



Daiichi-Sankyo

## Clinical Results Summary

### A clinical study to understand the effect of probenecid on the blood levels of pexidartinib in healthy participants

Protocol number: PL3397-A-U122

Thank You!



Daiichi Sankyo, Inc., the sponsor of this study, would like to thank the participants who took part in this study for pexidartinib, also known PLX3397. Each participant helped to advance medical research. 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 a 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?

Pexidartinib, also known as PLX3397, is a study drug that is being tested for its ability to stop the growth of tumor cells. A tumor is a type of cancer or abnormal growth of cells in the body, which can spread to other parts of the body.

Probenecid is a drug already available in the market for treating conditions like a type of arthritis (gout) and excess blood uric levels (hyperuricemia). Probenecid also blocks certain proteins that break down pexidartinib in the body. This may help to slow the breakdown of pexidartinib in the body.

In this study, researchers wanted to understand the effect of probenecid on the blood levels of pexidartinib and its breakdown product ZAAD-1006a in healthy participants.

### Treatments given in this study



#### **Pexidartinib** (Study drug)

A drug being studied for the treatment of tumors. When the study started, pexidartinib was not approved for use. This means that it could only be used in a research study such as this one.



#### **Probenecid** (Approved drug)

An approved drug for treating a type of arthritis (gout) and excess blood uric acid levels (hyperuricemia).

### Main goal of this study

The main question the researchers wanted to answer in this study was:



Was there a difference in the blood levels of pexidartinib when given with probenecid versus when given alone?

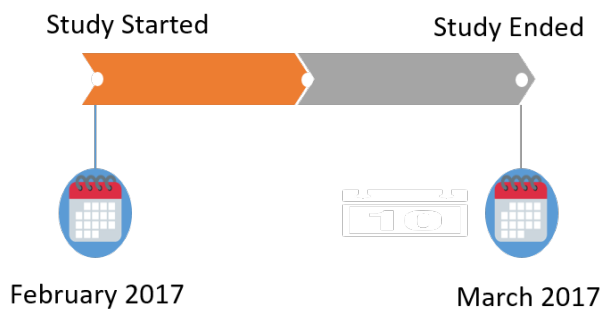
## Other goal of this study

Researchers also wanted to answer the following question:

- Was there a difference in the blood levels of ZAAD-1006a, when given pexidartinib with probenecid versus when given alone?

Researchers also monitored the health of the participants throughout the study.

## How long was this study?



An individual participant could have been in this study for about 1 month. The study started in February 2017 and ended in March 2017.

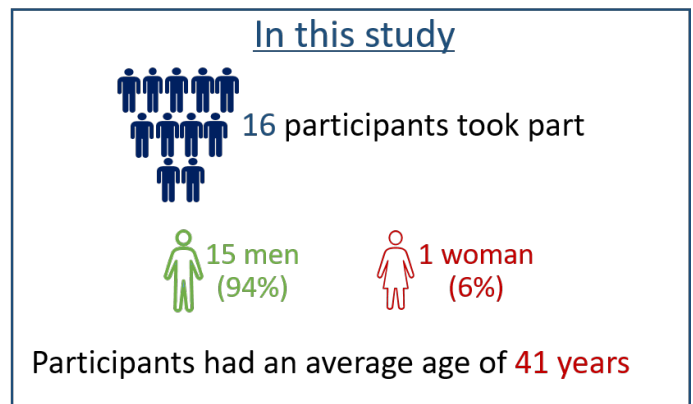
This study was completed as planned. When the study ended, the results were collected and a study report was created. This summary is based on that report.

## Who was in this study?

This study included 16 participants from a single site in the United States.

Healthy men and women could take part in this study if they were:

- between 18 years and 60 years of age,
- not underweight,
- using effective birth control methods during the study or were unable to have children.



