These Clinical Study Results are provided for informational purposes only.

This lay summary is a brief summary of the main results from a clinical study. The study listed may include approved and non-approved uses, formulations or treatment regimens. It is not intended to promote any product or indication and is not intended to replace the advice of a health care professional. The results reported in any single clinical trial may not reflect the results obtained across the full clinical development program. Only a physician can determine if a specific product is the appropriate treatment for a particular patient. If you have questions, please consult a health care professional. Before prescribing any product, healthcare professionals should consult the regional approved product labeling for indications and proper use of the product.

Table of Contents

Clinical Study Results

Study Sponsors: Mereo BioPharma and Ultragenyx Pharmaceutical Inc.

Treatment Studied: Setrusumab (BPS804 or UX143)

Study Purpose: This study was done to learn if setrusumab helped people with osteogenesis imperfecta

Protocol Number: MBPS205

Thank you!

Participants in clinical studies belong to a large community of people who take part in clinical research around the world. By taking part in this study, the participants helped the researchers learn more about using **setrusumab** (also called **BPS804** or **UX143**) to treat people with **osteogenesis imperfecta** (also called **OI**).

Thank you to the participants who took part in the clinical study for setrusumab. The sponsors of this study, Mereo BioPharma, in partnership with Ultragenyx, are grateful to those who participated and believe it is important to share the results.

This document provides a short summary of this study for a general audience. You can find more information about this study on the websites listed at the end of the document.

Why was the study needed?

Researchers designed this study to learn if a new treatment called setrusumab helps people with a rare genetic disorder called **osteogenesis imperfecta** (also called **OI**).

OI is a rare disorder that causes bones to be weaker and break more easily. There are many types of OI with different causes and symptoms. Most cases of OI are Types I–IV, which are caused by changes in genes. These genes affect how the body makes collagen, a protein that helps strengthen bones.

People with OI can have more frequent broken bones (also called brittle bones), weak bones, misshapen bones, curved spines (also called scoliosis), pain, muscle weakness, hearing loss, and shorter height than people without OI.

Who was in this study?

- This study included 112 adults with OI Type I, III, or IV.
- Everyone in the study was 19 to 74 years old when they joined.
- The study included people from Canada, Denmark, France, the United Kingdom, and the United States.

How long did this study take?

- The study started in September 2017 and ended in November 2020.

What treatment was studied?

- The participants gradually received setrusumab or a placebo over one hour through a needle put into a vein in the arm, also called an IV infusion, once a month for 12 months.
- Setrusumab is a fully humanized monoclonal antibody that may prevent a protein called sclerostin from blocking bone growth
- A placebo looks like a study treatment but has no medicine in it.

What were the main questions the study wanted to answer?

- Did setrusumab improve the health of the forearm bones?
- Did setrusumab improve the health of other bones?
- What side effects happened during the study?

What happened during the study?

At the start of this study, treatment groups were "double-blinded," which means that neither the researchers nor the participants knew which treatment the participant received (setrusumab or placebo). The researchers used a computer program to randomly assign participants to setrusumab or placebo groups. This helped make sure the treatments were chosen fairly and that comparing the results of the treatments was as accurate as possible.

