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Summary of Clinical Trial Results

For Laypersons

A study to learn how effective and safe a medicine called adalimumab works to treat children with moderate to severe ulcerative colitis

Overall Summary

- Ulcerative colitis (UC) is a long-lasting disease of the bowel that causes inflammation of the large intestine. Inflammation is part of the body's response to protect itself from harm. When this happens in the large intestine it can lead to symptoms such as abdominal pain, cramping, and diarrhea.
- Symptoms vary from person to person and can have changes 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.
- In this study, study doctors (investigators) tested a medicine called adalimumab in children who were treated for UC.
- The main goal of the study was to see how patients responded to standard or higher doses of adalimumab after 8 weeks (Part 1) and 52 weeks (Part 2) of treatment.
- The number and frequency of side effects in both the standard and higher dose groups were similar. The most common side effect in Part 1 and Part 2 was headache.
- The results of this study may be used by researchers to further develop this medicine.
- If you or your child 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 for a better way to treat children with ulcerative colitis (UC). Ulcerative colitis is an inflammatory bowel disease. Inflammation is 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), abdominal pain and 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 adalimumab. Adalimumab works to control the activity of the immune system to help patients with inflammatory diseases and is currently approved to treat moderate to severe UC in adults and children. The main goal of the study was to see how patients responded to standard or higher doses of adalimumab after 8 weeks (Part 1) and 52 weeks (Part 2) of treatment.

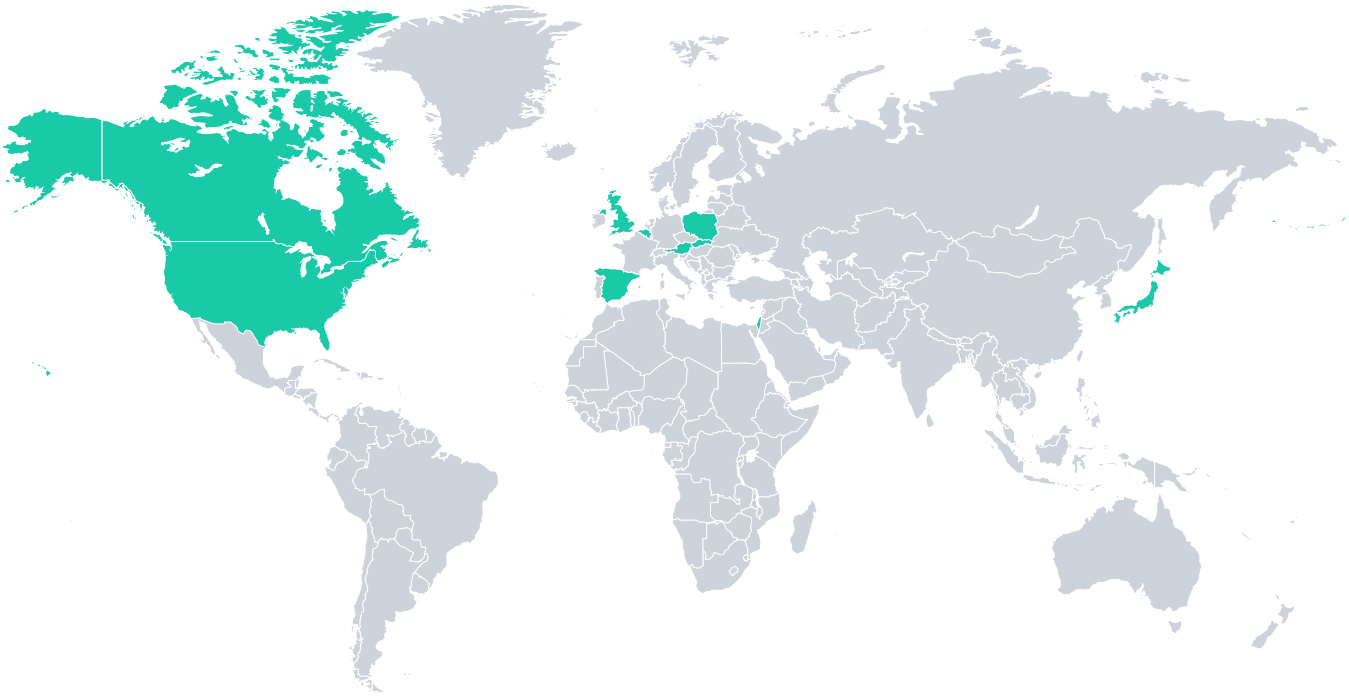
This medicine has been tested in many studies of people with different inflammatory diseases. This study looked at the benefits of adalimumab at a dose which was equivalent to the standard dose approved for adults and at a higher dose in patients who did not improve on other treatment.

