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 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:	Ritlecitinib
Protocol Number:	B7981045
Dates of Study:	22 October 2021 to 14 January 2022
Title of this Study:	A Target Occupancy Study with Ritlecitinib [An Open Label, Phase 1, Two-Arm Study to Assess Target Occupancy and Functional Inhibition of JAK3 and TEC Kinases by Single Doses of Ritlecitinib in Healthy Adult Participants]
Date(s) of this Report:	08 August 2022

– 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 alopecia areata?

Alopecia areata is an autoimmune disorder, which may be chronic and recurring, where a patient experiences non-scarring hair loss. It can affect adults and children across all ages, races, and sexes. Alopecia areata can have a large impact on the psychological health of both adult and pediatric patients, including damage to the patient's self-esteem, an increased occurrence of anxiety and depression and a general decline in quality of life.

What is Ritlecitinib?

Ritlecitinib is an investigational drug that is being studied to treat people with inflammatory conditions and diseases. An investigational drug is one that is still being studied and is not approved for use outside of research studies. Ritlecitinib is a small molecule medication that is taken orally (by mouth). Small molecules can move easily through the cell membrane and interact with targeted molecules present inside a cell. Ritlecitinib is thought to work by blocking the activity of specific enzymes (protein molecule in cells which speed up chemical reactions in the body) in immune cells called "Janus kinase 3" (JAK3) and the "TEC family kinases" (BTK, ITK, RLK/TXK, TEC and BMX). These proteins act like on/off switches for the cells of the immune system and are important regulators of inflammatory pathways. By turning off these switches, the cells of the immune system produce fewer cytokines (a type of protein), which may alleviate autoimmune diseases such as vitiligo as well as alopecia areata.

What was the purpose of this study?

The purpose of this study was to measure the amount of certain enzymes (JAK3 and TEC family kinases) in white blood cells that were bound by ritlecitinib after the participants took a single dose of ritlecitinib. The measurement of how much of an enzyme in a cell is bound by a drug at various times before and after dosing is called "target occupancy". After ritlecitinib was swallowed, ritlecitinib entered the blood

and organs and moved through the body (for example, stomach, liver, and kidneys). Afterwards, ritlecitinib was removed from the body through urine and feces.

This study did not test if the drug helps to improve inflammatory conditions and autoimmune diseases and only focused on how ritlecitinib interacted with certain enzymes in the body.

Researchers wanted to know:

- **How did 50 mg and 200 mg doses of ritlecitinib affect certain enzymes in the body?**
- **What medical problems did participants have during the study?**

What happened during the study?

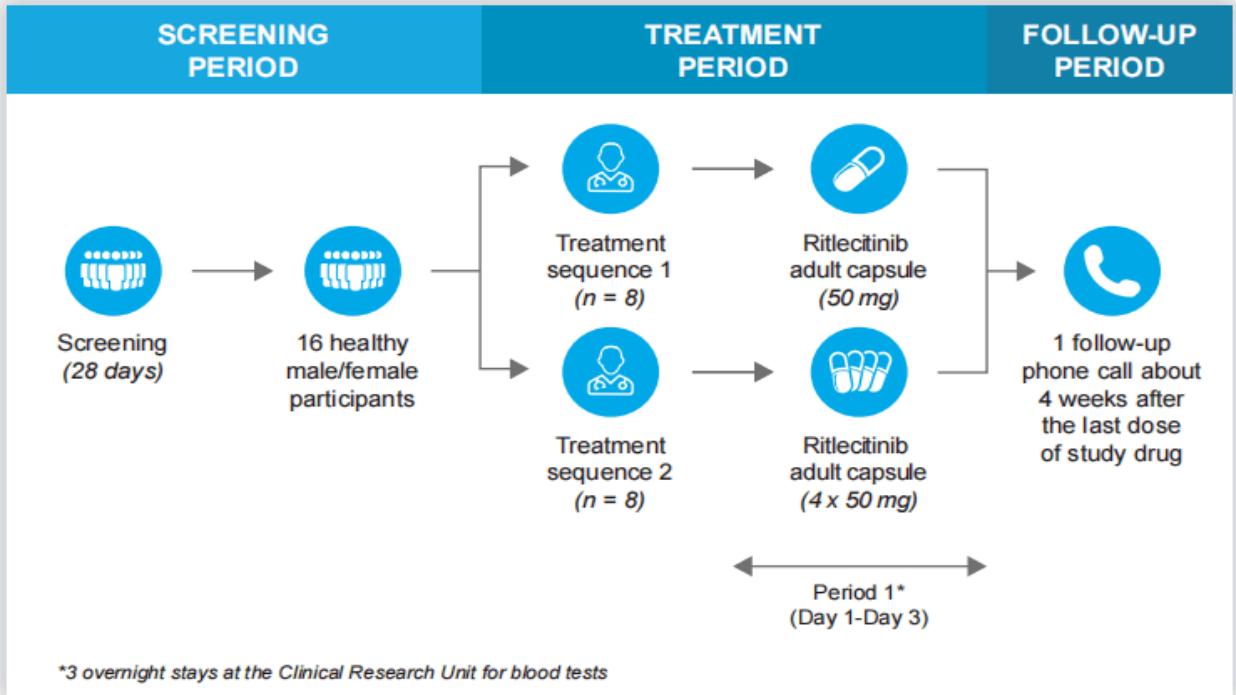
How was the study done?

