Clinical Study Results

Inspired by patients. Driven by science.

This is a summary of the main results of a clinical study for the drug certolizumab pegol.

This study is sometimes called the C-Early™ study.

UCB Pharma SA sponsored this study and wants to share the results with the participants and the public.

Thank you!

UCB thanks all the participants of this study. All the participants and caregivers helped the researchers learn about using certolizumab pegol in people with severe early rheumatoid arthritis.

We hope this summary helps the participants and their caregivers understand and feel proud of their important role in medical research.

This summary is for informational purposes only. If you need medical advice, please contact your doctor. If you participated in this study and have questions about the results, please speak with a doctor or staff at the study site.

Why was the research needed?

Before a treatment is available to all patients, researchers do clinical studies to get information about how well the treatment works and about how safe it is.

The researchers in this study wanted to learn how well certolizumab pegol worked in a large number of participants with severe, early rheumatoid arthritis (RA). They also wanted to learn if the participants had any medical problems during the study.

RA is an immune system disease that causes pain, swelling, and damage to joints. Some people have RA symptoms that start out severe. This is called severe early RA. People with severe early RA are more likely to have lasting damage to the joints.

Certolizumab pegol works by blocking a protein that is one of the causes of RA. When this study began, certolizumab pegol was approved for patients with RA to take if their other treatments had not helped their RA symptoms.

Protocol number: RA0055

In Year 1 of the study, the researchers wanted to learn how using certolizumab pegol plus methotrexate to treat severe early RA compared with using methotrexate alone. At the time of this study, methotrexate was commonly used by itself to treat people with early RA.

In Year 2 of the study, the researchers wanted to learn more about the participants who took certolizumab pegol plus methotrexate in Year 1 and had low RA disease activity at the final 2 clinic visits of Year 1.

What were the main questions studied?

The main questions the researchers wanted to answer in this study were:

- How many participants had their RA go into and stay in remission in Year 1?
- How many participants had their RA disease activity stay low in Year 2?
- What medical problems did the participants have during the study?

Who participated in the study?

Males and females with early RA participated in this study. They were 18 to 90 years old.

All the participants in the study had severe RA for less than 1 year when they joined the study. They also had never taken a medicine like methotrexate to treat their RA.

The study included 879 participants in 22 countries: Argentina, Australia, Austria, Belgium, Canada, Colombia, the Czech Republic, France, Germany, Hungary, Ireland, Italy, Mexico, Monaco, the Netherlands, Poland, Romania, Spain, Sweden, Switzerland, the United Kingdom, and the United States.

Each participant was in the study for up to a little more than two years, but the whole study lasted three and a half years. The study started in January 2012 and ended in July 2015.

What treatments did the participants take?

The participants in this study took either certolizumab pegol plus methotrexate or a placebo plus methotrexate. A placebo looks like a treatment but does not have any medicine in it.

This was a "double-blind" study. This means none of the participants, study doctors, or study staff knew what treatment each participant was taking. UCB also did not know. Some studies are done this way because knowing what treatment the participants are taking can affect the results of the study. After the study was completed, UCB learned what treatment each participant took so they could create a report of the results.

The researchers used a computer program to randomly choose the treatment the participants took during the study. This helped make sure the treatments were chosen fairly and that comparing the results of the treatments was as accurate as possible.

During Year 1, the participants took either certolizumab pegol plus methotrexate, or the placebo plus methotrexate.

The chart below shows the treatments the participants took during Year 1.

<table>
<tr><th colspan="2">Year 1</th></tr>
<tr><td>660 participants took:
  Certolizumab pegol injections under their skin every 2 weeks.
  Methotrexate pills every week.</td><td>219 participants took:
  Placebo injections under their skin every 2 weeks.
  Methotrexate pills every week.</td></tr>
<tr><td>  The first 3 injections of certolizumab pegol were 400 milligrams each.
  All other injections of certolizumab pegol were 200 milligrams each.
  The doses of methotrexate were 15 to 25 milligrams.</td><td>  The doses of methotrexate were 15 to 25 milligrams.</td></tr>
</table>

During Year 2, all the participants who took certolizumab pegol in Year 1 continued to take methotrexate. Of these participants:

- Some stopped taking certolizumab pegol
- Some took certolizumab pegol every 2 weeks as they did in Year 1
- Some took certolizumab pegol every 4 weeks

The participants who took the placebo plus methotrexate in Year 1 continued taking both during Year 2.

