abbvie

Summary of Clinical Trial Results

For Laypersons

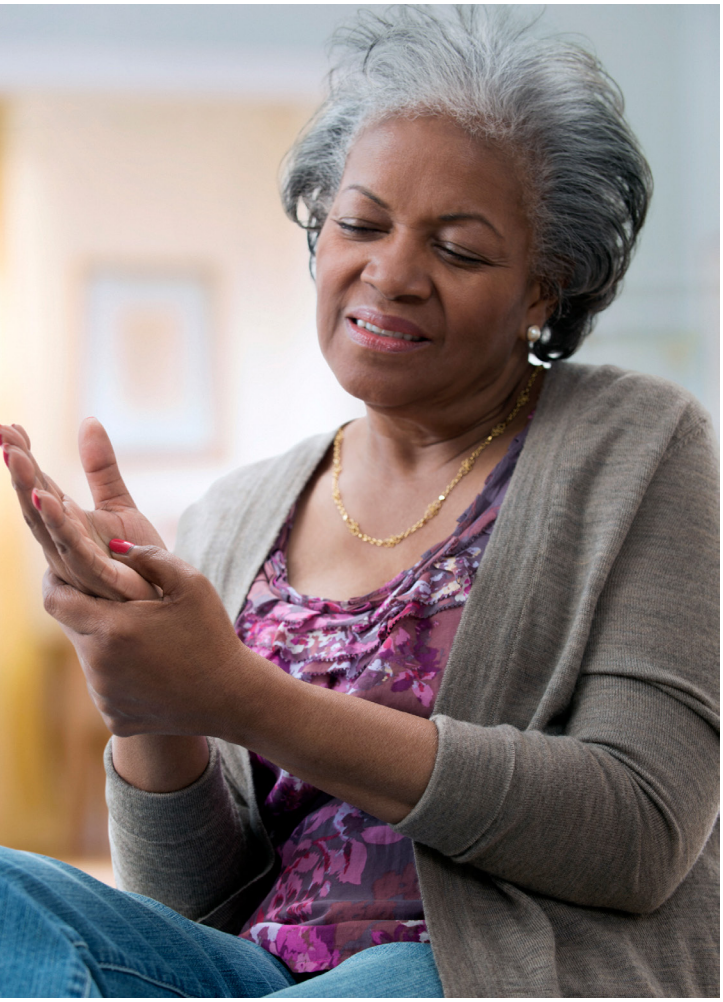
A study to learn how effective and safe elsubrutinib taken by itself or in combination with upadacitinib works to treat adult patients with rheumatoid arthritis compared to placebo

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 in the joints). These symptoms can disappear and return.
- The main goal of the study was to find out if elsubrutinib taken by itself or in combination with upadacitinib was safe and effective compared to placebo for the treatment of adult patients with rheumatoid arthritis.
- A total of 242 adult patients with active rheumatoid arthritis took part in the study, 215 of which completed the study. A total of 97 patients continued on to participate in the separate extension study.
- The study doctors put the patients into 1 of 6 groups. They tested different doses of elsubrutinib in this study including placebo (no real medicine) in addition to elsubrutinib + upadacitinib and upadacitinib itself.
- No patients had serious side effects during the study. The most common side effect was a cold (upper respiratory tract infection).
- Across the whole study, percentages of side effects were similar across patients who took elsubrutinib and/or upadacitinib and who took placebo.
- Across the treatment groups, the number and frequency of side effects were similar to those expected in patients with rheumatoid arthritis.
- The results of this study may be used by researchers to further develop this medicine.
- 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?



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 disappear and return.