Researchers tested 50 mg (single capsules) and 200 mg (4 x 50 mg capsules) of ritlecitinib on a group of healthy participants to learn how ritlecitinib interacted with certain enzymes in the body.

This study included 1 treatment period. Participants were randomized into 2 sequences of treatment.

- **Period 1 (Day 1):**
    - 8 participants took ritlecitinib as a single 50 mg capsule orally (by mouth) (Treatment sequence 1)
    - The remaining 8 participants took ritlecitinib 200 mg capsules orally (by mouth) (Treatment sequence 2)

Participants were assigned to each group by chance alone. This was an open-label study, which means that the participants and the researchers knew which treatments the participants received. The study design is shown below:



Researchers took samples of blood from participants during the study and measured the amount of certain enzymes (JAK3 and TEC family kinases) in specific types of white blood cells that were bound by ritlecitinib. Researchers also checked the participants' health during the study and asked them how they were feeling.

Researchers then compared the results of participants taking 50 mg of ritlecitinib to the results of participants taking 200 mg of ritlecitinib.

Where did this study take place?

The Sponsor ran this study at 1 location in the United States.

When did this study take place?

It began on 22 October 2021 and ended 14 January 2022.

Who participated in this study?

The study included healthy participants who met the inclusion criteria for things such as age, weight, body mass index (BMI), etc.

- A total of 10 men participated
- A total of 6 women participated
- All participants were between the ages of 24 and 56

Of the 16 participants who started the study, 16 (100%) finished it.

How long did the study last?

Individual study participants were in the study for about 30 days excluding the time between screening and dosing. The entire study took around 3 months to complete and was completed as planned.

When the study ended in January 2022, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

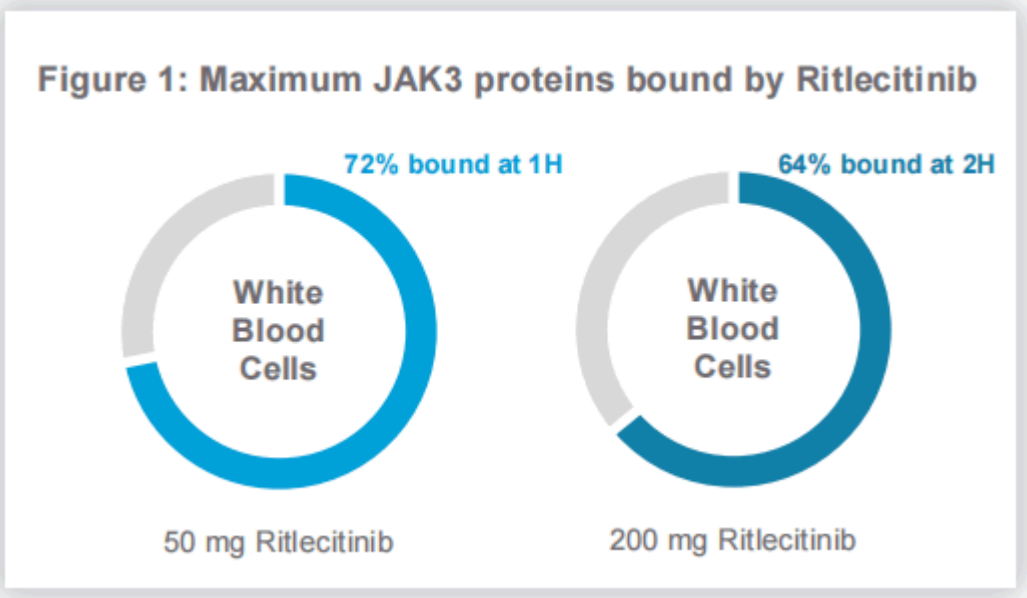
What were the results of the study?

How did 50 mg and 200 mg doses of ritlecitinib affect certain enzymes in the body?

