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Summary of Clinical Trial Results

For Laypersons

A study to learn how effective and safe adalimumab is compared to methotrexate in the treatment of adult patients with psoriatic arthritis

Overall Summary

- Psoriatic arthritis is a disease that causes pain, stiffness, and swelling of the joints.
- Psoriatic arthritis is long-lasting and can have changes in severity over time. Periods of more severe symptoms are called “flares”.
- The reason people have psoriatic arthritis is unknown, but researchers think it is caused by a combination of reasons that include genetics, the body’s immune system, and outside factors that can trigger the disease.
- This study took place from August 2016 to March 2020 in 14 countries.
- There were two parts to this study. A total of 246 adult patients with active psoriatic arthritis took part in the study, 227 of which completed Part 1 and continued on to Part 2.
- In Part 1, the patients were randomly (by chance) put into two groups. One group received methotrexate which was increased in dosage up to the highest tolerable dose. In the second group, patients were given adalimumab with a lower dose of methotrexate.
- In Part 2, patients were put into four groups, depending on how effective their treatment was in Part 1.
- The main aim of this study was to see how patients responded to adalimumab when added to the lower dose treatment of methotrexate versus an increased dose of methotrexate as defined by the percent of patients who reached minimal disease activity (MDA) in Part 1 of the study.
- The researchers found that 41.5% of patients who received adalimumab and methotrexate achieved MDA compared to 13.1% of patients who received methotrexate.
- The results of this study may be used by researchers to further develop adalimumab.
- If you participated in this study and have questions about your individual care, contact the doctor or staff at your study site.

1. General information about the study

1.1. What was the main objective of this study?

Researchers are looking to learn more about current treatments for a disease called psoriatic arthritis. Psoriatic arthritis is a long-lasting inflammatory disease that affects 0.3% to 1% of the adult world population. It causes pain, stiffness, and swelling in the joints. The exact cause of psoriatic arthritis is unknown. Researchers think it is caused by a combination of reasons that include genetics, the body's immune system, and outside factors that may trigger the disease.

There is no cure for psoriatic arthritis, but researchers are learning more about current psoriatic arthritis treatments, including methotrexate and adalimumab, that control the activity of the immune system to relieve patients' symptoms.

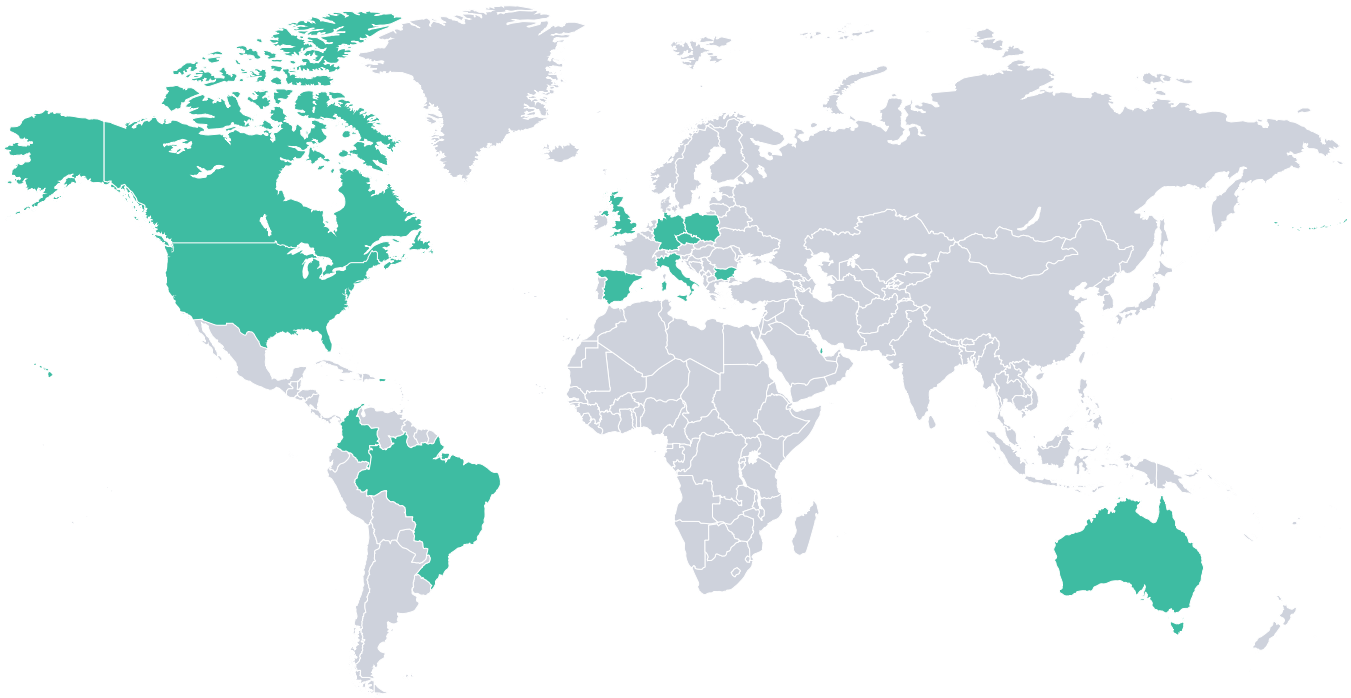
The main aim of the study was to find out if adding adalimumab to a lower dose treatment of methotrexate would provide better results than increasing the dose of methotrexate alone, for adult patients with psoriatic arthritis. Researchers planned this study as a Phase 4, open-label, randomized study.