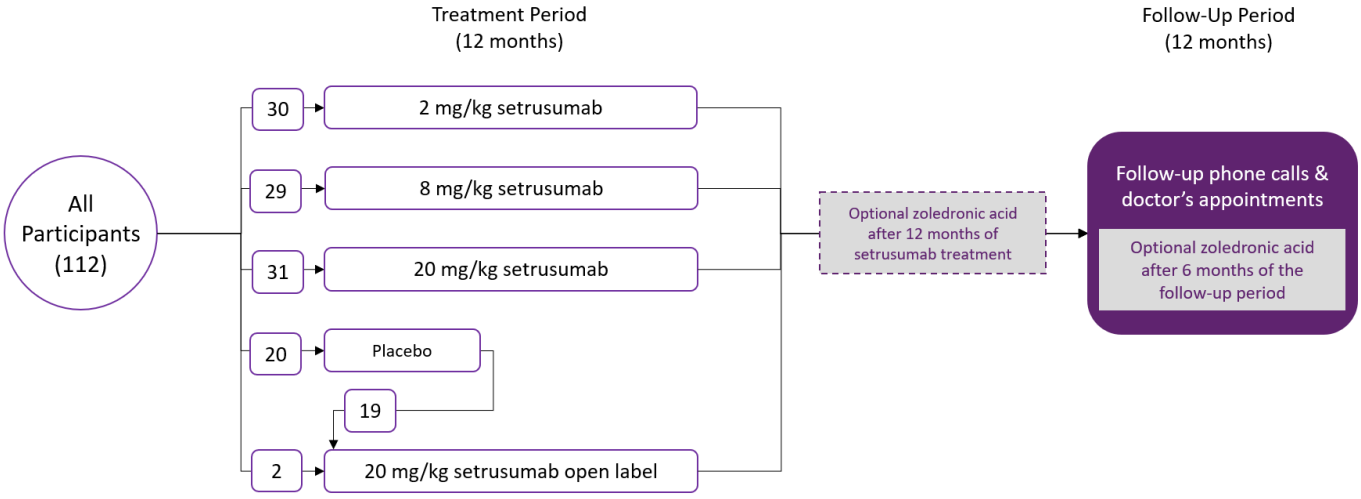
There were four treatment groups. Each group received a different dose of setrusumab for 12 months, or placebo. Setrusumab doses were measured in milligrams per kilogram of body weight (also called mg/kg). This means that the amount of setrusumab each participant received was based on their body weight.

After an average of 5 months, the participants in the placebo group were switched to "open label" setrusumab for an additional 12 months. "Open label" means that both the participants and researchers knew that these participants were receiving the high dose of setrusumab. The other groups remained double blinded through the end of the study.

After taking setrusumab for 12 months, treatment was stopped, and participants entered a follow-up period for an additional 12 months. During this period, participants continued to have doctor's appointments, blood tests, bone scans, and phone calls so researchers could see how long the effects of setrusumab lasted.

Participants were allowed to take a dose of an additional medication called zoledronic acid if their doctor thought it would help. Participants could receive this treatment two different times after they completed setrusumab therapy.

The chart below shows the treatments the participants took:



In this summary, we will refer to the different treatment groups as follows:

- 2 mg/kg setrusumab will be called the **low dose** group
- 8 mg/kg setrusumab will be called the **middle dose** group
- 20 mg/kg setrusumab will be called the **high dose** group
- 20 mg/kg setrusumab open label will be called the **high dose open label** group

What were the results of the study?

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

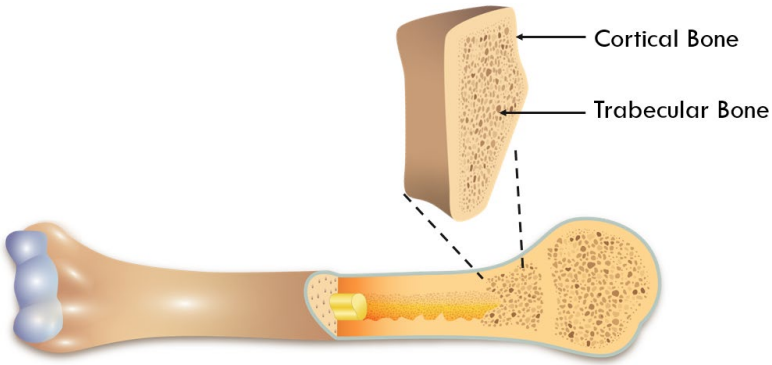
If you have questions about individual results, please contact the doctor or staff at the study site.