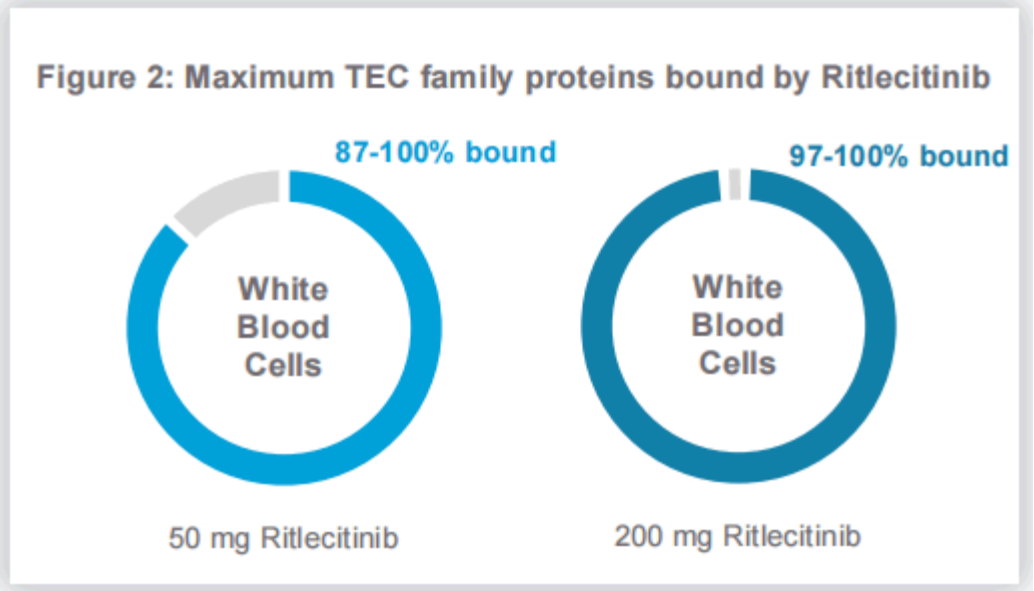
To answer this question, the researchers looked at the amount of JAK3 and TEC family kinases in white blood cells that was bound by ritlecitinib (also called the "median target occupancy"). The "median" value is the middle value, meaning that 50% of the values were higher than the median and 50% were lower than the median.

What was the percent target occupancy of JAK3 in white blood cells after participants took 50 mg or 200 mg doses of ritlecitinib?

- The highest median percent target occupancy of JAK3 kinases in the blood after participants took 50 mg and 200 mg of ritlecitinib is shown in Figure 1.
- The 50 mg dose reached the highest target occupancy at 1 hour after dosing. Ritlecitinib binding JAK3 lasted for 2 hours at this dose. The 200 mg dose of ritlecitinib took 2 hours to reach the highest target occupancy, but ritlecitinib bound some JAK3 for up to 48 hours after dosing.



- The highest median percent target occupancy of TEC family kinase proteins in the blood after participants took 50 mg and 200 mg of ritlecitinib is shown in Figure 2. The percentage target occupancy of TEC family kinase proteins in the blood depended on which TEC family kinase protein was measured. Researchers considered the differences in the results as minor.



- Overall, the percentage target occupancy of JAK3 appeared to be lower compared to the TEC family kinases.

These results showed that ritlecitinib binds to both JAK3 and TEC kinases when given at 50 mg or 200 mg doses. Higher percent target occupancies were seen in TEC kinase family proteins. 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.

Five out of 16 (31%) participants in this study had at least 1 medical problem. None of the participants left the study because of medical problems. The most common medical problems – those reported by one or more 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 1 or more participants are listed.
- The **2nd to 3rd** column tells how many of the 16 participants taking the study medication Treatment sequence 1 and Treatment sequence 2 reported each medical problem. Next to this number is the percentage of the 16 participants taking the study medication who reported the medical problem.
- Using these instructions, for example you can see that 1 out of the 8 (13%) participants taking the treatment sequence 1 of study medication reported swelling of the abdomen.

Table 1. Commonly reported medical problems reported by study participants		
Medical Problem	**Treatment sequence 1 Ritlecitinib 50 mg capsule (8 Participants)**	**Treatment sequence 2 Ritlecitinib 200 mg capsules (8 Participants)**
Swelling of the abdomen	1 out of 8 participants (13 %)	0 out of 8 participants (0 %)
Indigestion	1 out of 8 participants (13 %)	0 out of 8 participants (0 %)
Bacterial infection of the kidneys, bladder, or urethra	1 out of 8 participants (13 %)	0 out of 8 participants (0 %)
Stomach flu	0 out of 8 participants (0 %)	1 out of 8 participants (13 %)
Post operative dizziness	0 out of 8 participants (0 %)	1 out of 8 participants (13 %)
Arm or leg pain	1 out of 8 participants (13 %)	0 out of 8 participants (0 %)

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. No participants in this study had serious medical problems, and 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:

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

www.clinicaltrials.gov	Use the study identifier **NCT05128058**
www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number B7981045

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!