## What happened during this study?

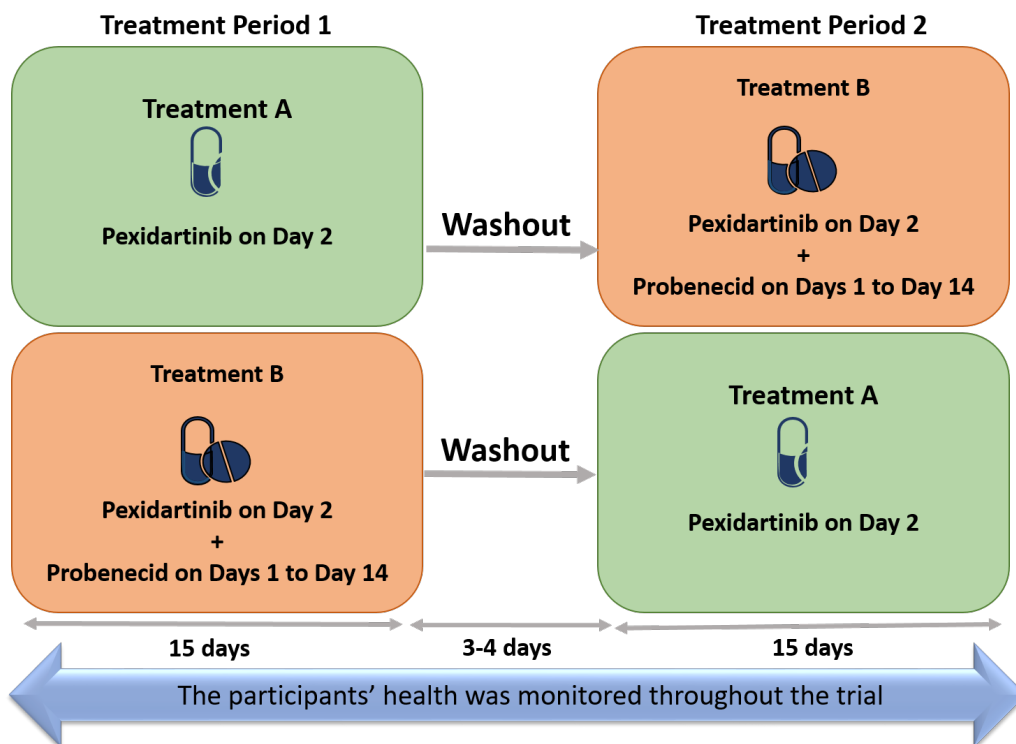
This was a Phase 1 study done in a small number of participants to learn what happens to the study drug in the body. This was an “open label” study. This means that both the researchers and participants knew which treatment was given to which participant.

Participants were screened to find out if they could take part in the study. Researchers then randomly assigned participants equally to 2 treatment groups using a computer system. This process is called randomization. It means that each participant could be assigned to any group to make sure the groups are distributed fairly.

Participants in each treatment group went through 2 treatment periods: Period 1 and Period 2. Each treatment period lasted for 15 days. Participants were given both the treatments based on the order shown in the figure below:

- **Treatment A:** Pexidartinib 600 milligram (mg) as capsules on Day 2.
- **Treatment B:** Probenecid 500 mg tablet 4 times a day for 14 days. Pexidartinib 600 mg as capsules on Day 2.

### What happened in this study



There was a washout period of 3 to 4 days between treatment periods. Participants were given no drugs during this time to allow drugs given during Period 1 to leave their body.

Researchers took blood samples at defined time points and monitored the participants' health throughout the study.

A total of 16 participants were enrolled in this study, but 1 participant in Treatment B (treatment sequence BA) discontinued the study due to the side effect of rash. So, 15 participants received Treatment A and 16 participants received Treatment B.