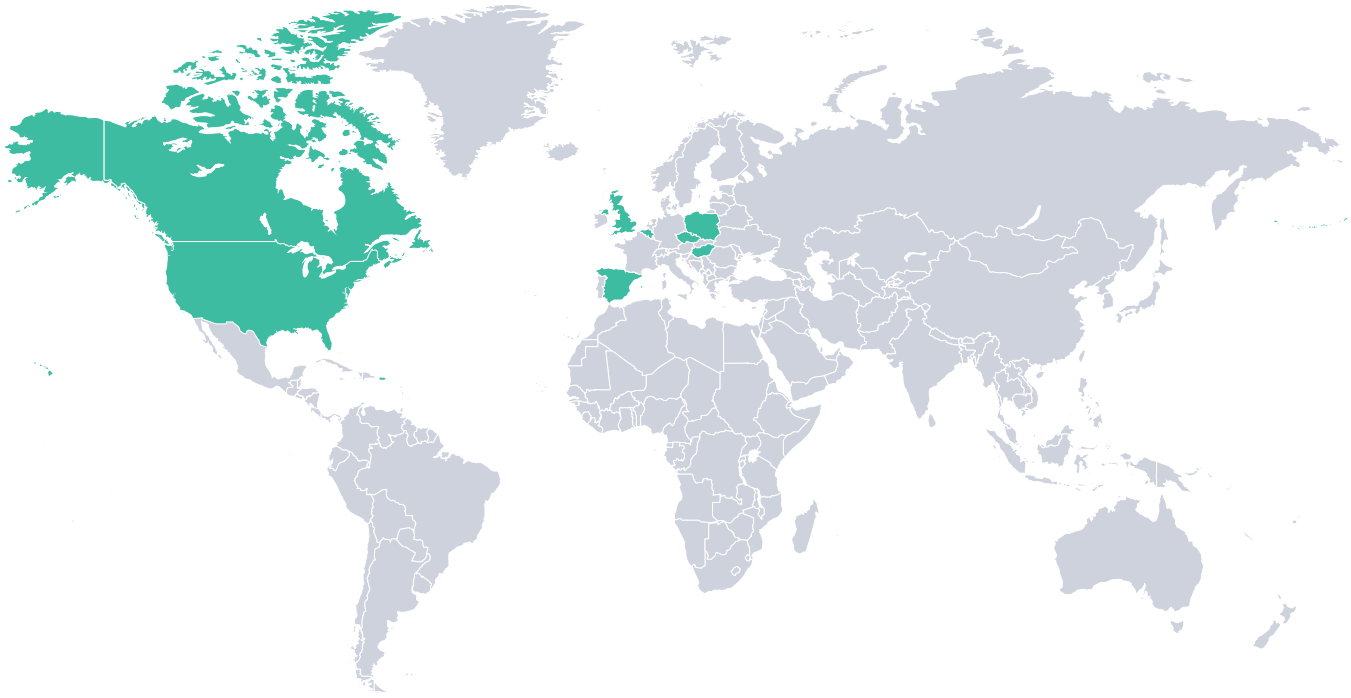
Researchers in this study used a medicine called elsubrutinib. Elsubrutinib is a new investigational drug being tested for the first time in people with rheumatoid arthritis to see if it can work on part of the immune system to help patients with inflammatory diseases. Researchers wanted to know if elsubrutinib could help relieve signs and symptoms of rheumatoid arthritis when given to patients by itself or in combination with upadacitinib, a drug used to treat autoimmune diseases.

The main goal of the study was to find out if elsubrutinib taken by itself or in combination with upadacitinib was safe and effective compared to placebo for the treatment of patients with rheumatoid arthritis. The doctors in this study treated adult patients who were diagnosed with rheumatoid arthritis whose symptoms had not improved after previous treatment with biologic disease-modifying anti-rheumatic drugs (bDMARDs), a type of drug used to slow the progression of rheumatoid arthritis. Researchers planned this study as a Phase 2, double-blinded, randomized study.

- **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 of elsubrutinib taken by itself or in combination with upadacitinib compared with placebo in patients with rheumatoid arthritis. The study doctors also looked for any side effects patients may have had after treatment with the study drugs. A side effect is a medical event considered by the study doctors to be at least possibly related to study drug/treatment.
- A **placebo** was used in this study. Placebo looks like the treatment but contains no medicine.
- This study was "**double-blinded**", which means that neither the patients nor the study doctors knew who was given which study drug/treatment. This ensures that no study results were influenced.
- This study was also **randomized**, which means a computer program was used to randomly (by chance) put the patients into one of six groups. This process is called "randomization", which reduces the differences between the groups. Randomization allows the results of each treatment to be compared as accurately as possible.

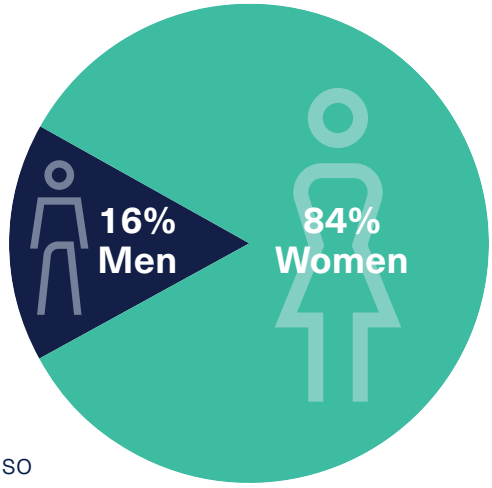
1.2. When and where was the study done?

