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Summary of Clinical Trial Results

For Laypersons

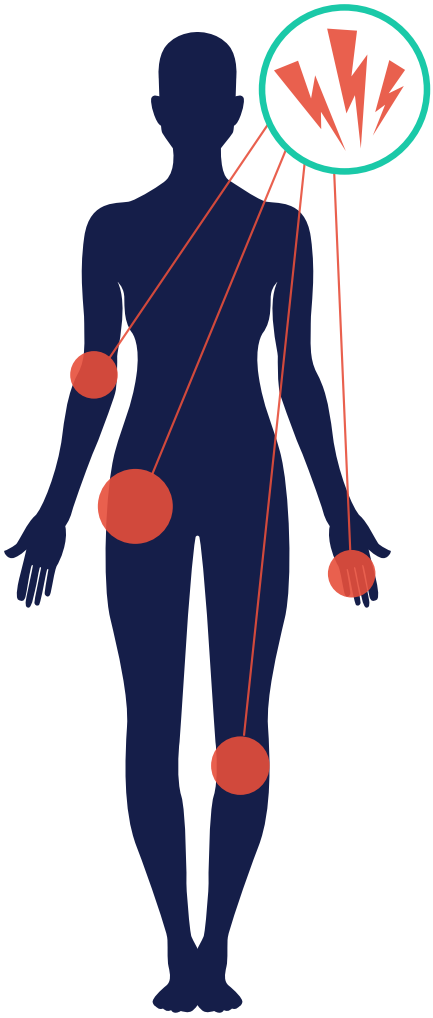
A study to learn if clinical disease activity measured by Magnetic Resonance Imaging (MRI) helped predict flares in adult patients with rheumatoid arthritis in remission who were being treated with dose-tapered adalimumab

Overall Summary

- Rheumatoid arthritis is an autoimmune disease of unknown origin that causes the body's immune system to attack itself. Rheumatoid arthritis targets the body's joints, causing inflammation (swelling, pain, and redness).
- When the symptoms leave for a long period of time (no clinical disease activity), it is called "remission". When the symptoms return while on medication, it is called a "flare".
- In this study, study doctors tested adult patients with rheumatoid arthritis in remission (no clinical disease activity) who had taken a medicine called adalimumab for at least 12 months.
- The study took place from January 2015 to August 2018 in 14 countries.
- A total of 149 adult patients with rheumatoid arthritis took part in the study.
- The study was divided into 4 parts: the screening period, the lead-in period, the double-blind period, and the open-label rescue arm.
- During the study, patients were measured for inflammation using an imaging technique called Magnetic Resonance Imaging (MRI).
- In the lead-in period, patients received adalimumab every other week.
- In the double-blind period, patients were randomized to either the taper arm or the withdrawal arm for 36 weeks. Patients in the taper arm were given adalimumab every 3 weeks, while patients in the withdrawal arm were given placebo (no medicine) every 3 weeks.
- If a patient in either arm had a flare at any time during the double-blind period, he or she entered the open-label rescue arm, wherein the patient received adalimumab every other week for 16 weeks.
- No relationship was found between the MRI scores (used to measure inflammation) in the lead-in period and the number of flares in the tapering arm.
- Most of the side effects were mild. Serious side effects considered possibly related to the study drug were uncommon.
- The results of this study may be used by researchers to further develop this medicine. If you participated in this study and wish to see your results, 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?



Rheumatoid arthritis is an autoimmune disease of unknown origin that causes the body's immune system to attack itself. Rheumatoid arthritis targets the body's joints, causing inflammation (swelling, pain, and redness in the joints). These symptoms can come and go.

The study doctors in this study used a medicine called adalimumab. Adalimumab works on part of the immune system to help patients with autoimmune diseases, like rheumatoid arthritis. Researchers have tested this medicine in many studies on patients with rheumatoid arthritis and have found that adalimumab helps relieve symptoms and stops joint damage. Sometimes doctors can extend the time between doses of adalimumab given to patients (a process called "tapering") and the medicine is still effective.

Researchers planned this study as a Phase 4 study with double-blind and open-label periods. 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 in patients with rheumatoid arthritis. The study doctors also looked for any side effects patients may have had after treatment with adalimumab. This study had a "double-blinded" period, which means that neither the patients nor the study doctors knew who was given which study drug during that period. This ensures that no study results were influenced. This study also had an "open-label" period, which means that both the patients and the study doctors knew which treatments were given during that period.