The results from several studies are needed to decide which treatments work best and are safest. Other studies may provide new information or different results. Always talk to a doctor before making any treatment changes.

Did setrusumab improve the health of forearm bones?

To answer this question researchers chose to focus on one of the bones of the forearm (also called the radius). The health of participants' radius was assessed based on the density of the spongy inside part of the bone (also called trabecular bone), the density of the radius as a whole, and a computer estimation of its strength. Measurements were taken before participants received setrusumab and again after taking setrusumab for 12 months to see if participants improved.

The anatomy of a bone is shown in the figure below.

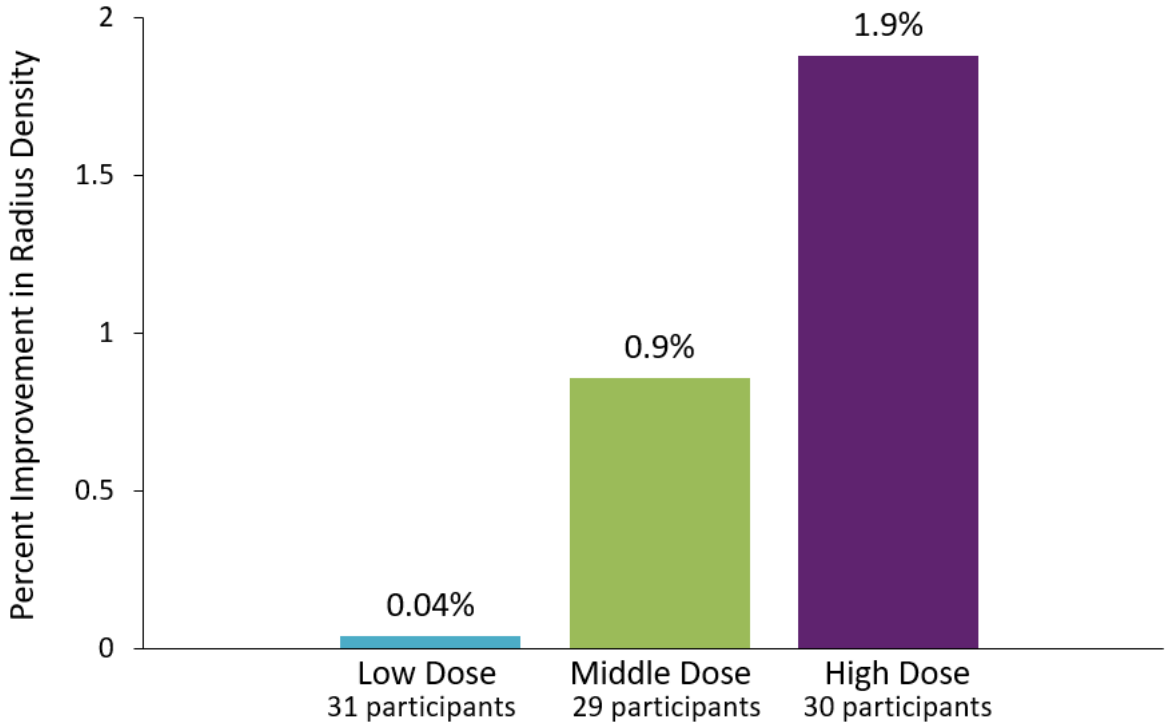


Overall, researchers found that the density of the trabecular bone did not improve in participants after 12 months of setrusumab treatment.

Researchers also looked at the density of the inner (trabecular) and outer (cortical) portions of the radius combined, as shown in the previous figure. Researchers found that the density of the entire radius improved the most after 12 months of high dose therapy. On average, the highest dose group improved by 1.9%, while the middle dose group improved by 0.9%, and the lowest dose group by 0.04%.

The graph below shows these results.

