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 participants. 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: B7981015

Dates of Study: 03 December 2018 to 24 June 2021

Title of this Study: A Placebo Controlled, Dose-Ranging Study to Investigate the Efficacy and Safety of PF-06651600 in Adult and Adolescent Alopecia Areata (AA) Subjects

[A Phase 2b/3 Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study to Investigate the Efficacy and Safety of PF-06651600 in Adult and Adolescent Alopecia Areata (AA) Subjects With 50% or Greater Scalp Hair Loss]

Date(s) of this Report: 23 May 2022

– Thank You –

If you or your child participated in this study, Pfizer, the Sponsor, would like to thank you for your or your child's 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 or your child's study site.

Why was this study done?

What is alopecia areata?

Alopecia areata is an autoimmune disorder, which may be chronic and reoccurring, 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 other psychological conditions, problems with social relationships, decreased health-related quality of life and a general decline in quality of life.

Patchy alopecia areata is the most common form of alopecia areata, which may develop into more widespread and often treatment-resistant forms of alopecia areata, especially when the disease starts at an earlier age. Alopecia areata involving 50% or greater scalp hair loss, including the loss of all the hair on the scalp (alopecia totalis) and the loss of all scalp, face and body hair (alopecia universalis) can be considered extensive forms of alopecia areata.

What is Ritlecitinib?

Ritlecitinib is a small molecule oral medication. Small molecules can move easily through the cell membrane to interact with targeted molecules present inside a cell. Ritlecitinib inhibits the enzymes (protein molecule in cells which speed up chemical reactions in the body) known as a Janus kinase 3 (JAK3) and tyrosine kinase expressed in hepatocellular carcinoma (TEC) family. These enzymes are important regulators of inflammatory pathways in the cell and cause the production of molecules known as cytokines. It is believed that these inflammatory pathways and cytokines are involved in dermatologic diseases such as vitiligo, atopic dermatitis, as well as alopecia areata.

What was the purpose of this study?

The purpose of this study was to compare ritlecitinib with a placebo to determine ritlecitinib's efficacy and safety in treating alopecia areata patients. Ritlecitinib is an investigational medication because it is not approved for use. The placebo looks like the study medication but does not contain any active ingredients. Researchers compared the results of taking the placebo to the results of taking ritlecitinib to see if there were any differences.

Researchers wanted to know:

Did the participants taking ritlecitinib have a better response than the participants taking placebo at Week 24?

What happened during the study?

How was the study done?

Researchers tested ritlecitinib on a group of study participants to find out if study participants taking ritlecitinib had a better response as measured by the Severity Alopecia Tool (SALT) in comparison to placebo at Week 24. Following Week 24, participants taking placebo were switched to ritlecitinib during the extension period. The SALT score measures the severity of alopecia by capturing the percentage of hair loss. It was calculated by dividing the scalp into 4 quadrants with allocated percentage scalp surface area in each area. The study was carried out as shown in Figure 1 below.

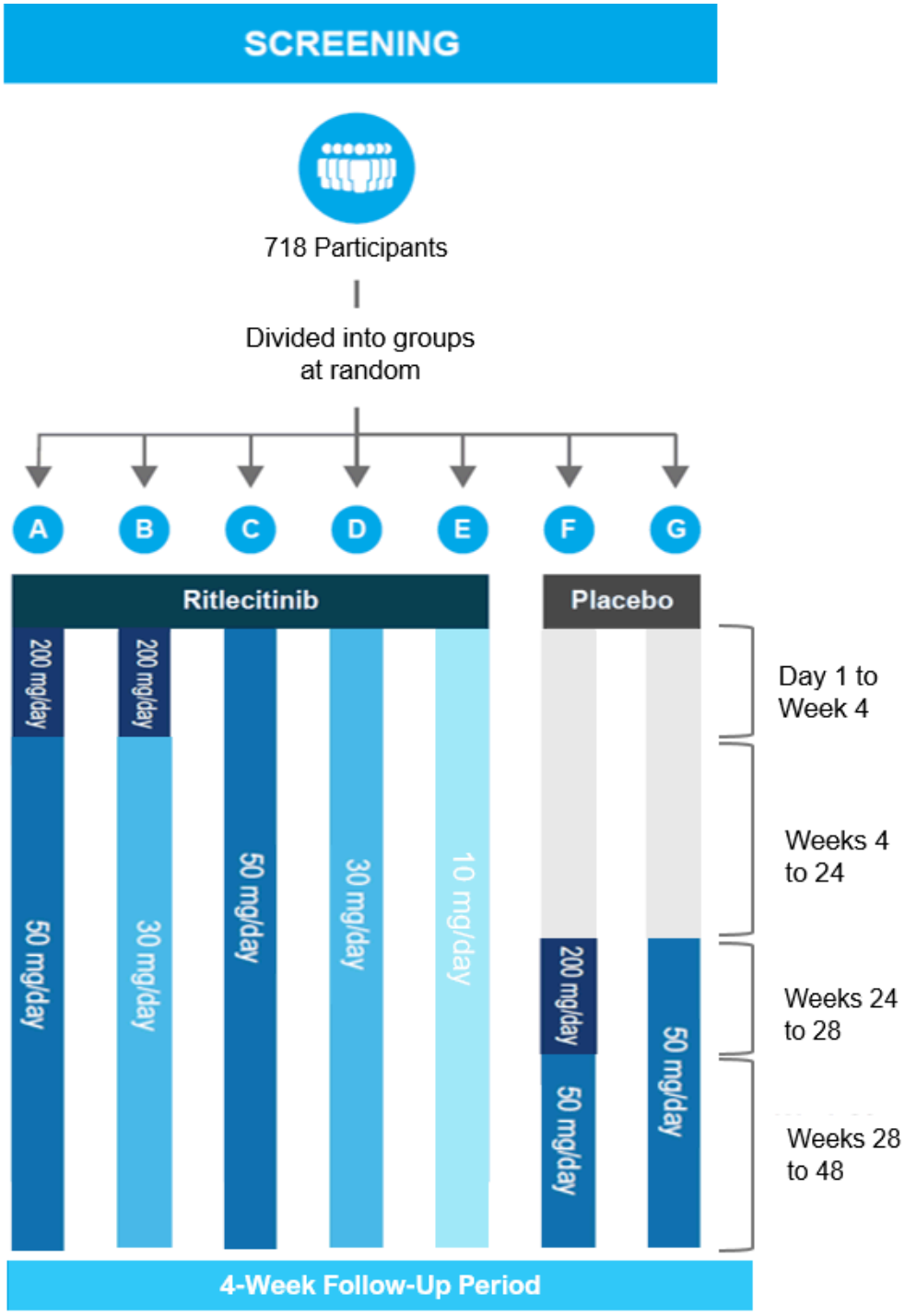

Figure 1: Overall study design

The study participants and researchers did not know who took ritlecitinib, what dosage was received, or who took the placebo. This is known as a "blinded" study. Study participants were assigned to each group by chance alone.

Where did this study take place?

The Sponsor ran this study at 118 locations in Argentina, Australia, Canada, Chile, China, Colombia, Czech Republic, Germany, Hungary, Japan, Mexico, Poland, Russia, Spain, South Korea, Taiwan, United Kingdom, and the United States.

When did this study take place?

It began 03 December 2018 and ended 24 June 2021.

Who participated in this study?

The study included participants who:

- Had a primary diagnosis of alopecia areata
- Had at least 50% hair loss on their scalp
- Were currently experiencing hair loss on their scalp
- Were at least 12 years old or older, depending on the study location

A total of 1097 participants were screened, and 718 participants were randomized or assigned to a treatment group by chance.

- A total of 272 males participated.
- A total of 446 females participated.
- Six hundred and thirteen out of 718 (85%) of participants were at least 18 years old.

Participants were to be treated until the planned end of treatment at 48 weeks. Of the 718 participants who started the study, 614 participants completed the study treatment.

Three participants were not treated, and 101 participants did not finish the study because:

- the participant left by their own choice,
- the participant experienced a medical problem,
- the participant discovered they were pregnant,
- a doctor decided it was best for a participant to stop being in the study,
- the participant could not be contacted,
- the treatment did not work for them,
- a protocol deviation occurred (an unplanned change from the study design),
- the participant was non-compliant while taking the study medication,
- or for other reasons.

How long did the study last?

Study participants were in the study for approximately 57 weeks. The entire study took approximately 2½ years to complete.

When the last participant's last visit occurred in June 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 have a better response than the participants taking placebo at Week 24?

The responses of the participants to treatment with ritlecitinib or placebo was measured using the SALT score. A response was defined as those participants whose SALT score improved to less than or equal to 20% at Week 24. In Figure 2 below, the response based on absolute SALT ≤20 at Week 24 is shown for the different treatment groups.

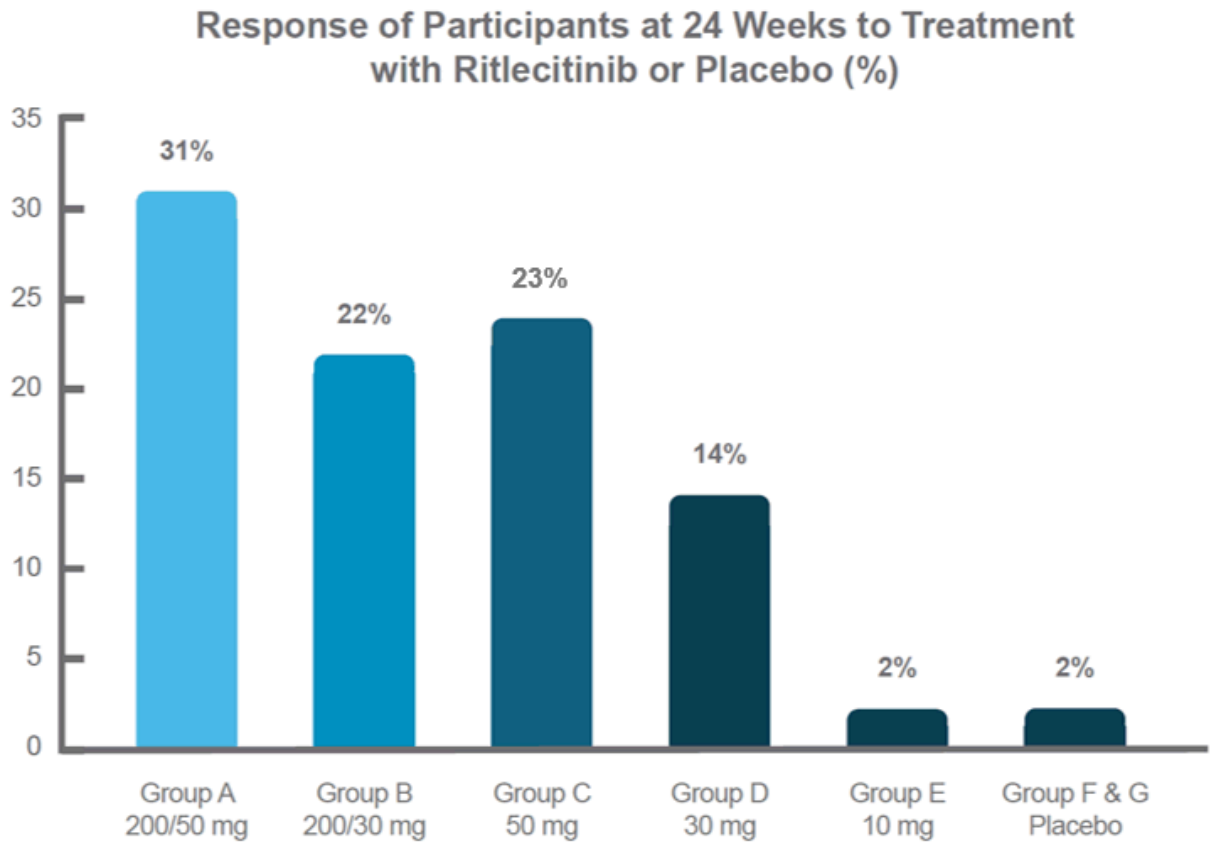

Figure 2: Response of participants to treatment with ritlecitinib or placebo at Week 24

At Week 24, the participants in the 200/50 mg, 200/30 mg, 50 mg, and 30 mg groups treated with ritlecitinib were significantly different from placebo.

- A significant difference between 2 groups means that there is a measurable difference between the groups and that, statistically, the probability of obtaining that difference by chance is very small (less than 0.125% for this study).

The percentage of responders ranged from 14% in the group treated with 30 mg of ritlecitinib to 31% in the 200/50 mg group. The group treated with ritlecitinib at 10 mg (2%) was not that different when compared to placebo (2%).

Based on these results, the researchers have decided that the results are not likely the result of chance. Ritlecitinib may help in the treatment of alopecia areata.

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

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 hundred and eighty-seven out of 715 participants (82%) that received study treatment in this study had at least 1 medical problem up to Week 48. A total of 22 participants left the study because of medical problems. The most common

medical problems – those reported by at least 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 at least 5% of participants are listed.
- The **2nd** to **6th** columns tells how many of the 584 participants who took different doses of ritlecitinib for 48 weeks reported each medical problem. Next to this number (the number in parenthesis) is the percentage of the participants who took each dose of ritlecitinib who reported the medical problem.
- The **7th** and **8th** columns tell how many of the 131 participants who took placebo during the first 24 weeks followed by treatment with ritlecitinib (either 200/50 mg [65 participants] or 50 mg [66 participants]) from Weeks 25 to 48 reported each medical problem. Next to this number (the number in parenthesis) is the percentage of the participants who took placebo during the first 24 weeks followed by either treatment with ritlecitinib (200/50 mg [65 participants] or 50 mg [66 participants]) from Weeks 25 to 48 who reported the medical problem.
- Using these instructions, you can see that 6 out of the 131 (5%) participants who took ritlecitinib in the 200/50 mg group during the first 24 weeks reported acne. A total of 5 out of the 65 (8%) participants who took placebo during the first 24 weeks followed by treatment with ritlecitinib (200/50 mg [65 participants]) from Weeks 25 to 48 reported acne.

Table 1. Commonly reported medical problems by study participants up to Week 48							
Medical Problem	Ritlecitinib					Placebo to Ritlecitinib	
	200/50 mg	200/30 mg	50 mg	30 mg	10 mg	200/50 mg	50 mg
No of Participants	131	129	130	132	62	65	66
Abdominal pain	1 out of 131 (1%)	5 out of 129 (4%)	5 out of 130 (4%)	3 out of 132 (2%)	0 out of 62 (0%)	4 out of 65 (6%)	0 out of 66 (0%)
Acne	6 out of 131 (5%)	10 out of 129 (8%)	12 out of 130 (9%)	12 out of 132 (9%)	3 out of 62 (5%)	5 out of 65 (8%)	8 out of 66 (12%)
Joint stiffness	4 out of 131 (3%)	5 out of 129 (4%)	2 out of 130 (2%)	4 out of 132 (3%)	2 out of 62 (3%)	2 out of 65 (3%)	6 out of 66 (9%)
Constipation	1 out of 131 (1%)	0 out of 129 (0%)	1 out of 130 (1%)	7 out of 132 (5%)	1 out of 62 (2%)	1 out of 65 (2%)	0 out of 66 (0%)
Cough	6 out of 131 (5%)	0 out of 129 (0%)	3 out of 130 (2%)	3 out of 132 (2%)	0 out of 62 (0%)	4 out of 65 (6%)	2 out of 66 (3%)
Diarrhea	9 out of 131 (7%)	4 out of 129 (3%)	12 out of 130 (9%)	8 out of 132 (6%)	0 out of 62 (0%)	4 out of 65 (6%)	1 out of 66 (2%)
Dizziness	9 out of 131 (7%)	8 out of 129 (6%)	4 out of 130 (3%)	8 out of 132 (6%)	1 out of 62 (2%)	0 out of 65 (0%)	2 out of 66 (3%)
Feeling tired	4 out of 131 (3%)	6 out of 129 (5%)	6 out of 130 (5%)	6 out of 132 (5%)	4 out of 62 (6%)	3 out of 65 (5%)	2 out of 66 (3%)
Infection of one or more of the pockets from which hair grows (follicles)	11 out of 131 (8%)	11 out of 129 (9%)	8 out of 130 (6%)	5 out of 132 (4%)	4 out of 62 (6%)	4 out of 65 (6%)	4 out of 66 (6%)
Headache	17 out of 131 (13%)	14 out of 129 (11%)	16 out of 130 (12%)	24 out of 132 (18%)	12 out of 62 (19%)	8 out of 65 (12%)	8 out of 66 (12%)