Researchers planned this study as a Phase 3, randomized study with double-blind and open-label part.

- **Phase 3 studies** test potential new treatments in patients with a condition or disease. In this Phase 3 study, the study doctors looked at the benefits of adalimumab in children with UC. The study doctors also looked for any side effects patients may have had after treatment with adalimumab. Side effects are medical events considered by the study doctors to be at least possibly related to study drug/ treatment.
- This study had a **double-blind** part, which means that neither the patients, caregivers, nor the study doctors knew who was given which treatment. 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 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 groups. This process is called "randomization", which helps make the groups similar and reduces the differences between the groups.
- This study used a **placebo**, which looks like the treatment but has no medicine in it.

1.2. When and where was the study done?

This study took place from October 2014 to February 2020 in the following countries: Austria, Belgium, Canada, Israel, Japan, Poland, Slovakia, Spain, United Kingdom, and the United States.

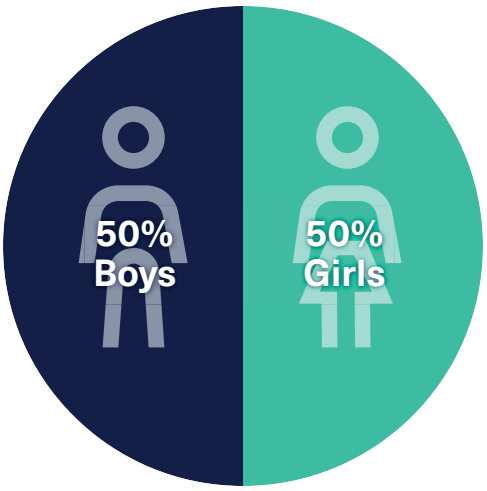


2. What patients were included in this study?

A total of 101 children took part in the study.

This study included children that had UC for at least 3 months prior to joining the study and had active, moderate to severe UC even while on other treatments for UC. Each patient's parent or guardian must have given written consent for t heir child to participate in the study.

There were an equal number of girls (50%) and boys (50%) in the study and ages ranged from 5 to 17 years.