- **Phase 4 studies** test treatments that have already been approved to treat patients with a condition or disease. In this Phase 4 study, the study doctors continued testing the benefits of adalimumab with methotrexate versus an increased dose of methotrexate in patients with psoriatic arthritis. The study doctors also looked for any side effects patients may have had after treatment with the study drug(s). Side effects are medical events considered by the study doctors to be at least possibly related to study drug/treatment.
- This study was "**open-label**", which means that both the patients and study doctors knew which treatment was given to patients.
- This study was also **randomized**, which means a computer program was used to randomly (by chance) put the patients into different groups. This process is called "randomization", which helps make the groups similar and reduces the differences between the groups. Randomization allows the results of each treatment to be compared as accurately as possible.

This summary only includes the results of this study, which may be different from the results of other studies.

1.2. When and where was the study done?

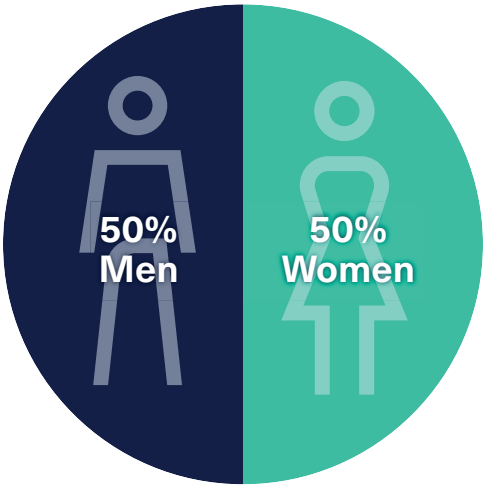
This study took place from August 2016 to March 2020 in the following countries: Australia, Brazil, Bulgaria, Canada, Colombia, the Czech Republic, Germany, Italy, Poland, Puerto Rico, Qatar, Spain, United Kingdom, and the United States.



2. What patients were included in this study?

A total of 246 adult patients with active psoriatic arthritis joined the study. Of these, 245 patients received treatment. A total of 227 patients completed Part 1 and continued on to Part 2.

There were about the same number of men (50%) and women (50%) in the study and patients ranged from 18 to 76 years of age. The average age of patients was 50.1 years old.



