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 (CP-690,550); immediate release tablet (5 mg) and weight-based equivalent oral formulation (1 mg/mL)

Protocol Number: A3921104

Dates of Trial: 10 June 2016 to 16 May 2019

Title of this Trial: Efficacy and safety of tofacitinib in young patients aged 2 to less than 18 years with polyarticular course Juvenile Idiopathic Arthritis (JIA)

[Efficacy, Safety, and Tolerability of Tofacitinib for Treatment of Polyarticular Course Juvenile Idiopathic Arthritis (JIA) in Children and Adolescent Subjects]

Date of this Report: 23 March 2020

– 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! 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?

Juvenile idiopathic arthritis (JIA) is the most common type of arthritis in children. The term "idiopathic" means "of unknown origin", and the term "juvenile" means that disease symptoms start before a person is 16 years old. This disease causes swelling, pain, and stiffness in the joints. JIA is an "autoimmune disease", which means that patients with JIA have an overactive immune system that mistakenly attacks healthy parts of the body, such as the joints. JIA can cause permanent damage to the joints if it goes unchecked, so researchers are looking for new treatment options for polyarticular course JIA.

The study drug, tofacitinib, is an oral (taken by mouth) medication that has been approved to treat adults with other types of arthritis. The body normally makes special proteins called "cytokines" that trigger activity in the immune system. In patients with JIA, the body makes too many cytokines, which causes the immune system to become overactive. Researchers think that the study drug works by lowering the amount of cytokines in the body, which helps to calm the activity of the immune system and decrease JIA symptoms.

The main purpose of this study was to find out if the study drug works to treat polyarticular course JIA. Some patients in this study also received placebo to find out if the study drug works in comparison with receiving no treatment at all. A placebo looks just like the medication, but doesn't have any medication in it.

Researchers wanted to know:

- **Did the study drug work to prevent JIA flares, improve JIA symptoms, and ease or reduce overall disability compared to placebo?**

To answer this question, researchers looked at how many patients had disease flares by the end of the study after being treated with the study drug, compared to patients who received placebo. A flare is a sudden, temporary episode of pain and inflammation which is usually associated with tiredness, stiffness or joint swelling. Researchers also looked at how many patients had 30%, 50%, and 70% improvement in their JIA symptoms and if there was any change in their overall disability by asking the patients or their parents certain questions.

WHAT HAPPENED DURING THE STUDY?

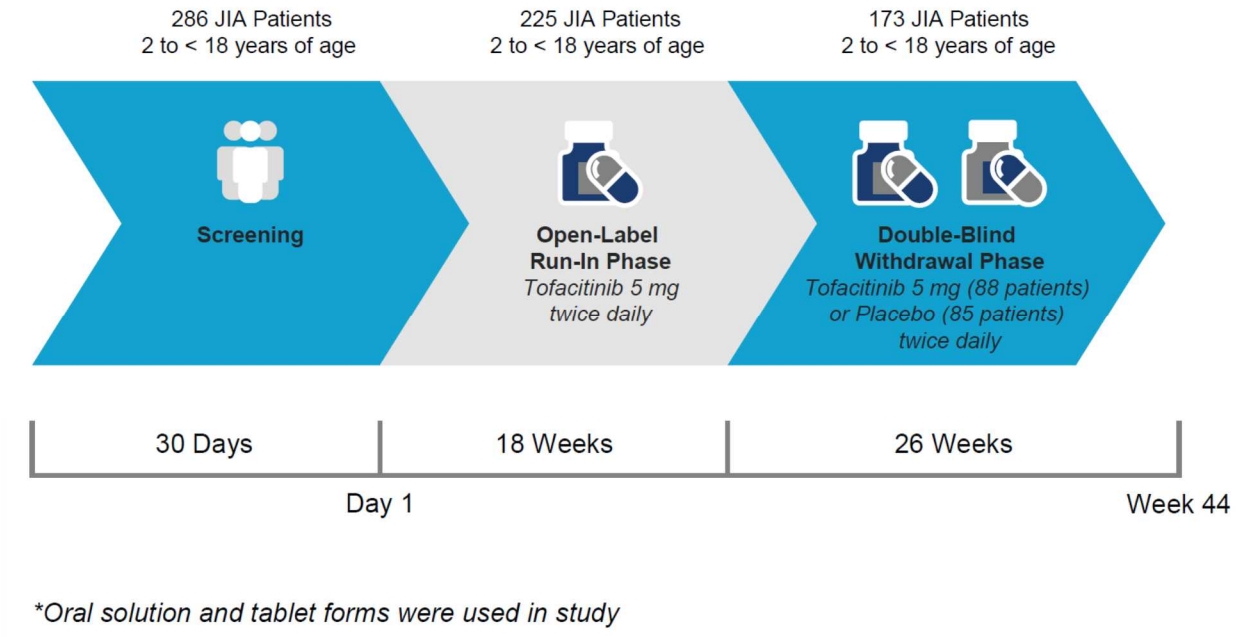
This study consisted of 2 parts. In the first part of the study, all patients received treatment with the study drug 2 times per day, for 18 weeks. This was called the "run-in phase". Only the patients who had at least 30% improvement in their symptoms after the run-in phase took part in the second part of the study, called the "double-blind phase".