3. Which medicines were studied?

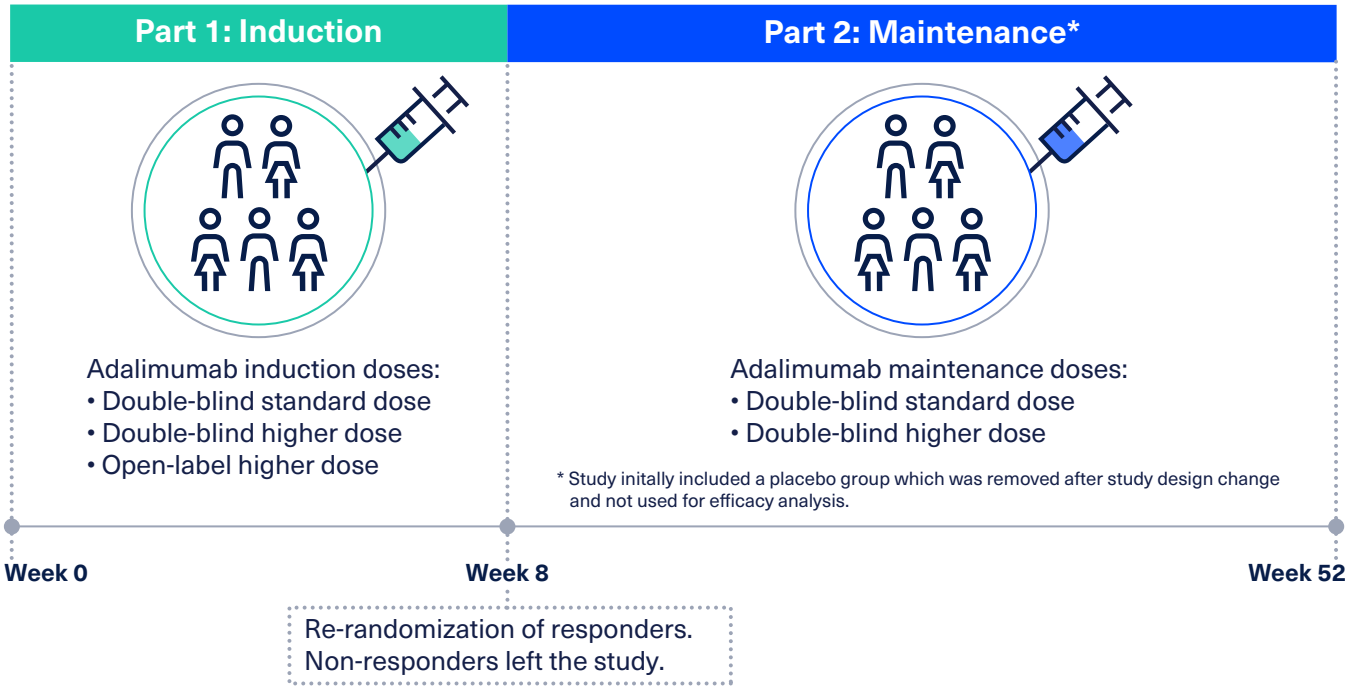
The medicine in this study was called adalimumab, given as an injection under the skin. The study was split into 2 parts, Part 1 (Induction) and Part 2 (Maintenance). Induction is the first round of treatment which aims to improve symptoms and make patients feel better. After induction treatment, patients continue to receive maintenance treatment to keep symptoms under control and try to avoid symptoms getting worse.

While the study was going on, the study design was changed to stop adding patients to the standard dose arm of Part 1 and the placebo (no medicine) arm of Part 2. Patients who had already been randomized to either of these arms at the time of the study design change continued the study as planned.

Part 1 (Induction): Patients were randomized to receive two different doses of adalimumab: a standard dose or a higher dose which were double-blind. After the study design change, the remaining patients received open-label adalimumab at the higher dose. Patients who did not respond to adalimumab at the end of Part 1 left the study.

Part 2 (Maintenance): Patients who responded to treatment with adalimumab in Part 1 were randomized to either the standard dose or a higher dose which were double-blind.

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 the 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.

- 4.0% of patients (4 patients) had serious side effects during Part 1, and 2.5% of patients (2 patients) had serious side effects during Part 2. No individual serious side effects occurred in more than 1 patient. The list of serious side effects included the following: fainting, headache, inflammation of the lining of the heart (pericarditis), inflammation of the pancreas (pancreatitis), meningitis aseptic, psoriasis, worsening of UC.
- 2.0% of patients (2 patients) stopped taking the study drug during Part 1 because of side effects. No patient stopped taking the study drug during Part 2 because of 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.