## 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 website listed at the end of this summary.

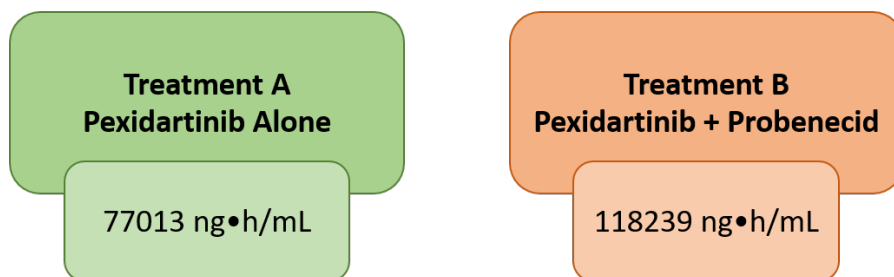
### Was there a difference in the blood levels of pexidartinib when given with probenecid versus when given alone?

The total blood level of pexidartinib measured over time was **60% higher** when given with probenecid compared with when given alone. This means that probenecid reduced the breakdown of pexidartinib in the body as expected.

#### *i* How was this measured?

Researchers took blood samples from participants at defined time points. They then measured the total levels of pexidartinib in participants' blood over time in units, nanograms hours per milliliter (ng•h/mL). This shows how much of pexidartinib in nanogram (one thousand-millionth of a gram) was found in each milliliter of blood over time.

#### Total levels of pexidartinib in participants' blood



## What were the other results of this study?

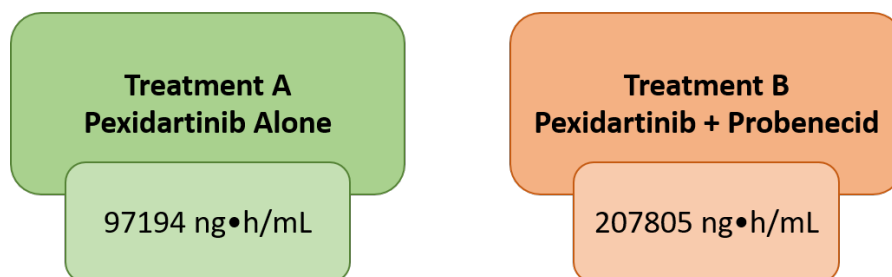
### Was there a difference in the blood levels of ZAAD-1006a, when pexidartinib was given with probenecid versus when given alone?

The total blood level of ZAAD-1006a measured over time was **2 times higher**, when pexidartinib was given with probenecid compared with when given alone. This means that probenecid reduced the breakdown of ZAAD-1006a in the body as expected.

#### How was this measured?

Researchers took blood samples from participants at defined time points. They then measured the total levels of ZAAD-1006a in participants' blood over time in units, nanograms hours per milliliter (ng•h/mL).

#### Total levels of ZAAD-1006a in participants' blood



## What medical problems did the study participants have?

Side effects are medical problems (such as feeling tired) that happened during the study which the study doctor (investigator) thought could be related to the treatments in the study. This section provides a summary of side effects related to pexidartinib. The website listed at the end of this summary has more information about the medical problems that happened in this study.