The chart below shows the treatments the participants took during Year 2.

Year 2

293 participants took certolizumab pegol plus methotrexate in Year 2.


84 participants took certolizumab pegol injections of 200 milligrams every 2 weeks.


127 participants took certolizumab pegol injections of 200 milligrams every 4 weeks. They also took placebo injections 2 weeks before their certolizumab pegol injections. This means they were taking injections every 2 weeks just like the other participants.


82 participants did not take certolizumab pegol anymore. They took placebo injections every 2 weeks.


All 293 participants took 15 to 25 milligrams of methotrexate once a week.

66 participants took the placebo plus methotrexate in Year 2.


All 66 participants took placebo injections every 2 weeks.


All 66 participants took 15 to 25 milligrams of methotrexate once a week.

What happened during the study?

Before the study started, all the participants decided to take part after learning about the study. This is called "informed consent." The study doctors and study staff then asked about their medical history and checked their health to make sure they could join the study.

During Year 1 and Year 2 of the study:

	The doctors counted the participants' number of swollen and painful joints.
	The study doctors kept track of any medical problems reported by the participants or observed by the study doctors or study staff.
	The participants rated how their arthritis was making them feel.
	The participants gave blood and urine samples at some clinic visits. They also had X-rays of their hands and feet to check their joints.

Participants who had some improvement in their RA by about halfway through Year 1 could continue in Year 1 of the study.

Participants with low RA disease activity at the final 2 clinic visits of Year 1 could enter Year 2.

About 10 weeks after participants stopped taking study treatment, the study doctor or nurse called each participant to see how he or she was feeling. After this, the participants left the study.

What were the results of the study?

This is a summary of the main results from this study. These are the results from all the participants combined. The individual results of each participant might be different and are not in this summary.

Deciding which treatments work best usually takes results from several studies. Other studies may provide new information or different results. Always talk to a doctor before making any treatment decisions.

To learn how the participants' RA was doing, the study doctors gave each participant an RA score. The score is called DAS28(ESR). The score was based on:

- The number of swollen and tender joints
- The results of a blood test called ESR that measured inflammation
- The participant's rating of how their arthritis was making them feel

How many participants had their RA go into and stay in remission in Year 1?

