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 Studied: Tofacitinib (Xeljanz)

Protocol Number: A3921165

Dates of Study: 10 May 2018 to 27 March 2024

Title of this Study: Effectiveness and Safety of Tofacitinib in Children and Adolescents With Systemic Juvenile Idiopathic Arthritis (sJIA) That Affects the Whole Body

[Efficacy, Safety, Tolerability and Pharmacokinetics of Tofacitinib for Treatment of Systemic Juvenile Idiopathic Arthritis (sJIA) With Active Systemic Features in Children and Adolescent Subjects]

Date of this Report: 22 November 2024

– Thank You –

Pfizer, the Sponsor, would like to thank you, as parents, for your child's participation in this clinical trial and provide you a summary of results representing everyone who participated. If you are the child or adolescent who participated, Pfizer would like to thank you directly!

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 systemic Juvenile Idiopathic Arthritis?

Arthritis is a condition that causes pain and inflammation in the joints. Juvenile idiopathic arthritis (JIA) is the most common type of arthritis in children. "Idiopathic" means "of unknown origin", and "juvenile" means the disease symptoms start before a person is 16 years old.

Young people with JIA may have a rare and serious type of JIA called "systemic" JIA (sJIA). Systemic means it may affect not only the joints but also other parts of the body, including the skin, liver, lungs, and heart. Young people with sJIA have an overactive immune system that mistakenly attacks healthy parts of the body, resulting in pain and inflammation. If untreated, sJIA can cause permanent damage to the joints. Treatments are available for people with sJIA but they don't help everyone. Researchers are looking for new treatment options for sJIA.

What is tofacitinib?

Tofacitinib (TOE-fa-SYE-ti-nib) is an oral (taken by mouth) medication that has been approved to treat adults and children with other types of arthritis. The body makes specific proteins called cytokines that trigger activity in the immune system. Patients with sJIA have increased cytokine levels which causes the immune system to become overactive or act incorrectly. Tofacitinib works by lowering the level of cytokines in the body. This may help to calm the activity of the immune system, help to control disease symptoms, and reduce joint damage.

What was the purpose of this study?

- The purpose of this study was to learn about the effects of tofacitinib in preventing the worsening of sJIA symptoms.

Some patients in this study also received placebo. A placebo does not have any medicine in it, but it looks just like the study medication.

Researchers wanted to know:

Did tofacitinib increase the amount of time it took for sJIA to worsen compared to placebo in Part 2 of the study?

What happened during the study?

How was the study done?

This study was done in 2 parts as shown in figure 1 below.

Part 1:

In **Part 1**, researchers wanted to learn how effective and safe tofacitinib was when given to study participants aged 2 to 17 years. Tofacitinib was given as tablets or in liquid form. Tablets were given at a dose of 5 mg to the study participants who weighed 40 kg or more. The liquid form of tofacitinib was given at a dose calculated according to body weight for study participants who weighed less than 40 kg. Part 1 was further divided into two parts: **Part 1A and Part 1B.**

In **Part 1 A**, all study participants aged 12 years and older who weighed at least 40 kg received tofacitinib 5 mg twice a day. When tofacitinib was shown to be safe and effective at this dose, study participants under 12 years who weighed less than 40 kg were then given the same dose.

If the study participants were taking corticosteroids (CS) before taking part in the study, they continued the same dose of CS during the study, for up to

16 weeks in Part 1A. Corticosteroids are medicines that help to reduce inflammation.

Participants who were not taking CS or taking lower dose of CS could go directly to Part 2 if their symptoms improved by 30% for at least 4 weeks and had been treated with tofacitinib for at least 12 weeks. Participants who were taking a higher dose of CS could continue to Part 1B once their symptoms improved by 30% and maintained for at least 4 weeks.

In **Part 1B**, the study doctor lowered the dose of CS the participants were taking in Part 1A. Study participants who had at least a 50% improvement in their sJIA symptoms while taking a lower dose of CS, could continue in Part 2 of the study.

Study participants took tofacitinib for up to 40 weeks during Part 1 of this study.

In Part 1, the parents' or guardians of the participants and researchers knew what medication the participants took. This is known as an open-label study.