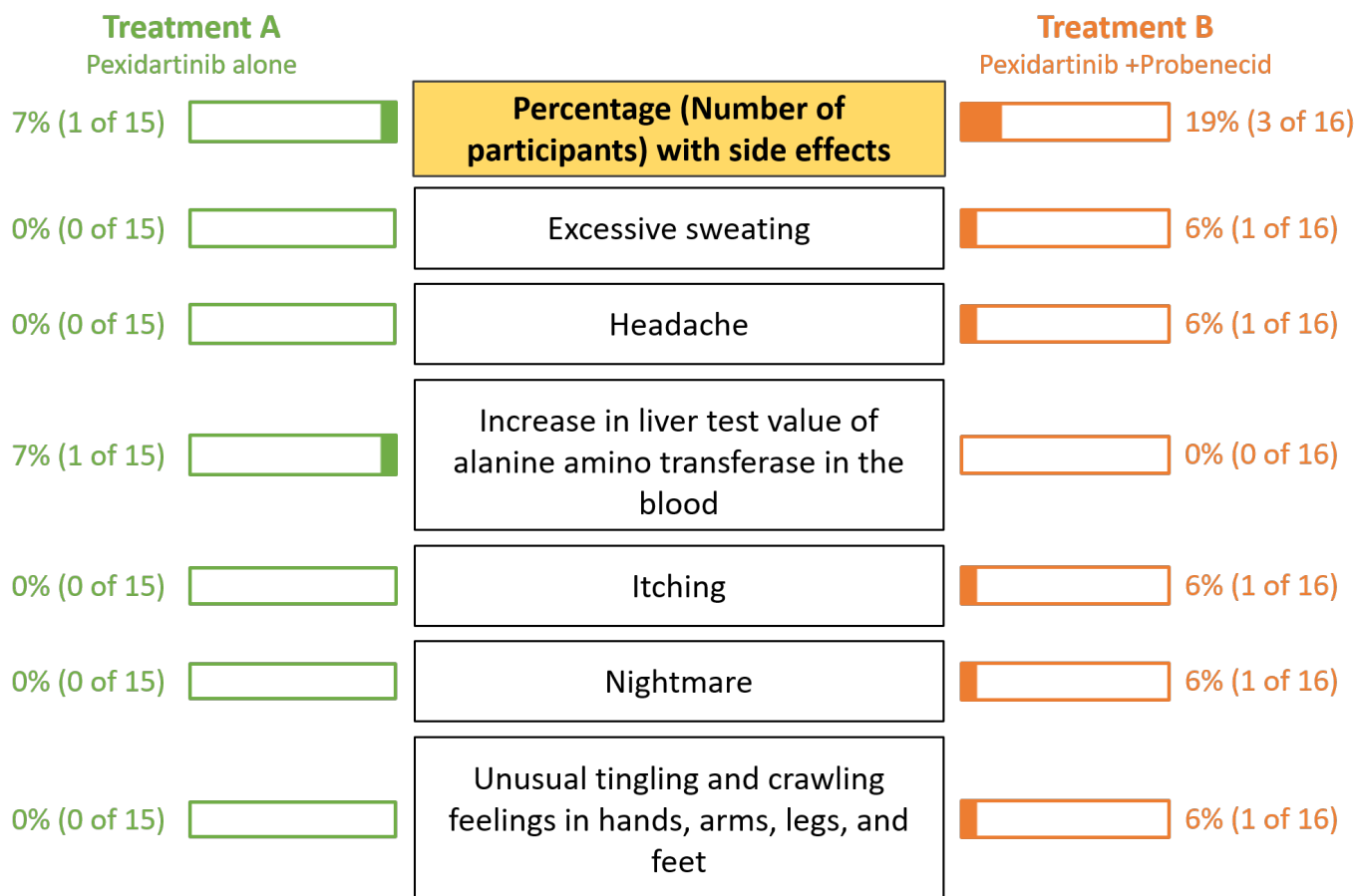
Side effects are considered serious if they cause death, are life-threatening, cause lasting problems, or require hospitalization. Some participants stop study treatment because of side effects.

### How many participants had serious side effects?

No participant had a serious side effect during this study. No deaths were reported due to side effects.

## How many participants had side effects during the study?

The side effects that happened during any treatment are presented below:



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

No participant stopped the study treatment due to a side effect related to pexidartinib.

## How was this study useful for patients and researchers?

This study helped researchers understand the effect of probenecid on the blood levels of pexidartinib and its breakdown product ZAAD-1006a in healthy participants.


Findings from this study may be used in other studies. Other studies for pexidartinib are ongoing.

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 website:

 [www.clinicaltrials.gov](http://www.clinicaltrials.gov): Use the NCT identifier NCT03138759 in the search field.

Please remember that the results on this website 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:** An Open-Label, Randomized, 2-Treatment, 2-Period, Crossover Study to Evaluate the Effect of Probenecid on the Pharmacokinetics of Pexidartinib in Healthy Subjects.

**Sponsor:** Daiichi Sankyo, Inc.

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