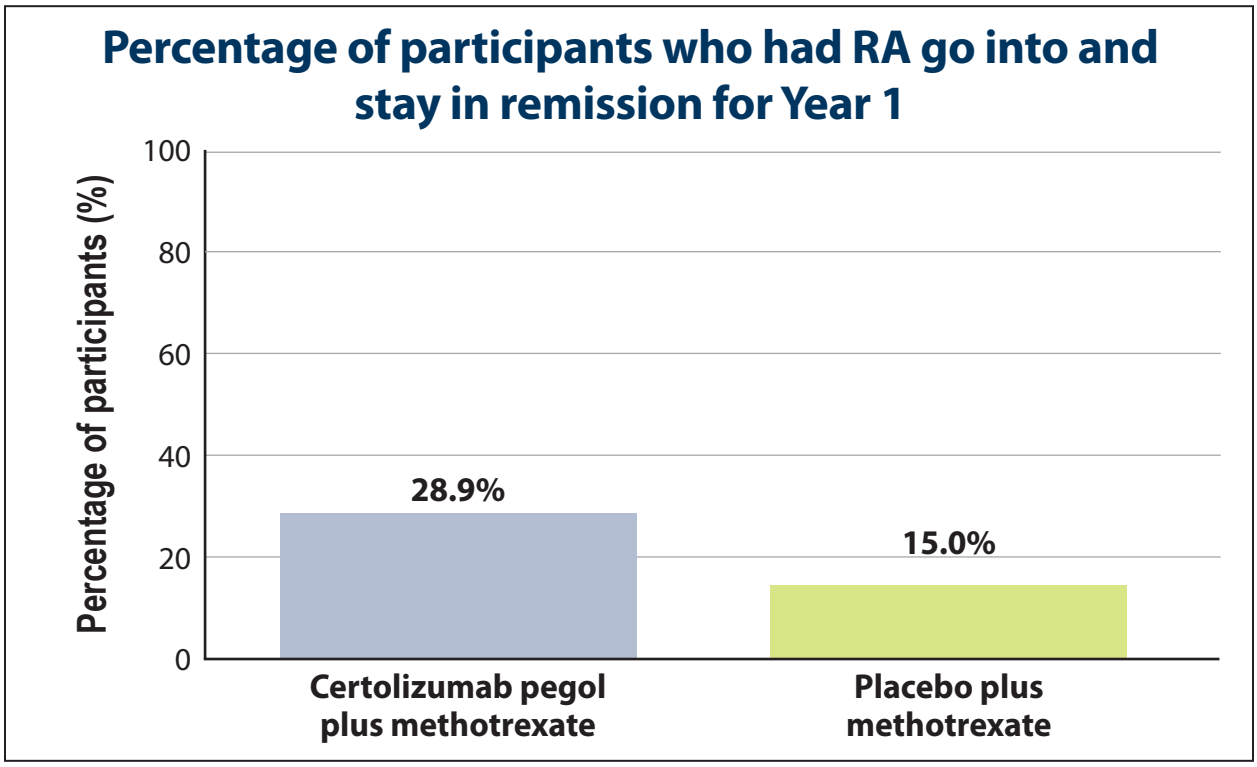
More participants who took certolizumab pegol plus methotrexate had their RA go into and stay in remission in Year 1 compared with the participants who took the placebo plus methotrexate.

For a participant's RA to be considered in and staying in remission, their score had to be less than 2.6 at both of the final 2 clinic visits in Year 1. Being in remission meant there were no or few swollen and/or painful joints, the ESR blood test showed little inflammation, and the participant rated himself or herself as feeling well.

In Year 1:

- 28.9% of participants who took certolizumab pegol plus methotrexate had their RA go into and stay in remission. This was 189 out of 655 participants.
- 15.0% of participants who took the placebo plus methotrexate had their RA go into and stay in remission. This was 32 out of 213 participants.

The graph below shows the results for Year 1:



How many participants had their RA disease activity stay low in Year 2?

