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: Abrilada (PF-06410293)

Protocol Number: B5381012

Dates of Study: 13 January 2020 to 22 June 2021

Title of this Study: Study Comparing Levels of Adalimumab in the Blood After Multiple Switches Between Humira® and Abrilada™ (PF-06410293) With Humira® Alone in Patients With Rheumatoid Arthritis

[A Randomized Comparative Study Assessing the Switching Between PF-06410293 and Humira® in Combination With Methotrexate in Participants With Moderately to Severely Active Rheumatoid Arthritis]

Date(s) of this Report: 04 February 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 rheumatoid arthritis?

Rheumatoid arthritis, or RA, is a disease that causes swelling, tenderness, pain, redness, and swelling in the joints. RA is an autoimmune disease, which means that patients with RA have an overactive immune system that mistakenly attacks healthy parts of the body, such as the joints. RA can cause permanent damage to the joints if it goes unchecked.

What is Abrilada?

There are many medicines that can be used to treat RA. One medicine that is approved for treatment of RA is called adalimumab. This medicine is also known as a biologic. A biologic is medicine that has been developed from materials from animals, plants, or micro-organisms that have been modified or changed in the laboratory. Adalimumab may help calm the activity of the immune system and decrease RA symptoms. Adalimumab was first licensed using the brand name Humira.

Abrilada (also known as PF-06410293) is an adalimumab biologic that is similar to Humira in structure and clinically equivalent (or biosimilar). This means Abrilada provides the same treatment benefits and has the same potential side effects as Humira. The reason for making a medicine that is similar to Humira is to help increase patient access.

What was the purpose of this study?

The Food and Drug Administration (FDA) in the United States has approved Abrilada as a biosimilar of Humira. The purpose of this study was to compare the level of adalimumab in the blood between 2 groups of participants. The first group received Humira throughout the study (non-switching group or arm). The second group started on Humira and then switched to Abrilada for a total of 3 times during the study (switching group or arm). Arm is another word for group in a clinical study.

This study did not test if Abrilada or Humira helps to improve RA as this has been previously studied.

Researchers wanted to know:

- **Do multiple switches between Humira and Abrilada change how adalimumab acts in the body compared to treatment with Humira alone?**

What happened during the study?

How was the study done?

Researchers tested Humira alone, compared with switching between Humira and Abrilada multiple times in 2 groups of study participants with RA to find out if switching between Humira and Abrilada changes how adalimumab acts in the body.

Participants were treated with Humira or Abrilada, which was given as an injection under the skin. The study doctor or nurse showed the participants or their care giver how to do the injection, then the participants were to give themselves the injections at home. The dose of Humira and Abrilada was 40 milligrams (mg) every other week. In addition, participants were required to continue taking methotrexate as prescribed by their doctor.