To participate in the study, patients had to have been diagnosed with psoriatic arthritis at least 4 weeks prior to the start of the study, and they had to have been treated with methotrexate 15 mg weekly for at least 4 weeks.

Patients could not participate if they had a known sensitivity to adalimumab or had a history of methotrexate intolerance.

3. Which medicines were studied?

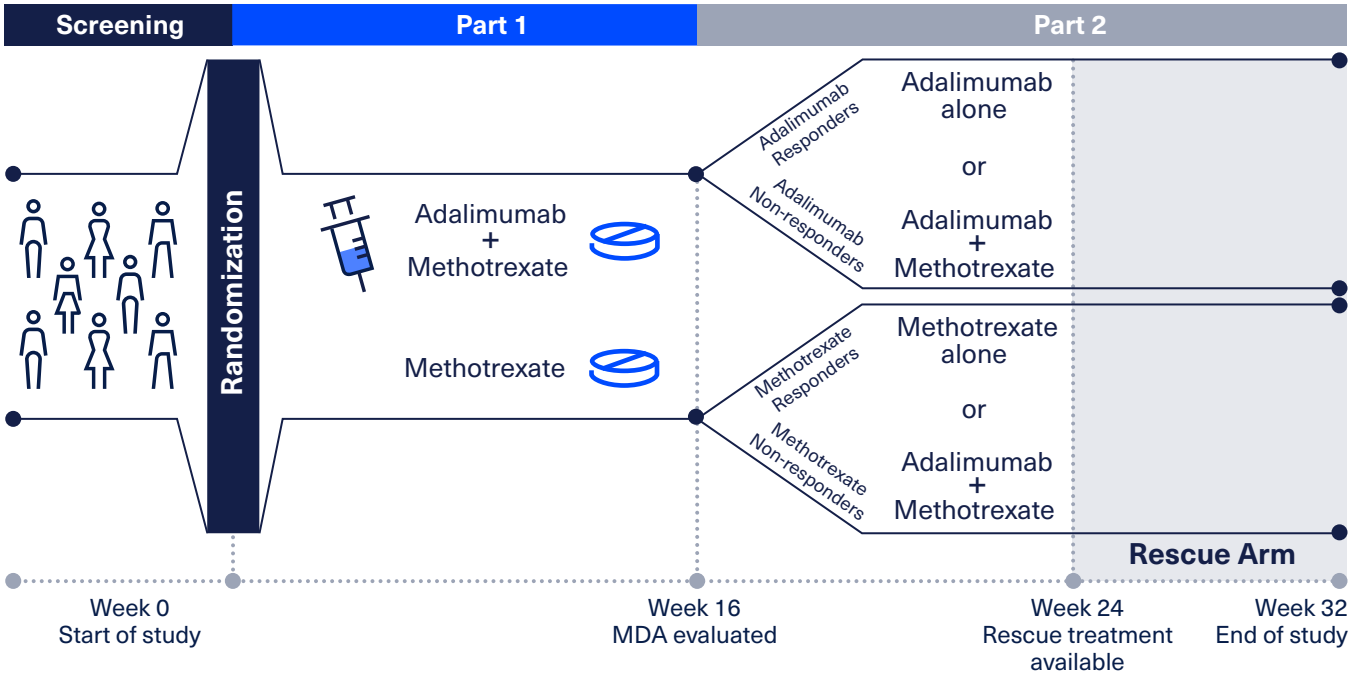
The medicines in this study were called adalimumab and methotrexate. Study doctors tested adalimumab taken with methotrexate, and also methotrexate taken by itself at a dose that increased over time. The study was split into 2 parts, each lasting 16 weeks. Part 1 was designed to see how patients responded to treatment with adalimumab with methotrexate versus an increased dose of methotrexate. Patient response to these medicines was measured by minimal disease activity (MDA). MDA is achieved when a patient has a low level of disease symptoms such as tender or swollen joints, skin psoriasis, and other related factors. Part 2 of the study was designed to evaluate the maintenance or achievement of MDA of four different treatments using adalimumab and/or methotrexate.