	Part 1: Induction			Part 2: Maintenance		
	I-SD (32 Patients)	I-HD (51 Patients)	I-HD-OL (18 Patients)	M-SD (33 Patients)	M-HD (36 Patients)	M-PL (12 Patients)
Number of patients with serious side effects	2 (6.3% of patients)	1 (2.0% of patients)	1 (5.6% of patients)	0 (0.0% of patients)	1 (2.8% of patients)	1 (8.3% of patients)
Number of patients who stopped taking study drug because of side effects	2 (6.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Reasons for stopping	Inflammation of the lining around the heart (pericarditis), injection site pain	–	–	–	–	–

I-SD = induction standard dose group; I-HD = induction higher dose group; I-HD-OL = induction higher dose open-label group; M-SD = maintenance standard dose group; M-HD = maintenance higher dose; M-PL = maintenance placebo group

14.9% of patients (15 patients) had side effects during Part 1, and 29.6% of patients (24 patients) had side effects during Part 2. The table below shows information about the common side effects (in at least 2 or more patients in any group) in this study. The most common side effect was headache.

	Part 1: Induction			Part 2: Maintenance		
	I-SD (32 Patients)	I-HD (51 Patients)	I-HD-OL (18 Patients)	M-SD (33 Patients)	M-HD (36 Patients)	M-PL (12 Patients)
Number of patients with at least one side effect	5 (15.6% of patients)	8 (15.7% of patients)	2 (11.1% of patients)	8 (24.2% of patients)	11 (30.6% of patients)	5 (41.7% of patients)
• Headache	1 (3.1%)	2 (3.9%)	0 (0.0%)	2 (6.1%)	0 (0.0%)	1 (8.3%)
• Worsening of UC	0 (0.0%)	0 (0.0%)	1 (5.6%)	1 (3.0%)	2 (5.6%)	0 (0.0%)
• Tiredness (fatigue)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.1%)	0 (0.0%)	0 (0.0%)
• Rash	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (5.6%)	0 (0.0%)

I-SD = induction standard dose group; I-HD = induction higher dose group; I-HD-OL = induction higher dose open-label group; M-SD = maintenance standard dose group; M-HD = maintenance higher dose; M-PL = maintenance placebo group

Across the whole study, patients who took higher doses of adalimumab did not necessarily have more side effects than those who took the standard dose.

5. What were the overall results of the study?

The main goal of this study was to see how young patients with UC respond to adalimumab after 8 weeks (Part 1) and 52 weeks (Part 2) of treatment. Response to treatment (clinical remission) was based on a scoring system called Mayo score, which looks at categories including stool frequency, rectal bleeding, endoscopic evaluation (a flexible tube is inserted into the rectum and a tiny video camera allows videos and images to be taken for review), and overall evaluation by the study doctor.

In Part 1, researchers found that both doses of adalimumab helped patients achieve clinical remission after 8 weeks of treatment. 58.8% of patients receiving the double-blind higher dose (30 patients) and 40.6% of patients receiving the standard dose (13 patients) achieved clinical remission at Week 8.

In Part 2, researchers looked at how many patients had clinical remission at the end of Part 2 among those with clinical response at the end of Part 1. They found that 42.9% of patients receiving the higher dose (15 patients) and 27.3% of patients receiving the standard dose (9 patients) had clinical remission at Week 52.

The number and frequency of side effects in both the standard and higher dose groups were similar to those expected in patients with moderate to severe UC. Higher doses did not give patients more side effects than standard doses.

In summary, the higher adalimumab doses were found to be a safe and most effective option for the treatment of moderate to severe UC in children.

6. How has the study helped patients and researchers?

This study showed that adalimumab at a higher dose is safe and effective for children with moderate to severe UC.

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.

Patients and/or caregivers should consult their physicians and/or study doctors with further questions about their individual care and should not make changes in treatment based on study results alone.

7. Are there any plans for future studies?

Long-term follow-up studies about adalimumab are ongoing. There may be future adalimumab studies.

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 Multicenter, Randomized, Double-Blind Study of the Human Anti-TNF Monoclonal Antibody Adalimumab in Pediatric Subjects With Moderate to Severe Ulcerative Colitis
Protocol Number	M11-290
Clinicaltrials.gov	NCT02065557 https://clinicaltrials.gov/ct2/show/NCT02065557
EudraCT	2013-003032-77 https://www.clinicaltrialsregister.eu/ctr-search/search?query=2013-003032-77
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!