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Summary of Clinical Trial Results

For Laypersons

A study to learn how safe and effective a medicine containing the study drug upadacitinib works compared to placebo (no medicine) to treat adult patients with moderate to severe atopic dermatitis

Overall Summary

- Atopic dermatitis is a skin disease that is the most common form of eczema.
- The skin of atopic dermatitis patients can become dry, swollen, red and itchy.
- Atopic dermatitis is long lasting and can have changes in severity (flares) over time.
- The reason people have atopic dermatitis is unknown, but researchers think it is caused by a mixture of reasons that include genetics and the body's immune system.
- Study doctors aimed to test a medicine called upadacitinib, which affects the immune system, to treat symptoms of atopic dermatitis.
- This study took place from October 2016 until January 2019 in 8 countries.
- In this study, doctors compared the effects and safety of upadacitinib with placebo (no medicine) in patients with moderate to severe atopic dermatitis.
- A total of 167 adult patients took part in the study. There were two parts of the study: Period 1 and Period 2. A total of 130 patients finished Period 1 of the study and could continue to Period 2. A total of 83 patients then finished Period 2.
- The study doctors looked at the patient's skin to measure the area and severity of atopic dermatitis after 16 weeks of treatment. The doctors saw fewer signs of disease in patients who took medicine.
- The number of side effects in patients given medicine was similar to the number of side effects seen in previous studies of this medicine.
- The results of this study will be used by researchers to further develop this medicine.
- If you participated in this study and wish to learn more, contact the doctor or staff at your study site.

1. General information about the study

1.1 Why did we perform this study?

Researchers are looking for a better way to treat a skin disease called atopic dermatitis. Atopic dermatitis is the most common form of eczema, affecting 1–3% of the adult world population. It causes the skin to become very dry, swollen, red and itchy. The exact cause of atopic dermatitis is unknown. Researchers think that it is caused by a mixture of reasons that include genetics and the body's immune system.

There is no cure for atopic dermatitis, but researchers are looking for a treatment that weakens the activity of the immune system to relieve patients' symptoms. In this study, a drug called upadacitinib was tested for benefits and safety in atopic dermatitis patients compared to placebo (no medicine).

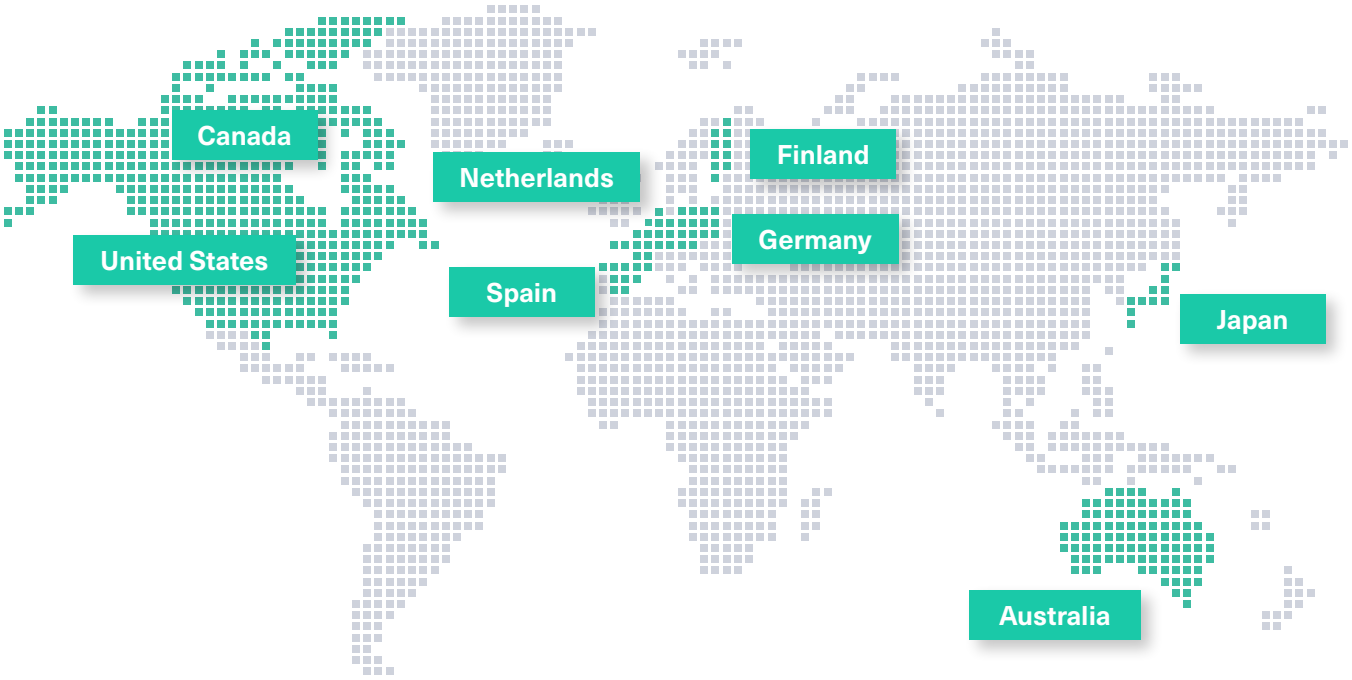
Researchers planned this Phase 2 study in patients with moderate to severe atopic dermatitis (atopic dermatitis covering at least 10% of the body and not helped with other types of medications). Phase 2 studies test potential new treatments in a small number of patients with a condition or disease. In this Phase 2 study, the study doctors looked at the benefits and side effects of upadacitinib in patients with atopic dermatitis. This study was "double-blinded", which means that neither the patients nor the study doctors knew who was given study drug. This ensures that no study results were influenced.