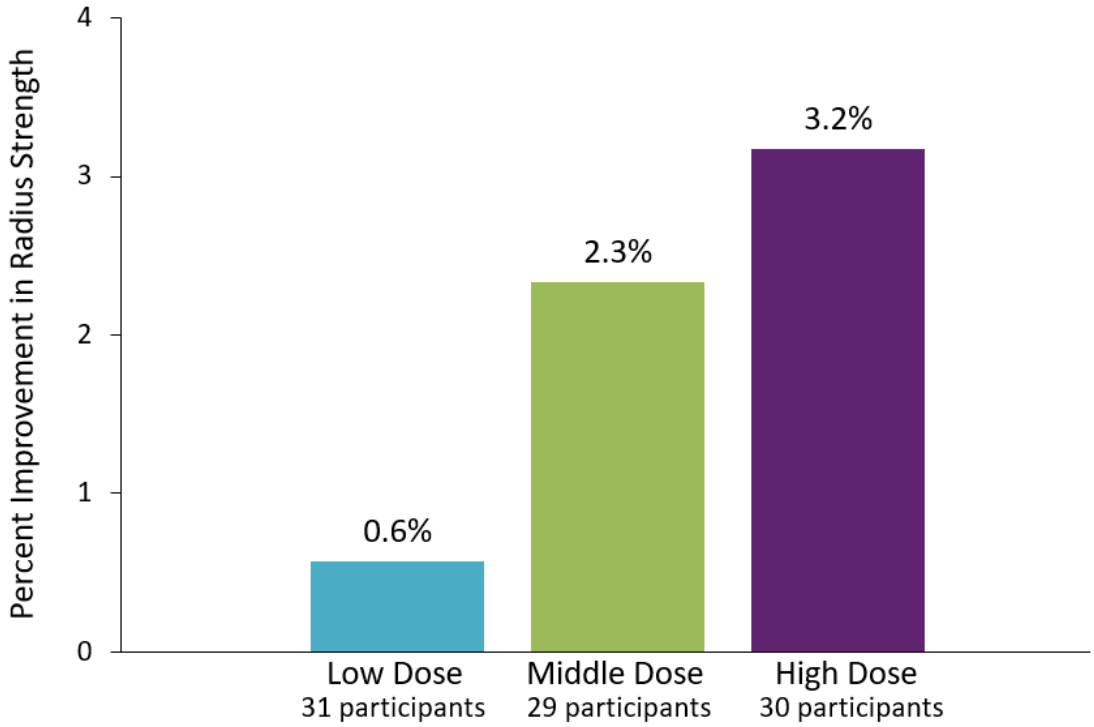
Overall Radius Density After 12 Months of Setrusumab



Researchers also looked at how strong a participant's radius was before and after taking setrusumab for 12 months to see if the medicine improved bone strength. To do this, researchers used a computer estimation (also called Finite Element Analysis, or FEA) of the amount of force the bone could withstand before breaking (also called failure load). Improvements in failure load of 3.2% were seen in the highest dose group, followed by 2.3% in the middle dose group, and 0.6% in the lowest dose group.

The graph below shows these results.