Part 2:

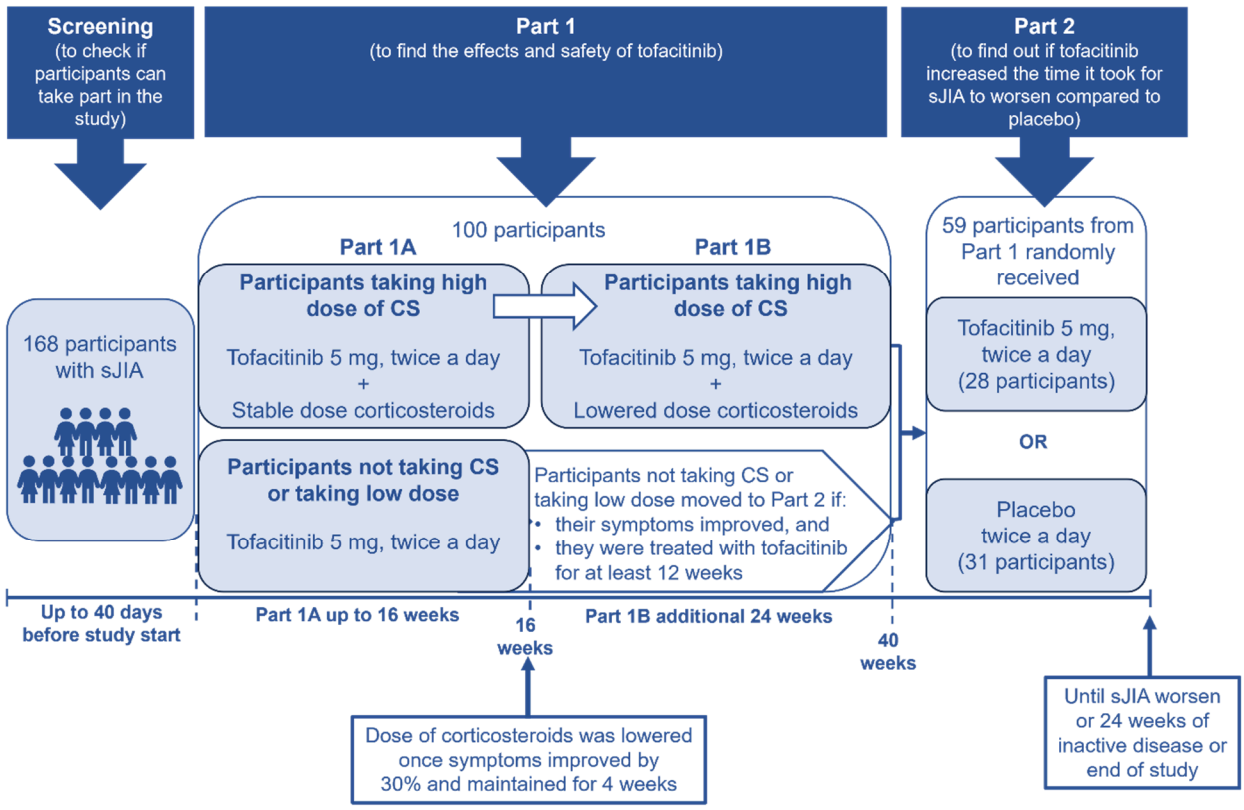
In Part 2, researchers wanted to find out if tofacitinib increased the time it took for the symptoms of sJIA to worsen compared to placebo. Study participants were assigned to 1 of the 2 groups by chance alone. This is known as "randomization". "Randomization" is done to make comparing the groups more fair.

- Tofacitinib: 5 mg tablets or liquid form (1 mg/mL) 2 times a day
- Placebo: tablets or liquid form 2 times a day.

The parents or guardians of the study participants and researchers did not know who took tofacitinib and who took the placebo during Part 2. This is known as a double-blind study.

Researchers then compared the results of study participants taking tofacitinib to the results of study participants taking placebo. Study participants remained in Part 2 of the study until they experienced worsening of their sJIA, or achieved 24 weeks of inactive disease, or until the end of the study.

Figure 1: What happened during the study



Where did this study take place?

The Sponsor ran this study at 101 locations in 16 countries in North America, South America, Europe, Asia, Middle East, and Africa.

When did this study take place?

It began on 10 May 2018 and ended on 27 March 2024.

Who participated in this study?

The study included participants who had sJIA with fever and at least 2 joints with active symptoms of arthritis, or at least 5 affected joints. Participants were allowed to take methotrexate and/or corticosteroids, at a stable dose, during the study. They could not have a history of untreated or inadequately treated tuberculosis infection (bacterial infection in the lungs).