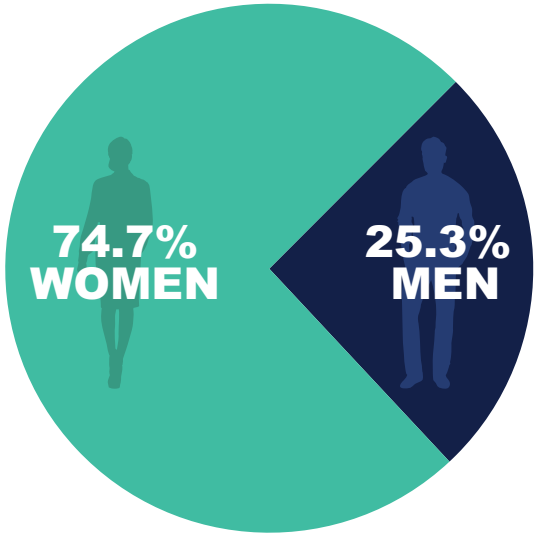
The main aim of the study was to find if an imaging technique called Magnetic Resonance Imaging (MRI) could help measure inflammation of clinical disease activity and predict flares in adults with rheumatoid arthritis that have tapered their treatment with adalimumab and are in remission. Researchers also checked if there were any unwanted side effects. 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?

The study took place from January 2015 to August 2018 in the following countries:

2. What patients were included in this study?

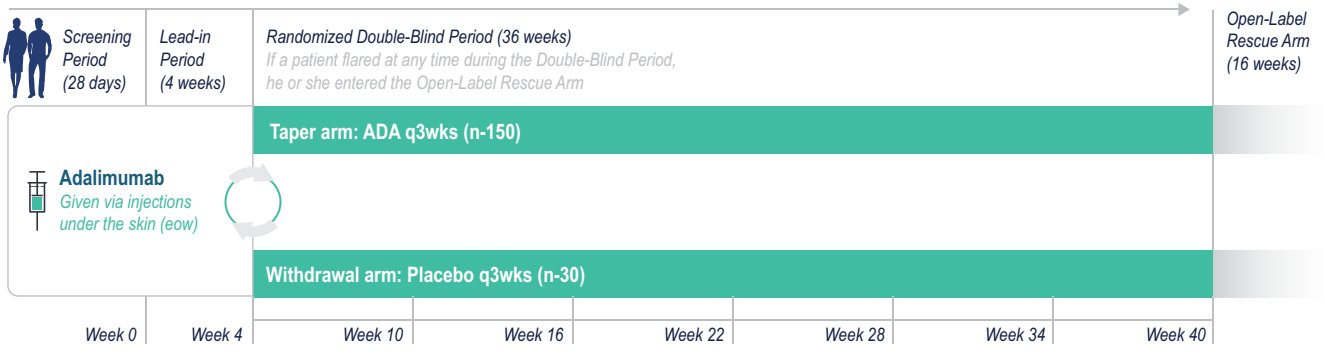
A total of 149 adult patients with rheumatoid arthritis took part in the study; of these, 146 patients participated in the lead-in period. A total of 102 patients continued on to the double-blind period taper arm and 20 patients continued on to the double-blind period withdrawal arm. Lastly, 31 patients flared and entered the open-label rescue arm. Patients mostly withdrew from the study due to personal choice, side effects, or other reasons.



There were more women (74.7%) than men (25.3%) in the study, as rheumatoid arthritis mostly affects women. Study doctors selected only adults in this study. Patients ranged from 32 to 83 years of age. Each patient was in remission and had been receiving adalimumab for at least 12 months.

3. Which medicines were studied?

The medicine in this study was adalimumab. The diagram below shows how the study was organized.



ADA = adalimumab, q3wks = every 3 weeks, eow = every other week

The study was divided into 4 parts: the screening period, the lead-in period, the double-blind period, and the open-label rescue arm.

At the beginning of the study, the study doctors selected patients who met all the requirements of the planned study in the screening period. During the lead-in period, patients were measured for inflammation using an imaging technique called Magnetic Resonance Imaging (MRI).

In the lead-in period, patients were given medicine for 4 weeks. All patients got the same dose of medicine. Patients received adalimumab every other week via an injection underneath the skin.