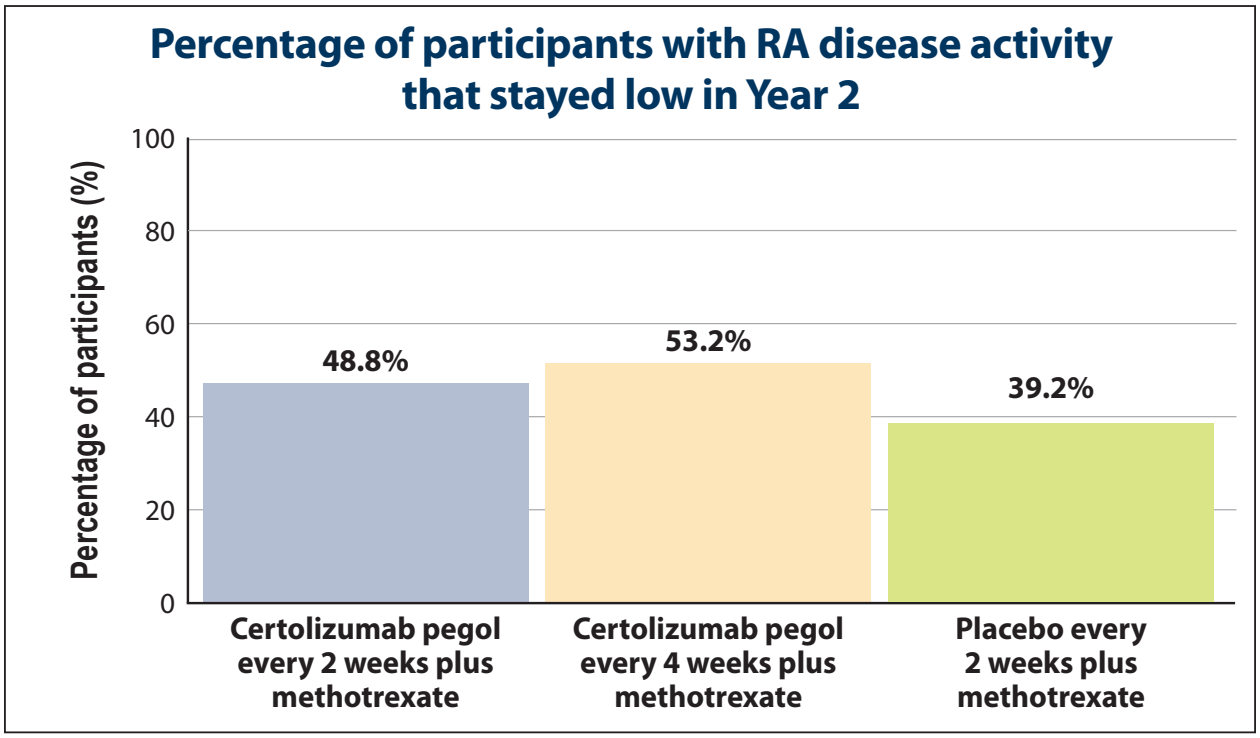
The researchers found that there was a difference between the number of participants with disease activity that stayed low when they took certolizumab pegol every 2 weeks plus methotrexate compared with the placebo plus methotrexate. But, the difference between these treatments was too small for the researchers to know if taking certolizumab pegol every 2 weeks plus methotrexate helped more participants have their RA disease activity stay low compared with those taking the placebo plus methotrexate. The difference between the treatments could have been due to chance. Because of this, the researchers did not compare taking certolizumab pegol every 4 weeks with the placebo in Year 2.

For a participant's RA to be considered as staying low, their score had to be 3.2 or less at all the clinic visits in Year 2. Having low RA disease activity that stays low is not as good as remission, but is an acceptable treatment goal.

In Year 2:

- 48.8% of participants who took certolizumab pegol every 2 weeks plus methotrexate had RA disease activity that stayed low. This was 41 out 84 participants.
- 53.2% of participants who took certolizumab pegol every 4 weeks plus methotrexate had RA disease activity that stayed low. This was 67 out of 126 participants.
- 39.2% of participants who took placebo plus methotrexate had RA disease activity that stayed low. This was 31 out of 79 participants.

The graph below shows the results for Year 2:



What medical problems did the participants have?

This section is a summary of the medical problems the participants had during the study that the study doctors thought might be related to the treatments. These medical problems are called “adverse reactions.” Some participants had more than 1 adverse reaction.

An adverse reaction is considered “serious” when it puts the participant’s life at risk, requires hospitalization, causes disability, causes a baby being born with medical problems, or may have turned into one of these problems if not treated.

These adverse reactions may or may not be caused by the treatments in the study. The results from several studies are needed to decide if a treatment causes an adverse reaction.

How many participants had serious adverse reactions?

In Year 1, the percentage of participants taking certolizumab pegol plus methotrexate who had serious adverse reactions was about the same as participants taking the placebo plus methotrexate. There were 3.1% of participants who had serious adverse reactions. This was 27 out of 876 participants.

One participant who took certolizumab pegol plus methotrexate died due to serious adverse reactions. These serious adverse reactions were:

- Lung disease caused by a germ called Mycobacterium
- Problem in the stomach or bowels caused by a germ called Mycobacterium
- Sudden, severe trouble breathing caused by inflammation and fluid in the lungs

None of the participants who took the placebo plus methotrexate died due to serious adverse reactions.

In Year 2, the percentage of participants who had serious adverse reactions was about the same for each of the treatment groups. There were 1.1% of participants who had serious adverse reactions. This was 4 out of 357 participants.

None of the participants died due to serious adverse reactions in Year 2.

