Clinical Study Results

1. Study Name

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.

Title of the Study:	A Randomized, Double-Blind, Phase 3 Study of ABP 501 Efficacy and Safety Compared to Adalimumab in Subjects with Moderate to Severe Rheumatoid Arthritis
Brief Title:	How Did ABP 501 Compare to Adalimumab in Improving Symptoms of Rheumatoid Arthritis?
Protocol Number:	20120262
EU Trial Number:	2013-000525-31
Other Identifiers (ClinicalTrials.gov):	NCT01970475
Date of This Summary:	08 October 2018

2. Who Sponsored This Study?

Amgen Inc.
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Amgen Inc. is the sponsor of the study and manufactured ABP 501, 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 Trial

Where and when was the study done?

- This study took place in Bulgaria, Canada, Czech Republic, Germany, Hungary, Mexico, Poland, Romania, Russian Federation, Spain, United Kingdom, and the United States.
- The study began in October 2013 and ended in November 2014.
- 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 (MTX): A medicine that lowers immune system activity
- Adalimumab (HUMIRA®): An injected medicine that attaches to TNF and keeps it from activating the immune system

Adalimumab 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 501 (AMJEVITA™ or AMGEVITA™) is another injected biologic. It also attaches to TNF to keep it from triggering the immune system. ABP 501 was created to be highly similar to adalimumab (HUMIRA®). 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 501 is called an investigational medicine, and adalimumab 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
	**Adalimumab** was the reference product in this study	**ABP 501** was tested as a biosimilar in this study

This was a phase 3 study, which is usually the latest 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 501 to those who were given the adalimumab reference product, 24 weeks after starting treatment.

4. What Patients/People Were Included in This Study?

Who took part in the study?

This study included 526 adult men and women with moderate to severe RA. Of the 526 participants, 426 participants (81%, or about 8 out of 10) were women and 100 participants (19%, or about 2 out of 10) were men. Participants ranged in age from 21 to 80 years old. The average age of all participants was about 56 years old.

The study took place at 92 study centers across Europe, North America, and Latin America. The numbers of participants in each country are shown in the map below:

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 (Class IV) type of RA, 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, and did not take adalimumab in the past

5. Which Medicines Were Studied?

What investigational medicines were studied?

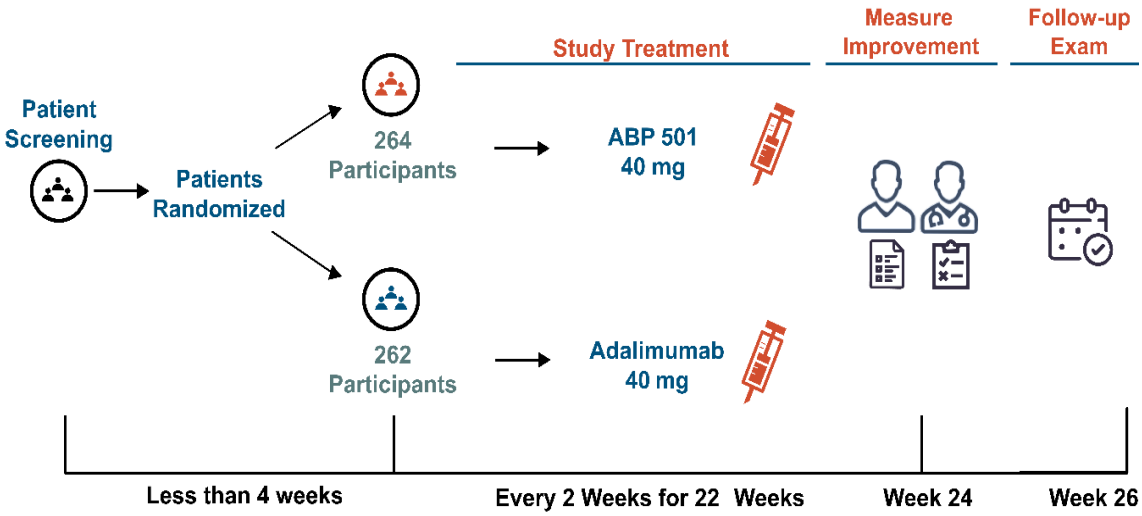
In this study, ABP 501 was compared with adalimumab. Participants had an equal chance (50/50) of receiving either of these medicines as their study treatment.

