Clinical Study 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 medication 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 Study:	16 November 2017 to 18 March 2022
Title of this Study:	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:	17 January 2023

– Thank You –

If you participated in this study, Pfizer, the Sponsor, would like to thank you for your participation.

This summary will describe the study results. If you have any questions about the study or the results, please contact the doctor or staff at your study site.

Why was this study done?

What is ulcerative colitis?

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.

What is tofacitinib?

Tofacitinib (tow-fah-sit-in-ib) (Xeljanz®) 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.

What was the purpose of this study?

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 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.

Researchers wanted to know:

- **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?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

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 were to come to the study site 17 times over 42 months and have their UC assessed. At 4 of these visits, participants were 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:

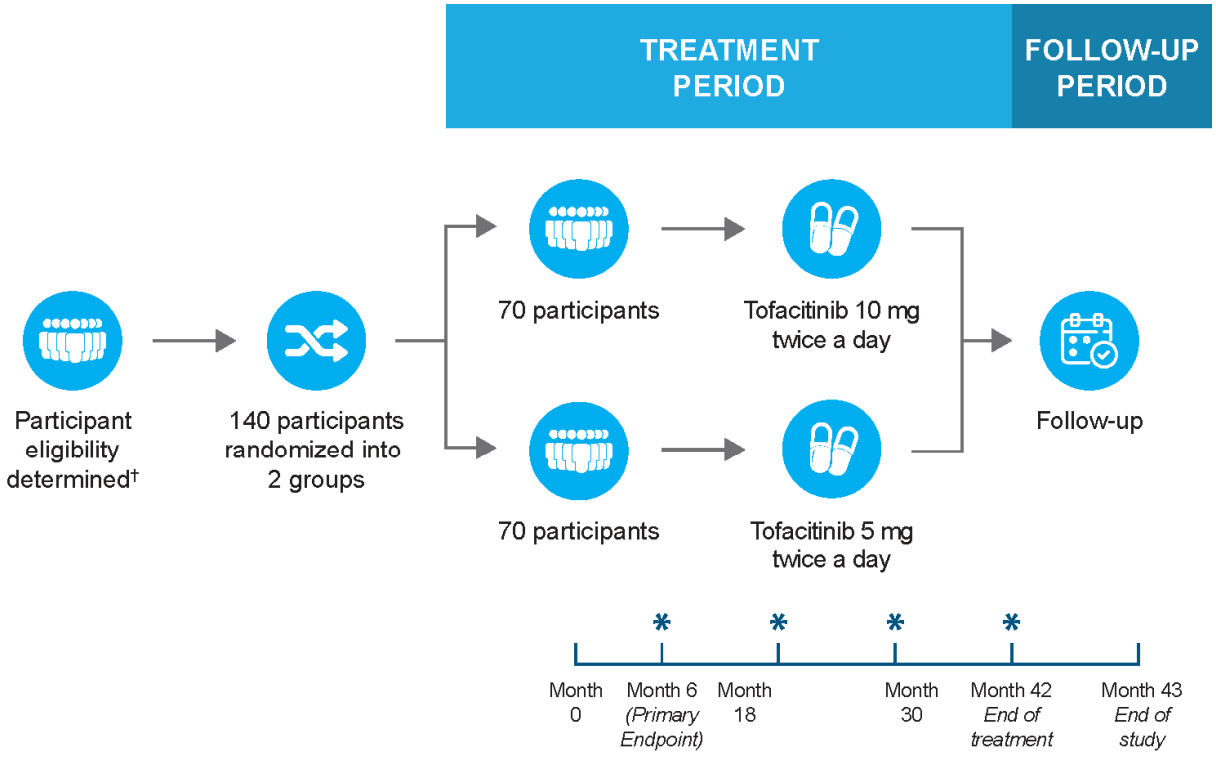
- Category related to stool frequency (was there a change in the number of bowel movements per day)
- Category related to rectal bleeding (is blood seen in the stool)
- Category related to endoscopy results (how does the lining of the colon look)

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 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. In addition, this report summarizes the medical issues that participants had during the entire study.

The figure below shows what was 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.*

Where did this study take place?

The Sponsor ran this study at 69 locations in 20 countries in Europe, North America, Asia, Africa, and Oceania.

When did this study take place?

It began 16 November 2017 and ended 18 March 2022.

Who participated in this study?

The study included adult 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.

Overall, 92 men and 48 women participated. All participants were between the ages of 21 and 81.

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, 63 finished the study. Seventy-seven (77) participants did not finish the study. The most common reason participants did not finish the study was due to the Sponsor ending the study earlier than originally planned (31 participants [22%]).

How long did the study last?

Study participants were in the study for 42 months. The entire study took 52 months to complete.