The double-blind phase of the study compared 2 groups of patients to find out if the study drug works to treat JIA compared to placebo:

- Study drug (tofacitinib): 5 mg tablets or oral solution (1 mg/mL) 2 times per day
- Placebo: tablets or oral solution 2 times per day

The study included patients with JIA who were 2 years and older, but less than 18 years old. The patient's JIA symptoms had to start before they were 16 years old. Patients were assigned to one of the 2 groups by chance alone. This is known as a "randomized" study. "Randomization" is done to make comparing the groups more fair.

The patients and researchers did not know who took the study drug and who took the placebo during the study. This is known as a "blinded" study. This was done to make sure the results of the study could not be unfairly influenced by anyone. In case of urgent need, the study team could learn quickly which study drug the patients were receiving.



**Oral solution and tablet forms were used in study*

While each patient was only in the study for up to approximately 44 weeks, the entire study took almost 3 years to complete. The Sponsor ran this study at 64 locations in 14 countries in different parts of the world. It began 10 June 2016 and ended 16 May 2019. In the run-in phase, 56 boys and 169 girls participated. In the double-blind phase, 43 boys and 130 girls participated. All patients were older than 2 and less than 18 years old.

Patients were to be treated until the end of the double-blind phase, or until their symptoms worsened. Of the 225 patients who started the study, 185 finished the run-in phase. Forty (40) patients left by their own choice or because a doctor decided it was best for a patient to stop the study. Of the 185 patients who finished the run-in phase, 12 did not continue into the double-blind phase.

