Daiichi-Sankyo

Clinical Results Summary

A clinical study to learn about the safety and effects of DS-1211b in people with pseudoxanthoma elasticum

Protocol number: DS1211-A-U201

Thank You!

Daiichi Sankyo, Inc., the sponsor of this study, would like to thank the participants who took part in this study for DS-1211b. Each participant helped to advance medical research for people affected with pseudoxanthoma elasticum. Their contribution to medicine and healthcare is greatly appreciated.

Important note: This summary only shows the results of a single study. Other studies may have different findings. Researchers and health authorities look at the results of many studies to understand which treatments work and how they work. It takes a lot of people in many studies around the world to advance medical science and healthcare.

Do not use the results of this study to make health decisions. Please talk to your doctor before changing any treatment you are taking or if you have any questions about these study results.

What was the main purpose of this study?

Pseudoxanthoma elasticum

Pseudoxanthoma elasticum (PXE) is a rare genetic condition that causes minerals such as calcium to buildup in the body. PXE mainly affects the elastic tissues in the skin, eyes, and blood vessels. Elastic tissues help the skin and blood vessels stretch and bounce back to their original shape. PXE can lead to stiffening and breaks in the elastic tissues, and symptoms including yellowish bumps on the skin, eye problems, and blood flow issues. Currently, there is no cure for PXE, so treatments focus on managing the symptoms.

Most people with PXE have changes in a gene called ABCC6. This leads to lower levels of a substance or chemical called inorganic pyrophosphate (PPi). PPi helps to prevent a harmful buildup of calcium in the body. The study drug, DS-1211b, blocks an enzyme called tissue-nonspecific alkaline phosphatase (TNAP). Researchers have shown that DS-1211b blocks TNAP and increases PPi levels which reduce calcium buildup.

Biomarkers are often proteins or other substances that are easy to measure in the body. Researchers can use biomarkers in the body to measure changes in illness or in response to treatment.

Researchers checked the levels of specific biomarkers in this study:

- Alkaline Phosphatase (ALP): This enzyme disables PPi.
- Pyridoxal 5'-Phosphate (PLP): This is the active form of vitamin B6 and is modified by the activity of ALP.

Each cell in the body contains genes that carry coding information. People with PXE have changes in the ABCC6 gene which affects the levels of certain substances in the body. The biomarkers ALP, PPi, and PLP can serve as indicators of changes after taking DS-1211b, and these changes can be measured in the body.

Researchers wanted to understand the effectiveness of treatment by examining how different doses of DS-1211b affect blood levels of specific biomarkers (ALP, PPi, and PLP).

Treatments given in this study

The treatments given in this study were:

DS-1211b
(Study drug)

A drug being studied for the treatment of PXE. Currently, DS-1211b is not approved for use. This means that it could only be used in a research study such as this one. DS-1211b was taken as tablets by mouth.

Placebo

A placebo looks like the study treatment and is given in the same way, but does not have any medicine in it. Researchers sometimes use a placebo to understand if the changes seen were due to the study treatment or if they happened by chance.

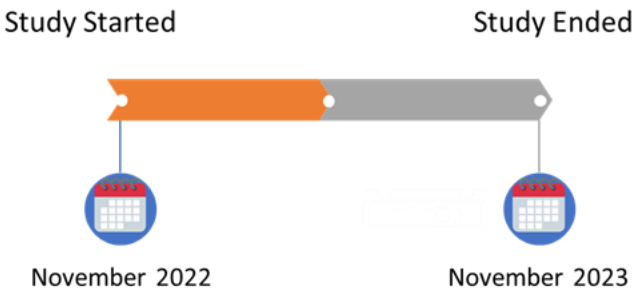
Main purpose of this study

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

- How many participants had side effects using different doses of DS-1211b during this study?
- How did different doses of DS-1211b affect blood levels of the biomarkers ALP, PPi, and PLP?

There were some additional questions that the researchers wanted to answer but these are not discussed in this summary.

How long was this study?



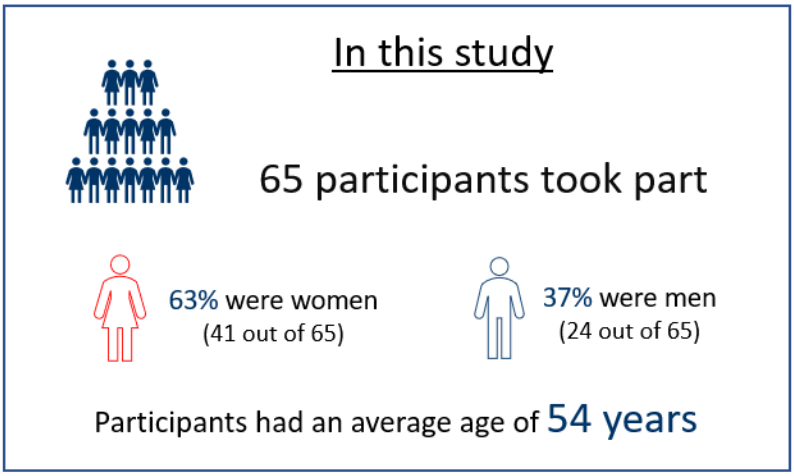
An individual participant could have been in this study for about 3 and a half months. The study started in November 2022 and ended in November 2023. The study was completed as planned.