- A total of 56 boys participated, of which 38 participated in Part 2.
- A total of 44 girls participated, of which 21 participated in Part 2.
- All participants were between the ages of 2 and 17 years.

Participants in Part 2 were treated until they experienced worsening of their sJIA, 24 weeks of inactive disease or end of study.

How long did the study last?

The total duration of the study was for 6 years. Most of the participants were in the study for about 2 years and a small number of participants were in the study for up to 6 years. The study was stopped early as there was little to no chance that the study would demonstrate any benefit when participants took tofacitinib compared to placebo for the treatment of sJIA. Tofacitinib did not increase the amount of time it takes for sJIA to worsen compared to placebo.

When the study ended in March 2024, 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?

Did tofacitinib increase the amount of time it took for sJIA to worsen compared to placebo in Part 2 of the study?

In this study, the time taken for sJIA to worsen in participants who took tofacitinib was not different than for participants who took placebo.

This means the study results did not show that one treatment was better than another at preventing the worsening of sJIA.

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 Part 1, 55 out of 100 (55%) participants in Part 1A had at least 1 medical problem. Twenty-four (24) out of 54 (44%) participants in Part 1B had at least 1 medical problem. A total of 6 participants left the study because of medical problems in Part 1A. No participants left because of medical problems during Part 1B.

In Part 2, 23 out of 28 (82%) participants in the tofacitinib treated group, and 25 out of 31 (81%) in the placebo treated group had at least 1 medical problem. A total of 10 participants in the tofacitinib treated group, and 16 participants in the placebo treated group left the study because of medical problems in Part 2.

The most common medical problems – those reported by more than 7% of participants – are described below in Table 1 for Part 1 and Table 2 for Part 2 of the study.

Below are instructions on how to read tables.

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 more than 7% of participants are listed.
- The **2nd** column tells how many of the 100 participants taking the study medication in Part 1A reported each medical problem. Next to this number is the percentage of the 100 participants taking the study medication who reported the medical problem.
- The **3rd** column tells how many of the 54 participants taking the study medication in Part 1B reported each medical problem. Next to this number is the percentage of the

54 participants taking the study medication who reported the medical problem.

- Using these instructions, you can see that 0 out of the 100 (0%) participants taking the study medication in Part 1A reported Covid-19. A total of 5 out of the 54 (9%) participants taking the study medication in Part 1B reported Covid-19.

Table 1. Commonly reported medical problems by study participants, in Part 1 of the study

Medical Problem	PART 1A Tofacitinib 5 mg (100 Participants)	PART 1B Tofacitinib 5 mg (54 Participants)
COVID-19	0 out of 100 participants (0%)	5 out of 54 participants (9%)
Infection in the nose or throat	10 out of 100 participants (10%)	7 out of 54 participants (13%)

Table 2. Commonly reported medical problems by study participants, in Part 2 of the study		
Medical Problem	**Tofacitinib 5 mg (28 Participants)**	**Placebo (31 Participants)**
Fever	4 out of 28 participants (14%)	1 out of 31 participants (3%)
Inflammation of the airways that carry air to lungs	0 out of 28 participants (0%)	3 out of 31 participants (10%)
Infection in the nose or throat	3 out of 28 participants (11%)	5 out of 31 participants (16%)
Infection in the urinary system	0 out of 28 participants (0%)	3 out of 31 participants (10%)
Worsening of sJIA	8 out of 28 participants (29%)	14 out of 31 participants (45%)
Vomiting	3 out of 28 participants (11%)	1 out of 31 participants (3%)

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.

Seven (7) participants (7%, or 7 out of 100 participants) had serious medical problems in Part 1A. No participants had serious medical problems in Part 1B. In Part 2, 2 participants (7%, or 2 out of 31 participants) in the placebo group had serious medical problems.

- In Part 1A, 3 participants had worsening of their sJIA, 3 participants had certain rare diseases that affect the immune system, and 1 participant reported depression and overdose.
- In Part 2, 1 participant had inflammation of the airways that carry air to lungs, and 1 participant had kidney stones in the placebo group.

No participants died during the study.

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.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number **A3921165**

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

www.clinicaltrials.gov	Use the study identifier **NCT03000439**
www.clinicaltrialsregister.eu	Use the study identifier **2017-002018-29**

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 your child 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!