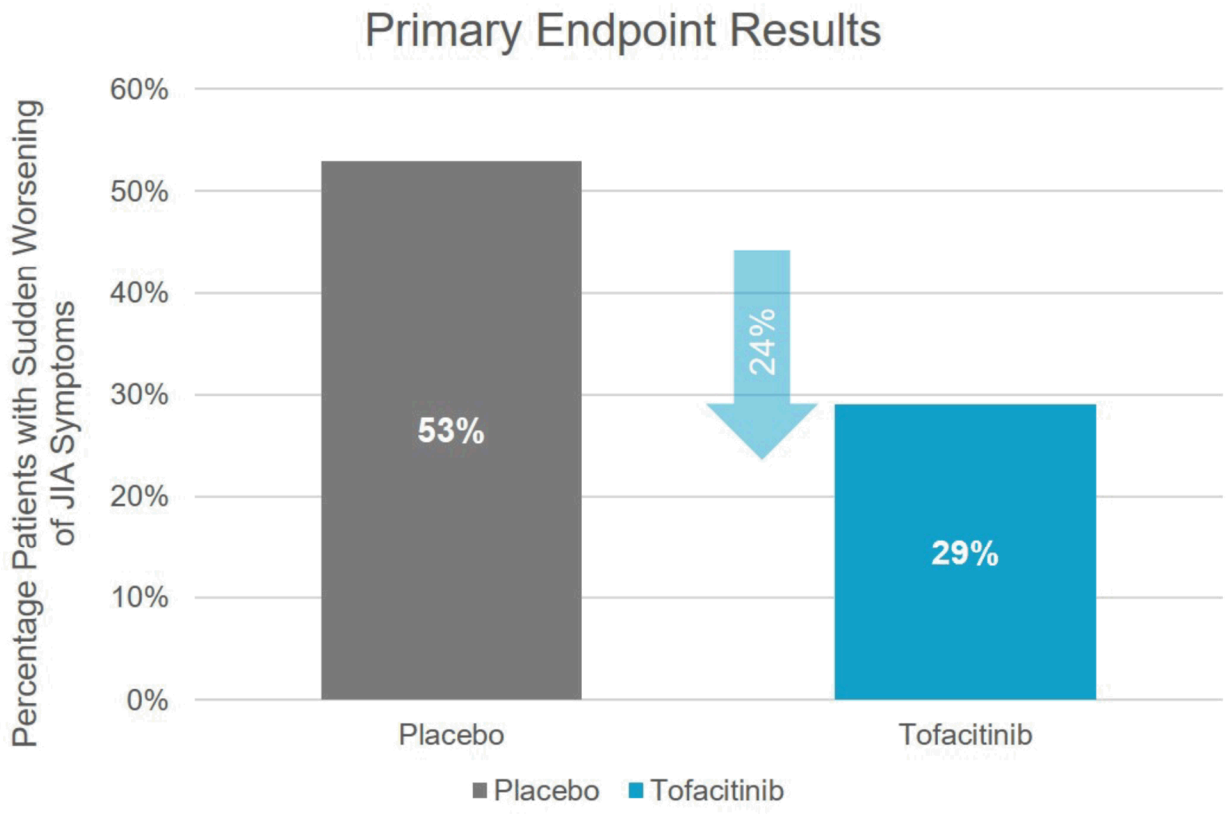
Of the 173 patients who started the double-blind phase of the study, 99 finished the double-blind phase. Seventy-four (74) patients left by their own choice or because a doctor decided it was best for a patient to stop the study.

When the study ended in May 2019, the Sponsor reviewed 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 the study drug work to prevent JIA flares, compared to placebo?

Of the 72 patients treated with the study drug in the double-blind phase, 21 patients (29%) had disease flares by the end of the study. Of the 70 patients treated with placebo, 37 patients (53%) had disease flares by the end of the study. The researchers determined that these results were not likely due to chance, and that the study drug may help prevent JIA flares.

