



## Clinical Results Summary

# A clinical study to learn about the effects of PLX3397 when given to people with advanced solid tumors in addition to paclitaxel

Protocol number: PLX108-07

### Thank You!



Daiichi Sankyo, Inc., the sponsor of this study, would like to thank the participants who took part in this study for PLX3397, also known as pexidartinib. Each participant helped to advance medical research for people affected with advanced solid tumors. 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?

### Advanced solid tumor

A solid tumor is a type of cancer that starts in an organ, muscle, or bone of the body. A tumor is considered to be “advanced” if it has spread to other parts of the body. The most common symptoms of advanced tumors are pain, breathing problems, loss of appetite, weight loss, feeling very tired, depression, vomiting, and feeling sick to the stomach. Researchers have found that certain kind of protein called ‘kinase’ helps tumor cells divide and grow. It is believed that by stopping this protein from working, the growth of the tumor cells can be stopped. PLX3397, also known as pexidartinib, is a study drug that is being tested for its ability to stop the growth of tumor cells by preventing this protein from working.

Some types of advanced solid tumors include:

- **epithelial ovarian cancer** develop from the cells that cover the outer surface of the ovary. Ovaries are female organs that produce eggs.
- **primary peritoneal cancer** is a rare cancer that develops in a thin layer of tissue that lines the stomach, uterus, bladder, and rectum.
- **fallopian cancer** starts in the fallopian tubes. Fallopian tubes connect the ovaries to the womb.

All 3 types of cancers are similar and are not easily diagnosed at early stages. At later stages, the symptoms of all 3 cancers are similar.

A few treatments, such as paclitaxel, are available for advanced solid tumors. However, some people either do not respond to treatment or their cancer comes back after being treated.

In this study, researchers wanted to learn if giving participants both pexidartinib and paclitaxel together can help decrease the size of their tumors.

## Treatments given in this study



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

Drug being studied for advanced solid 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.



### **Paclitaxel** (Approved drug)

Chemotherapy medication approved to treat advanced solid tumors.

## Main goals of this study

This study had 3 parts. The main questions the researchers wanted to answer in each part were:

### Parts 1 and 2:



How many participants had side effects during this study?

### Part 3:



How many participants had tumors that completely disappeared or became at least 30% smaller after treatment?

## Other goals of this study

Researchers also wanted to answer the following questions:

### Parts 1 and 2:

- How many participants had tumors that completely disappeared or became at least 30% smaller after treatment?

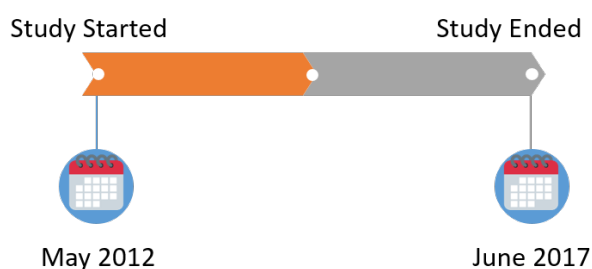
- For participants whose tumors completely disappeared or became at least 30% smaller, how long did the effect of treatment last?

### Part 3:

- For participants whose tumors completely disappeared or became at least 30% smaller, how long did the effect of treatment last?
- How long did participants live with their cancer before it got worse or led to death?

Researchers monitored the health of the participants throughout the study.

## How long was this study?



The study was designed so that participants could continue in it as long as their cancer did not get worse, or they did not have serious side effects, or they did not ask to be removed.

The study started in May 2012 and ended in June 2017. The study was completed as planned.