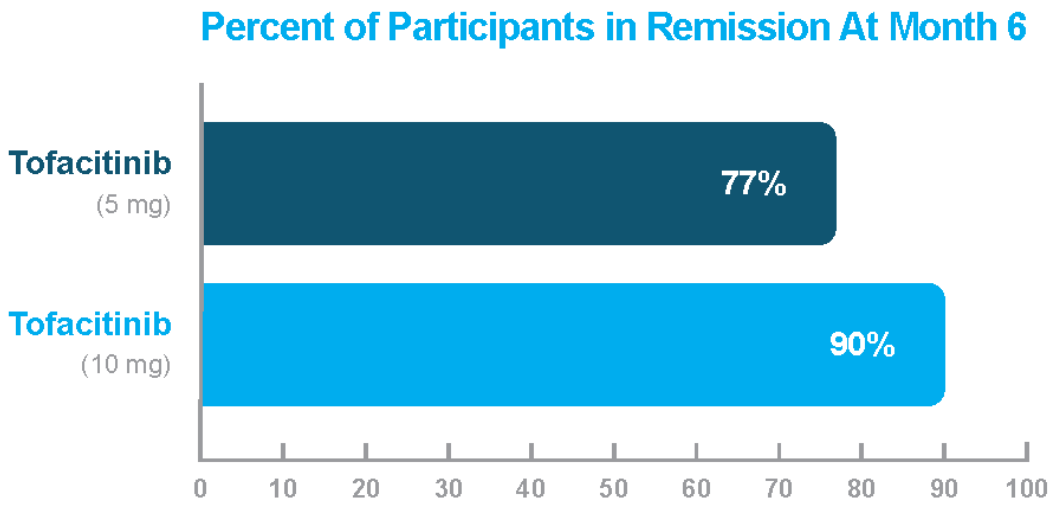
The study was stopped early because the primary objective of this study had been achieved. There were no concerns about the safety or effectiveness of tofacitinib.

When the study ended in March 2022, 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?

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 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%).



This does not mean that everyone in this study had these results. This is a summary of just some of the main results of this study. Other studies may have different results.

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 effects a study medication might have on a participant.

In this study, 113 out of 140 (81%) participants had at least 1 medical problem. A total of 24 participants (11 participants in the tofacitinib 5 mg group and 13 participants in the tofacitinib 10 mg group) left the study because of medical problems. Of these, 2 participants in the tofacitinib 5 mg group and 3 participants 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 – those reported by 5% or more of participants – are described below.

Below are instructions on how to read Table 1.

Instructions for Understanding Table 1.

- The **1st** column of Table 1 lists medical problems that were commonly reported during the study. All medical problems reported by 5% or more of participants are listed.
- The **2nd** column tells how many of the 70 participants in the tofacitinib 5 mg group reported each medical problem. Next to this number is the percentage of the 70 participants in the tofacitinib 5 mg group who reported the medical problem.
- The **3rd** column tells how many of the 70 participants in the tofacitinib 10 mg group reported each medical problem. Next to this number is the percentage of the 70 participants in the tofacitinib 10 mg group who reported the medical problem.
- Using these instructions, you can see that 16 out of the 70 participants (23%) in the tofacitinib 5 mg group reported worsening of ulcerative colitis. A total of 14 out of the 70 participants (20%) in the tofacitinib 10 mg group reported worsening of ulcerative colitis.

Table 1. Medical problems reported by 5% or more of study participants		
Medical Problem	**Tofacitinib 5 mg (70 Participants)**	**Tofacitinib 10 mg (70 Participants)**
Worsening of ulcerative colitis	16 out of 70 participants (23%)	14 out of 70 participants (20%)
Common cold	7 out of 70 participants (10%)	8 out of 70 participants (11%)
High blood pressure	4 out of 70 participants (6%)	5 out of 70 participants (7%)
Joint pain	4 out of 70 participants (6%)	5 out of 70 participants (7%)
Positive test for the virus that causes COVID-19	2 out of 70 participants (3%)	7 out of 70 participants (10%)
Fever	5 out of 70 participants (7%)	2 out of 70 participants (3%)
Stomach pain	5 out of 70 participants (7%)	3 out of 70 participants (4%)
Shingles	2 out of 70 participants (3%)	6 out of 70 participants (9%)
Headache	4 out of 70 participants (6%)	3 out of 70 participants (4%)
Nose, sinus, or throat infection	3 out of 70 participants (4%)	4 out of 70 participants (6%)
Increased level of a certain protein in the blood (creatine phosphokinase)	2 out of 70 participants (3%)	5 out of 70 participants (7%)
Low white blood cell count	2 out of 70 participants (3%)	5 out of 70 participants (7%)

Did study participants have any serious medical problems?

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

Overall, 23 participants (16%) in the study had serious medical problems.

- In the tofacitinib 5 mg group, 7 participants (10%) had at least 1 serious medical problem. Of these, researchers did not believe any were related to study medication.
- In the tofacitinib 10 mg group, 16 participants (23%) had at least 1 serious medical problem. Of these, researchers believed 4 participants (6%) had serious medical problems that were related to study medication.

One (1) participant in the tofacitinib 10 mg group died during the study. Researchers do not believe the death was related to study medication.

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 **NCT03281304**
www.clinicaltrialsregister.eu	Use the study identifier **2017-002274-39**
www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number **A3921288**

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

Again, if you participated in this study,
thank you for volunteering.
We do research to try to find the
best ways to help patients, and you helped
us to do that!