoing. When it has finished, additional information will be available to better understand the benefits and the risks of different doses of tofacitinib for maintaining remission in patients with UC.

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!