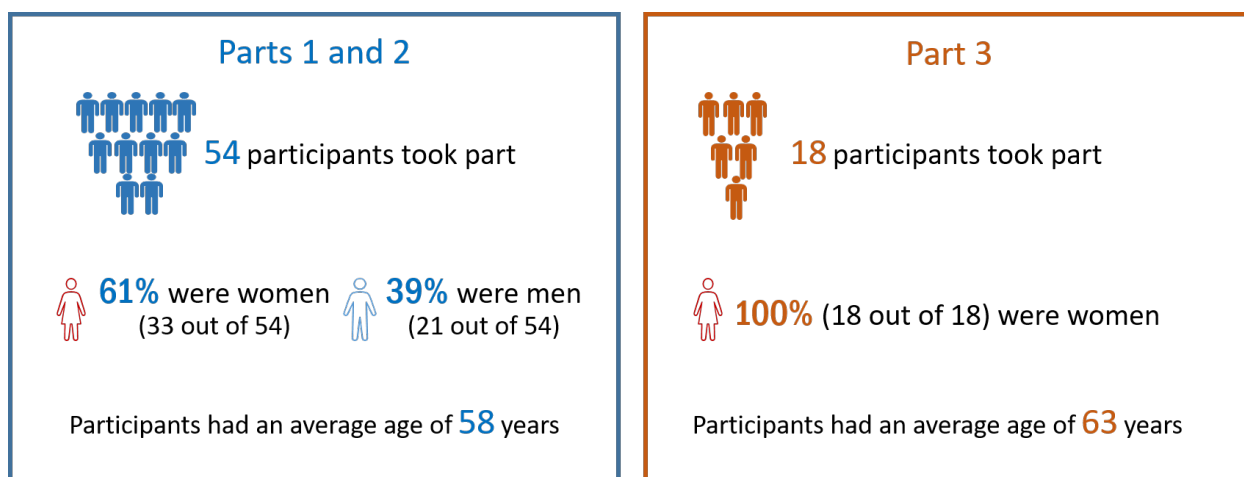
## Who was in this study?

The study included 72 participants from 8 study sites in the United States.

Participants could take part in this study if they:

- were at least 18 years of age,
- had an advanced solid tumor (for [Parts 1 and 2](#)),
- had advanced epithelial ovarian cancer, primary peritoneal cancer, or fallopian tube cancer (for [Part 3](#)),
- had stopped previous therapies at least 15 days before the start of treatment, and
- were fully active, OR unable to do a hard physical activity but able to walk and do light housework or office work, OR unable to work but able to walk and take care of themselves.

Participants included in this study:



## What happened during this study?

This was a Phase 1b study that was divided into 3 parts. Phase 1b studies are sometimes done to find the highest dose of a drug that can be safely given to participants. This study was also “open-label”. This means that both the researchers and the participants knew which treatment was given to which participants.

**Part 1** was done to find the highest dose of a pexidartinib that can be safely given to participants in addition to paclitaxel. In **Part 2**, researchers wanted to see if the highest safe dose of pexidartinib determined in Part 1, when given in addition to paclitaxel, was effective in reducing tumor size for participants. In **Part 3**, researchers were trying to learn if 1200 milligrams (mg) of pexidartinib daily, when given in addition to paclitaxel, can reduce tumor size for participants with epithelial ovarian cancer, primary peritoneal cancer, or fallopian tube cancer.

Participants first completed a screening period to find out if they could take part in the study.

