A study to learn how effective and safe a medicine called upadacitinib is to treat patients with moderate to severe ulcerative colitis

Overall Summary

• Ulcerative colitis (UC) is a long-lasting bowel disease that causes inflammation of the large intestine.

• Symptoms can vary from person to person and may include abdominal pain, cramping, diarrhea and other symptoms. These symptoms can change in severity over time. Increases in severity are called flares.

• The reason people have UC is unknown, but researchers think it is caused by a combination of reasons that include genetics and the body’s immune system, which helps fight infection.

• In this study, doctors (investigators) tested a medicine called upadacitinib compared to placebo (no medicine) in patients with moderate to severe UC.

• The study took place from October 2018 to November 2020 in 40 countries and included 522 patients between the ages of 17 and 75 years.

• This study included two parts. In Part 1, patients received either upadacitinib or placebo for 8 weeks. In Part 2, patients who did not respond well to treatment in Part 1, received additional treatment with upadacitinib or placebo for another 8 weeks.

• The main goal of the study was to see how patients with moderate to severe UC responded to upadacitinib or placebo after 8 weeks of treatment (Part 1).

• Response to treatment (clinical remission) was based on stool frequency, rectal bleeding, and endoscopic evaluation (a long flexible tube is inserted into the rectum with a tiny video camera that allows the study doctor to see the inside of the body).

• The study showed that patients treated with upadacitinib had greater responses to treatment compared to patients treated with placebo.

• The most common side effects were acne, increased blood creatine phosphokinase (a chemical primarily released from damaged body muscle), and a small decrease in a type of white blood cell (neutrophil) that helps fight infection in Part 1 and rash, acne, and increased blood creatine phosphokinase in Part 2. Side effects are unwanted medical events considered at least possibly related to treatment.

• 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.
Researchers are looking for a better way to treat people with moderate to severe ulcerative colitis (UC). UC is an inflammatory bowel disease. Inflammation is a part of the body’s response to protect itself from harm. When this happens in the large intestine, it can lead to many different symptoms including urgent or frequent bowel movements (passing poop), stomach pain, cramping, and diarrhea. Symptoms are different for every patient.

The medicines used to treat UC do not work the same for all patients. Symptoms do not improve for some patients receiving treatment. Because of this, study doctors are looking for different medicines to treat the disease.

The medicine in this study was upadacitinib. Upadacitinib works to change the way the immune system responds to help patients with inflammatory diseases. Upadacitinib has been tested in many studies with different inflammatory diseases.

Researchers planned this study as a Phase 3, randomized study with a double-blind part (Part 1) and open-label part (Part 2).

- **Phase 3** studies test potential new treatments in a large number of patients with a condition or disease. In this Phase 3 study, the study doctors looked at the benefits of upadacitinib compared to placebo. A placebo looks like the treatment but has no medicine in it. The study doctors also looked for any side effects patients may have had after treatment with study drug.

- **Side effects** are medical events considered by the study doctors to be at least possibly related to treatment.

- This study had a **double-blind** part, which means that neither the patients nor the study doctors knew who was given upadacitinib or placebo. This ensures that no study results were influenced. This study also had an **open-label** part, which means that patients, caregivers, and study doctors knew that upadacitinib was given to patients.

- This study was **randomized**, which means a computer program was used to randomly (by chance) put the patients into 1 of 2 groups at the start of the study. 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.

1. **General information about the study**

1.1. **What was the main objective of this study?**
1.2. When and where was the study done?

This study took place from October 2018 to November 2020 in the following countries: Argentina, Australia, Austria, Belgium, Bosnia and Herzegovina, Brazil, Canada, Chile, China, Colombia, Croatia, Czech Republic, Estonia, France, Germany, Greece, Hungary, Israel, Italy, Japan, Korea, Latvia, Lithuania, Malaysia, Mexico, Norway, Poland, Portugal, Russia, Serbia, Singapore, Slovakia, South Africa, Spain, Switzerland, Taiwan, Turkey, Ukraine, United Kingdom, and United States (including Puerto Rico).

2. What patients were included in this study?

A total of 522 patients participated in the study. One patient left the study early before receiving any treatment.

All patients had moderate to severe UC for at least 3 months prior to joining the study and had poor response, loss of response, or were unable to tolerate other treatments for UC.

There were more men (62%) than women (38%) in the study and ages ranged from 17 to 75 years.
3. Which medicines were studied?

The medicine in this study was called upadacitinib which was compared to placebo (no medicine). Both upadacitinib and placebo were given as a tablet by mouth.

At the start of the study, patients were randomized into 1 of 2 groups. In Part 1, patients received placebo or upadacitinib for 8 weeks. At the end of Part 1, patients who did not achieve clinical response to treatment could continue to Part 2 where all patients received upadacitinib for another 8 weeks. Clinical response was achieved when a person's symptoms of UC were gone, or mostly gone.

Patients who achieved clinical response at the end of Part 1 or end of Part 2 could join a different study of upadacitinib compared to placebo for additional treatment with upadacitinib in order to evaluate how effective and safe upadacitinib is with a longer length of treatment.

Patients who did not achieve clinical response by the end of Part 2 discontinued treatment.

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:
• 1.1% of patients (2 patients) treated with placebo and 0.3% of patients (1 patient) treated with upadacitinib had serious side effects during the study.
• 1.1% of patients (2 patients) treated with placebo and 0.9% of patients (3 patients) treated with upadacitinib stopped taking the study drug because of side effects during the study.

