# 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:** Ritlecitinib (PF-06651600)

**Protocol Number:** B7981069

**Dates of Study:** 02 November 2021 to 10 January 2022

**Title of this Study:** Study to Evaluate the Effect of Multiple-Dose Ritlecitinib on the Pharmacokinetics (PK) of Tolbutamide

[Phase 1, Open-Label, Fixed-Sequence, 2-Period Study to Estimate the Effect of Multiple-Dose Ritlecitinib (PF-06651600) on the Pharmacokinetics of Single-Dose Tolbutamide in Healthy Participants]

**Date(s) of this Report:** 05 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 disease, which means that the immune system mistakenly attacks healthy parts of the body.

With alopecia areata, patients experience non-scarring hair loss, which may be chronic and recurring. It can affect adults and children across all ages, races, and sexes.

Treatments for autoimmune diseases focus on changing the activity of the immune system. However, these treatments do not work for all patients, may cause health problems, or may only be used for a brief period of time, depending on the treatment. Researchers are looking for new treatments for autoimmune diseases such as alopecia areata that work well for the disease, cause fewer health problems, and can be taken for longer periods of time.

## What are Ritlecitinib and Tolbutamide?

Ritlecitinib is an investigational drug that is being studied to treat people with inflammatory conditions and autoimmune diseases. An investigational treatment is one that is still being studied and is not approved for use outside of research studies. Ritlecitinib is a small molecule oral treatment drug. Small molecules can move easily through the cell membrane and interact with molecules present inside a cell. Ritlecitinib is thought to work by blocking the activity of specific proteins in immune cells called "Janus kinase 3" and the "TEC family kinases". These proteins act like on/off switches for the cells of the immune system. If these switches are turned off, the cells of the immune system may produce fewer cytokines (a type of protein), which is expected to make autoimmune diseases better.

Tolbutamide is usually used to treat diabetes (a condition where the body can't control the amount of sugar in the blood and can't use sugar efficiently). Tolbutamide lowers blood sugar.

Researchers wanted to find out if ritlecitinib would have an effect on the amount of tolbutamide in the body.

## What was the purpose of this study?

The purpose of this study was to estimate the effect of multiple doses of ritlecitinib on the pharmacokinetics (PK) of a single dose of tolbutamide in healthy adult participants. Pharmacokinetics is the study of the way the body breaks down a drug and removes it.

All participants received a single dose of tolbutamide at 2 different times during the study. The first dose was taken alone in the beginning of the study, and the second dose was taken after multiple doses of ritlecitinib.

After the tolbutamide tablet was swallowed, the drug entered the blood and organs (for example, stomach, liver, and kidneys) as it moved through the body. Afterwards, the tolbutamide was removed from the body through urine and feces. The effect of multiple doses of ritlecitinib on the amount of tolbutamide in the blood over time was measured.

This study did not test if ritlecitinib helped to improve alopecia areata as participants in this study were healthy and did not have alopecia areata.

## Researchers wanted to know:

- **How did multiple doses of ritlecitinib affect the amount of tolbutamide in the blood over time?**
- **What medical problems did participants have when ritlecitinib was taken with a single dose of tolbutamide?**

# What happened during the study?

## How was the study done?

There were 2 treatment periods in the study:

- **Period 1:** One (1) dose of tolbutamide (one 500 mg tablet) was given.
- **Period 2:** Ritlecitinib was given once a day for 10 days (four 50 mg capsules were given together, which provided a total dose of 200 mg). On the morning of Day 10 a single dose of tolbutamide (one 500 mg tablet) was also given shortly after the daily dose of ritlecitinib.

There was no washout period between the study periods. A washout is when a participant is not given any other treatment and it allows the body time to remove the drug out of the body.

The researchers assessed blood levels of tolbutamide in all participants before both periods began, as well as for 36 hours after tolbutamide was given on Day 1 of Period 1 and Day 10 of Period 2.

A summary of how the study was done is shown in Figure 1 below:

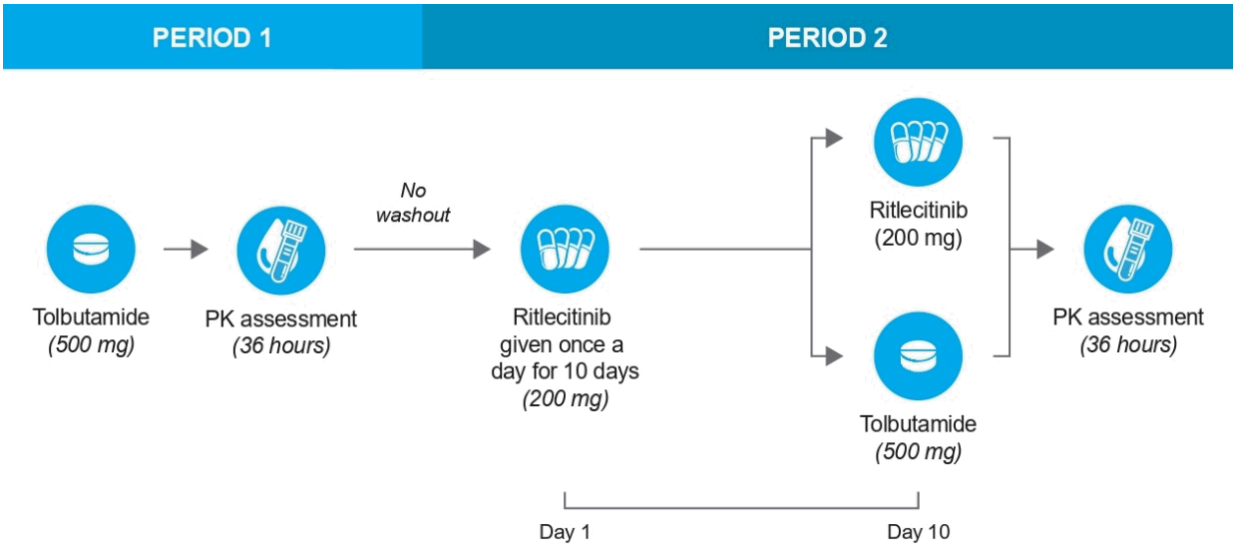


**Figure 1. Overall study design**

Researchers took samples of blood from participants during the study and measured the amount of tolbutamide. Researchers also checked the participants' health during the study and asked them how they were feeling.

The participants and researchers knew who took the study medications. This is known as an "open label" study.

## 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 02 November 2021 and ended on 10 January 2022.

## Who participated in this study?

The study included 12 healthy adult participants who met the inclusion/exclusion criteria (for example, age, weight, etc.).

- A total of 9 males participated.

- A total of 3 females participated.
- All participants were between the ages of 18 and 64 years old.

All 12 participants were treated in Period 1 (tolbutamide treatment alone). Two (2) participants stopped the study after Period 1 because of a medical issue and a personal reason.

Ten (10) participants were treated in Period 2 (multiple doses of ritlecitinib and a single dose of tolbutamide) and completed the study.

### How long did the study last?

The entire study took 10 weeks to complete. Individual study participants were in the study for 12 days.

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 multiple doses of ritlecitinib affect the amount of tolbutamide in the blood over time?

The study was done to see how multiple doses of ritlecitinib affected the amount of tolbutamide in the body. Researchers used different measurements to understand how much tolbutamide was in the blood over time. These measurements are shown below.

**What was the amount of tolbutamide in the blood after participants took a single dose of tolbutamide (500 mg) alone, and after participants took multiple doses of ritlecitinib (200 mg) with a single dose of tolbutamide?**

The highest (peak) amount of tolbutamide in the blood (known as $C_{max}$) after participants took tolbutamide alone and after multiple doses of ritlecitinib is shown in Figure 2 below. The amount of tolbutamide in the blood was measured in nanograms per milliliter, also called ng/mL.

- The highest amount of tolbutamide in the blood after participants took a single dose of tolbutamide was 44,240 ng/mL (Study Period 1).
- The highest amount of tolbutamide in the blood after participants took a single dose of tolbutamide following multiple doses of ritlecitinib was 45,740 ng/mL (Study Period 2).

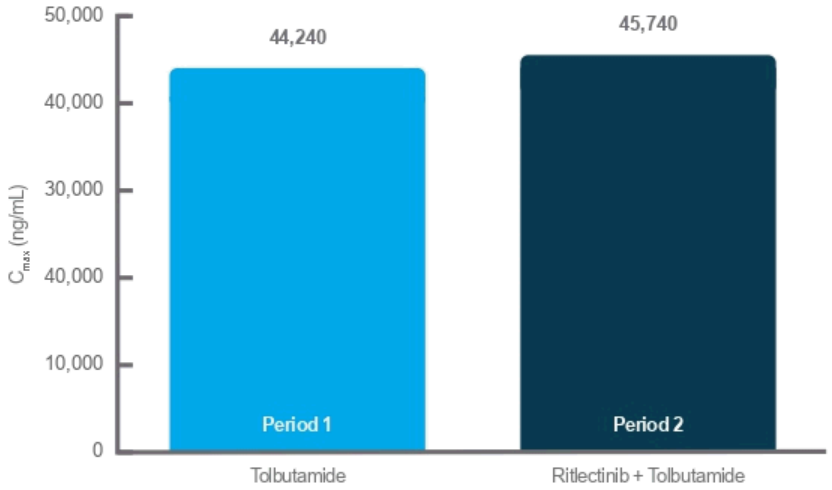


**Figure 2. Peak Amount of Tolbutamide in the Blood**

## How long did it take for tolbutamide to be removed from the body after participants took a single dose of tolbutamide?