In Part 1, patients were randomized to two different groups. Randomization is when a computer program is used to randomly (by chance) put patients into similar groups. One group was given methotrexate which was increased in dosage up to the highest tolerable dose. In the second group, patients were given a lower dose of methotrexate with adalimumab.

In Part 2, patients were split into 4 groups depending on how effective their treatment was for them in Part 1, as measured by MDA achievement:

1. Patients who took adalimumab + methotrexate in Part 1 and achieved MDA continued taking adalimumab in Part 2 but stopped taking methotrexate.
2. Patients who took adalimumab + methotrexate in Part 1 but did not achieve MDA continued taking both medicines in Part 2. However, they took adalimumab every week in Part 2 rather than every other week in Part 1.
3. Patients who took methotrexate in Part 1 and achieved MDA continued taking the same methotrexate increased dose in Part 2.
4. Patients who took methotrexate in Part 1 but did not achieve MDA took methotrexate increased dose and added adalimumab in Part 2 of the study.

Starting at Week 24, there was a “rescue” treatment option available to patients who did not achieve MDA. The diagram below shows how the study was organized.



4. What were the side effects?

Side effects are unwanted medical events that were considered by the study doctor to be at least possibly related to study drug.

A side effect is serious if it leads to death, is life-threatening, puts a patient in the hospital, keeps a patient in the hospital for a long time, or causes a disability that lasts a long time.

- In Part 1 of the study, no patients had serious side effects. In Part 2 of the study, 1.1% of patients (1 patient) in the Methotrexate Non-responders and 4.8% of patients (3 patients) in the Adalimumab Non-responders group had serious side effects. No patients in the Methotrexate Responders group or Adalimumab Responders group had serious side effects.
- In Part 1, 1.6% of patients (2 patients) in both the Methotrexate Increased Dose group and the Adalimumab + Methotrexate group stopped taking the study drug(s) because of side effects. In Part 2, 1.1% of patients (1 patient) in the Methotrexate Non-responders group, 1.8% of patients (1 patient) in the Adalimumab Responders group, and 3.2% of patients (2 patients) in the Adalimumab Non-responders group stopped taking the study drug(s) because of side effects. No patients in the Methotrexate Responders group stopped taking methotrexate because of side effects.
- No patients died during the study.

The tables below show information about the serious side effects patients had in the study, as well as side effects that led to the patient stopping study drug.

Part 1

	Methotrexate Increased Dose (122 Patients)	Adalimumab + Methotrexate (123 Patients)
Number of patients with serious side effects	0 (0.0% of patients)	0 (0.0% of patients)
Number of patients who stopped taking study drug because of side effects	2 (1.6%)	2 (1.6%)
Reasons for stopping	Herpes simplex (type of viral infection), injection site reaction	Injection site reaction, nerve damage of the brain and spinal cord (peripheral sensory neuropathy)

Part 2				
	Methotrexate Responders (15 Patients)	Methotrexate Non-responders (95 Patients)	Adalimumab Responders (54 Patients)	Adalimumab Non-responders (63 Patients)
Number of patients with serious side effects	0 (0.0% of patients)	1 (1.1% of patients)	0 (0.0% of patients)	3 (4.8% of patients)
Serious Side Effects				
• Abscess (area of pus) under the skin (subcutaneous abscess)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
• Asthma	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.6%)
• Redness of the stomach lining (gastric mucosa erythema)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.6%)
• Inflammation of the stomach lining (gastritis)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.6%)
Number of patients who stopped taking study drug because of side effects	0 (0.0%)	1 (1.1%)	1 (1.8%)	2 (3.2%)
Reasons for stopping	–	Nausea	Hives (urticaria)	Enlarged liver (hepatomegaly), lung disease which causes difficulty breathing (chronic obstructive pulmonary disease)

In Part 1, side effects were seen in:

- 41.0% of patients (50 patients) in the Methotrexate Increased Dose group.
- 38.2% of patients (47 patients) in the Adalimumab + Methotrexate group.

