Clinical Study Results

1. STUDY NAME

Title of the Study:	A Randomized, Double-Blind Phase 3 Study to Assess the Efficacy and Safety of ABP 710 Compared to Infliximab in Subjects with Moderate to Severe Rheumatoid Arthritis
Brief Title:	How Did ABP 710 Compare to Infliximab in Improving Symptoms of Rheumatoid Arthritis?
Protocol Number:	20140111
EU Trial Number:	2014-004704-29
Other Identifiers (ClinicalTrials.gov):	NCT02937701
Date of This Summary:	22 May 2019

What does this summary cover?

This summary shows the main results from one clinical study. The results are only for this study. Other studies may find different results. Researchers and health authorities look at the results of many studies to decide which medicines work best and are safest for patients.

2. WHO SPONSORED THIS STUDY?

Amgen Inc.
One Amgen Center Drive
Thousand Oaks, CA 91320-1799 USA
Phone (United States): +1 805-447-1000

Amgen Inc. is the sponsor of the study and manufactured ABP 710, the investigational medicine in this study. Amgen would like to thank everyone who participated in this study and feels it is important to share the results of this study.

3. General Information About the Clinical Study

Where and when was the study done?

- This study took place in Australia, Bulgaria, Canada, Czech Republic, Germany, Hungary, Poland, Spain, and the United States.
- The study began in October 2016 and ended in August 2018.
- The study was completed as planned.

Why was the study done?

This study was done to help patients with rheumatoid arthritis (also known as "RA"). RA is a disease that causes pain and swelling (known as inflammation) in or around the joints. These joint problems are caused when the immune system – whose job is to attack foreign invaders like viruses and other germs – mistakenly attacks the joints instead.

Patients with RA tend to have a high level of a protein called TNF (stands for tumor necrosis factor) in their blood, which makes their immune systems more active. If RA inflammation is left untreated, joints can become loose or stiff, and even deformed.

Common treatments for RA include medicines that control pain, reduce swelling, and lower the activity of the immune system. Some patients need more than one medicine to treat their RA. Doctors may prescribe more than one medicine together, including:

- Methotrexate (also called "MTX"): A medicine that lowers immune system activity
- Infliximab (also known as Remicade®): A medicine delivered into the vein through a needle (called 'intravenous' or 'IV') that attaches to TNF and keeps it from activating the immune system

Infliximab is a type of medicine called a "biologic." Biologics are made of a complex mix of sugars, proteins, genetic material, living cells, or groups of cells called tissues.

ABP 710 is another IV biologic medicine. It also attaches to TNF to keep it from triggering the immune system. ABP 710 was created to be highly similar to infliximab. Once a new biologic product has been tested and is shown to be highly similar to a reference biologic product, it is called a "biosimilar." In clinical studies like this one, ABP 710 is called an investigational medicine, and infliximab is called the reference product.

	Biologic (Reference Product)	Biosimilar (Investigational Medicine)
	Complex mixture from human, animal, or microscopic living sources	Similar structure and quality features as the biologic
	Approved for use by a country's health authority	Must be highly similar in makeup, safety, and function to be approved for use
	Has been shown in studies to improve specific health problems	No clinically meaningful differences compared to results of the biologic
	Has been tested for safety in clinical studies	No clinically meaningful differences in safety results compared to biologic
	**Infliximab** was the reference product in this study	**ABP 710** was tested as a biosimilar in this study

This was a phase 3 study, which is usually the last stage for testing investigational medicines in humans before they are approved for use. The main purpose of the study was to compare RA symptom improvement in participants who were given ABP 710 to those who were given the infliximab reference product, 22 weeks after starting treatment.

4. WHAT PATIENTS/PEOPLE WERE INCLUDED IN THIS STUDY?

Who took part in the study?

This study included 558 adult men and women with moderate to severe RA. Of the 558 participants, 437 participants (78%, or about 8 out of 10) were women and 121 participants (22%, or about 2 out of 10) were men. Participants ranged in age from 19 to 77 years old. The average age of all participants was about 55 years old.

The study took place at 75 study centers across Europe, North America, and Australia. The numbers of participants in each country are shown in the following map:

Participants were examined by a study doctor and chose to be in the study if they:

- were between 18 and 80 years old
- were diagnosed with RA and had moderate to severe RA for at least 3 months before starting the study
- had at least 6 swollen joints and at least 6 tender joints
- were taking MTX for at least 12 weeks, on a dose that did not change in the 8 weeks leading up to the study, and were willing to continue their MTX during the study
- had no history or symptoms of the lung infection tuberculosis
- did not have a severe type of RA (called Class IV),
- did not have additional joint diseases, uncontrolled diabetes, heart failure, high blood pressure, liver, kidney, or nervous system diseases, or certain types of cancer
- had not taken 2 or more biologic medicines in the past, did not take certain RA medicines recently, and did not take infliximab in the past
- were not pregnant, or were willing to prevent pregnancy in a female partner

5. WHICH MEDICINES WERE STUDIED?

In this study, ABP 710 was compared with infliximab. Participants had an equal chance (50/50) of receiving either of these medicines as their study treatment.