This study took place from October 2018 to March 2020 in the following countries: Belgium, Canada, Czechia, Hungary, Poland, Puerto Rico, Spain, United Kingdom, and the United States.



2. What patients were included in this study?

A total of 242 adult patients with active rheumatoid arthritis took part in the study, 215 of which completed the study. A total of 97 patients continued to participate in a separate extension study. In the extension study, patients chose to extend their time in the trial for an additional 48 weeks. The patients who originally received placebo were switched to receive a combination of elsubrutinib and upadacitinib during the extension study.



There were more women (84%) than men (16%) in the study, as this disease occurs more often in women. Patients ranged from 23 to 80 years of age. The average age of patients was 58 years.

To participate in this study, patients had to have been diagnosed with active rheumatoid arthritis for at least 3 months. Patients must have also been treated previously with bDMARDs for at least 3 months but continued to experience symptoms of rheumatoid arthritis or were having too many side effects from the bDMARD treatment.

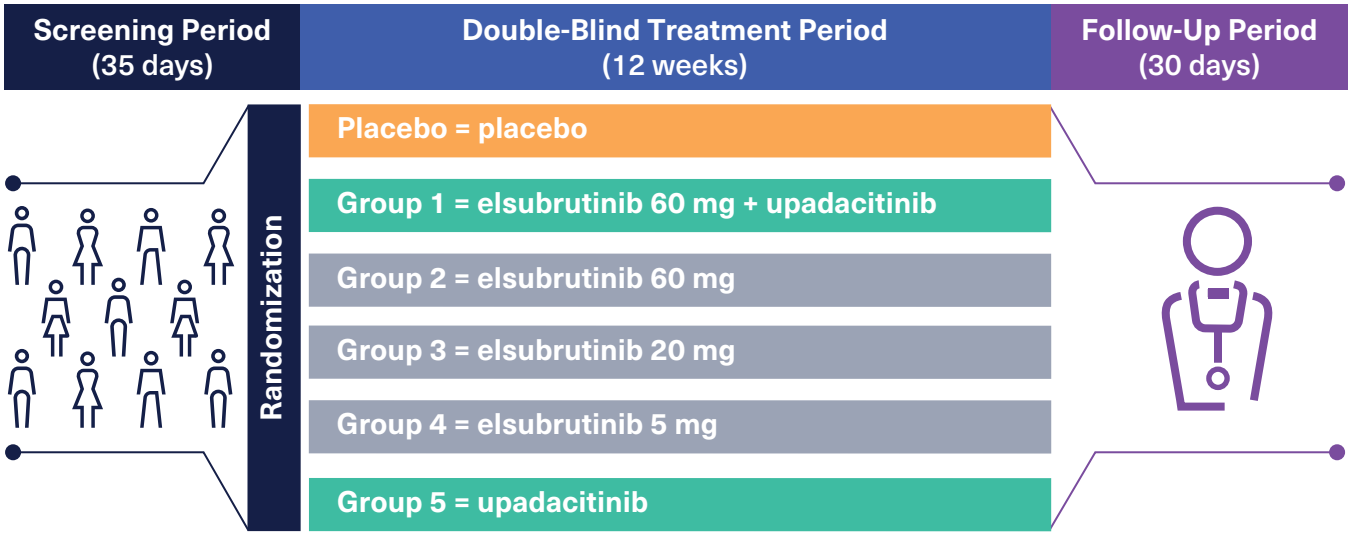
3. Which medicines were studied?

The medicine in this study was elsubrutinib. Study doctors tested this medicine given by itself, and also given in combination with a medicine called upadacitinib. Study doctors tested different doses of elsubrutinib with placebo (looks like the treatment but contains no real medicine), in addition to elsubrutinib with upadacitinib, upadacitinib with placebo, and placebo by itself.

At the beginning of the study, the study doctors selected patients who met all the requirements of the planned study in the Screening Period of 35 days.

In the Double-Blind Treatment Period, the study doctors used a computer program to randomly (by chance) put the patients into 1 of 6 groups. Patients received different doses of elsubrutinib and/or placebo and upadacitinib and/or placebo for 12 weeks, depending on which group they were in. The drugs were capsules/tablets for the patients to swallow, taken once daily. Patients did not know which dose of drug they were given or if they were given placebo.

During the Follow-Up Period, patients who had received study drug were again contacted by study doctors after getting the last dose of medicine. Patients were then given the option to participate in the separate extension study.



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 longer time, or causes a disability that lasts a long time.