Radius Failure Load After 12 Months of Setrusumab



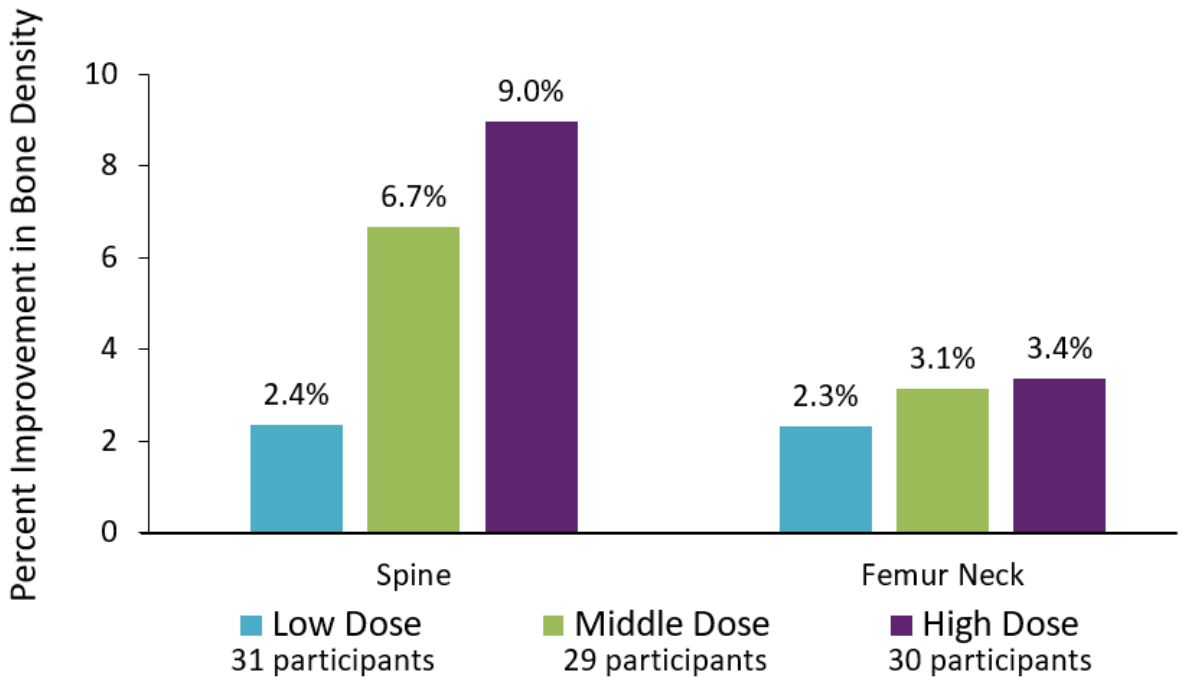
It is important to know that this study was designed to get the most accurate answers to the question of whether setrusumab improves the health of the radius. The results in the next section were not the main question the study was designed to answer, but the researchers believe they may be interesting to people with OI and their caregivers.

Did setrusumab improve the health of other bones?

Researchers looked at the densities of other bones where fractures can occur in participants with OI, including the spine and the top portion of the thigh bone, called the femur neck, to see if they improved after 12 months of setrusumab therapy. In both of these bones, densities increased after 12 months of taking setrusumab, with the most improvement seen in the highest and middle dose groups.

The graph below shows these results.

Spine and Femur Neck Bone Densities After 12 Months of Setrusumab



Overall, the effects on bone density and strength seen in participants who received placebo before switching to 12 months of high dose open label setrusumab treatment were similar to those seen in the high dose setrusumab group.

Researchers also compared the effects of setrusumab treatment in participants with OI Type I with those in participants with OI Types III or IV. Researchers found that the effects of setrusumab on bone density and strength were similar in all OI types examined.

What side effects occurred during the study?

What is a side effect?

A **side effect** is an unwanted or unexpected experience that occurs after taking the study treatment. Side effects may or may not be related to setrusumab, to other drugs taken while in the study, to the participants' medical history, or to any of the tests performed in the study.

A lot of research is needed to know whether a treatment causes a side effect.

What is a serious side effect?

A side effect is **serious** when it:

- Is considered medically important by a doctor
- Requires hospital care
- Causes a birth defect or disability
- Is life-threatening
- Causes death

This section is a summary of the side effects that occurred during the study that doctors thought might be related to setrusumab. Side effects were reported from the time setrusumab treatment or placebo first began through the end of the follow-up period.

Four out of the 111 participants who received setrusumab, or 4%, had serious side effects during this study that doctors thought might be related to setrusumab treatment.

These serious side effects included one allergic reaction (also called anaphylaxis), one case of chills and headache, and one case each of high blood pressure in the lungs and headache in a patient who had fluid in the brain. Each of these participants had received the high or high open label doses of setrusumab.