Doctors looked at the benefits of 3 different doses of upadacitinib compared to placebo after 16 weeks of treatment. The placebo looks like upadacitinib but contains no real medicine. Researchers use placebos in studies to compare the results for patients who take study drug with the results for patients who take no medicine at all. The study doctors also reported any side effects patients may have had during and after treatment.

The main aim of the study was to find out if patients had fewer symptoms of atopic dermatitis after 16 weeks of treatment and if there were any unwanted side effects. This summary only includes the results from this study, which may be different from the results from other studies.

1.2 When and where was the study done?

This study took place from October 2016 to January 2019 in the following countries:

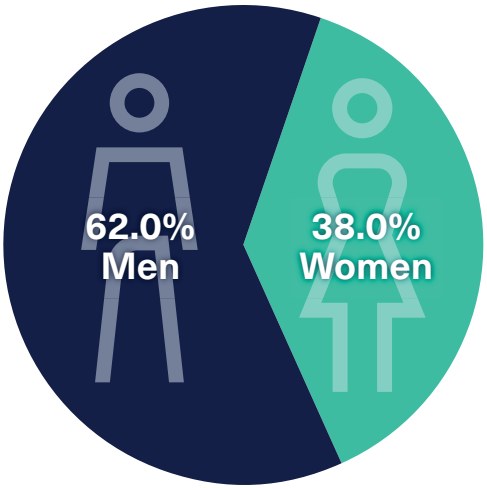


2. What patients were included in this study?

A total of 167 adult patients took part in the study. One patient left the study before being given any study drug. All the patients had moderate to severe atopic dermatitis for at least 1 year and, on average, had almost half of their body covered with atopic dermatitis. Patients who had taken upadacitinib before or had taken similar types of drugs were not included in the study.

There were 2 parts of the study called Period 1 and Period 2. A total of 166 patients started Period 1 and 130 of those patients finished Period 1 of the study. Patients who completed Period 1 could continue to Period 2 and receive drug or placebo for 72 weeks in an extension period. A total of 83 patients finished Period 2. Most patients that did not finish the study stopped due to lack of improvement in their atopic dermatitis symptoms.

There were more men (62%) than women (38%) in the study. Study doctors selected only adults to participate in this study and patients ranged from 18 to 75 years of age.