Table 1. Commonly reported medical problems by study participants up to Week 48							
Medical Problem	Ritlecitinib					Placebo to Ritlecitinib	
	200/50 mg	200/30 mg	50 mg	30 mg	10 mg	200/50 mg	50 mg
No of Participants	131	129	130	132	62	65	66
Flu	8 out of 131 (6%)	1 out of 129 (1%)	3 out of 130 (2%)	3 out of 132 (2%)	3 out of 62 (5%)	1 out of 65 (2%)	0 out of 66 (0%)
Trouble sleeping	3 out of 131 (2%)	0 out of 129 (0%)	2 out of 130 (2%)	1 out of 132 (1%)	1 out of 62 (2%)	1 out of 65 (2%)	4 out of 66 (6%)
Muscle aches and pain	6 out of 131 (5%)	3 out of 129 (2%)	3 out of 130 (2%)	5 out of 132 (4%)	6 out of 62 (10%)	0 out of 65 (0%)	1 out of 66 (2%)
Blocked nose	1 out of 131 (1%)	1 out of 129 (1%)	2 out of 130 (2%)	3 out of 132 (2%)	4 out of 62 (6%)	1 out of 65 (2%)	1 out of 66 (2%)
Infection of nose and throat (cold)	19 out of 131 (15%)	21 out of 129 (16%)	18 out of 130 (14%)	21 out of 132 (16%)	7 out of 62 (11%)	7 out of 65 (11%)	4 out of 66 (6%)
Nausea	11 out of 131 (8%)	3 out of 129 (2%)	3 out of 130 (2%)	12 out of 132 (9%)	3 out of 62 (5%)	8 out of 65 (12%)	1 out of 66 (2%)
Throat pain	4 out of 131 (3%)	6 out of 129 (5%)	6 out of 130 (5%)	1 out of 132 (1%)	0 out of 62 (0%)	2 out of 65 (3%)	5 out of 66 (8%)
Itching	4 out of 131 (3%)	7 out of 129 (5%)	1 out of 130 (1%)	3 out of 132 (2%)	1 out of 62 (2%)	1 out of 65 (2%)	1 out of 66 (2%)
Rash	5 out of 131 (4%)	3 out of 129 (2%)	7 out of 130 (5%)	1 out of 132 (1%)	0 out of 62 (0%)	1 out of 65 (2%)	1 out of 66 (2%)

Table 1. Commonly reported medical problems by study participants up to Week 48							
Medical Problem	Ritlecitinib					Placebo to Ritlecitinib	
	200/50 mg	200/30 mg	50 mg	30 mg	10 mg	200/50 mg	50 mg
No of Participants	131	129	130	132	62	65	66
Nose, sinus, or throat infection	18 out of 131 (14%)	12 out of 129 (9%)	11 out of 130 (8%)	16 out of 132 (12%)	2 out of 62 (3%)	7 out of 65 (11%)	6 out of 66 (9%)
Infection of the kidneys, bladder, or urethra	11 out of 131 (8%)	3 out of 129 (2%)	1 out of 130 (1%)	5 out of 132 (4%)	0 out of 62 (0%)	4 out of 65 (6%)	2 out of 66 (3%)
Raised, itchy rash	9 out of 131 (7%)	9 out of 129 (7%)	7 out of 130 (5%)	5 out of 132 (4%)	1 out of 62 (2%)	4 out of 65 (6%)	4 out of 66 (6%)
Vomiting	6 out of 131 (5%)	7 out of 129 (5%)	2 out of 130 (2%)	5 out of 132 (4%)	1 out of 62 (2%)	2 out of 65 (3%)	3 out of 66 (5%)

Did study participants have any serious medical problems?

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

Fourteen participants (2%) had serious medical problems up to Week 48.

- Eleven participants in the groups that received ritlecitinib for 48 weeks experienced a serious medical problem.
    - In the 200/50 mg group (4 participants) experienced a serious medical problem including:
        - inflammation of the appendix (appendicitis)

        - infection of the lung tissue (empyema) and overactive and toxic response to an infection (sepsis)
        - a type of breast cancer that begins in the milk-producing glands of the breast called invasive lobular breast carcinoma
        - miscarriage
    - In the 200/30 mg group (2 participants) experienced:
        - inflammation of the appendix (appendicitis)
        - chemical poisoning & suicidal behavior
    - In the 50 mg group (2 participants) experienced:
        - breast cancer
        - blockage in an artery in the lungs (pulmonary embolism)
    - In the 30 mg group (1 participant) experienced infection or inflammation of pouches that formed in the intestines (diverticulitis).
    - In the 10 mg group (2 participants) experienced:
        - suicidal behavior
        - inflammatory condition of the skin (eczema)
- Three participants in the groups that received placebo for the first 24 weeks followed by treatment with ritlecitinib from weeks 25 to 48 experienced a serious medical problem. These medical problems were all reported during the first 24 weeks when the participants were taking placebo.
    - In the placebo to 200/50 mg group no serious medical problems were experienced by participants
    - In the placebo to 50 mg group (3 participants) experienced:
        - miscarriage

- A mental condition in which a person experiences blindness, paralysis, or other nervous system (neurologic) symptoms that cannot be explained by illness or injury (conversion disorder)
- heavy period

No participants died during the study.

Where can I learn more about this study?

If you have questions about the results of your or your child's study, please speak with the doctor or staff at your or your child's study site.

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

www.clinicaltrials.gov	Use the study identifier NCT03732807
www.clinicaltrialsregister.eu	Use the study identifier 2018-001714-14
www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number B7981015

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

Again, if you or your child participated in this study, **thank you** for volunteering. We do research to try to find the best ways to help study participants, and you or your child helped us to do that!