Fifty-four out of 111 participants who received setrusumab, or 49%, had any side effects during this study, including those considered serious and non-serious, that doctors thought might be related to setrusumab treatment.

Infusion site reactions, which include infusion-related reactions, infusion site pain, irritation, swelling, or other local reactions, were reported in 16 out of 111 participants who received setrusumab, or 14%. These reactions were more frequent in participants who received the high or high open label doses of setrusumab, affecting 10 out of 52 participants, or 19%. In comparison, infusion site reactions were reported in 1 out of 20 participants treated with placebo, or 5%. All infusion site reactions were mild or moderate in severity and happened near where the infusion needle was placed.

The table below shows the most common side effects that occurred in at least 10% of participants in any treatment group that doctors thought might be related to setrusumab. Participants had other side effects, but the side effects occurred in fewer participants or were believed to be unrelated to setrusumab.

Most common side effects in this study*

Side Effect	Low Dose (30 participants)	Middle Dose (29 participants)	High Dose (31 participants)	High Dose Open Label (21 participants)	Total Setrusumab (111 participants)	Placebo (20 participants)
Headache	3% (1)	10% (3)	10% (3)	14% (3)	9% (10)	5% (1)
Infusion-related reaction	0	10% (3)	10% (3)	0	5% (6)	0
Nausea	10% (3)	3% (1)	3% (1)	6% (5)	5% (5)	10% (2)
Neck pain	10% (3)	0	0	0	3% (3)	0
Dizziness	10% (3)	0	0	0	3% (3)	5% (1)

*Side effects that occurred in participants who received setrusumab during the 12-month treatment period or the 12-month follow-up period, or in participants who received placebo for an average of 5 months are included.

Five participants left the study because of serious or non-serious side effects, including four participants who received setrusumab and one from the placebo group. None of the participants died during this study.

How has this study helped people with OI and researchers?

While this study did not show improvements in the density of the inner portion of the radius of participants, overall, the researchers in this study found that setrusumab increased radius strength and the density of the whole radius, spine, and femur neck in people with OI.

The results from additional studies may be needed to decide whether this treatment improves bone health and is safe. The results presented here are for a single study. Other studies may provide new information or different results. Always talk to a doctor before making any treatment changes.

Further clinical research by Ultragenyx is planned for setrusumab in people with OI.

Where can I learn more about this study?

You can find more information about this study on the websites listed below. A full report of the study's results is available on these websites:

- https://clinicaltrials.gov/ct2/show/NCT03118570
- https://www.clinicaltrialsregister.eu/ctr-search/search?query=2016-005096-27

If you have questions about the results, please speak with a doctor or staff at the study site.

Official Study Title: A Study in Adult Patients With Type I, III or IV Osteogenesis Imperfecta Treated With BPS804 (ASTEROID)

National Clinical Trial number: NCT03118570 **EudraCT number:** 2016-005096-27

The phone number for Ultragenyx is (+1) 415 483 8800 and the email is patientadvocacy@ultragenyx.com

The phone number for Mereo BioPharma is (+44) 0333 023 7300 and the email is asteroidstudy@mereobiopharma.com

Thank you!

Your involvement is essential and ensures that the research process moves forward. Thank you for both your participation in this study, throughout the challenges of COVID-19, and for your commitment to research.

Mereo BioPharma is a biopharmaceutical company committed to Improving lives of patients with cancer and rare diseases by unlocking the potential of novel targets.

Mereo BioPharma
1 Cavendish Place • London, W1g 0QF UK
+44 333 0237 300
www.mereobiopharma.com

Ultragenyx is a biopharmaceutical company committed to bringing to patients products for the treatment of rare and ultra-rare diseases, with a focus on serious, debilitating genetic diseases.

Ultragenyx
60 Leveroni Court • Novato, CA 94949
+1 415 483 8800
www.ultragenyx.com

Notes: