Clinical Study Results

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Study Sponsor: Amgen Inc.

Treatment Studied: Romosozumab

Protocol Number: 20110142

Short Study Title: A study to learn how romosozumab worked in women with osteoporosis who had gone through menopause

Thank you

UCB and Amgen thank all the participants of this study. All the participants helped the researchers learn more about using romosozumab in women who have osteoporosis. Romosozumab is also called AMG 785. While Amgen conducted this study, UCB and Amgen have worked together to develop romosozumab.

This is a summary of the main results of this study. This study is sometimes called the ARCH study. An independent, non-profit organization called CISCRP helped prepare this summary of the study results.

We think it is important to share the results with the participants and the public. We hope this summary helps the participants understand and feel proud of their important role in medical research.

The purpose of this summary is only to share information. If you need medical advice, please contact your study doctor. If you participated in this study and have questions about the results, please speak with a study doctor or study staff.

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 if romosozumab worked in a large number of female participants with osteoporosis who have gone through menopause. They also wanted to learn if the participants had any medical problems during the study.

In people with osteoporosis, bones break down and become weak. When this happens, it becomes more likely that their bones will fracture. Women are more likely to have osteoporosis after their periods have stopped. This is known as menopause.

The study drug, romosozumab, was developed to help slow down or stop osteoporosis. It works by helping new bone to form.

In this study, the researchers compared romosozumab to alendronate, which is also called Fosamax®. Doctors already use alendronate to treat osteoporosis in women who have gone through menopause. It works by stopping the breakdown of bone.

In this study, the researchers wanted to find out if romosozumab lowered the number of bone fractures and new fractures in the spine in women who had gone through menopause.

What were the main questions studied?

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

- Did romosozumab lower the number of new bone fractures?
- What medical problems did the participants have during the study?

Who participated in the study?

There were 4,093 women who participated in this study and took study treatment. They were 55 to 90 years old.

The study included participants who took study treatment in 41 countries and territories: Argentina, Australia, Austria, Belgium, Brazil, Bulgaria, Canada, Chile, Colombia, the Czech Republic, Denmark, the Dominican Republic, Estonia, Finland, France, Germany, Greece, Guatemala, Hong Kong, Hungary, Israel, Italy, Latvia, Lithuania, Mexico, Netherlands, New Zealand, Norway, Peru, Poland, Romania, the Russian Federation, Slovakia, South Africa, South Korea, Spain, Sweden, Taiwan, Turkey, the United Kingdom, and the United States.

In this study, the researchers planned to include women with osteoporosis who had both:

- Gone through menopause
- Low bone density in the hip or at the top of the thigh bone

The participants also had either:

- At least 1 medium or severe fracture in the spine, or at least 2 mild fractures in the spine
- At least 2 medium or severe fractures in the spine, or a fracture in the leg that happened up to 2 years before the start of the study

Each participant was in the study for at least 2 years, but the whole study lasted for a little more than 5 years. The study started in May 2012 and ended in June 2017.

What treatments did the participants take?

During the first year of the study, the participants got either:

- Romosozumab and a placebo that looked like alendronate
- Alendronate and a placebo that looked like romosozumab

Alendronate is an existing treatment for osteoporosis. A placebo looks like a study treatment, but does not have study treatment in it. The researchers used placebos to help make sure that the participants did not know what study treatment they were getting.

Romosozumab and its placebo were given through a needle under the skin, also known as an injection. Alendronate and its placebo were taken as tablets by mouth.

The doses of romosozumab and alendronate were measured in milligrams, also called mg. The participants who were given romosozumab got 210 mg once a month. The participants who were given alendronate took 70 mg once a week.

During the first part of the study, none of the participants, study doctors, or study staff knew what treatment each participant was getting. Amgen and UCB staff also did not know. Some studies are done this way because knowing what treatment the participants are getting can affect the results of the study. After the study was completed, Amgen and UCB learned what treatment each participant got so they could create a report of the results.

The researchers used a computer program to randomly choose if the participants got romosozumab or alendronate. This helped make sure the treatments were chosen fairly and comparing the results for the treatments was as accurate as possible.

During the second year of the study, all the participants took alendronate as tablets by mouth. The participants, study doctors, study staff, and Amgen and UCB staff knew that all the participants in this part were taking alendronate.

The chart below shows an overview of the study:

	First year	Second year
	• 2,046 participants were planned to get romosozumab and a placebo that looked like alendronate • 2,047 participants were planned to take alendronate and a placebo that looked like romosozumab	• 3,480 of the participants took alendronate
	• The participants got romosozumab or its placebo through an injection under the skin • The participants took alendronate or its placebo as tablets by mouth	• The participants took alendronate as tablets by mouth
	• The participants got a romosozumab or placebo injection once a month • The participants took alendronate or placebo tablets once a week	• The participants took alendronate tablets once a week

What happened during this study?

This section shows how the study was planned to be done.

Before joining the study, the participants visited the study clinic 1 time. All the participants first learned about the study, including potential risks due to the study drug or their participation in the study, and then decided to join. This is called “informed consent”. Then, the study doctors and study staff asked the participants about their medical history and checked their health to make sure they could join the study. This part lasted up to 5 weeks.

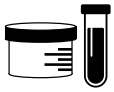
During the first year of the study, the participants visited the study clinic once every month. They got their randomly chosen study treatment.

During the second year of the study, the participants visited the study clinic once every 6 months. In between these visits, the participants had phone calls with the study staff every month. During this time, all of the participants took alendronate.

During the study, the participants:

Took Vitamin D and calcium supplements to help with overall bone health

Had physical exams



Gave blood and urine samples at some clinic visits

Answered questionnaires about their overall health and their symptoms

The study doctors:

Kept track of any medical problems reported by the participants or observed by the study doctors or study staff

Did X-rays to check bone density and fractures at some clinic visits

After getting the last treatment, the participants visited the study clinic 1 more time. The study doctors asked about their health and any medical problems they were having. The participants had a phone call from the study staff after their last visit.

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.

The results below include 3,659 out of 4,093 participants. This is because some participants left the study before having all of their study measurements or treatments.

Did romosozumab lower the number of new bone fractures?

Yes. In this study, the participants who got romosozumab had fewer new bone fractures than those who took alendronate.

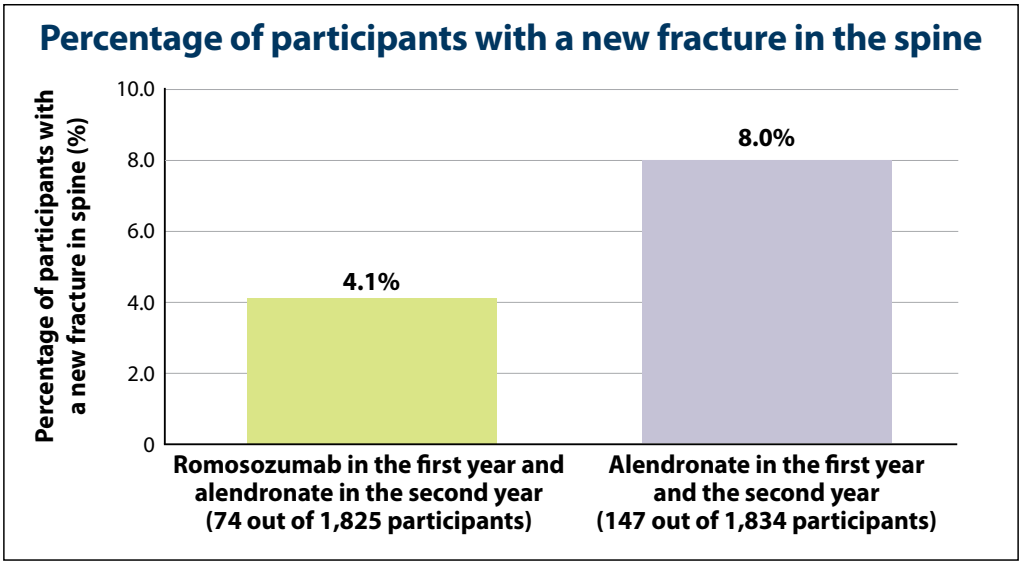
To answer this question, the researchers counted the percentage of participants who had a new fracture in the spine. They also counted the number of bone fractures overall. Then, they calculated the risk of new bone fractures.

After getting study treatment for at least 2 years:

- 4.1% of the participants who got romosozumab in the first year and took alendronate in the second year had a new fracture in the spine. This was 74 out of 1,825 participants.
- 8.0% of the participants who took alendronate in both years had a new fracture in the spine. This was 147 out of 1,834 participants.

This meant that the participants who were given romosozumab in the first year and took alendronate in the second year had a lower risk of getting a new fracture in the spine compared with the participants who took alendronate in both years.

The graph below shows these results.

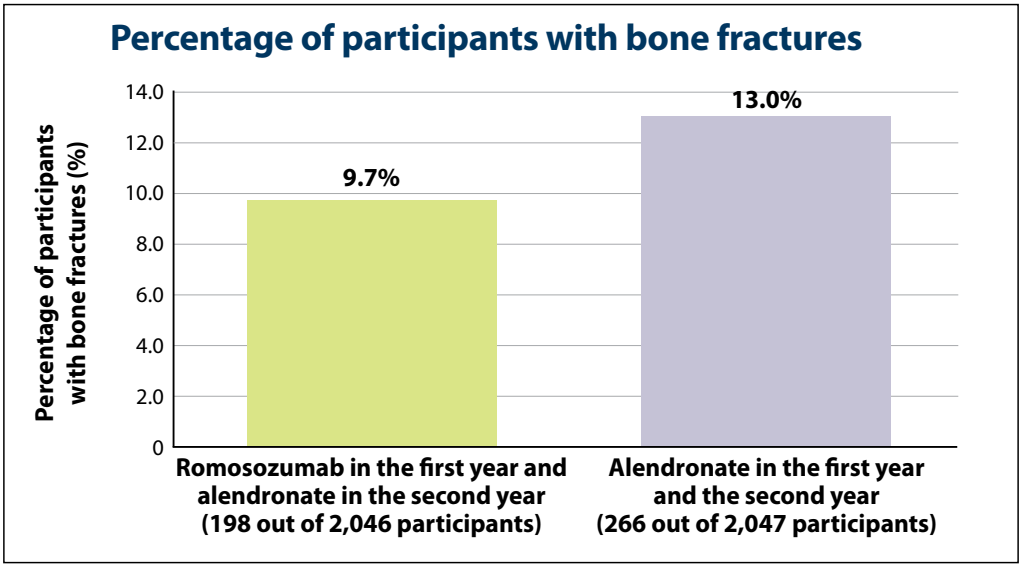


After getting study treatment through 2 years:

- 9.7% of the participants who were given romosozumab in the first year and took alendronate in the second year had any bone fractures. This was 198 out of 2,046 participants.
- 13.0% of the participants who took alendronate in both years had any bone fractures. This was 266 out of 2,047 participants.

This meant that participants who got romosozumab in the first year and took alendronate in the second year had a lower risk of getting any bone fractures, including fractures of the spine and other fractures not in the spine, compared with the participants who took alendronate in both years.

The graph below shows these results.



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. In this summary, these medical problems are called “adverse reactions”.

This summary also includes information about serious adverse reactions. 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 1 of these problems if not treated.

Other studies may or may not show that these adverse reactions were related to the treatments in the study. The final decision about if the treatments actually cause an adverse reaction or not will be based on all the information collected for the treatments and will be shown in the Patient Information Leaflet.

The results below include 4,054 participants who got at least 1 dose of study treatment.

How many participants had serious adverse reactions?

The table below shows the number of serious adverse reactions and deaths in this study. The serious adverse reactions that happened in the first year were also counted for the whole study.

Participants with serious adverse reactions during the study

	During the first year only		During the whole study	
	Romosozumab (out of 2,040 participants)	**Alendronate (out of 2,014 participants)**	**Romosozumab in the first year and alendronate in the second year (out of 2,040 participants)**	**Alendronate in both years (out of 2,014 participants)**
How many participants had serious adverse reactions?	0.6% (13)	0.6% (12)	1.1% (23)	1.6% (32)
How many participants died due to serious adverse reactions?	0.0% (0)	0.1% (3)	0.1% (3)	0.2% (4)

What serious adverse reactions did the participants have?

The table below shows the serious adverse reactions that happened in more than 1 participant. Some of the participants had more than 1 serious adverse reaction. There were other serious adverse reactions, but these only happened in 1 participant during either year of the study.