In Part 2, side effects were seen in:

- 26.7% of patients (4 patients) in the Methotrexate Responders group.
- 30.5% of patients (29 patients) in the Methotrexate Non-responders group.
- 20.4% of patients (11 patients) in the Adalimumab Responders group.
- 34.9% of patients (22 patients) in the Adalimumab Non-responders group.

The tables below show information about the common side effects (in at least 4 or more patients) in any dosing group. The most common side effects across the whole study were nausea and common cold (upper respiratory tract infection).

Part 1

	Methotrexate Increased Dose (122 Patients)	Adalimumab + Methotrexate (123 Patients)
Number of patients with at least one side effect	50 (41.0% of patients)	47 (38.2% of patients)
Nausea	10 (8.2%)	4 (3.3%)
Sensitivity to drug (drug intolerance)	8 (6.6%)	0 (0.0%)
Common cold (upper respiratory tract infection)	7 (5.7%)	7 (5.7%)
Increased alanine aminotransferase in the blood (which may be sign of liver damage)	6 (4.9%)	4 (3.3%)
Increased aspartate aminotransferase in the blood (which may be sign of liver damage)	3 (2.5%)	4 (3.3%)
Injection site reaction	1 (0.8%)	5 (4.1%)
Headache	1 (0.8%)	4 (3.3%)
Injection site redness (erythema)	0 (0.0%)	4 (3.3%)

Part 2

	Methotrexate Responders (15 Patients)	Methotrexate Non-responders (95 Patients)	Adalimumab Responders (54 Patients)	Adalimumab Non-responders (63 Patients)
Number of patients with at least one side effect	4 (26.7% of patients)	29 (30.5% of patients)	11 (20.4% of patients)	22 (34.9% of patients)
Upper respiratory tract infection	0 (0.0%)	7 (7.4%)	1 (1.9%)	3 (4.8%)
Nausea	1 (6.7%)	4 (4.2%)	0 (0.0%)	1 (1.6%)

5. What were the overall results of the study?

The study was completed as planned. The main aim of this study was to see how patients responded to adalimumab when added to the lower dose treatment of methotrexate versus an increased dose of methotrexate, as defined by MDA achieved in Part 1 of the study. The study doctors found that 41.5% of patients who received adalimumab + methotrexate achieved MDA compared to 13.1% of patients who received an increasing dose of methotrexate.

6. How has the study helped patients and researchers?

The study has helped researchers to learn more about the safety and effectiveness of adalimumab with methotrexate versus increased doses of methotrexate for the treatment of adult patients with psoriatic arthritis. It showed that MDA achievement was greater in patients who received adalimumab + methotrexate in Part 1 of the study compared to patients who received methotrexate.

This summary only shows the results from this study, which may be different from the results of other studies. Findings from this study may be used in other studies to learn whether patients are helped by adalimumab.

7. Are there any plans for future studies?

Multiple adalimumab studies are ongoing for a wide range of conditions.

8. Who sponsored this study?

This study was sponsored by AbbVie. This summary was reviewed for readability by a patient advocacy group.

9. Where can I find out more information about this study?

Title of Study	A Phase 4 Open-label Randomized Controlled Study COmparing the Effectiveness of Adalimumab iNTROduction and Methotrexate Dose escaLation in Subjects with Psoriatic Arthritis (CONTROL)
Protocol Number	M14-496
Clinicaltrials.gov	NCT02814175 https://clinicaltrials.gov/ct2/show/NCT02814175
EudraCT	2016-000191-21 https://www.clinicaltrialsregister.eu/ctr-search/search?query=2016-000191-21
Study Sponsor	AbbVie, Inc. Phone: +1 800-633-9110 Email: abbvieclinicaltrials@abbvie.com

Thank You

AbbVie wants to thank all the participants for their time and effort that went into making this study possible.

Clinical study participants help advance science!