In Part 2:
• 1.5% of patients (1 patient) treated with placebo in Part 1 and changed to upadacitinib in Part 2 and 1.7% of patients (2 patients) treated with upadacitinib in Part 1 who continued on to upadacitinib in Part 2 stopped taking the study drug because of side effects during the study.
• No patients had serious side effects.

No patient died during the study.

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

<table>
<thead>
<tr>
<th>Part 1</th>
<th>Part 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Placebo (177 Patients)</strong></td>
<td><strong>Upadacitinib (344 Patients)</strong></td>
</tr>
<tr>
<td>Number of patients with serious side effects</td>
<td>2 (1.1% of patients)</td>
</tr>
<tr>
<td>Serious Side Effects</td>
<td></td>
</tr>
<tr>
<td>• Low level of red blood cells (anemia)</td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>• Blood clot in vein in pelvis (pelvic venous thrombosis)</td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>• Blood clot that travels to your lung from elsewhere in the body (pulmonary embolism)</td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>• Worsening ulcerative colitis</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Number of patients who stopped taking study drug because of side effects</td>
<td>2 (1.1%)</td>
</tr>
<tr>
<td>Reasons for stopping</td>
<td>Blood clot in vein in the pelvis (pelvic venous thrombosis), blood clot that travels to your lung from elsewhere in the body (pulmonary embolism), tiredness, weakness (asthenia)</td>
</tr>
</tbody>
</table>
In Part 1, 6.8% of patients (12 patients) treated with placebo and 23.5% of patients (81 patients) treated with upadacitinib had side effects during the study.

In Part 2, 14.7% of patients (17 patients) treated with placebo in Part 1 and changed to upadacitinib in Part 2 and 16.2% of patients (11 patients) treated with upadacitinib in Part 1 and continued on upadacitinib in Part 2 had side effects during the study.

The table below shows information about the common side effects (in 3 or more patients in any group) in this study. The most common side effects were acne, increased blood creatine phosphokinase (a chemical primarily released from damaged body muscle), and a small decrease in a type of white blood cell (neutrophil) that helps fight infection in Part 1 and rash, acne, and increased blood creatine phosphokinase in Part 2.

<table>
<thead>
<tr>
<th>Common Side Effects</th>
<th>Placebo (177 Patients)</th>
<th>Upadacitinib (344 Patients)</th>
<th>Placebo to Upadacitinib (116 Patients)</th>
<th>Upadacitinib to Upadacitinib (68 Patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash</td>
<td>1 (0.6%)</td>
<td>4 (1.2%)</td>
<td>4 (3.4%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Acne</td>
<td>1 (0.6%)</td>
<td>14 (4.1%)</td>
<td>3 (2.6%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Increase in blood creatine phosphokinase (a chemical released from damaged body muscles)</td>
<td>0 (0.0%)</td>
<td>12 (3.5%)</td>
<td>2 (1.7%)</td>
<td>3 (4.4%)</td>
</tr>
<tr>
<td>Small decrease in a type of white blood cell (neutrophil) that helps fight infection</td>
<td>0 (0.0%)</td>
<td>9 (2.6%)</td>
<td>0 (0.0%)</td>
<td>1 (1.5%)</td>
</tr>
<tr>
<td>Decrease in the number of white blood cells</td>
<td>0 (0.0%)</td>
<td>7 (2.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Large decrease in a type of white blood cell called neutrophil that may affect the body's ability to fight infection (neutropenia)</td>
<td>0 (0.0%)</td>
<td>6 (1.7%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Upper respiratory tract infection (common viral infection of the nose, throat and airways)</td>
<td>0 (0.0%)</td>
<td>3 (0.9%)</td>
<td>0 (0.0%)</td>
<td>1 (1.5%)</td>
</tr>
<tr>
<td>Headache</td>
<td>1 (0.6%)</td>
<td>3 (0.9%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Tiredness</td>
<td>1 (0.6%)</td>
<td>3 (0.9%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>
5. What were the overall results of the study?

The main goal of this study was to see how patients with moderate to severe UC respond to upadacitinib compared to placebo after 8 weeks of treatment (Part 1).

Response to treatment (clinical remission) was based on a scoring system called Adapted Mayo score which looks at categories including stool frequency, rectal bleeding, and endoscopic evaluation (a flexible tube is inserted into the rectum and a tiny video camera allows video and images to be taken for review).

After 8 weeks of treatment, this study showed that 33.5% of patients treated with upadacitinib achieved clinical remission per Adapted Mayo score compared to 4.1% of patients treated with placebo.

6. How has the study helped patients and researchers?

This study showed that upadacitinib is safe and effective for patients with moderate to severe UC. This summary only shows the results from this study, which may be different to the results from other studies.

7. Are there any plans for future studies?

Additional studies of upadacitinib are ongoing and future studies may be planned.

8. Who sponsored this study?

This study was sponsored by AbbVie. This summary was reviewed for readability by a patient advocacy group.
Title of Study: A Multicenter, Randomized, Double-Blind, Placebo-Controlled Induction Study to Evaluate the Efficacy and Safety of Upadacitinib (ABT-494) in Subjects With Moderately to Severely Active Ulcerative Colitis

Protocol Number: M14-675

Clinicaltrials.gov: NCT03653026
https://clinicaltrials.gov/ct2/show/NCT03653026?term=m14-675&draw=2&rank=1

EudraCT: 2016-000642-62
https://www.clinicaltrialsregister.eu/ctr-search/search?query=M14-675

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

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!