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 501 or adalimumab

after the study was over. This was done to make sure the study results were not influenced in any way.

After being randomly assigned to a treatment group, participants were given either 40 mg of ABP 501 or 40 mg of the adalimumab reference product as an injection under their skin. Participants continued the same treatment every 2 weeks for up to 22 weeks. Participants were examined by study doctors at each visit to the study center, up to 24 weeks after starting treatment. At some of these visits, participants answered questions on several different forms about their RA symptoms. 2 weeks after the treatment finished, participants had a final checkup to see how they were feeling after the study treatment ended.



All 526 participants in the study were given at least 1 dose of either ABP 501 or adalimumab. Of those who started the study, 494 participants (243 in the ABP 501 group and 251 in the adalimumab group) completed the study. 32 participants did not complete the study for these reasons: 17 participants chose not to take part anymore, 5 left due to side effects, 5 left for other reasons, 4 lost contact with the study site, and 1 left after not following the study instructions.

6. What Were the Side Effects?

What is an adverse reaction (sometimes called side effects)?

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 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 caused a birth defect. In this study, no participants died due to a side effect.

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

Side Effects During the Study		
	ABP 501 Group (264 participants)	**Adalimumab Group (262 participants)**
How many participants had serious side effects?	4 participants (2%)	1 participant (less than 1%)
How many participants had non-serious side effects?	48 participants (18%)	54 participants (21%)
How many participants died from side effects?	0 participants	0 participants
How many participants stopped taking the study medicine because of side effects?	4 participants (2%)	1 participant (less than 1%)

The table below shows the serious side effects that occurred.

Serious Side Effects During the Study		
Serious Side Effect	**ABP 501 Group (264 participants)**	**Adalimumab Group (262 participants)**
Blood infection	2 participants (less than 1%)	0 participants
Burst appendix	1 participant (less than 1%)	0 participants
Heart failure	1 participant (less than 1%)	0 participants
Allergic reaction	1 participant (less than 1%)	0 participants
High blood pressure	1 participant (less than 1%)	0 participants
Infected fluid in the belly	1 participant (less than 1%)	0 participants
Lung infection (pneumonia) caused by bacteria or a virus	1 participant (less than 1%)	0 participants
Lung infection (pneumonia) caused by a fungus	0 participants	1 participant (less than 1%)

The table below shows the non-serious side effects that occurred in at least 2 participants in either treatment group.

Non-serious Side Effects During the Study		
Non-serious Side Effect	**ABP 501 Group (264 participants)**	**Adalimumab Group (262 participants)**
Redness at the injection site	3 participants (1%)	5 participants (2%)
Common cold	3 participants (1%)	5 participants (2%)
Rash at the injection site	3 participants (1%)	4 participants (2%)
Cold sores around the mouth	3 participants (1%)	4 participants (2%)
Higher level of a liver blood test (called ALT)	3 participants (1%)	2 participants (less than 1%)
Sinus infection	4 participants (2%)	1 participant (less than 1%)
Bladder (or urinary) infection	3 participants (1%)	2 participants (less than 1%)
Hair loss	3 participants (1%)	1 participant (less than 1%)
Painful irritation of the tubes in the lungs (bronchitis)	3 participants (1%)	1 participant (less than 1%)
Headache	2 participants (less than 1%)	2 participants (less than 1%)
Shingles	3 participants (1%)	1 participant (less than 1%)
High blood pressure	2 participants (less than 1%)	2 participants (less than 1%)
Swollen sore throat	2 participants (less than 1%)	2 participants (less than 1%)
Cough	1 participant (less than 1%)	2 participants (less than 1%)
Infection of nose and upper throat	1 participant (less than 1%)	2 participants (less than 1%)
Joint pain	0 participants	2 participants (less than 1%)
Heavy sweating	2 participants (less than 1%)	0 participants
Itching at the injection site	0 participants	2 participants (less than 1%)
Low number of white blood cells	2 participants (less than 1%)	0 participants
Sensitivity to light	0 participants	2 participants (less than 1%)
Swelling and pain in the chest cavity lining and lungs	2 participants (less than 1%)	0 participants
Rash	2 participants (less than 1%)	0 participants
Blood test results that could suggest a liver problem	0 participants	2 participants (less than 1%)
Itchy red welts (hives)	0 participants	2 participants (less than 1%)

Treatments that work on the immune system (like ABP 501 and adalimumab) are known to cause certain side effects. Researchers looked at all the "known" side effects in this study and found they were similar in both treatment groups.

This section only shows the most frequently reported side effects. Information about other side effects may be available at the websites listed at the end of this summary.

7. What Were the Overall Results of the Study?

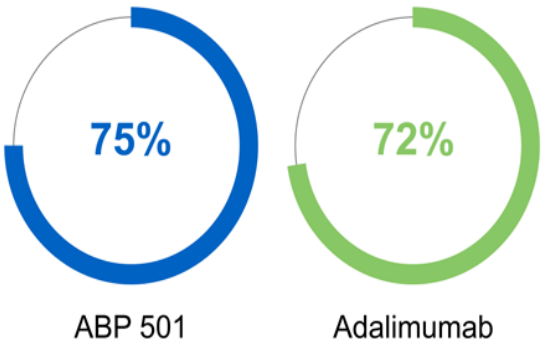
How did participants' RA symptoms improve after 24 weeks of treatment with ABP 501 compared with adalimumab?

In this study, researchers looked at the RA symptoms of participants after 24 weeks of treatment with ABP 501 or adalimumab. 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 20% (or 1 in 5) of their joints show improvement after 24 weeks of treatment. The participant also had to be doing or feeling 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 24 weeks after starting treatment. 75% of participants in the ABP 501 group and 72% of participants in the adalimumab group showed a 20% improvement in their RA symptoms after 24 weeks.



Researchers also used a calculation called “risk ratio” to compare the results of the 2 treatment groups. The closer a risk ratio is to 1, the more alike the treatments are. In this study:

ABP 501 vs. Adalimumab → Risk Ratio = 1.039

Researchers studied these findings. Based on the above results, they determined that ABP 501 worked the same as adalimumab in this study.

These are just some of the main results of the study. More results may be available at the websites listed at the end of this summary.

8. How Has This Study Helped Patients and Researchers?

What is important to know about these results?

These results are only for this clinical study, which looked at a sample of 526 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 their group. These results are not an explanation of what a treatment can and cannot do for an individual. No single clinical study can give a complete picture of the benefits and risks of a medicine. 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.

9. Are There Plans for Further Studies?

Will there be more studies with ABP 501?

If more clinical studies are done, they may be listed on public websites, such as those below. Search for the study medicine name ABP 501 or AMJEVITA™ (AMGEVITA™) on these or other websites:

- www.clinicaltrials.gov
- www.clinicaltrialsregister.eu
- www.amgentrials.com

10. Where Can I Find More Information About This Study?

Where can I learn more?

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.

Some information in this summary may be different from the approved labelling for AMJEVITA™ (AMGEVITA™). Your healthcare professional should refer to the full prescribing information for proper use of AMJEVITA™ (AMGEVITA™).

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

- www.clinicaltrials.gov. Use the study identifier NCT01970475
- www.clinicaltrialsregister.eu. Use the study identifier 2013-000525-31
- www.amgentrials.com. Use the study identifier 20120262

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.