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: PF-06651600 (Ritlecitinib), PF-06700841 (Brepocitinib)

Protocol Number: B7981005

Dates of Study: 03 February 2017 to 10 May 2021

Title of this Study: Study to Compare Oral PF-06651600, PF-06700841 and Placebo in Subjects With Moderate to Severe Ulcerative Colitis

[A Phase 2b, Double-Blind, Randomized, Placebo-Controlled, Parallel Group, Dose Ranging Study of Oral PF-06651600 and PF-06700841 as Induction and Chronic Therapy in Subjects With Moderate to Severe Ulcerative Colitis]

Date(s) of this Report: 10 May 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 ulcerative colitis?

Ulcerative Colitis (or "UC") is a long-term inflammatory medical condition that affects the large intestines (also known as the colon). Symptoms include cramping, constipation, diarrhea, rectal bleeding, and fatigue (feeling very tired).

The exact cause of UC is not known. It is thought that UC is caused by an overactive immune system, which is normally responsible for fighting infections.

Medicines are available that lower the activity of the immune system, but some people with UC do not get better when taking these medicines. Some people who do get better when taking these medicines still have worse UC over time.

Researchers are looking for new treatments that can help treat patients with UC.

What are Ritlecitinib and Brepocitinib?

Ritlecitinib is a "small molecule" oral medication (swallowed). Small molecules can move easily through the cell membrane to interact with other molecules, such as enzymes, inside a cell.

Ritlecitinib prevents (inhibits) certain enzymes from working. Enzymes are protein molecules in cells which speed up chemical reactions in the body. The enzymes that ritlecitinib inhibits are known as janus kinase 3 (JAK3) and the tyrosine-protein (TEC) kinase family.

Both of these enzymes help control inflammatory pathways in the cell. They also cause molecules known as cytokines to be released. Cytokines cause inflammation. This inflammation is usually used by the immune system to fight infections that may be caused by viruses or bacteria. In people with UC, the body's immune system causes inflammation even although they are healthy.

Brepocitinib is another small molecule oral medication. It inhibits enzymes known as janus kinase 1 (JAK1) and tyrosine kinase 2 (TYK2). These enzymes control signals to the immune system cells that produce cytokines. By stopping the function of JAK1 and TYK2, brepocitinib may prevent the abnormal immune system response and inflammation in people with UC.

What was the purpose of this study?

The main purpose of the study was to find out if ritlecitinib or brepocitinib was more effective at relieving UC symptoms. In addition, both study medications were compared to placebo. A placebo does not have any medicine in it, but it looks just like the study medication.

Researchers wanted to know:

Did the participants taking Ritlecitinib or Brepocitinib have more relief from their UC symptoms?

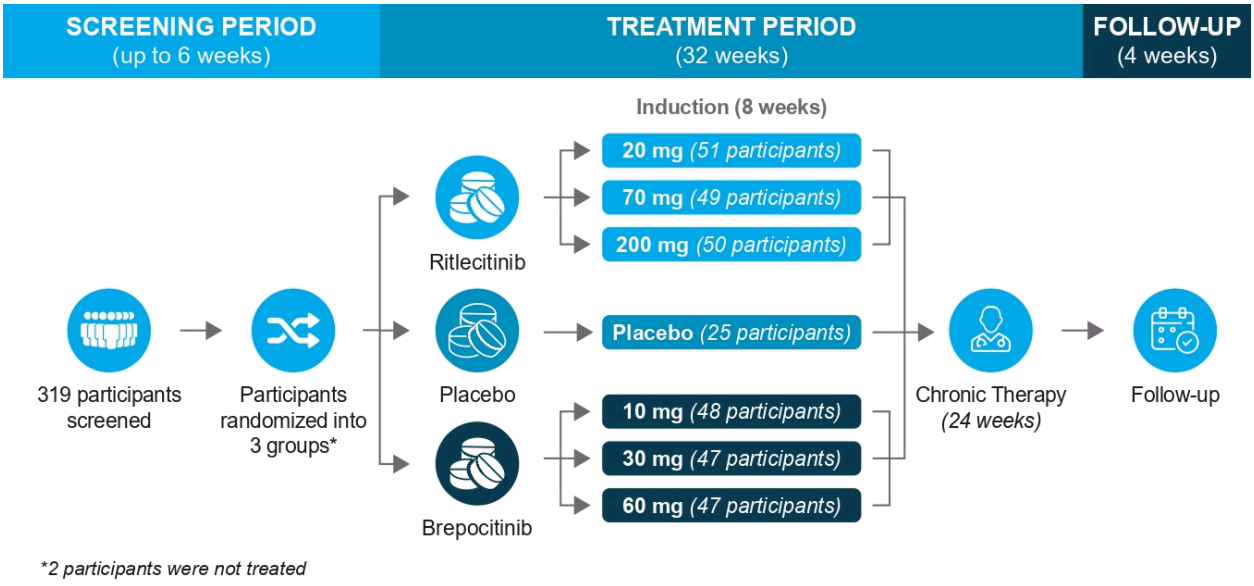
What happened during the study?

How was the study done?

Researchers tested various doses of ritlecitinib or brepocitinib on groups of study participants to find out if study participants taking these study medicines experienced relief from their UC symptoms.

- Ritlecitinib (total of 150 participants):
    - 51 participants received 20 mg
    - 49 participants received 70 mg
    - 50 participants received 200 mg

- Brepocitinib (total of 142 participants):
    - 48 participants received 10 mg
    - 47 participants received 30 mg
    - 47 participants received 60 mg
- Placebo (total of 25 participants)



The study participants and researchers did not know who took ritlecitinib or brepocitinib and who took the placebo. This is known as a "double-blinded" study. Study participants were assigned to each group by chance alone.

Researchers measured the symptom relief of UC for each treatment group by using a Mayo score. This is a scoring system that measures how many stools were passed each day, amount of rectal bleeding (if any), mucosal appearance (doctors use a camera on the end of a tube to look at the inside lining of the colon), and a rating of the disease by a doctor (normal, mild, moderate or severe).

The Mayo score ranges from 0 to 12:

- Mayo score 0 to 2: Participant is in remission (no disease activity)

- Mayo score 3 to 5: Participant has mild disease
- Mayo score 6 to 10: Participant has moderate disease
- Mayo score 10 and higher: Participant has severe disease

All participants in the study started with moderate to severe UC according to their Mayo score. The difference in their score after the induction period would indicate how effective the study treatment was.

Where did this study take place?

The Sponsor ran this study at 154 locations in 19 countries (United States, Australia, Bulgaria, Czech Republic, Denmark, Georgia, Germany, Hungary, Israel, Italy, Republic of Korea, Romania, Russian Federation, Serbia, Slovakia, Spain, Poland, Turkey and Ukraine).

When did this study take place?

It began 03 February 2017 and ended 10 May 2021.

Who participated in this study?

The study included participants who had moderate to severe UC, even although they had tried other treatments.

- A total of 182 men participated
- A total of 135 women participated
- All participants were between the ages of 18 and 73.

Participants were to be treated in the induction period for 8 weeks. Of the 317 participants who started the study, 281 finished the induction phase.

Ten (10) participants in the ritlecitinib group, 4 participants in the brepocitinib group, and zero participants in the placebo group, did not finish the induction phase because of medical problems.

Overall, 36 participants left before the study was over by their choice or a doctor decided it was best for a participant to stop being in the study.

How long did the study last?

Study participants were in the induction phase of the study for 8 weeks. The entire study took 51 months to complete. The study was completed as planned.

When the study ended in May 2021, 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 the participants taking Ritlecitinib or Brepocitinib have more relief from their UC symptoms?

After 8 weeks of treatment, these were the results.

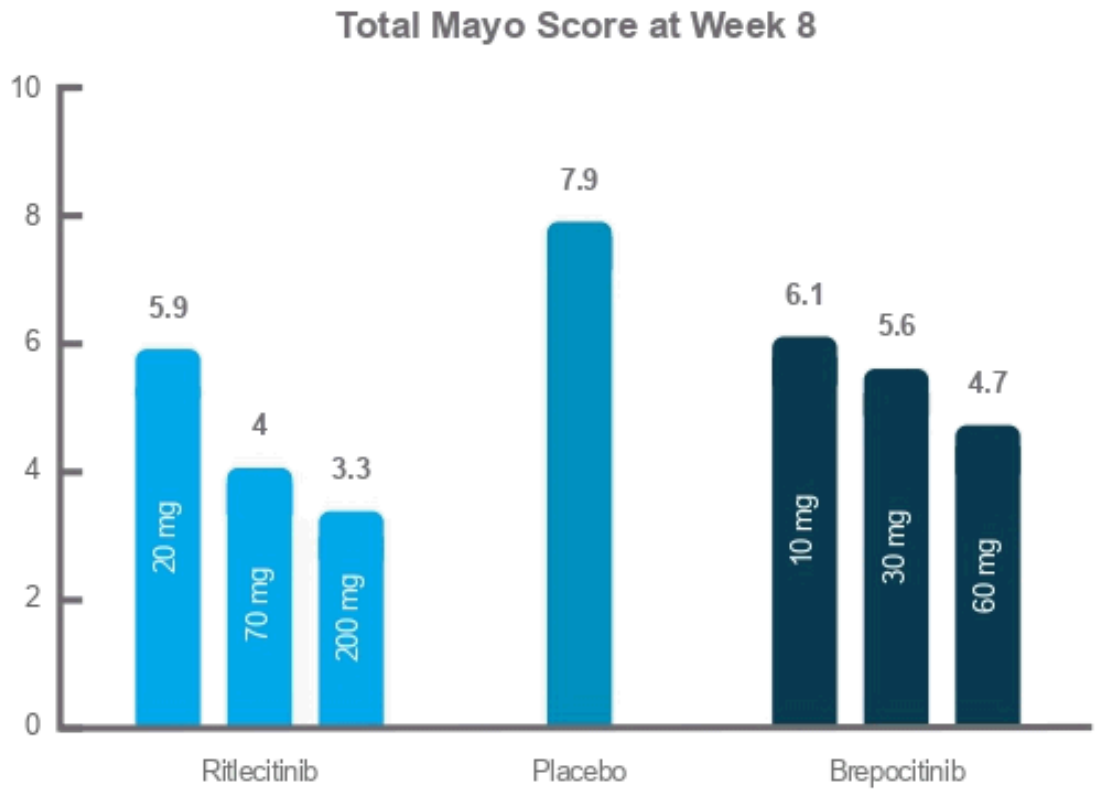
The average Mayo score for participants taking ritlecitinib were as follows:

- 20 mg dose: 5.9
- 70 mg dose: 4.0
- 200 mg dose: 3.3

The average Mayo score for participants taking brepocitinib were as follows:

- 10 mg dose: 6.1
- 30 mg dose: 5.6
- 60 mg dose: 4.7

The average Mayo score for participants taking placebo was 7.9



Did the study medications help relieve the symptoms of UC compared to placebo?

On average, participants who took the study medications (ritlecitinib or brepocitinib) had a lower Mayo score (fewer UC symptoms), while participants taking placebo had a higher Mayo score (more UC symptoms).

Based on these results, the researchers have decided that the results are not likely the result by chance. Ritlecitinib and brepocitinib may help with decreasing the symptoms and severity of UC.

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.

One-hundred and forty-six (146) out of 317 (46%) participants in the induction of this study had at least 1 medical problem. A total of 14 participants left the study because of medical problems. The most common medical problems – those reported by more than 5% 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 during the study. All medical problems reported by more than 5% of participants are listed.
- The **2nd** column tells how many of the 150 participants taking ritlecitinib reported each medical problem. Next to this number is the percentage of the 150 participants taking the ritlecitinib who reported the medical problem.
- The **3rd** column tells how many of the 142 participants taking brepocitinib reported each medical problem. Next to this number is

the percentage of the 140 participants taking the brepocitinib who reported the medical problem.

- The **4th** column tells how many of the 25 participants taking a placebo reported each medical problem. Next to this number is the percentage of the 25 participants taking a placebo who reported the medical problem.
- Using these instructions, you can see that 6 out of the 150 (4%) participants taking ritlecitinib reported having a headache, and 5 out of 142 (4%) participants taking brepocitinib reported having a headache. A total of 2 out of the 25 (8%) participants taking a placebo reported having a headache.

Table 1. Commonly reported medical problems by study participants during 8-week induction period

Medical Problem	PF-06651600 (150 Participants)	PF-06700841 (142 Participants)	Placebo (25 Participants)
Anemia (low number of red blood cells)	7 out of 150 participants (5%)	6 out of 142 participants (4%)	1 out of 25 participants (4%)
Headache	6 out of 150 participants (4%)	5 out of 142 participants (4%)	2 out of 25 participants (8%)

Table 1. Commonly reported medical problems by study participants during 8-week induction period			
Medical Problem	**PF-06651600 (150 Participants)**	**PF-06700841 (142 Participants)**	**Placebo (25 Participants)**
Infection of nose and throat	3 out of 150 participants (2%)	8 out of 142 participants (6%)	0 out of 25 participants (0%)
Stomach pain	2 out of 150 participants (1%)	4 out of 142 participants (3%)	2 out of 25 participants (8%)
Fever	2 out of 150 participants (1%)	5 out of 142 participants (4%)	1 out of 25 participants (4%)
Joint pain	3 out of 150 participants (2%)	5 out of 142 participants (4%)	0 out of 25 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.

Eleven (11) participants (3%, or 11 out of 317 participants) had serious medical problems.

- 6 participants in the ritlecitinib group had serious medical problems. These included lung infection, severe UC, heart attack, brain inflammation (encephalitis), and lung damage.
- 5 participants in the brepocitinib group had serious medical problems. These included severe UC, haemorrhoid (swollen veins in rectum/anus) operation, blood clots, fever, and anaemia.
- No participants in the placebo group had serious medical problems.

One (1) participant died during the study from a heart attack. This was determined to not be related to the study treatment.

Researchers believe most of the serious medical problems reported by participants were not related to study medications, except for 1 case of severe UC (ritlecitinib 20 mg group) and 1 case of fever (brepocitinib 30 mg group).

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 **NCT02958865**

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!