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 study participants. The results of this study might be different than the results of other studies that the researchers review.

Sponsor:	Pfizer, Inc.
Medicine(s) Studied:	CP-690,550 (Tofacitinib)
Protocol Number:	A3921133
Dates of Study:	14 March 2014 to 22 July 2020
Title of this Study:	Safety Study of Tofacitinib Versus Tumor Necrosis Factor (TNF) Inhibitor in Subjects With Rheumatoid Arthritis [Phase 3b/4 Randomized Safety Endpoint Study of 2 Doses of Tofacitinib in Comparison to A Tumor Necrosis Factor (TNF) Inhibitor in Subjects with Rheumatoid Arthritis]
Date(s) of this Report:	9 July 2021

– 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 rheumatoid arthritis?

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 unchecked.

What is tofacitinib?

Tofacitinib is a medicine that works to reduce the activity of the immune system. It is an oral (taken by mouth) prescription medicine that is used treat adults with active, moderate to severe RA that did not respond well to medicines known as disease-modifying anti-rheumatic drugs (DMARDs), like methotrexate ("MTX"). Tofacitinib may help calm the activity of the immune system and decrease RA signs and symptoms.

What was the purpose of this study?

Researchers did this study to learn more about the safety of 2 different doses of tofacitinib, compared to a tumor necrosis factor inhibitor (TNF inhibitor). TNF inhibitors are another type of medicine that work to reduce the activity of the immune system.

Cardiovascular disease is a disease of the heart or blood vessels.

Researchers wanted to know:

How many participants developed cancer?
How many participants developed cardiovascular disease?
How many participants had medical problems?

What happened during the study?

How was the study done?

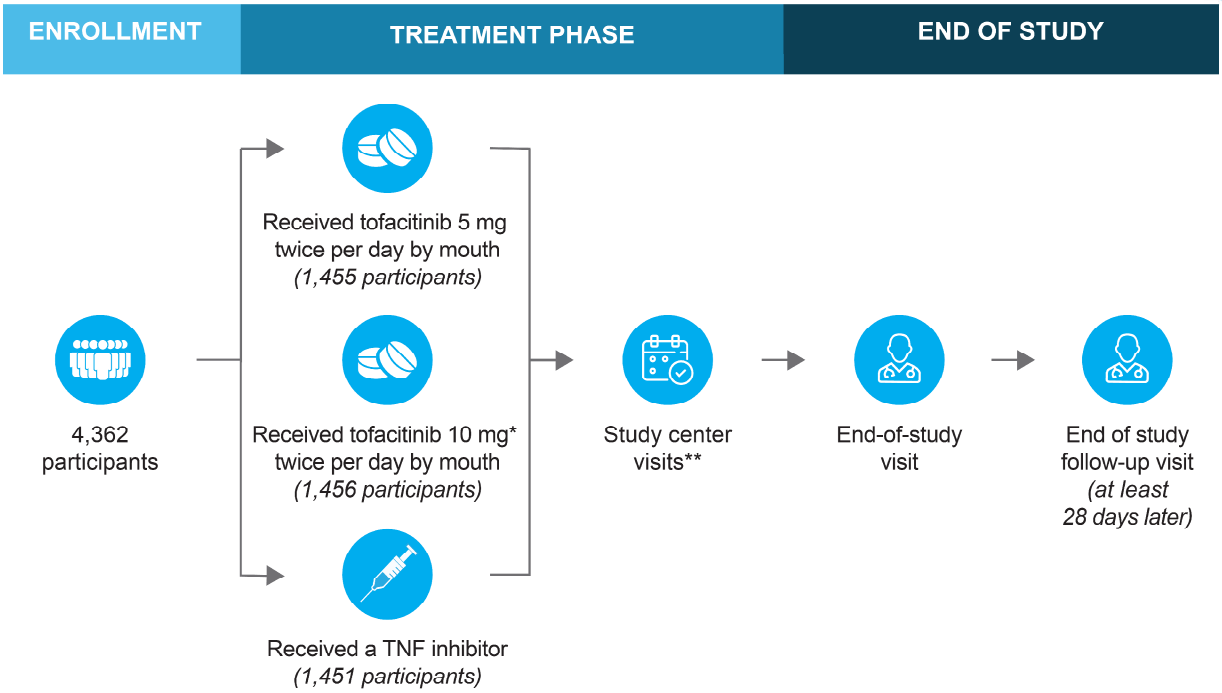
Participants were checked (screened) to make sure they were a good fit for the study. Participants who were a good fit were assigned by chance to receive either:

- tofacitinib 5 milligrams (mg) twice per day by mouth,
- tofacitinib 10 mg twice per day by mouth (these participants were later switched to tofacitinib 5 mg twice per day, due to new safety information about tofacitinib),
- or a TNF inhibitor (participants in the United States, Puerto Rico, and Canada received adalimumab 40 mg every other week by injection under the skin, participants in other countries received etanercept 50 mg once per week by injection under the skin)

This was an "open-label" study, which means that the participants and doctors knew which treatment and dose the participants received.

Participants were expected to attend visits at the study center for the baseline visit, at Month 2, Month 3, then every 3 months thereafter, and to complete an end-of-study visit, and an end-of study visit at least 28 days later.

The figure below shows what happened during this study.



*These participants were later switched to tofacitinib 5 mg twice per day, due to new safety information about tofacitinib
**Participants were expected to attend visits at the study center for the baseline visit, at Month 2, Month 3, then every 3 months thereafter

Where did this study take place?

The Sponsor ran this study at 323 locations in 30 countries in Africa, Asia, Australia, Europe, North America, and South America.

When did this study take place?

It began on 14 March 2014 and ended 22 July 2020.

Who participated in this study?

This study included adult men and women who:

- Were 50 years of age or older
- Had moderate to severe RA
- Had an inadequate response to treatment with methotrexate alone
- Had at least one additional risk factor for cardiovascular disease

- A total of 952 men (22%) participated

- A total of 3,410 women (78%) participated
- All participants were between the ages of 50 and 88

Participants could continue taking study treatment as long as they continued to benefit from it, or until the study ended. Of the 4,362 participants who started the study and received treatment, 3,111 completed it.

A total of 1,615 participants stopped taking study treatment early

- by their choice,
- because they did not see significant improvement in RA symptoms,
- because they had a medical problem, or
- because a doctor decided it was best for them to stop the study

How long did the study last?

The amount of time that each participant was in this study varied. The entire study took more than 6 years to complete.

When the study ended in July 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?

How many participants developed cancer?

To answer this question, the researchers looked at the number of participants from each group who developed any cancer besides non-melanoma skin cancer during the study:

- 62 out of 1,455 (4%) participants who received tofacitinib 5 mg developed cancer.
- 60 out of 1,456 (4%) participants who received tofacitinib 10 mg developed cancer.
- 42 out of 1,451 (3%) participants who received a TNF inhibitor developed cancer.

How many participants developed cardiovascular disease?

To answer this question, the researchers looked at the number of participants from each group who developed cardiovascular disease within 60 days of their last study treatment:

- 47 out of 1,455 (3%) participants who received tofacitinib 5 mg developed cardiovascular disease.
- 51 out of 1,456 (4%) participants who received tofacitinib 10 mg developed cardiovascular disease.
- 37 out of 1,451 (3%) participants who received a TNF inhibitor developed cardiovascular disease.

These are just some of the main findings 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.

3,985 out of 4,362 (91%) participants had at least 1 medical problem within 28 days of their last study treatment:

- 1,333 out of 1,455 (92%) participants who received tofacitinib 5 mg had a medical problem.
- 1,344 out of 1,456 (92%) participants who received tofacitinib 10 mg had a medical problem.
- 1,308 out of 1,451 (90%) participants who received a TNF inhibitor had a medical problem.

A total of 684 out of 4,362 (16%) participants stopped taking study treatment because of medical problems:

- 199 out of 1,455 (14%) participants who received tofacitinib 5 mg stopped taking study treatment because of medical problems.
- 288 out of 1,456 (20%) participants who received tofacitinib 10 mg stopped taking study treatment because of medical problems.
- 197 out of 1,451 (14%) participants who received a TNF inhibitor stopped taking study treatment because of medical problems.

