Clinical Study Results

Study Name

Title of the study:	A Multicenter Double-blind, Randomized Controlled Study of Etanercept and Methotrexate in Combination or as Monotherapy in Subjects With Psoriatic Arthritis
Brief Title:	How did Etanercept Alone and in Combination with Methotrexate Improve Symptoms of Psoriatic Arthritis?
Protocol Number:	20130207
EU Trial Number	2014-004869-24
Other Identifiers	NCT02376790
Date of This Summary	3 December 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.

1. 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., authorized marketer of etanercept in the United States and Canada and owner of subsidiary Immunex Corporation, etanercept's manufacturer, is the sponsor of the study. Amgen would like to thank everyone who participated in this study and feels it is important to share the results of this study.

Approved

2. General Information About The Clinical Trial

Where and when was the study done?

- This study took place at 124 centers in Europe, Latin America, North America, and South Africa.
- The study began in March 2015 and ended in July 2018.
- The study was completed as planned.

Why was the study done?

This study was done to help patients with a condition called psoriatic arthritis (also known as "PsA"). PsA can cause pain, stiffness, and swelling in or around the joints. This type of arthritis often happens in people with psoriasis. Psoriasis is a condition that causes itchy, red patches with silvery scales on the skin.

PsA is caused when the immune system, whose job is to attack foreign invaders like viruses and other germs, mistakenly attacks healthy parts of the body instead.

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

Methotrexate (or MTX) is a medicine commonly used to treat PsA because it lowers immune system activity. Some patients still have PsA symptoms while taking MTX. Etanercept (also called Enbrel) is a medicine approved by the government health agencies in some countries to treat PsA. When used in studies like this one, it is called an "investigational medicine."

This was a phase 3 study, the late stage of the development process of medicines for humans. This study included investigational medicines and a "placebo." A placebo does not contain any medicine and helps researchers compare the effects of a new medicine to taking no medicine.

The main purpose of the study was to compare PsA symptom improvement in participants who were given one of the following treatment combinations for 24 weeks:

- Etanercept injection + placebo pills
- Etanercept injection + MTX pills
- Placebo injection + MTX pills

Approved

3. Who Was Included In This Study?

Who took part in the study?

This study included 851 participants with PsA. 432 participants (51%, or about half) were women and 419 participants (49%, or about half) were men. They ranged in age from 18 to 87 years old. The average age of participants was about 48 years old. Most of the participants had PsA symptoms for less than 1 year when the study began.

This study took place at 124 study centers across around the world. The numbers of participants in each country are listed below:

United States	347	Canada	25
Russia	77	Greece	18
Mexico	73	Portugal	16
Poland	61	Latvia	12
Chile	53	Argentina	10
Bulgaria	45	Spain	9
South Africa	32	United Kingdom	9
Czech Republic	32	France	1
Hungary	31		

Approved

Men and women at least 18 years old were examined by a study doctor and chosen to be in the study if they:

- had been diagnosed with PsA
- had at least 3 swollen joints, 3 tender joints, and had at least 1 patch of psoriasis on their skin that was about 1 inch (2 centimeters) or larger
- were not using MTX, and had not used etanercept or a medicine similar to etanercept in the past
- had not changed their current PsA treatment recently
- did not have serious medical conditions, such as uncontrolled diabetes, heart failure, liver disease, kidney disease, or immune system diseases
- were not pregnant and were not planning to become pregnant, and were willing to prevent pregnancy in a female partner