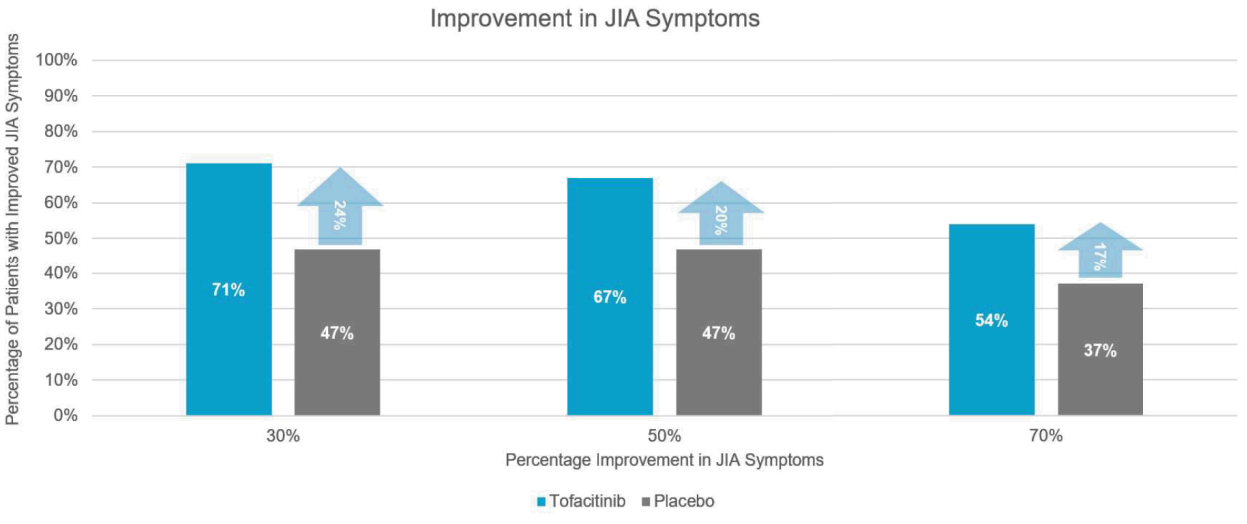


Did the study drug work to improve JIA symptoms, compared to placebo?

At the end of the double-blind phase:

- Thirty-nine (39) out of 72 patients (54%) treated with the study drug and 26 out of 70 patients (37%) treated with placebo had 70% improvement in their symptoms.
- Forty-eight (48) out of 72 patients (67%) treated with the study drug and 33 out of 70 patients (47%) treated with placebo had 50% improvement in their symptoms.
- Fifty-one (51) out of 72 patients (71%) treated with the study drug and 33 out of 70 patients (47%) treated with placebo had 30% improvement in their symptoms.

The researchers determined that these results were not likely due to chance, and that the study drug may help improve JIA symptoms.



Did the study drug work to reduce overall disability, compared to placebo, based on the Child Health Assessment Questionnaire?

In this study, patients treated with the study drug in the double-blind phase had a greater reduction in disability compared with patients treated with placebo. On average, their disability score improved by 0.09, while the placebo score slightly worsened, by 0.03, from the time of randomization. The study showed that these results were not likely due to chance, and that the study drug may help improve overall disability.

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 patients had during the study. Patients 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 patient 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.

One-hundred and fifty-three (153) out of 225 patients (68%) in the run-in phase had at least 1 medical problem. In the double-blind phase, 68 out of 88 patients (77%) in the study drug group and 63 out of 85 patients (74%) in the placebo group had at least 1 medical problem. A total of 26 out of 255 patients (12%) in the run-in phase left the study because of medical problems. In the double-blind phase, 16 out of 88 patients (18%) in the study drug group and 29 out of 85 patients (34%) in the placebo group left the study because of medical problems.

The most common medical problems for patients in the run-in phase were upper respiratory tract infection (24 out of 225 patients [11%]), headache (16 out of 225 patients [7%]), nausea (13 out of 225 patients [6%]), and vomiting (13 out of 225 patients [6%]).

The most common medical problems for patients in the study drug group of the double-blind phase were upper respiratory tract infection (13 out of 88 patients [15%]), worsening of disease (8 out of 88 patients [9%]), and common cold (nasopharyngitis) (7 out of 88 patients [8%]).

The most common medical problems for patients in the placebo group of the double-blind phase were worsening of disease (13 out of 85 patients [15%]), JIA (12 out of 85 patients [14%]), and upper respiratory tract infection (9 out of 85 patients [11%]).

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

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

Seven (7) out of 225 patients (3%) in the run-in phase had serious medical problems. In the double-blind phase, 1 out of 88 patients (1%) in the study drug group, and 2 out of 85 patients (2%) in the placebo group had serious medical problems. No patients 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 this study protocol, please visit:

www.clinicaltrials.gov	Use the study identifier **NCT02592434**
www.clinicaltrialsregister.eu	Use the study identifier **2015-001438-46**
www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number **A3921104**

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

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!