Clinical Study Results

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Study Sponsor: Amgen Inc.

Treatment Studied: Romosozumab

Protocol Number: 20070337

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 FRAME 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 wanted to find out if romosozumab lowered the number of 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 fractures in the spine?
- What medical problems did the participants have during the study?

Who participated in the study?

There were 7,180 women with osteoporosis 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 24 countries and territories: Argentina, Australia, Belgium, Brazil, Canada, Colombia, the Czech Republic, Denmark, the Dominican Republic, Estonia, Germany, Hong Kong, Hungary, India, Japan, Latvia, Lithuania, Mexico, New Zealand, Poland, Romania, Spain, Switzerland, the United Kingdom, and the United States.

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

- Had gone through menopause
- Had low bone density in the hip or at the top of the thigh bone when measured on a scan. This is the amount of bone minerals, like calcium, in the bone tissue
- Did not have very low bone density in the hip or top of thigh bone or were already taking osteoporosis treatments
- Did not have a severe fracture or more than 2 moderate fractures in their spine and did not have any fractures in their hips

Each participant was in the study for about 3 years and 1 month, but the whole study lasted for 3 years and 10 months. The study started in March 2012 and ended in December 2015.

What treatments did the participants take?

The participants in this study got romosozumab or a placebo through a needle under the skin. This is also known as an injection. The placebo injection looked like the romosozumab injection but did not have any treatment in it. The researchers used the placebo to help make sure the effects of romosozumab they found in the study were actually caused by it.

The dose of romosozumab in the injection was 210 milligrams, also called mg. The participants got romosozumab or placebo injections once a month for 12 months.

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 were given romosozumab or placebo. This helped make sure the treatments were chosen fairly and comparing the results for the treatments was as accurate as possible.

After the first part of the study, all of the participants stopped getting romosozumab or placebo and started getting denosumab as an injection. Denosumab is a treatment that doctors currently use to treat osteoporosis. The participants were given 60 mg of denosumab every 6 months for 24 months.

The participants, study doctors, study staff, and Amgen and UCB staff knew that all the participants in this part of the study were getting denosumab.

There were 3,589 participants who were planned to get romosozumab and 3,591 who were planned to get the placebo during this study.

The chart below shows the treatments the researchers planned to study at the start:

	• 3,589 participants were planned to get romosozumab • 3,591 participants were planned to get the placebo • 7,118 of the participants got denosumab after 12 months
	• The participants were given all of the study treatments as injections
	• The participants were given romosozumab or placebo injections every month for 12 months, then denosumab injections every 6 months for 24 months

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.

There were 3 parts to this study:

During the first year of the study, the participants visited the study clinic 13 times. During this part, the participants were given romosozumab or placebo.

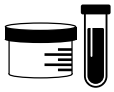
During the second year of the study, the participants visited the study clinic 5 times. During this part, all the participants were given denosumab.

During the third year of the study, the participants visited the study clinic 2 times. During this part, all the participants were given denosumab.

During the study, the participants:

Were given romosozumab or the placebo through an injection once a month during the first year
Were all given denosumab through an injection once every 6 months during the next 2 years

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



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.

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 6,643 out of 7,180 participants for the first year and 6,652 out of 7,180 participants for the first two years. This is because some participants left the study before having all of their study measurements or treatments.

The results from the third year are not included below. This is because it was not a part of the main question that the researchers wanted to answer.

Did romosozumab lower the number of new fractures in the spine?

Yes. In this study, participants who took romosozumab had fewer new bone fractures in the spine than participants who took the placebo.

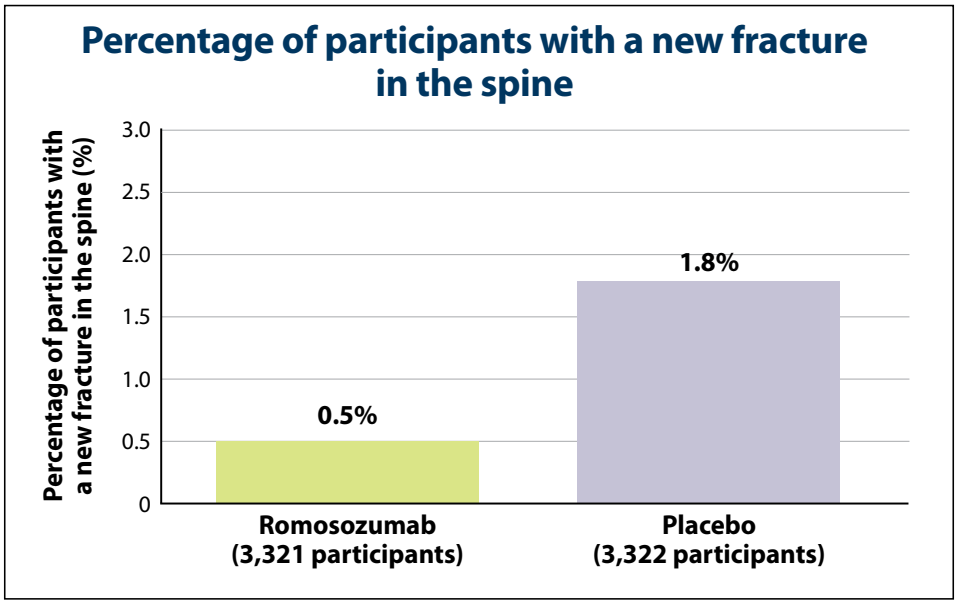
To answer this question, the researchers counted the percentage of participants who had a new fracture of the spine in each part of the study. The researchers then calculated the risk of getting a new fracture in the spine for each group.

At the end of the first year:

- 0.5% of the participants who were given romosozumab had a new fracture in the spine. This was 16 out of 3,321 participants.
- 1.8% of the participants who were given the placebo had a new fracture in the spine. This was 59 out of 3,322 participants.

This meant that the participants who were given romosozumab had a lower risk of getting a new fracture in the spine compared with the participants who were given the placebo.

The graph below shows these results.

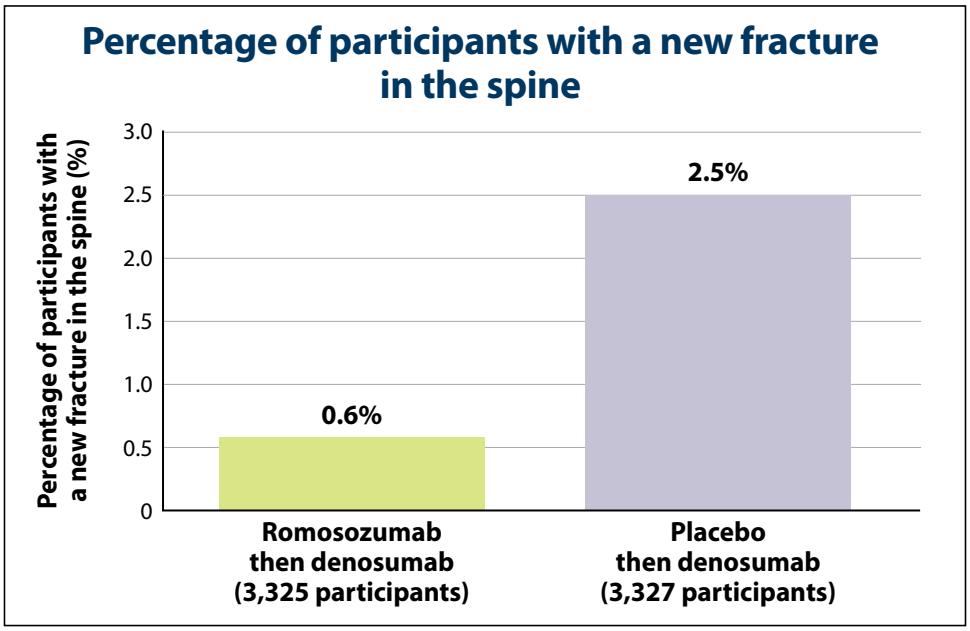


At the end of the second year, the percentage of participants who had a new fracture of the spine in the first 2 years were:

- 0.6% of the participants who were given romosozumab followed by denosumab. This was 21 out of 3,325 participants.
- 2.5% of the participants who were given the placebo followed by denosumab. This was 84 out of 3,327 participants.

This meant that the participants who were given romosozumab followed by denosumab had a lower risk of getting a new fracture in the spine, compared with the participants who were given placebo followed by denosumab.

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 7,157 participants who got at least 1 dose of the 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 3,581 participants)	**Placebo (out of 3,576 participants)**	**Romosozumab followed by denosumab (out of 3,581 participants)**	**Placebo followed by denosumab (out of 3,576 participants)**
How many participants had serious adverse reactions?	0.4% (16)	0.4% (13)	0.9% (31)	0.6% (20)
How many participants died due to serious adverse reactions?	0.03% (1)	0.03% (1)	0.06% (2)	0.03% (1)

What serious adverse reactions did the participants have?

There were 0.7% of participants who had a serious adverse reactions during the study. This was 51 out of 7,157 participants. The table below shows the serious adverse reactions that happened in more than 1 participant during the first 2 years of the study.

There were other serious adverse reactions that happened in 1 participant each during the study. Some of the participants may have had more than 1 serious adverse reaction.

Serious adverse reactions in more than 1 participant during the study

	During the first year		During the first 2 years	
Serious adverse reaction	**Romosozumab (out of 3,581 participants)**	**Placebo (out of 3,576 participants)**	**Romosozumab followed by denosumab (out of 3,581 participants)**	**Placebo followed by denosumab (out of 3,576 participants)**
Long-term kidney disease	0.0% (0)	0.06% (2)	0.0% (0)	0.06% (2)
Bone marrow cancer	0.03% (1)	0.0% (0)	0.03% (1)	0.03% (1)
Lung tumor	0.0% (0)	0.03% (1)	0.03% (1)	0.03% (1)
Increase of proteins called transaminases	0.03% (1)	0.03% (1)	0.03% (1)	0.03% (1)

How many participants had any adverse reactions?

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

- 16.6% of participants who were given romosozumab during the study. This was 596 out of 3,581 participants.
- 13.8% of participants who were given the placebo during the study. This was 494 out of 3,576 participants.

In the first 2 years of the study, adverse reactions that were serious or not serious happened in:

- 18.2% of participants who were given romosozumab followed by denosumab during the study. This was 653 out of 3,581 participants.
- 15.6% of participants who were given the placebo followed by denosumab during the study. This was 557 out of 3,576 participants.

What adverse reactions did the participants have?

The most common adverse reaction was having joint pain. This was the only adverse reaction that happened in 2.0% or more participants in any group. There were other adverse reactions, but these happened in fewer participants. The adverse reactions that happened in the first year were also counted during the first 2 years.

In the first year of the study, the adverse reaction of joint pain happened in:

- 2.0% of participants who got romosozumab. This was 72 out of 3,581 participants.
- 1.7% of participants who got the placebo. This was 62 out of 3,576 participants.

In the first 2 years of the study, the adverse reaction of joint pain happened in:

- 2.2% of participants who got romosozumab followed by denosumab. This was 79 out of 3,581 participants.
- 1.9% of participants who got the placebo followed by denosumab. This was 67 out of 3,576 participants.

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 have 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/NCT01575834
- www.clinicaltrialsregister.eu/ctr-search/search?query=2011-001456-11

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

Study Information

Protocol Number: 20070337

Study Sponsor: Amgen, Inc.

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

National Clinical Study Number: NCT01575834

EudraCT Number: 2011-001456-11

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
Long-term kidney disease	Chronic kidney disease or CKD
Bone marrow cancer	Plasma cell myeloma
Lung tumor	Lung neoplasm malignant
Increase of proteins called transaminases	Transaminases are proteins made by the liver and other parts of the body. An increase is also called “transaminases increased”.
Joint pain	Arthralgia

This summary was last updated on 13 April 2021.
The final clinical study report is dated 14 April 2017.