The most common medical problems – those reported by at least 10% 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 within 28 days of the last study treatment. All medical problems reported by at least 10% of participants are listed.
- The **2nd** column tells how many of the 1,455 participants taking tofacitinib 5 mg reported each medical problem. Next to this number is the percentage of the 1,455 participants taking tofacitinib 5 mg who reported the medical problem.
- The **3rd** column tells how many of the 1,456 participants taking tofacitinib 10 mg reported each medical problem. Next to this number is the percentage of the 1,456 participants taking tofacitinib 10 mg who reported the medical problem.
- The **4th** column tells how many of the 1,451 participants taking a TNF inhibitor reported each medical problem. Next to this number is the percentage of the 1,451 participants taking a TNF inhibitor who reported the medical problem.
- Using these instructions, you can see that 176 out of the 1,455 (12%) participants taking tofacitinib 5 mg reported shingles. A total of 167 out of 1,456 (12%) participants taking tofacitinib 10 mg reported shingles. A total of 55 out of 1,451 (4%) participants taking a TNF inhibitor reported shingles.

Table 1. Commonly reported medical problems by study participants within 28 days of last study treatment

Medical Problem	Tofacitinib 5 mg (1,455 Participants Treated)	Tofacitinib 10 mg (1,456 Participants Treated)	TNF Inhibitor (1,451 Participants Treated)
Low level of a type of white blood cell called a lymphocyte	104 out of 1,455 participants (7%)	150 out of 1,456 participants (10%)	32 out of 1,451 participants (2%)
Infection affecting the larger airways (bronchitis)	222 out of 1,455 participants (15%)	237 out of 1,456 participants (16%)	163 out of 1,451 participants (11%)
Shingles	176 out of 1,455 participants (12%)	167 out of 1,456 participants (12%)	55 out of 1,451 participants (4%)
Common cold	164 out of 1,455 participants (11%)	165 out of 1,456 participants (11%)	158 out of 1,451 participants (11%)
Nose, sinus, or throat infection	308 out of 1,455 participants (21%)	312 out of 1,456 participants (21%)	255 out of 1,451 participants (18%)
Infection of the kidney, bladder, or urethra	186 out of 1,455 participants (13%)	221 out of 1,456 participants (15%)	184 out of 1,451 participants (13%)
Fall	169 out of 1,455 participants (12%)	154 out of 1,456 participants (11%)	151 out of 1,451 participants (10%)
Worsening rheumatoid arthritis	176 out of 1,455 participants (12%)	168 out of 1,456 participants (12%)	179 out of 1,451 participants (12%)
High blood pressure	125 out of 1,455 participants (9%)	145 out of 1,456 participants (10%)	123 out of 1,451 participants (9%)

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.

1,047 out of 4,362 (24%) participants in this study had at least 1 serious medical problem within 28 days of their last study treatment:

- 351 out of 1,455 (24%) participants who received tofacitinib 5 mg had serious medical problems.
- 390 out of 1,456 (27%) participants who received tofacitinib 10 mg had serious medical problems.
- 306 out of 1,451 (21%) participants who received a TNF inhibitor had serious medical problems.

Pneumonia was the most common serious medical problem, which happened in 136 (3%) total participants within 28 days of last study treatment, including:

- 46 out of 1,455 (3%) participants who received tofacitinib 5 mg.
- 52 out of 1,456 (4%) participants who received tofacitinib 10 mg.
- 38 out of 1,451 (3%) participants who received a TNF inhibitor.

A total of 82 participants died during study treatment or within 28 days of their last study treatment:

- 26 out of 1,455 (2%) participants who received tofacitinib 5 mg died.
- 39 out of 1,456 (3%) participants who received tofacitinib 10 mg died.
- 17 out of 1,451 (1%) participants who received a TNF inhibitor died.

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 **NCT02092467**
www.clinicaltrialsregister.eu	Use the study identifier **2013-003177-99**

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

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