The tables below and on the next page show these results:

Number of participants with serious adverse reactions in Year 1

	Placebo plus methotrexate (out of 217 participants)	Certolizumab pegol plus methotrexate (out of 659 participants)
How many participants had serious adverse reactions?	2.8% (6)	3.2% (21)
How many participants died due to serious adverse reactions?	0.0% (0)	0.2% (1)

Number of participants with serious adverse reactions in Year 2				
Year 1 treatment:	**Placebo plus methotrexate**	**Certolizumab pegol plus methotrexate**		
Year 2 treatment:	**Placebo plus methotrexate (out of 66 participants)**	**Placebo plus methotrexate (out of 81 participants)**	**Certolizumab pegol every 4 weeks plus methotrexate (out of 127 participants)**	**Certolizumab pegol every 2 weeks plus methotrexate (out of 83 participants)**
How many participants had serious adverse reactions?	0.0% (0)	2.5% (2)	0.8% (1)	1.2% (1)
How many participants died due to serious adverse reactions?	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)

What serious adverse reactions did the participants have?

In Year 1, more participants had lung infections than any other serious adverse reactions. Two participants in each treatment group had lung infections.

The table below shows the serious adverse reactions that happened in 2 or more participants in Year 1. There were other serious adverse reactions, but these happened in fewer participants.

Serious adverse reactions in 2 or more participants in Year 1

	Placebo plus methotrexate (out of 217 participants)	Certolizumab pegol plus methotrexate (out of 659 participants)
Lung infection	0.9% (2)	0.3% (2)
Disease that affects tissue in the lungs and causes inflammation and scarring	0.0% (0)	0.3% (2)
Inflammation of the lungs	0.9% (2)	0.0% (0)
Low number of certain blood cells	0.0% (0)	0.3% (2)

The following serious adverse reactions happened in Year 2:

- Infection caused by a germ called Mycobacterium, without it causing sickness in 1 participant who took certolizumab pegol every 2 weeks plus methotrexate
- Prostate cancer in 1 participant who took certolizumab pegol every 2 weeks plus methotrexate
- Infection of the lungs or airways to the lungs in 1 participant who took placebo plus methotrexate in Year 2 and had taken certolizumab pegol plus methotrexate in Year 1
- Lung infection in 1 participant who took certolizumab pegol every 2 weeks plus methotrexate in Year 2 and had taken certolizumab pegol plus methotrexate in Year 1

No other participants had serious adverse reactions during Year 2.

How many participants had any adverse reactions?

In Year 1, a higher percentage of participants taking certolizumab pegol plus methotrexate had adverse reactions than participants taking the placebo plus methotrexate. Overall, 39.6% of participants had adverse reactions that were either serious or not serious. This was 347 out of 876 participants.

The table below shows these results:

Number of participants with adverse reactions in Year 1

	Placebo plus methotrexate (out of 217 participants)	Certolizumab pegol plus methotrexate (out of 659 participants)
How many participants had adverse reactions?	31.8% (69)	42.2% (278)

In Year 2, higher percentages of participants taking certolizumab pegol plus methotrexate had adverse reactions than participants taking placebo plus methotrexate. Overall, 22.1% of participants had adverse reactions that were either serious or not serious. This was 79 out of 357 participants.

Number of participants with adverse reactions in Year 2

Year 1 treatment:	Placebo plus methotrexate	Certolizumab pegol plus methotrexate		
Year 2 treatment:	Placebo plus methotrexate (out of 66 participants)	Placebo plus methotrexate (out of 81 participants)	Certolizumab pegol every 4 weeks plus methotrexate (out of 127 participants)	Certolizumab pegol every 2 weeks plus methotrexate (out of 83 participants)
How many participants had adverse reactions?	15.2% (10)	17.3% (14)	23.6% (30)	30.1% (25)

What adverse reactions did the participants have?

In Year 1, the adverse reaction of feeling sick to the stomach happened in more than 5% of participants in any treatment group. This adverse reaction happened in about the same percentage of participants taking certolizumab pegol plus methotrexate as participants taking placebo plus methotrexate.