- No patients had serious side effects during the study.
- About 2.5% of patients (6 patients) stopped taking the study drug because of side effects during the study.
- 1 patient in Group 4 (elsubrutinib 5mg) died from cardiac arrest which was not considered related to the study drug.

The table below shows information about the side effects patients had that led to the patient stopping treatment.

Overall Study						
	Placebo (19 Patients)	Group 1 (62 Patients)	Group 2 (41 Patients)	Group 3 (39 Patients)	Group 4 (41 Patients)	Group 5 (40 Patients)
Number of patients who stopped taking study drug because of side effects	0 (0.0% of patients)	3 (4.8% of patients)	2 (4.9% of patients)	1 (2.6% of patients)	0 (0.0% of patients)	0 (0.0% of patients)
Reasons for stopping	–	Common cold (upper respiratory tract infection), inflammation of the salivary glands, inflammation of the stomach lining (gastritis), lymph node enlargement (lymphadenitis)	Swelling of the arms or legs (peripheral swelling), stomachache (upper abdominal pain)	Hives (urticaria)	–	–

Group 1 = elsubrutinib 60 mg + upadacitinib
Group 2 = elsubrutinib 60 mg
Group 3 = elsubrutinib 20 mg
Group 4 = elsubrutinib 5 mg
Group 5 = upadacitinib

26.8% of patients (65 patients) had side effects during the study. The table below shows information about the common side effects (in at least 2 or more patients in any group) in the study. The most common side effect was a cold (upper respiratory tract infection).

Overall Study						
	Placebo (19 Patients)	Group 1 (62 Patients)	Group 2 (41 Patients)	Group 3 (39 Patients)	Group 4 (41 Patients)	Group 5 (40 Patients)
Number of patients with at least one side effect	7 (3.7% of patients)	16 (25.8% of patients)	16 (3.9% of patients)	11 (2.8% of patients)	4 (9.7% of patients)	11 (27.5% of patients)
Common cold (upper respiratory tract infection)	1 (5.3%)	3 (4.8%)	1 (2.4%)	1 (2.6%)	0 (0.0%)	0 (0.0%)
Worsening rheumatoid arthritis	1 (5.3%)	0 (0.0%)	3 (7.3%)	1 (2.6%)	1 (2.4%)	1 (2.5%)
Urinary tract infection	0 (0.0%)	0 (0.0%)	2 (4.9%)	2 (5.1%)	1 (2.4%)	2 (5.0%)
Increased alanine aminotransferase (which may be a sign of liver damage)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (5.0%)

Group 1 = elsubrutinib 60 mg + upadacitinib
Group 2 = elsubrutinib 60 mg
Group 3 = elsubrutinib 20 mg
Group 4 = elsubrutinib 5 mg
Group 5 = upadacitinib

Across the whole study, percentages of side effects were similar across patients who took elsubrutinib and/or upadacitinib and who took placebo.

5. What were the overall results of the study?

The study was completed as planned. The study doctors found that the patients in the elsubrutinib 60 mg + upadacitinib group and patients in the upadacitinib group showed fewer signs and symptoms of rheumatoid arthritis compared to the other groups after 12 weeks of treatment. In general, groups treated with elsubrutinib and/or upadacitinib showed fewer signs and symptoms of rheumatoid arthritis after 12 weeks compared to the placebo group.

Across the whole study, percentages of side effects were similar across patients who took elsubrutinib and/or upadacitinib and who took placebo. Across the treatment groups, the number and frequency of side effects were similar to those expected in patients with rheumatoid arthritis.

6. How has the study helped patients and researchers?

The study has helped researchers to learn more about the safety and effectiveness of elsubrutinib and upadacitinib for the treatment of patients with rheumatoid arthritis. It showed that signs and symptoms of rheumatoid arthritis, such as tender and swollen joints, morning stiffness, and fatigue, were improved in the elsubrutinib 60 mg + upadacitinib group and the upadacitinib treatment groups.

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 elsubrutinib and upadacitinib.

7. Are there any plans for future studies?

There are currently no elsubrutinib studies ongoing or planned for the treatment of rheumatoid arthritis.

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 2 Study to Investigate the Safety and Efficacy of ABBV-105 Given Alone or in Combination with Upadacitinib (ABBV-599 Combination) with a Background of Conventional Synthetic DMARDs in Subjects with Active Rheumatoid Arthritis with Inadequate Response or Intolerance to Biologic DMARDs
Protocol Number	M16-063
Clinicaltrials.gov	NCT03682705 https://clinicaltrials.gov/ct2/show/NCT03682705
EudraCT	2018-000666-10 https://www.clinicaltrialsregister.eu/ctr-search/search?query=2018-000666-10
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!