The estimated total amount of tolbutamide in the blood, from when tolbutamide was taken until it was gone from the blood (known as $AUC_{inf}$) is shown in Figure 3. This was measured in nanogram hours per milliliter, also called ng.hr/mL. The ng.hr/mL is a unit used to measure total amount of drug in the blood over time.

- The $AUC_{inf}$ after participants took a single dose of tolbutamide alone was 608,600 ng.hr/mL (Study Period 1).

- The $AUC_{inf}$ after participants took a single dose of tolbutamide following multiple doses of ritlecitinib was 586,500 ng.hr/mL (Study Period 2).

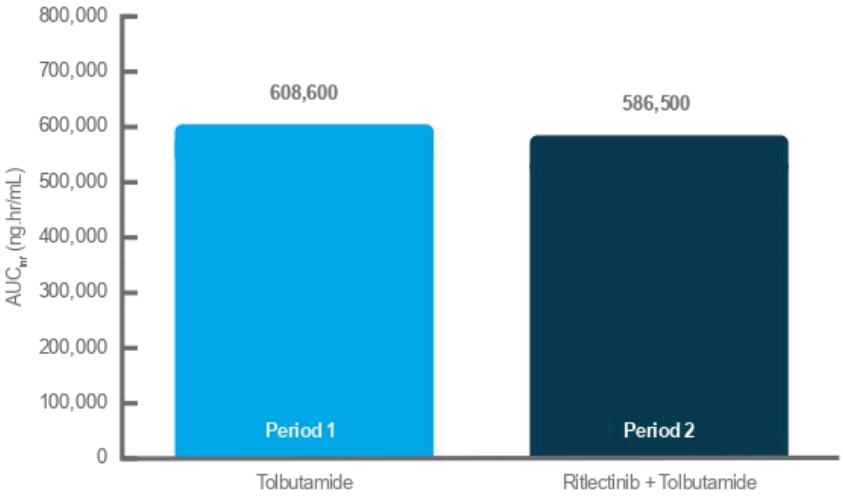


**Figure 3. Amount Of Tolbutamide In The Blood From When It Was Taken Until It Was Removed From The Blood**

In summary, the amount of tolbutamide in the blood was very similar when participants took a single dose of tolbutamide alone (Period 1) compared to when participants took a single dose of tolbutamide following multiple doses of ritlecitinib (Period 2).

Based on these results, the researchers concluded that tolbutamide is not moved differently through the body following multiple doses of ritlecitinib.

This does not mean that everyone in this study had these results. This is a summary of 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.

Three (3) out of 12 (25%) participants in this study had at least 1 medical problem.

One (1) participant in Period 2 was treated for low blood glucose levels. The study doctor considered this to be related to tolbutamide. One (1) participant left the study because of a medical problem (COVID-19) which was not related to the study treatments. All the medical problems 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 reported during the study. All medical problems reported are listed.
- The **2nd** column tells how many of the 12 participants taking tolbutamide alone reported each medical problem. Below this number is the percentage of the 12 participants taking tolbutamide who reported the medical problem.
- The **3rd** column tells how many of the 10 participants taking ritlecitinib alone reported each medical problem. Below this number is the percentage of the 10 participants taking ritlecitinib who reported the medical problem.

- The **4th** column tells how many of the 10 participants taking tolbutamide and ritlecitinib together on the same day reported each medical problem. Below this number is the percentage of the 10 participants taking tolbutamide and ritlecitinib together who reported the medical problem.
- For example, using these instructions, you can see that 1 out of the 12 (8%) participants taking tolbutamide alone had COVID-19. No participants taking ritlecitinib reported COVID-19, and 1 out of the 10 (10%) participants taking tolbutamide and ritlecitinib on the same day reported COVID-19.

**Table 1. Medical problems reported by study participants**

| Medical Problem | Tolbutamide (12 Participants) | Ritlecitinib alone (Days 1-9) (10 Participants) | Ritlecitinib and Tolbutamide (Day 10) (10 Participants) |
|---|---|---|---|
| **Pain** | 0 out of 12 participants (0%) | 1 out of 10 participants (10%) | 0 out of 10 participants (0%) |
| **COVID-19** | 1 out of 12 participants (8%) | 0 out of 10 participants (0%) | 1 out of 10 participants (10%) |
| **Low blood glucose levels** | 0 out of 12 participants (0%) | 0 out of 10 participants (0%) | 1 out of 10 participants (10%) |
| **Nail disorder** | 0 out of 12 participants (0%) | 1 out of 10 participants (10%) | 0 out of 10 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 had serious medical problems in this study. No participants died during this 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 **NCT05097716** |
| www.pfizer.com/research/research_clinical_trials/trial_results | Use the protocol number B7981069 |

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!