Who was in this study?

This study included 65 participants from the United States and the Netherlands.

Participants could take part in this study if they:

- were between the ages of 18 years and 75 years,
- had a confirmed diagnosis of PXE.



What happened during this study?

This was a Phase 2 study that compared DS-1211b with placebo. In Phase 2 studies, the study treatment is given to a small number of participants with the disease condition to gather information about the effects and safety of the study treatment in participants.

This study was “double blind”. This means that neither participants nor the researchers knew who was given which treatment. Studies are sometimes done this way to make sure that study results are not biased by this information.

The study was divided into three periods: screening, treatment, and safety follow-up.

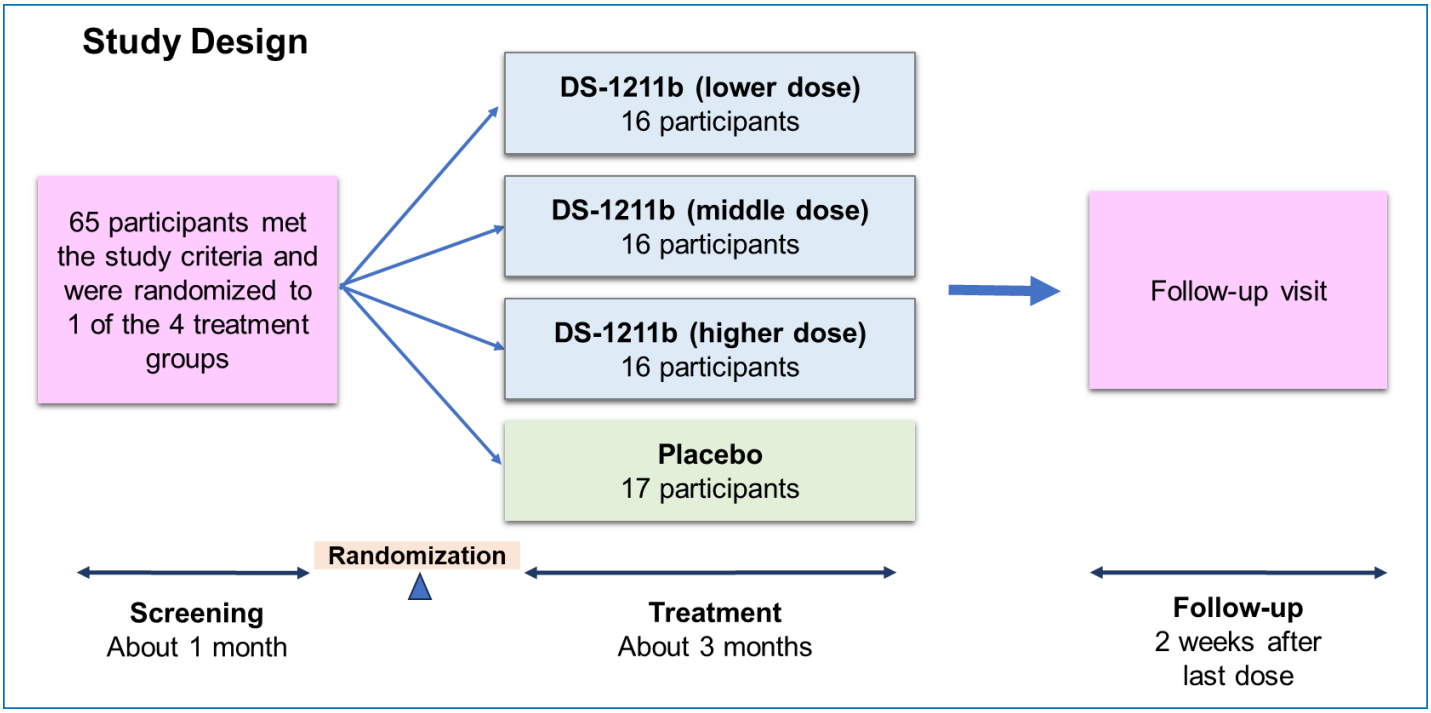
Screening period (about 1 month): The researchers checked if the participants met the requirements to take part in this study based on their medical history and health.