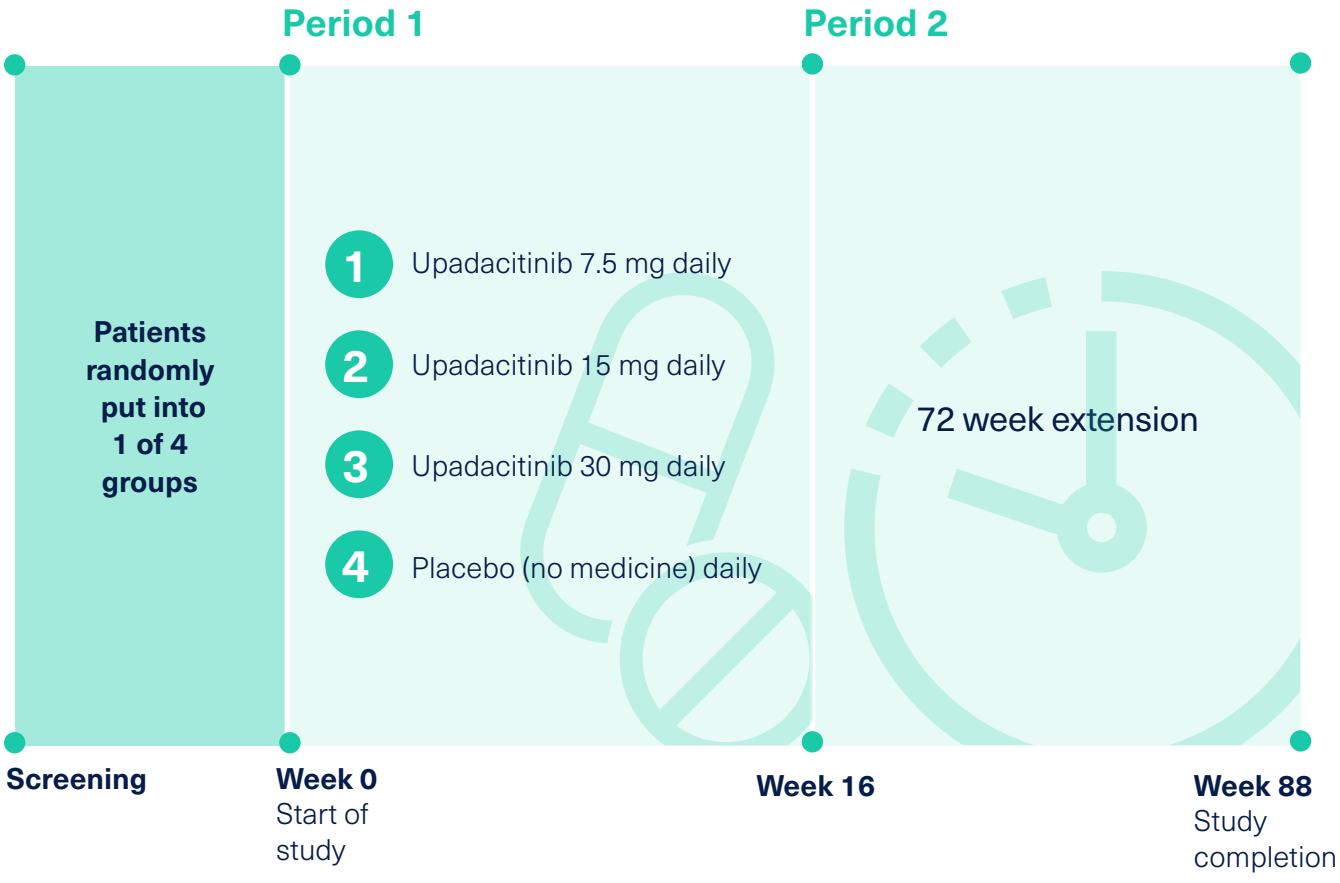
3. Which medicines were studied?

The medicine in this study was upadacitinib which was compared to placebo. Both upadacitinib and placebo were given as a tablet by mouth once a day.

Before the study started, a screening period of about 5 weeks took place to check if patients could join the study. At the beginning of the study, a computer program was used to randomly (by chance) put the patients into 1 of 4 groups. This process is called "randomization", which helps make the groups equal and reduces the differences between the groups. Randomization allows the results of each treatment to be compared as accurately as possible. After the screening period, the study was separated into 2 parts, called Period 1 and Period 2.

In Period 1, study doctors gave the patients the study drug or placebo as a tablet to swallow depending on their assigned group. Tablets were taken by mouth once a day from the start of the study until the end of Week 16. The patients did not know what dose of study drug they were given or if they were given placebo. At the end of Period 1, patients could join Period 2 for a 72-week extension period.