Serious adverse reactions in more than 1 participant in any treatment group during the study

	During the first year		During the first 2 years	
Serious adverse reaction	Romosozumab (out of 2,040 participants)	Alendronate (out of 2,014 participants)	Romosozumab in the first year and alendronate in the second year (out of 2,040 participants)	Alendronate in both years (out of 2,014 participants)
Heavy bleeding in the upper part of the gastrointestinal tract	0.05% (1)	0.0% (0)	0.1% (2)	0.0% (0)
Heavy bleeding from a stomach ulcer	0.0% (0)	0.05% (1)	0.0% (0)	0.1% (2)
Inflammation of the stomach lining	0.0% (0)	0.05% (1)	0.0% (0)	0.1% (2)
Fracture of the thigh bone	0.0% (0)	0.0% (0)	0.05% (1)	0.1% (2)
Irregular heartbeat	0.0% (0)	0.0% (0)	0.0% (0)	0.1% (2)
Breast cancer	0.0% (0)	0.0% (0)	0.0% (0)	0.1% (2)

How many participants had any adverse reactions?

During the first year of the study, adverse reactions that were serious or not serious happened in:

- 14.7% of participants who were given romosozumab. This was 299 out of 2,040 participants.
- 15.4% of participants who took alendronate. This was 310 out of 2,014 participants.

During the whole study, adverse reactions that were serious or not serious happened in:

- 18.5% of participants who were given romosozumab in the first year and took alendronate in the second year. This was 377 out of 2,040 participants.
- 18.6% of participants who took alendronate in both years. This was 374 out of 2,014 participants.

What adverse reactions did the participants have?

In this study, the adverse reactions that happened in the first year were also counted in the whole study.

During the first year of the study, the only adverse reaction that happened in 1.0% or more participants in any group was pain at the site of an injection. There were other adverse reactions, but these happened in fewer participants.

This adverse reaction of pain at the site of an injection happened in:

- 1.1% of participants who were given romosozumab. This was 22 out of 2,040 participants.
- 0.7% of participants who took alendronate. This was 15 out of 2,014 participants.

The adverse reactions that happened in 1.0% or more participants in any group during the whole study are shown in the table below. There were other adverse reactions, but these happened in fewer participants.

Adverse reactions in 1.0% or more of participants in any treatment group during the whole study

Adverse reaction	Romosozumab in the first year and alendronate in the second year (out of 2,040 participants)	Alendronate in both years (out of 2,014 participants)
Joint pain	1.2% (24)	1.2% (25)
Pain in the upper abdomen	1.1% (23)	1.2% (24)
Pain at the site of an injection	1.1% (22)	0.7% (15)
Indigestion	0.8% (17)	1.2% (25)
Muscle pain	0.6% (13)	1.1% (22)
Headache	0.6% (12)	1.1% (23)

How has this study helped patients and researchers?

The results of this study have helped researchers learn more about using romosozumab in women with osteoporosis who had gone through menopause.

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.

The purpose of this summary is only to share information. If you need medical advice about your own health or situation, please contact your doctor.

The results of this study may be used in other studies to compare romosozumab with other treatments for people who have osteoporosis.

At the time this study ended, further clinical studies of romosozumab in people with osteoporosis were planned.

Where can I learn more about this study?

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

- www.clinicaltrials.gov/ct2/show/study/NCT01631214
- www.clinicaltrialsregister.eu/ctr-search/search?query=2011-003142-41

If you have questions about this study, contact information for UCB is available at www.ucb.com/UCBCares.

Study Information

Protocol Number: 20110142

Study Sponsor: Amgen, Inc.

Full Study Title: A Multicenter, International, Randomized, Double-blind, Alendronate-controlled Study to Determine the Efficacy and Safety of Romosozumab in the Treatment of Postmenopausal Women With Osteoporosis

National Clinical Study Number: NCT01631214

EudraCT Number: 2011-003142-41

Thank you

Participants in clinical studies belong to a large community of people who take part in clinical research around the world. They help researchers answer important health questions and find medical treatments for patients.

Glossary

Description	Also called
Heavy bleeding in the upper part of the gastrointestinal tract	The gastrointestinal tract is a tube that carries food through the body. Heavy bleeding along the upper part of the tube is called “upper gastrointestinal haemorrhage”.
Heavy bleeding from a stomach ulcer	Gastric ulcer haemorrhage
Inflammation of the stomach lining	Gastritis
Fracture of the thigh bone	Femur fracture
Irregular heartbeat	Atrial fibrillation
Joint pain	Arthralgia
Pain in the upper abdomen	Abdominal pain upper
Pain at the site of an injection	Injection site pain
Indigestion	Dyspepsia
Muscle pain	Myalgia

This summary was last updated on 13 April 2021.
The final clinical study report is dated 26 July 2017.