No other adverse reaction happened in more than 5% of participants. This means no other adverse reaction happened in more than 5 out of every 100 participants. There were other adverse reactions, but these happened in fewer participants.

The table below shows these results.

Adverse reactions in 5% or more of participants in either treatment group in Year 1

	Placebo plus methotrexate (out of 217 participants)	Certolizumab pegol plus methotrexate (out of 659 participants)
Feeling sick to the stomach	5.5% (12)	7.6% (50)

In Year 2, the adverse reaction of inflammation of the nose and throat area happened in more than 5% of participants in any treatment group. This adverse reaction happened in more participants taking certolizumab pegol every 4 weeks plus methotrexate than other treatments.

No other adverse reaction happened in more than 5% of participants. This means no other adverse reaction happened in more than 5 out of every 100 participants. There were other adverse reactions, but these happened in fewer participants.

The table below shows these results.

Adverse reactions in 5% or more of participants in any treatment group in Year 2

Year 1 treatment:	Placebo plus methotrexate	Certolizumab pegol plus methotrexate		
Year 2 treatment:	Placebo plus methotrexate (out of 66 participants)	Placebo plus methotrexate (out of 81 participants)	Certolizumab pegol every 4 weeks plus methotrexate (out of 127 participants)	Certolizumab pegol every 2 weeks plus methotrexate (out of 83 participants)
Inflammation of the nose and throat area	0.0% (0)	1.2% (1)	5.5% (7)	0.0% (0)

How has this study helped patients and researchers?

The results of this study have helped researchers learn more about using certolizumab pegol in people with severe, early RA.

Deciding which treatments work best for patients almost always takes results from several studies. This summary shows only the main results from this one study. Other studies may provide new information or different results.

At the time this study ended, further clinical studies in early rheumatoid arthritis with certolizumab pegol were not planned.

This summary is provided for informational purposes only. If you need medical advice about your own health or situation, please contact your physician.

Where can I learn more about this study?

You can find more information about this study at the websites listed below:

- For Year 1: www.clinicaltrials.gov/ct2/show/study/NCT01521923
- For Year 2: www.clinicaltrials.gov/ct2/show/study/NCT01519791
- For Year 1 and Year 2: www.clinicaltrialsregister.eu/ctr-search/search?query=2011-001729-25

If you have questions about this study, you can contact UCB by email at datasharing@ucb.com.

Study Information

Protocol Number: RA0055

Study Sponsor: UCB Pharma SA sponsored this study. It is now called UCB Biopharma SPRL and is referred to as UCB in this summary.

Treatment Studied: Certolizumab pegol

Short Study Title: This study was done to see how certolizumab pegol works and to learn about its safety in people with severe early rheumatoid arthritis.

Full Study Title: A multi-center, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of certolizumab pegol in combination with methotrexate for inducing and sustaining clinical response in the treatment of DMARD-naïve adults with early active rheumatoid arthritis

National Clinical Study numbers: NCT01521923 for Part 1, NCT01519791 for Part 2

EudraCT number: 2011-001729-25

Glossary

Disease that affects tissue in the lungs and causes inflammation and scarring:	Also called “interstitial lung disease.”
Feeling sick to the stomach:	Also called “nausea.”
Infection caused by a germ called Mycobacterium, without it causing sickness:	Also called “latent tuberculosis.”
Infection of the lungs or the airways to the lungs:	Also called “respiratory tract infection.”
Inflammation of the nose and throat area:	Also called “nasopharyngitis.”
Inflammation of the lungs:	Also called “pneumonitis.”
Low number of certain blood cells:	A lower than normal number of red blood cells, white blood cells, and platelets. Also called “pancytopenia.”
Lung disease caused by a germ called Mycobacterium:	Also called “pulmonary tuberculosis.”
Lung infection:	Also called “pneumonia.”
Problem in the stomach or bowels caused by a germ called Mycobacterium:	Also called “tuberculosis gastrointestinal.”
Sudden severe trouble breathing caused by inflammation and fluid in the lungs:	Also called “acute respiratory distress syndrome.”

Last updated on 12 March 2019.