The diagram below displays how different doses were given to patients in different groups.



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 participant in the hospital, keeps a participant in the hospital for a long time, or causes a disability that lasts a long time.

Related side effects are side effects that were considered by the study doctor to be at least possibly related to the study drug.

In Period 1, about 2.4% of patients (3 patients) who were given study drug had serious side effects. None of the serious side effects were considered possibly related to the study drug.

About 7.9% of patients (10 patients) who were given study drug stopped taking the study drug because of side effects during the study. The total number of patients that stopped study drug because of side effects considered possibly related to the study drug was 3.2% of patients (4 patients).

No patients died during Period 1 of the study. During Period 2 of the study, 1 patient died from complications due to a routine heart procedure and 1 patient died from a heart attack after study drug was finished. Both deaths were considered possibly related to the study drug.

The table below shows information about the related serious side effects patients had in Period 1 of the study, as well as related side effects that led to patients stopping study drug.

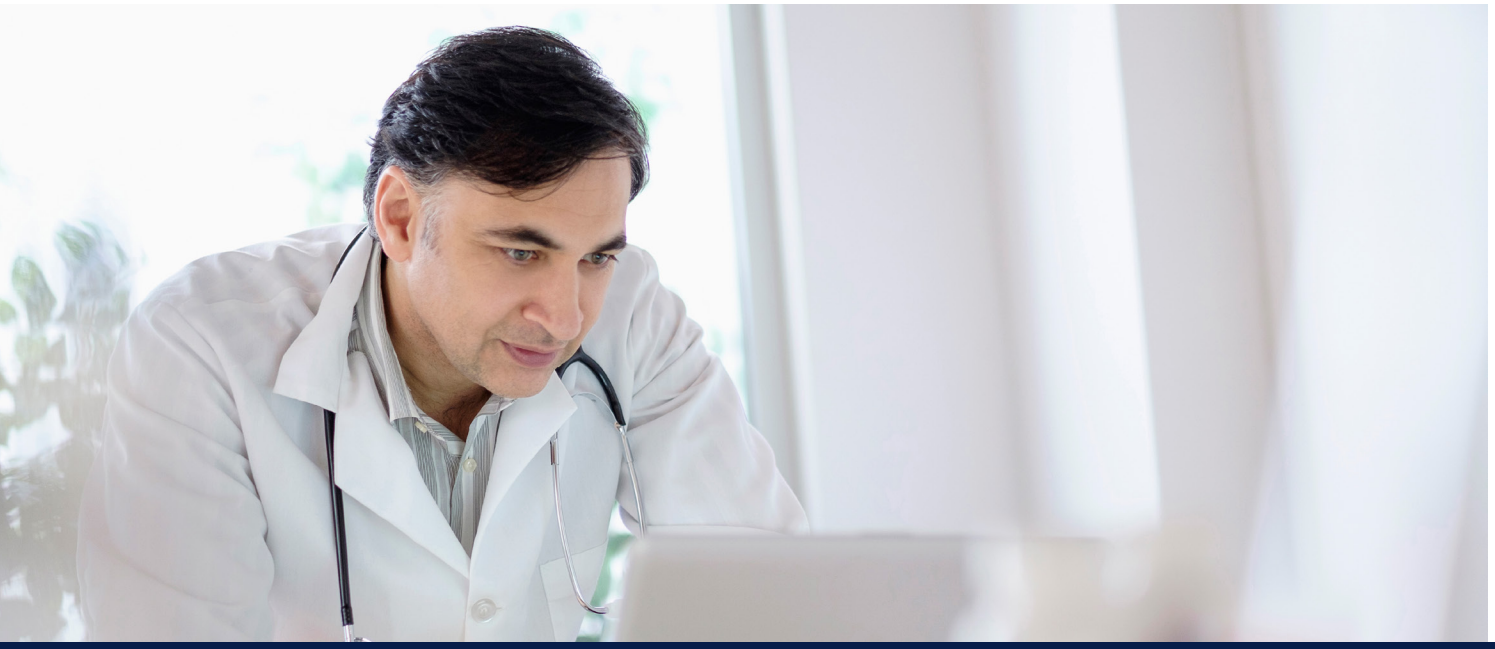
Period 1		
	Placebo (N=40)	Upadacitinib (N=126)
Number of patients with related serious side effects	1 (2.5% of patients)	0 (0% of patients)
Related Serious Side Effects • Atrial fibrillation (irregular heartbeat)	1 (2.5% of patients)	0 (0% of patients)
Number of patients who stopped taking study drug because of related side effects • Reasons for stopping	2 (0% of patients) Patient decision, lack of improvement, lost to follow-up, worsening of symptoms, other reasons	4 (0% of patients) Patient decision, lack of improvement, lost to follow-up, worsening of symptoms, other reasons
Number of related side effects leading to death	0 (0% of patients)	0 (0% of patients)