4. Which Medicines Were Studied?

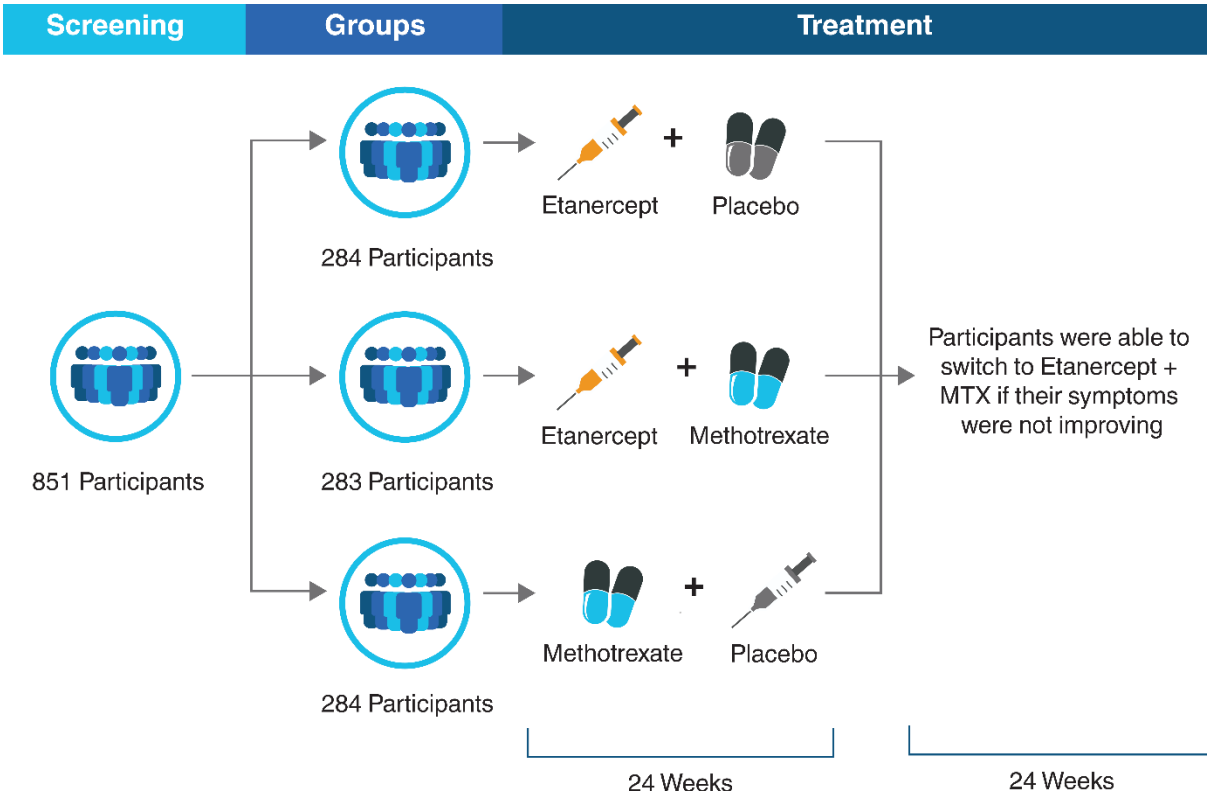
In this study, etanercept + MTX was compared to MTX + placebo, and etanercept + placebo was compared to MTX + placebo. Participants had an equal chance of receiving any of the 3 study medicine combinations.

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 which treatment the participant was given after the initial treatment period was over and the entire study was completed. 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. After 24 weeks of treatment, any participants who still had PsA symptoms received etanercept + MTX treatment. This was called the "rescue period". After another 24 weeks of treatment, all participants had a final checkup to see how they were feeling.

Approved



5. 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 participant is receiving. These are also called "adverse reactions."

What side effects related to the investigational medicine or placebo 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 important enough to record as "serious". No participant died due to a side effect. The table below shows how many participants had side effects that were considered related to treatment.

Approved

Side Effects During the Study			
	Etanercept + Placebo (282 participants)	**Etanercept + MTX (284 participants)**	**MTX + Placebo (282 participants)**
How many participants had serious side effects?	3 participants (1%)	3 participants (1%)	5 participants (2%)
How many participants had non-serious side effects?	66 participants (23%)	76 participants (27%)	57 participants (20%)
How many participants died from side effects?	0 participants (0%)	0 participants (0%)	0 participants (0%)
How many participants stopped taking the study medicine because of side effects?	5 participants (2%)	9 participants (3%)	8 participants (3%)

The table below 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			
Serious side effect	**Etanercept + Placebo (282 participants)**	**Etanercept + MTX (284 participants)**	**MTX + Placebo (282 participants)**
Bronchitis	1 participant (less than 1%)	0 participants (0%)	0 participants (0%)
Serious infection of the soft tissue	1 participant (less than 1%)	0 participants (0%)	0 participants (0%)
Respiratory infection caused by fungus	0 participants (0%)	0 participants (0%)	1 participant (less than 1%)
Increased level of liver enzyme 'alanine aminotransferase' in the blood	0 participants (0%)	0 participants (0%)	2 participants (1%)
Skin infection causing redness and swelling	1 participant (less than 1%)	0 participants (0%)	0 participants (0%)

Approved

Serious Side Effects During the Study			
Serious side effect	**Etanercept + Placebo (282 participants)**	**Etanercept + MTX (284 participants)**	**MTX + Placebo (282 participants)**
Abnormal liver function	0 participants (0%)	1 participant (less than 1%)	0 participants (0%)
Cancer that starts in pigment-containing cells in skin, mouth, intestines, or eye	0 participants (0%)	1 participant (less than 1%)	0 participants (0%)
Nerve damage that may cause pain, tingling, or numbness	0 participants (0%)	0 participants (0%)	1 participant (less than 1%)
Abnormally fast heart beat	0 participants (0%)	1 participant (less than 1%)	0 participants (0%)
Urinary tract infection	0 participants (0%)	0 participants (0%)	1 participant (less than 1%)

The table below shows the non-serious side effects considered by the study doctor as related to treatment that occurred in at least 1% of all participants (or about 1 out of 100).