Treatment period (about 3 months): Researchers randomly assigned 65 participants to 4 different treatment groups using a computer system. This process is called randomization. It means that each participant could be assigned to any group, and it helps to make sure the groups are distributed fairly.

Out of the 4 treatment groups, 3 groups received different doses of DS-1211b: a lower dose, a middle dose, or a higher dose. The fourth treatment group received a placebo. All participants took either DS-1211b or placebo as tablets by mouth, once daily in the morning.

Follow-up (2 weeks): The researchers checked each participant’s health about 2 weeks after they received their last dose of study treatment.

The study design was as follows:



The researchers took blood samples from participants at different timepoints during the study. They checked for DS-1211b levels in the blood, assessed the biomarkers, and monitored each participant's overall health throughout the study.

What were the key results of this study?

Key results from this study are shown for the total group of participants as average results. This summary does not show the results from each individual participant. An individual participant's results could be different from the total group of participants. A full list of the questions the researchers wanted to answer, and a detailed presentation of the results, can be found on the websites listed at the end of this summary.

The key results are summarized below and show the effect and safety of DS-1211b in this study.

How many participants had side effects using different doses of DS-1211b during this study?

Side effects are medical problems (such as feeling tired) that happened during the study which the study doctor thought could be related to the study treatment.

The answer to this question is presented in the next section 'What side effects did the study participants have?'.

How did different doses of DS-1211b affect blood levels of the biomarkers ALP, PPi, and PLP?

To answer this question, the researchers took blood samples from participants before and after they received DS-1211b, and at different time points during each visit.

The results showed that during the 3 months treatment period, all 3 doses of DS-1211b (lower, middle, and higher) lowered ALP levels and increased PPi and PLP levels, in the blood of the participants. By the end of the treatment period, and during follow-up visits, levels of ALP, PPi, and PLP had returned to their initial levels before treatment.

However, the researchers would emphasize that a 3-month study is too short to assess the effect of DS-1211b on the participants' PXE symptoms.

What side effects did the study participants have?

This section provides a summary of side effects from this study. The websites listed at the end of this summary have more information about the side effects and other medical problems that happened in this study.

Side effects are considered serious if they cause death, are life-threatening, cause disability, cause lasting problems, cause birth defects, or require hospitalization. Some participants may stop study treatment because of side effects.

How many participants had serious side effects?

In this study, side effects were monitored for all 65 study participants.

No serious side effects were reported for any of the participants. No participants died during the study.

How many participants had non-serious side effects?

10% (5 out of 48) of participants who received different doses of DS-1211b reported non-serious side effects. Of these participants, 13% (2 out of 16) who received a lower dose, 13% (2 out of 16) who received a middle dose, and 6% (1 out of 16) who received a higher dose of DS-1211b reported non-serious side effects. Additionally, 6% (1 out of 17) of participants who received the placebo reported non-serious side effects.

The non-serious side effects that happened in any group are shown below as a percentage (number of participants) of that group. Some participants experienced more than 1 non-serious side effect.

	DS-1211b			Placebo (17 participants)
	Lower dose (16 participants)	Middle dose (16 participants)	Higher dose (16 participants)	
Eye-related migraine headache	6% (1)	0	0	0
Indigestion	6% (1)	0	0	0
Involuntary shaking	6% (1)	0	0	0
Loss of detail vision	6% (1)	0	0	0
Hot flashes	0	6% (1)	0	0
Menstrual problems	0	6% (1)	0	0
Vomiting	0	6% (1)	0	0
Head discomfort	0	0	6% (1)	0
Headache	0	0	0	6% (1)

How many participants had to stop study treatment because of side effects?

One participant who received a lower dose of DS-1211b stopped treatment early because of a side effect of loss of detail vision. This participant reported similar symptoms before the start of study participation.

How was this study useful for patients and researchers?

This study helped researchers learn about the safety and effects of DS-1211b in people with PXE.

Findings from this study may be used in other studies to learn whether patients with PXE are helped by this treatment.

Please remember, this summary only shows the results of a single study. Other studies may have different findings. Please talk to a doctor before changing any treatment you are taking or if you have any questions about these study results.

Where can I learn more about this study?

You can find more information about this study on the following websites:

- www.clinicaltrials.gov: Use the NCT identifier NCT05569252 in the search field.
- www.clinicaltrialsregister.eu/ctr-search/search: Use the EudraCT identifier 2022-000676-19 in the search field.

Please remember that the results on these websites may be presented in a different way. If you were a study participant and have questions about the results of this study, please speak with the doctor or staff at your study site.

Full study title: A Phase 2, 12-Week, Randomized, Double-Blind, Placebo-Controlled Study of DS-1211b in Individuals with Pseudoxanthoma Elasticum

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