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

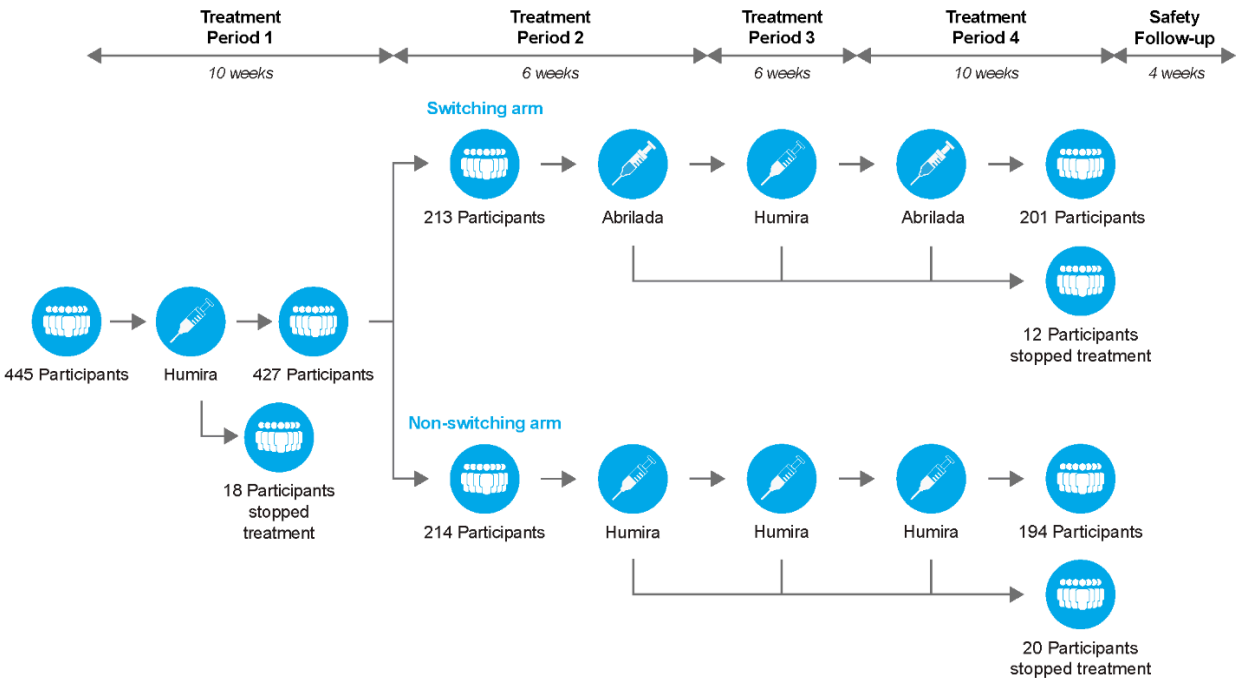
Researchers then compared the results of study participants who switched between Humira and Abrilada (switching arm) to the results of study participants who only took Humira (non-switching arm).

Participants were assigned to the switching arm or the non-switching arm by chance alone. The participants and researchers knew who took each type of medicine. This is known as an open-label study.

This study was split up into 4 treatment periods and 1 safety follow-up period as follows:

- In Treatment Period 1 and Treatment Period 3, all participants received Humira. Treatment Period 1 was for 10 weeks and Treatment Period 3 was for 6 weeks
- In Treatment Period 2 and Treatment Period 4, participants in the switching arm received Abrilada and participants in the non-switching arm received Humira. Treatment Period 2 was for 6 weeks and Treatment Period 4 was for 10 weeks
- In the Safety Follow-up Period, treatment with Abrilada in the switching arm and Humira in the non-switching arm was stopped and all participants remained in the study for a further 4 weeks for safety checks

The following figure shows what happened during the study.



All participants continued their methotrexate during the study and were treated with 40 mg Humira or 40 mg Abrilada every 2 weeks for 32 weeks.
Blood samples were collected throughout the study for testing.
All participants had safety follow-up (safety checks) for 4 weeks after their last dose of study drug (Humira or Abrilada).

Where did this study take place?

The Sponsor ran this study at 61 locations in 10 countries in Europe, Northern Asia, South Africa, and North America.

When did this study take place?

It began 13 January 2020 and ended 22 June 2021.

Who participated in this study?

The study included adult participants who had moderately to severely active RA and who were also taking methotrexate.

In Treatment Period 1:

- A total of 77 men participated
- A total of 368 women participated

- All participants were between the ages of 20 and 71 years.

Of these 445 participants, 427 were treated in Treatment Period 2.

In Treatment Period 2:

- A total of 73 men participated
- A total of 354 women participated
- All participants were between the ages of 20 and 71 years.

Of the 445 participants who started the study, 427 finished treatment with Humira in Treatment Period 1 and 18 stopped treatment early. Of the 427 participants who continued the study in Treatment Periods 2 to 4, there were 213 participants who were treated in the switching arm with Humira and Abrilada and 214 participants who were treated in the non-switching arm with Humira alone.

Of the 213 in the switching arm, 201 participants finished the study, and 12 stopped treatment early. Of the 214 participants in the non-switching arm, 194 finished the study, and 20 stopped treatment early.