Non-Serious Side Effects During the Study			
Non-serious side effect	**Etanercept + Placebo (282 participants)**	**Etanercept + MTX (284 participants)**	**MTX + Placebo (282 participants)**
Viral infection of nose, throat, and airways	10 participants (4%)	7 participants (3%)	5 participants (2%)
Bronchitis	2 participants (1%)	6 participants (2%)	3 participants (1%)
Redness at injection site	5 participants (2%)	4 participants (1%)	1 participant (less than 1%)
Irritation or pain at injection site	5 participants (2%)	8 participants (3%)	0 participants (0%)
Sinus infection	5 participants (2%)	3 participants (1%)	2 participants (1%)
Headache	4 participants (1%)	6 participants (2%)	2 participants (1%)
Rash at injection site	4 participants (1%)	4 participants (1%)	1 participant (less than 1%)

Approved

Non-Serious Side Effects During the Study			
Non-serious side effect	**Etanercept + Placebo (282 participants)**	**Etanercept + MTX (284 participants)**	**MTX + Placebo (282 participants)**
Diarrhea	3 participants (1%)	3 participants (1%)	5 participants (2%)
Common cold	3 participants (1%)	3 participants (1%)	6 participants (2%)
Increased level of liver enzyme 'alanine aminotransferase' in the blood	1 participant (less than 1%)	3 participants (1%)	4 participants (1%)
Nausea	1 participant (less than 1%)	8 participants (3%)	4 participants (1%)
Vomiting	1 participant (less than 1%)	2 participants (1%)	3 participants (1%)

The researchers also looked at the side effects that happened during the rescue period (when patients switched to etanercept + MTX treatment if their symptoms were not improving). The table below shows how many participants had side effects that were considered related to treatment during the rescue period.

Side Effects During the Rescue Period			
	Etanercept + Placebo (282 participants)	**Etanercept + MTX (284 participants)**	**MTX + Placebo (282 participants)**
How many participants had serious side effects?	0 participants (0%)	0 participants (0%)	2 participants (1%)
How many participants had non-serious side effects?	6 participants (2%)	2 participants (1%)	9 participants (3%)
How many participants died from side effects?	0 participants (0%)	0 participants (0%)	0 participants (0%)
How many participants stopped taking the study medicine because of side effects?	0 participants (0%)	0 participants (0%)	2 participants (1%)

Approved

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

Serious Side Effects During the Rescue Period

Serious side effect	Etanercept + Placebo (282 participants)	Etanercept + MTX (284 participants)	MTX + Placebo (282 participants)
Increased level of liver enzyme 'alanine aminotransferase' in the blood	0 participants (0%)	0 participants (0%)	1 participant (less than 1%)
Increased level of bilirubin in blood (a substance formed when red blood cells break down)	0 participants (0%)	0 participants (0%)	1 participant (less than 1%)
Non-Hodgkin's lymphoma (a type of cancer)	0 participants (0%)	0 participants (0%)	1 participant (less than 1%)

The table below shows the non-serious side effects considered by the study doctor as related to treatment, which occurred in at least 2 participants during the rescue period. The other non-serious side effects considered by the study doctor as related to treatment occurred in 1 participant each.

Non-Serious Side Effects During the Rescue Period

Non-serious side effect	Etanercept + Placebo (282 participants)	Etanercept + MTX (284 participants)	MTX + Placebo (282 participants)
Bronchitis	1 participant (less than 1%)	1 participant (less than 1%)	0 participants (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.

Approved

6. What Were The Overall Results Of The Study?

How did participants' symptoms improve after 24 weeks of treatment?

In this study, researchers looked at the PsA symptoms of participants after their first 24 weeks of treatment with etanercept, MTX, or both. Researchers used several methods to evaluate PsA symptoms, including 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 PsA.

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 PsA symptoms keep participants from doing every day activities
- laboratory tests that measure inflammation

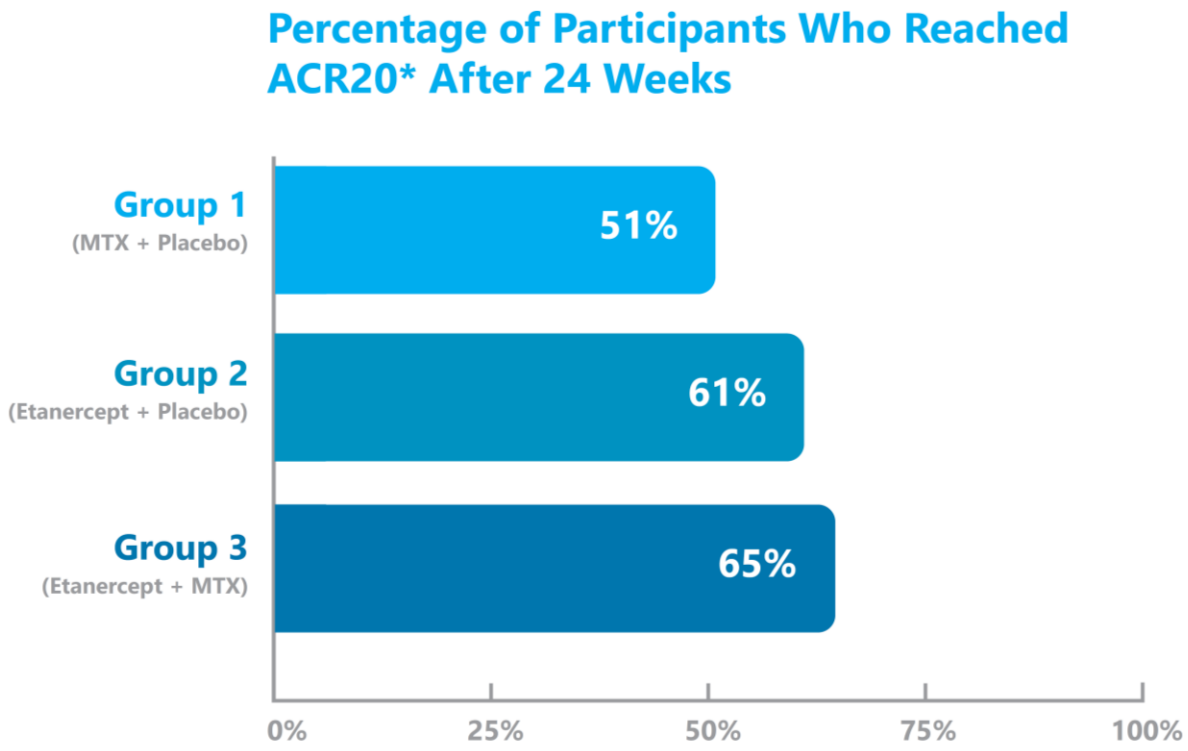
A score of ACR20 was used in this study. To reach that score, a participant had to have at least 20% (or 1 in 5) of his or her joints show improvement after 24 weeks of treatment. The participant also had to be doing or feeling at least 20% better in 3 of the other 5 categories listed above.

The results of this study included:

- 65% (184 out of 283 participants) in the etanercept + MTX group showed improvement in their PsA symptoms after 24 weeks of treatment
- 51% (144 out of 284 participants) in the MTX + placebo group showed improvement in their PsA symptoms after 24 weeks of treatment
- 61% (173 out of 284 participants) in the eteranercept + placebo group showed improvement in their PSA symptoms after 21 weeks of treatment

The results in the figure below shows the percentage of participants in each group who reached an ACR20 score 24 weeks after starting treatment.

Approved



*ACR20 score is used to measure the amount of improvement people have when being treated for PsA

The response rates of the etanercept + MTX group and the etanercept + placebo group were higher than the MTX + placebo, and this was not likely not due to chance. This is only one measure of participants' improvement after treatment. More results may be available at the websites listed at the end of this summary.

7. How Has This Study Helped Participants And Researchers? What is important to know about these results?

These results are only for this clinical study, which looked at a sample of 851 people with PsA. 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. Other studies may find different results. These results are not an explanation of what a treatment can and cannot do for an individual. Many studies are needed to show the benefits and risks of an investigational medicine. This research may help future participants and families by helping doctors understand more about the treatments being studied.

8. 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 study medicine name "etanercept" and "Enbrel" on the websites below.

Approved

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

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 labeling for etanercept. Your healthcare professional should refer to the full prescribing information for proper use of etanercept.

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

- www.clinicaltrials.gov. Use the study identifier NCT02376790
- www.clinicaltrialsregister.eu. Use the study identifier 2014-004869-24

More information is also available in this publication:

Mease PJ, Gladman DD, Collier DH, Ritchlin CT, Helliwell PS, Liu L, Kricorian G, Chung JB. Etanercept and methotrexate as monotherapy or in combination for psoriatic arthritis: primary results from a randomized, controlled phase 3 trial. Arthritis Rheum. 2019; 71 (7): 1112-1124.

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.

Approved