Neither the participants nor the study doctors could choose which treatment participants were given. Participants agreed to be put into a treatment group by

chance (“randomized”) using an automated computer system. This is like flipping a coin or drawing numbers out of a hat.

This was a “double-blinded” study, which means that the participants and the study doctors could only find out whether the participant was given ABP 710 or infliximab after the study was over. This was done to make sure the study results were not influenced in any way.

Participants were examined by study doctors at each visit to the study center. At some of these visits, participants answered questions on several different forms about their RA symptoms. About half way through the study, some participants were randomly chosen to be switched to receive a different treatment from what they started. 4 weeks after the treatment finished, all participants had a final checkup to see how they were feeling. This study had 2 main parts:

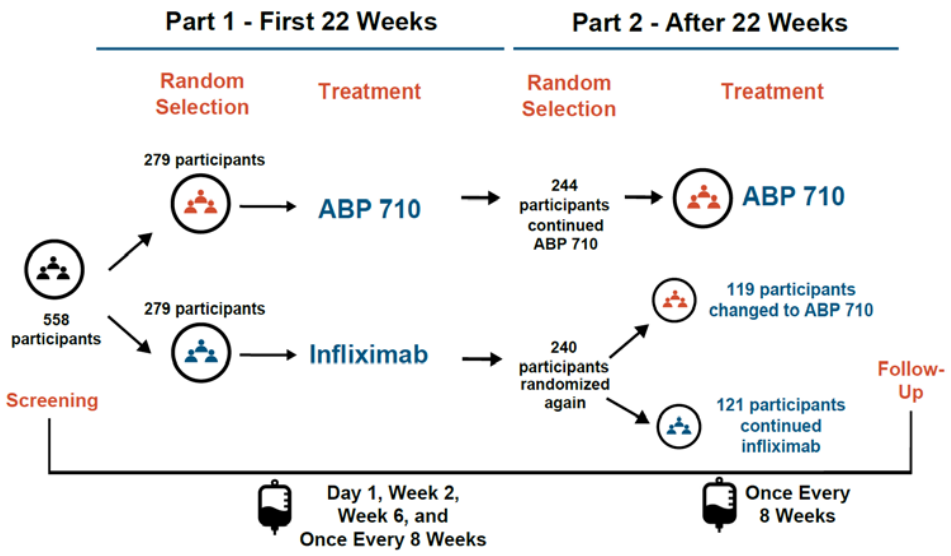
Part 1 – First 22 Weeks of Treatment

After being randomly assigned to a treatment group, participants were given either ABP 710 or the infliximab reference product as through an IV into their vein. The amount of medicine (the dose) was calculated for each participant based on his or her weight. Participants were given their first treatment at their first visit. They continued their same treatment again at week 2, week 6, and once every 8 weeks after that for 22 weeks.

Part 2 – After 22 Weeks of Treatment

After 22 weeks of treatment, participants who started in the infliximab group were randomly separated into different treatment groups again. These participants had an equal chance (about 50/50) to either stay on infliximab or be switched to ABP 710 until the study was over.

Participants who started in the ABP 710 group continued for another 24 weeks on ABP 710. Treatment during the final 24 weeks was also blinded. Participants and study doctors did not know who was being given ABP 710 and who was being given infliximab. Participants received their assigned treatment once every 8 weeks for another 24 weeks.



Of the 558 participants who were screened, 556 participants in this study were given at least 1 dose of either ABP 710 or infliximab. 484 participants (244 in the ABP 710 group and 240 in the infliximab group) completed the first 22 weeks of study treatment. Overall, 435 participants (78%, or about 8 out of 10) completed the entire study and 123 participants (22%, or about 2 out of 10) left the study before it ended.

6. WHAT WERE THE SIDE EFFECTS?

What is an adverse reaction (sometimes called a side effect)?

A lot of research is needed to know whether a medicine causes a side effect. All medicines can cause side effects, or unwanted medical problems that may happen when you take a medicine. In a clinical study, the study doctors record all unwanted medical problems that occur during the study, including side effects that they believe are possibly caused by the investigational medicine each patient is receiving. These are also called “adverse reactions.”

What side effects related to the treatment were seen?

When reporting side effects in this study, the study doctor did not know which treatment a participant was receiving. A side effect was recorded as “serious” if it caused death, was life threatening, required the participant to stay in a hospital, or the study doctor thought it was clinically significant enough to be recorded as “serious”.

During the study, 1 participant in the ABP 710 group was diagnosed with pneumonia, a lung infection caused by viruses and bacteria. The participant was hospitalized and treated for the infection but died while in the hospital. Study doctors believe the infection may have been related to the study treatment.

The following table shows how many participants had side effects that were considered related to treatment.

Participants with Side Effects During the Study

	Part 1 – First 22 Weeks		Part 2 – After 22 Weeks		
	ABP 710 (278 participants)	Infliximab (278 participants)	ABP 710 only (241 participants)	Infliximab only (121 participants)	Infliximab then ABP 710 (119 participants)
How many participants had serious side effects?	4 (1%)	3 (1%)	3 (1%)	0	0
How many participants had non-serious side effects?	53 (19%)	57 (21%)	47 (20%)	29 (24%)	26 (22%)
How many participants died from side effects?	1 (less than 1%)	0	0	0	0
How many participants stopped taking the study medicine because of side effects?	11 (4%)	10 (4%)	7 (3%)	4 (3%)	2 (2%)

The following table shows the serious side effects considered by the study doctor as related to treatment that occurred during the study.

Serious Side Effects During the Study

	Part 1 – First 22 Weeks		Part 2 – After 22 Weeks		
	ABP 710 (278 participants)	Infliximab (278 participants)	ABP 710 only (241 participants)	Infliximab only (121 participants)	Infliximab then ABP 710 (119 participants)
Reduced pumping of the heart	0	0	1 (less than 1%)	0	0
Heart or blood vessel problems that cause swelling in the body	0	0	1 (less than 1%)	0	0
Skin infection	0	0	1 (less than 1%)	0	0
Chest pain	1 (less than 1%)	0	0	0	0
Infection with a fever	0	0	1 (less than 1%)	0	0
Lung infection caused by bacteria	0	1 (less than 1%)	0	0	0
Lung infection caused by pneumococcal bacteria	2 (less than 1%)	0	0	0	0
Lung infection caused by a virus	0	1 (less than 1%)	0	0	0
Blood clot	0	1 (less than 1%)	0	0	0
Higher level of a liver blood test (called ALT)	0	0	1 (less than 1%)	0	0
Bladder cancer	0	1 (less than 1%)	0	0	0

The following table shows the most common non-serious side effects considered by the study doctor as related to treatment. These side effects occurred in at least 1% of participants in any treatment group.

Most Common Non-serious Side Effects During the Study

	Part 1 – First 22 Weeks		Part 2 – After 22 Weeks		
	ABP 710 (278 participants)	Infliximab (278 participants)	ABP 710 only (241 participants)	Infliximab only (121 participants)	Infliximab then ABP 710 (119 participants)
Common cold	8 (3%)	4 (1%)	6 (3%)	4 (3%)	3 (3%)
Low white blood cell count	2 (1%)	0	4 (2%)	0	3 (3%)
Allergic reaction	1 (less than 1%)	2 (less than 1%)	2 (less than 1%)	3 (3%)	0
Infection of nose and upper throat	3 (1%)	2 (less than 1%)	0	3 (3%)	2 (2%)
Rheumatoid arthritis	5 (2%)	3 (1%)	4 (2%)	1 (less than 1%)	1 (less than 1%)
Nausea	4 (1%)	3 (1%)	0	0	0
Painful irritation of the tubes in the lungs (bronchitis)	4 (1%)	1 (less than 1%)	4 (2%)	1 (less than 1%)	1 (less than 1%)
Allergic skin reaction	0	5 (2%)	1 (less than 1%)	1 (less than 1%)	2 (2%)
Skin redness	1 (less than 1%)	4 (1%)	1 (less than 1%)	2 (2%)	1 (less than 1%)
Headache	3 (1%)	2 (less than 1%)	0	1 (less than 1%)	1 (less than 1%)
Sore throat	4 (1%)	1 (less than 1%)	1 (less than 1%)	2 (2%)	0
Dizziness	4 (1%)	0	0	0	0
Cold sores around the mouth	4 (1%)	0	2 (less than 1%)	1 (less than 1%)	0
Rash	3 (1%)	1 (less than 1%)	1 (less than 1%)	1 (less than 1%)	1 (less than 1%)
Infection of breathing passages or lungs	3 (1%)	1 (less than 1%)	2 (less than 1%)	0	0
Higher level of a liver blood test (called ALT)	2 (less than 1%)	0	3 (1%)	1 (less than 1%)	0
High blood pressure	1 (less than 1%)	0	1 (less than 1%)	0	2 (2%)
Vomiting	2 (less than 1%)	1 (less than 1%)	1 (less than 1%)	0	2 (2%)
Ear infection	0	0	0	2 (2%)	0
Lower than normal number of white blood cells called neutrophils	0	0	0	0	2 (2%)
Bladder (or urinary) infection	0	2 (less than 1%)	0	2 (2%)	0

This section only shows the most frequently reported side effects considered by the study doctor as related to treatment. No single clinical study can give a complete picture of the benefits and risks of a medicine. Information about other side effects may be available at the websites listed at the end of this summary.

Treatments that work on the immune system (like ABP 710 and infliximab) are known to cause certain types of side effects. In this study, researchers looked at all the side effects that are known to be associated with treatments such as infliximab or ABP 710. These types of side effects (listed below) were found to be similar in all treatment groups. No participants reported some other known side effects such as, new or worsening liver infection called Hepatitis B, or diseases caused when the brain or spinal cord are mistakenly attacked by the immune system.

- Allergic reaction
- Abnormal numbers of blood cells
- Liver problems
- Cancers
- Infections that happen because of a weakened immune system, including serious infections
- Heart or blood vessel problems that cause swelling in the body
- Other diseases where the immune system attacks healthy cells

7. WHAT WERE THE OVERALL RESULTS OF THE STUDY?

How did participants' RA symptoms improve after 22 weeks of treatment with ABP 710 compared with infliximab?

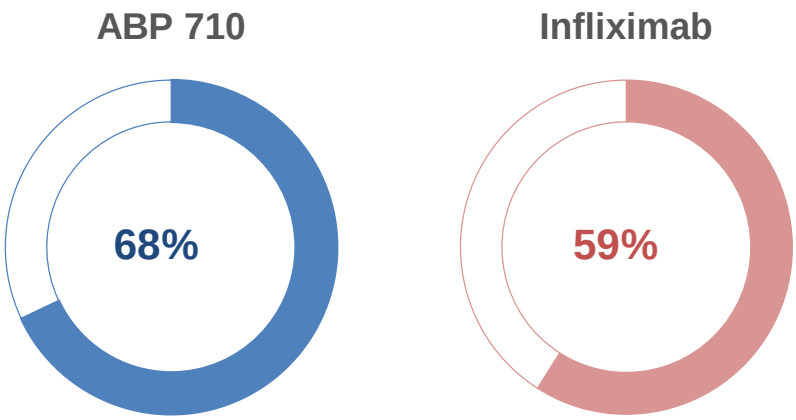
In this study, researchers looked at the RA symptoms of participants after 22 weeks of treatment with ABP 710 or infliximab. Researchers used a scale called the ACR score (which stands for the American College of Rheumatology). The ACR score is used to measure the amount of improvement people have when being treated for RA. The ACR score counts the number of swollen and tender joints, plus:

- how the participants feel they are doing,
- how their doctors feel they are doing,
- how much pain the participants are in,
- how much the RA symptoms keep participants from doing every day activities, and
- laboratory tests that measure inflammation.

A score of ACR20 was used in this study. To reach that score, a participant had to have at least 20% (or 1 in 5) of his or her joints show improvement after 22 weeks of

treatment. The participant also had to be doing or feeling at least 20% better in 3 of the 5 other categories listed above.

The results in the figure below show the percentage of participants in each group who reached an ACR20 score 22 weeks after starting treatment. 68% of participants in the ABP 710 group and 59% of participants in the infliximab group showed at least a 20% improvement in their RA symptoms after 22 weeks.



Researchers reviewed the results from both treatment groups. Researchers predicted that the results would be very similar between the ABP 710 and infliximab groups. The difference in this study, 9% higher for ABP 710, was a slightly higher response rate than predicted.

Other measurements showing similarity between ABP 710 and infliximab are available at the websites listed at the end of this summary.

8. How Has This Study Helped Patients and Researchers?

These results are only for this clinical study, which looked at a sample of 558 people with RA. Not all participants in the study had the same results. The results for any individual participant could have been better or worse than the results for his or her group. Other studies may find different results.

This research may help future patients and their families by helping doctors understand more about the treatment being studied. These results are not an explanation of what a treatment can and cannot do for an individual.

9. ARE THERE PLANS FOR FURTHER STUDIES?

If more clinical studies are done, they may be listed on public websites, such as those below. Search for the study medicine name ABP 710 on the websites listed below.

10. WHERE CAN I FIND MORE INFORMATION ABOUT THIS STUDY?

To find out more about this study, check these websites:

www.clinicaltrials.gov. Use the study identifier NCT02937701
www.clinicaltrialsregister.eu. Use the study identifier 2014-004704-29
www.amgentrials.com. Use the study identifier 20140111

Amgen has committed to make research results available to the public. This summary has been provided as part of that commitment and should not be used for any other purpose. It should not be considered to make a claim for any product or to guide treatment decisions.

If you participated in the study and have questions about the study results, the doctor or staff at your study site may be able to answer them.