After the lead-in period, patients were then “randomized” in the double-blind period to either the taper arm or the withdrawal arm for 36 weeks. Randomization is the process where patients are randomly (by chance, by flip of a coin) placed into different groups. Study doctors gave the patients doses of the medicine, or a placebo (no medicine), depending on which group they were in. Patients in the taper arm were given adalimumab every 3 weeks, while patients in the withdrawal arm were given placebo (a treatment that looks like the treatment medicine but has no active drug in it) every 3 weeks.

If a patient in either arm had a flare at any time during the double-blind period, he or she entered the open-label rescue arm, wherein the patient received adalimumab every other week for 16 weeks.

4. What were the side effects?

Side effects are unwanted medical events that happen during a study. They may or may not be caused by the treatment in the study. 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.

Related side effects are side effects that were at least possibly related to the study drug.

4.1. What were the serious side effects?

In the lead-in period, about 2.7% of patients (4 patients) had serious side effects. None of these side effects were considered possibly related to the study drug. About 0.7% of patients (1 patient) stopped taking the study drug because of side effects; this patient stopped taking the study drug because of the side effect (herpes zoster [herpes virus]) that was considered possibly related to the study drug. No patients died during the lead-in period.

In the double-blind period, about 1.0% of patients (1 patient) in the tapering arm and no patients in the withdrawal arm had serious side effects. The patient's serious side effect in the tapering arm was considered possibly related to the study drug (breast cancer). About 2.0% of patients (2 patients) in the tapering arm and no patients in the withdrawal arm stopped taking the study drug because of side effects; one of these patients in the tapering arm stopped taking the study drug because of the side effect (breast cancer) that was considered possibly related to the study drug. The other patient stopped taking the study drug because of the side effect (cough) that was not considered possibly related to the study drug. No patients died during the double-blind period.

In the open-label rescue arm, about 7.7% of patients (3 patients) had serious side effects. One of these patients had a side effect considered possibly related to the study drug (pleural effusion [extra fluid around the lungs]). No patients stopped taking the study drug because of side effects. No patients died during the open-label rescue arm.

The table below shows information about the related serious side effects patients had in the study, as well as related side effects patients had that led to the patient stopping the study drug, and related side effects leading to death.

	Lead-In Treated Patients (n=146)	Double-Blind Treated Patients Tapering Arm (n=102)	Withdrawal Arm (n=20)	Open-Label Rescue Arm Treated Patients (n=39)
Number of patients with related serious side effects	0 (0% of patients)	1 (1.0% of patients)	0 (0% of patients)	1 (2.6% of patients)
Serious related side effects	-	Breast cancer	-	Pleural effusion (extra fluid around the lungs)
Number of patients who stopped taking study drug because of related side effects	1 (0.7% of patients)	1 (1.0% of patients)	0 (0% of patients)	0 (0% of patients)
Reason(s) for stopping	Herpes zoster (herpes virus)	Breast cancer	-	-
Number of patients with related side effects leading to death	0 (0% of patients)	0 (0% of patients)	0 (0% of patients)	0 (0% of patients)

4.2. What were the most common side effects?

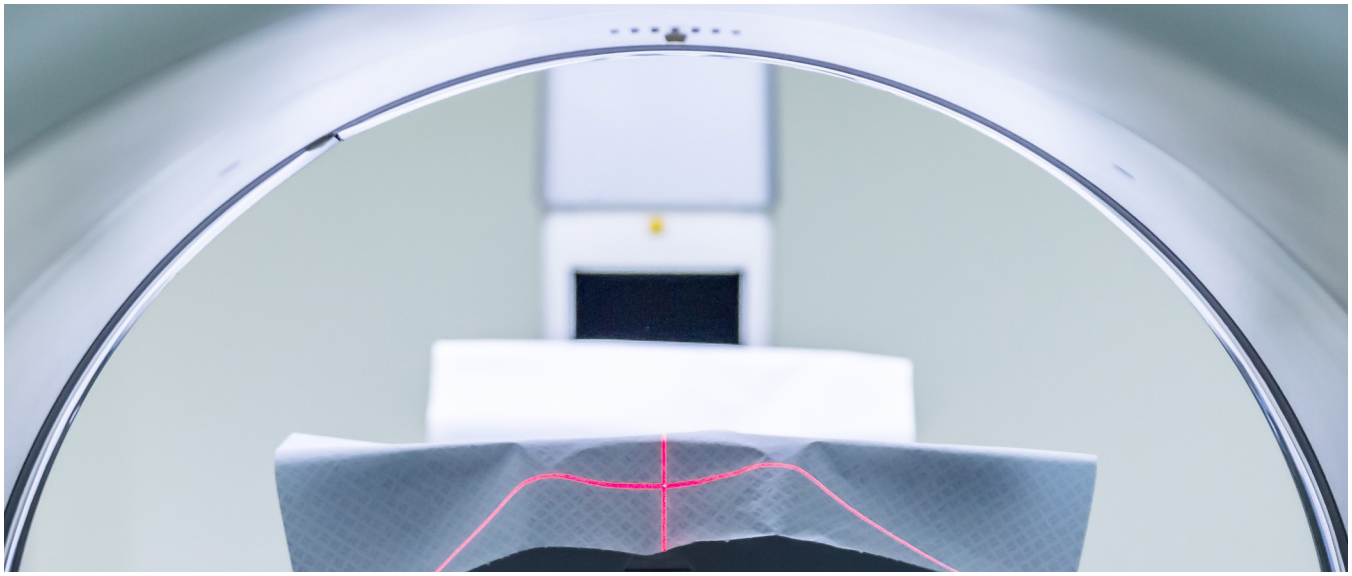
About 24.7% of patients (36 patients) had side effects during the lead-in period. The total number of patients that had side effects considered possibly related to the study drug was 7.5% of patients (11 patients). The table below shows information about the most common related side effects in 2 or more patients in the lead-in period.