There were 50 participants who stopped treatment early 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 study for 36 weeks. The entire study took nearly 18 months to complete.

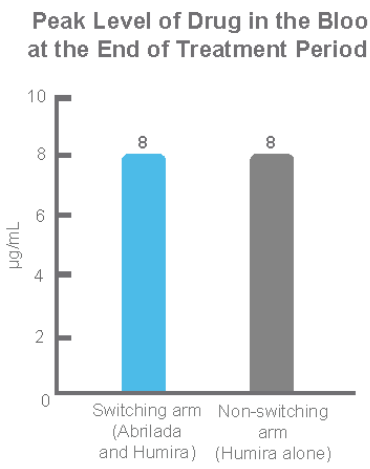
When the study ended in June 2021, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

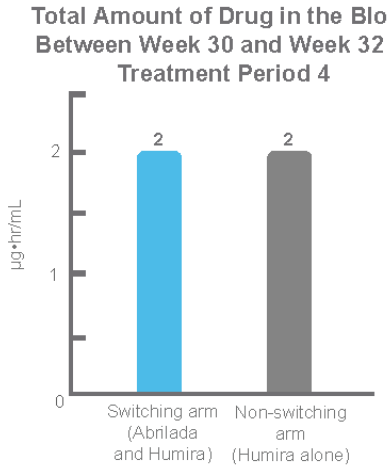
What were the results of the study?

Do multiple switches between Humira and Abrilada change how adalimumab acts in the body compared to treatment with Humira alone?

What was the amount of adalimumab in the blood after participants were treated with Humira or multiple switches of Humira and Abrilada?

- The highest amount of adalimumab in the blood at the end of Treatment Period 4 is shown in the first figure below. The amount of drug in the blood was measured in micrograms per milliliter, also called µg/mL. This was approximately 8 µg/mL in the switching arm and similar in the non-switching arm.
- The calculated amount of adalimumab in the blood during the 15 days between Week 30 and Week 32 in Treatment Period 4 is shown in the second figure below. The units for the total amount of drug in the blood over time is microgram hours per milliliter or µg•hr/mL. This was approximately 2 µg•hr/mL in the switching arm and similar in the non-switching arm.





Based on these results, the researchers have decided that switching between Abrilada and Humira does not make any clinically meaningful difference compared to continuous treatment with Humira.

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.

In Treatment Period 1, 107 out of 445 (24%) participants in this study had at least 1 medical problem and there were 12 (3%) participants who left the study because of medical problems. The medical problems seen were as expected for participants treated with Humira.

In Treatment Period 2 to the end of the study, 82 out of the 213 (38%) participants in the switching arm and 62 out of the 214 (29%) participants in the non-switching arm had at least 1 medical problem. The most common medical problems – those reported by more than 1% of participants – are described in Table 1 for Treatment Period 2 to the end of the study. A total of 8 (4%) participants in the switching arm and 9 (4%) participants in the non-switching arm left the study because of medical problems.

Below are instructions on how to read Table 1. These instructions can also be used to understand Table 2.

Instructions for Understanding Table 1.

- The **1st** column of Table 1 lists medical problems that were commonly reported from Treatment Period 2 to the end of the study. All medical problems reported by more than 1% of participants are listed.
- The **2nd** column tells how many of the 213 participants in the switching arm reported each medical problem. Next to this number is the percentage of the 213 participants in the switching arm who reported the medical problem.
- The **3rd** column tells how many of the 214 participants in the non-switching arm reported each medical problem. Next to this number is the percentage of the 214 participants in the non-switching arm who reported the medical problem.
- Using these instructions, you can see that 46 out of the 213 (22%) participants in the switching arm had medical problems compared with 38 out of the 214 (18%) participants in the non-switching arm during Treatment Period 2 to the end of the study.

Table 1. Commonly reported medical problems by study participants during Treatment Period 2 to the end of the study

Medical problem	Switching Arm: Humira and Abrilada (213 Participants)	Non-switching Arm: Humira (214 Participants)
Any	46 out of 213 participants (22%)	38 out of 214 participants (18%)
Abdominal pain in the upper part of the tummy	3 out of 213 participants (1%)	0 out of 214 participants (0%)
Reaction at or around the injection site	6 out of 213 participants (3%)	4 out of 214 participants (2%)

Swelling	3 out of 213 participants (1%)	1 out of 214 participants (Less than 1%)
COVID-19	16 out of 213 participants (8%)	10 out of 214 participants (5%)
COVID-19 infection of the lung	2 out of 213 participants (1%)	4 out of 214 participants (2%)
Infection of the nose and throat (nasopharyngitis)	0 out of 213 participants (0%)	7 out of 214 participants (3%)
Common cold (upper respiratory tract infection)	3 out of 213 participants (1%)	3 out of 214 participants (1%)
Infection of the kidneys, bladder, or urethra	4 out of 213 participants (2%)	3 out of 214 participants (1%)
Liver test levels increased for ALT	3 out of 213 participants (1%)	1 out of 214 participants (Less than 1%)
Liver test levels increased for AST	3 out of 213 participants (1%)	1 out of 214 participants (Less than 1%)
Positive COVID-19 test	18 out of 213 participants (8%)	14 out of 214 participants (7%)
Rheumatoid arthritis	3 out of 213 participants (1%)	1 out of 214 participants (Less than 1%)
Headache	4 out of 213 participants (2%)	4 out of 214 participants (2%)
Cough	3 out of 213 participants (1%)	1 out of 214 participants (Less than 1%)
Reddening of the skin	6 out of 213 participants (3%)	4 out of 214 participants (2%)
Rash	3 out of 213 participants (1%)	0 out of 214 participants (0%)
High blood pressure	2 out of 213 participants (1%)	5 out of 214 participants (2%)

ALT: alanine aminotransferase (one of the liver enzymes tested in liver function tests); AST: aspartate aminotransferase (one of the liver enzymes tested in liver function tests); COVID-19: Coronavirus disease 2019.

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.

In Treatment Period 1, 13 out of 445 (3%) participants in this study had at least 1 serious medical problem while taking Humira. The serious medical problems seen were as expected for participants taking Humira.

In Treatment Period 2 to the end of the study, 3 out of the 213 (1%) participants in the switching arm and 8 out of the 214 (4%) participants in the non-switching arm had at least 1 serious medical problem as shown in Table 2 (instructions on how to read this type of table are provided earlier).

Table 2. Serious medical problems by study participants during Treatment Period 2 to the end of the study

Serious medical problems	Switching Arm: Humira and Abrilada (213 Participants)	Non-switching Arm: Humira (214 Participants)
Any	3 out of 213 participants (1%)	8 out of 214 participants (4%)
Blood loss and low red blood cell count	0 out of 213 participants (0%)	1 out of 214 participants (Less than 1%)
Inflammation or swelling in the eye	1 out of 213 participants (Less than 1%)	0 out of 214 participants (0%)
Inflammation or swelling of the gall bladder	0 out of 213 participants (0%)	1 out of 214 participants (Less than 1%)
Tender lump filled with pus (abscess) on a limb	1 out of 213 participants (Less than 1%)	0 out of 214 participants (0%)
COVID-19	0 out of 213 participants	1 out of 214 participants

	(0%)	(Less than 1%)
COVID-19 infection of the lung	1 out of 213 participants (Less than 1%)	2 out of 214 participants (1%)
Infection of the lung	0 out of 213 participants (0%)	1 out of 214 participants (Less than 1%)
Bleeding on the surface of the brain	0 out of 213 participants (0%)	1 out of 214 participants (Less than 1%)
Stroke	0 out of 213 participants (0%)	1 out of 214 participants (Less than 1%)

COVID-19: Coronavirus disease 2019.

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:

www.clinicaltrials.gov	Use the study identifier NCT04230213
www.clinicaltrialsregister.eu	Use the study identifier 2019-000284-24

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!