About 76.2% of patients (96 patients) who were given study drug had side effects during the study. The number of patients who were given study drug and had side effects considered possibly related to the study drug was 44.4% (56 patients).

The table below shows information about the common related side effects (in at least 5.0% or more patients in either group) in this study. The most common related side effects were diarrhea, upper respiratory tract infection (an infection of the upper part of the body and includes the common cold, infection of the throat and tonsils), hematuria (blood in the urine), and acne.

Period 1		
	Placebo (N=40)	Upadacitinib (N=126)
Number of patients with at least one related side effect	11 (27.5% of patients)	56 (44.4% of patients)
Common Related Side Effects (Side effects reported in at least 5% of patients in either group)		
• Diarrhea	2 (5% of patients)	3 (2.4% of patients)
• Upper respiratory tract infection (an infection of the upper part of the body and includes the common cold, infection of the throat and tonsils)	1 (2.5% of patients)	8 (6.3% of patients)
• Hematuria (blood in the urine)	2 (5% of patients)	0 (0% of patients)
• Acne	1 (2.5% of patients)	12 (9.5% of patients)

Across the whole study, patients who took higher doses did not necessarily suffer from more side effects. This meant that there was no link between the dose and the number of side effects patients had.



5. What were the overall results of the study?

The study was completed as planned. Study doctors aimed to find out if the study drug worked to treat the symptoms of atopic dermatitis and was safe when compared to placebo. To find out the main results of the study, study doctors looked at the change in the patients' Eczema Area and Severity Index (EASI) score, which measures the size and severity of atopic dermatitis, and the patients' level of itchiness from before starting study drug compared to EASI score and itchiness after 16 weeks of treatment.

In Period 1, study doctors found that patients in the groups who had taken the study drug had less symptoms of atopic dermatitis compared to patients who had taken placebo. Based on EASI score, average improvements in atopic dermatitis symptoms were:

- 23% in patients given placebo
- 39% in patients given 7.5 mg
- 62% in patients given 15 mg
- 74% in patients given 30 mg

Study doctors also found that patients in the groups who had taken the study drug had less itchiness after 16 weeks of study drug compared to patients who had taken placebo. A decrease in itchiness was seen in:

- 6% of patients given placebo
- 24% of patients given 7.5mg
- 59% of patients given 15 mg
- 53% of patients given 30 mg

In Period 2, study doctors found that longer use of the study drug did not give patients more side effects and patients' atopic dermatitis symptoms stayed the same as at Week 16 or got better.

The number and frequency of side effects were like those expected in patients with moderate to severe atopic dermatitis. Higher doses did not give patients more side effects than lower doses.

6. How has the study helped patients and researchers?

The study helped researchers learn the safety and benefits of upadacitinib over placebo in the treatment of atopic dermatitis. They also learned that the study drug is well tolerated.

Findings from this study may be used in other studies to learn whether patients are helped by the study drug.

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?

Upadacitinib is currently being studied in adults and children with atopic dermatitis around the world.

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 2b Multicenter, Randomized, Placebo-Controlled, Double-Blind Dose-Ranging Study to Evaluate ABT-494 (Upadacitinib) in Adult Subjects With Moderate to Severe Atopic Dermatitis
Protocol Number	M16-048
Clinicaltrials.gov	NCT02925117 https://clinicaltrials.gov/ct2/show/NCT02925117?term=M16-048&draw=2&rank=1
EudraCT	2016-002451-21 https://www.clinicaltrialsregister.eu/ctr-search/search?query=2016-002451-21
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!