	Lead-In Treated Patients (n=146 patients)
Number of patients with at least one related side effect	11 (7.5% of patients)
Most common side effects in 2 or more patients	
Nasopharyngitis (common cold)	2 (1.4% of patients)
Cough	2 (1.4% of patients)

About 60.8% of patients (62 patients) in the tapering arm and 60.0% of patients (12 patients) in the withdrawal arm had side effects during the double-blind period. The total number of patients that had side effects considered possibly related to the study drug was 25.5% of patients (26 patients) in the tapering arm and 25.0% of patients (5 patients) in the withdrawal arm. The table below shows information about the most common related side effects in 3 or more patients in the double-blind period.

Double-Blind Period	Tapering Arm (n=500 patients)	Withdrawal Arm (n=20)
Number of patients with at least one related side effect	26 (25.5% of patients)	5 (25.0% of patients)
Most common side effects in 3 or more patients		
Nasopharyngitis (common cold)	9 (8.8% of patients)	2 (10.0% of patients)
Rheumatoid arthritis	5 (4.9% of patients)	1 (5.0% of patients)
Lower respiratory tract infection	3 (2.9% of patients)	1 (5.0% of patients)
Oral herpes (cold sore)	3 (2.9% of patients)	0 (0% of patients)

About 61.5% of patients (24 patients) had side effects during the open-label rescue arm. The total number of patients that had side effects considered possibly related to the study drug was 23.1% (9 patients). No related side effect occurred in more than one patient.



5. What were the overall results of the study?

The study was completed as planned. No relationship was found between inflammation measured by MRI scoring and the number of flares in the tapering arm up to Week 40.

Most of the side effects were mild. Serious side effects considered possibly related to the study drug were uncommon.

6. How has the study helped patients and researchers?

The results of this study showed there was no relationship between inflammation measured by MRI scoring and the risk of flaring (symptoms returning) in patients with rheumatoid arthritis in remission (no clinical disease activity).

Findings from this study may be used in other studies to show that tapering adalimumab can be an option for some patients with rheumatoid arthritis who are in remission.

This summary only shows the results from this study, which may be different from the results of other studies. Patients should consult their physicians and/or study doctors with further questions about their individual care and should not make changes in their treatment based on the results of a single study.

7. Are there any plans for future studies?

There is a possibility for future studies that include the medicine that was used in this study.

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 Trial Assessing the ImPact of Residual Inflammation Detected Via Imaging TEchniques, Drug Levels and Patient Characteristics on the Outcome of Dose TaperIng of Adalimumab in Clinical Remission Rheumatoid ArThritis (RA) Subjects (PREDICTRA)
Protocol Number	M14-500
ClinicalTrials.gov	NCT02198651 https://clinicaltrials.gov/ct2/show/NCT02198651
EudraCT	2014-001114-26 https://www.clinicaltrialsregister.eu/ctr-search/search?query=2014-001114-26
Study Sponsor	Global Medical Services, AbbVie Phone: +1 800-633-9110 Email: abbvieclinicaltrials@abbvie.com

23 Oct 2019. This document includes known facts as of the time the document was finalized.

THANK YOU!

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

Clinical study participants help advance science!