### Part 1

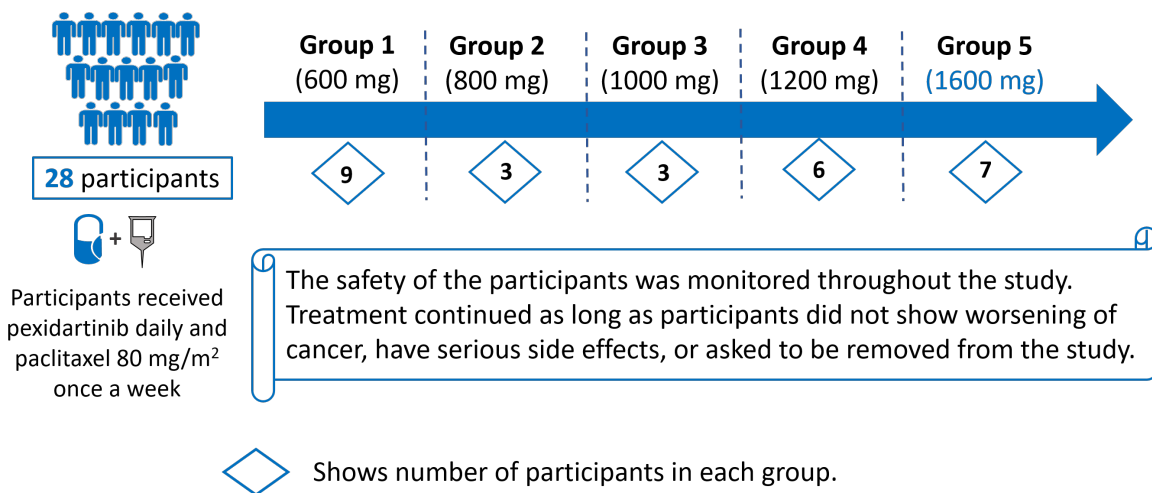
In **Part 1**, researchers started by giving the first group of participants 600 mg of pexidartinib daily in addition to 80 mg/m<sup>2</sup> of paclitaxel once a week. Meter squared, or m<sup>2</sup>, means the dose of paclitaxel was based on the participants’ individual body surface area. If this dose was considered to be safe by the researchers, the next group of participants received a higher dose of pexidartinib. This process was repeated with increasingly higher doses, as shown in the study design figure, until the highest safe dose was identified.

For all groups, pexidartinib was given by mouth as 2 divided doses, one in the morning and one in the evening each day. For example, the 600 mg daily group received 300 mg in the morning and 300 mg in the evening. Paclitaxel was given as an injection in a vein once a week. The researchers identified 1600 mg daily as the highest dose of pexidartinib that could safely be given to participants.

Participants continued to receive treatment as long as they did not show a worsening of cancer, have serious side effects, or asked to be removed from the study.

## What happened in this study

### Part 1

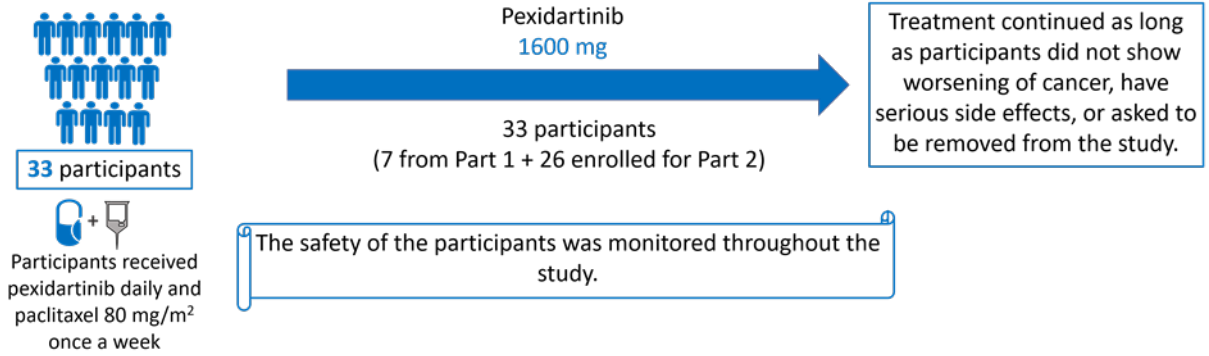


### Part 2

In [Part 2](#), 1600 mg of pexidartinib daily was given to all participants in addition to 80 mg/m<sup>2</sup> of paclitaxel once a week. Participants continued to receive treatment as long as they did not show a worsening of cancer, have serious side effects, or asked to be removed from the study.

## What happened in this study

### Part 2

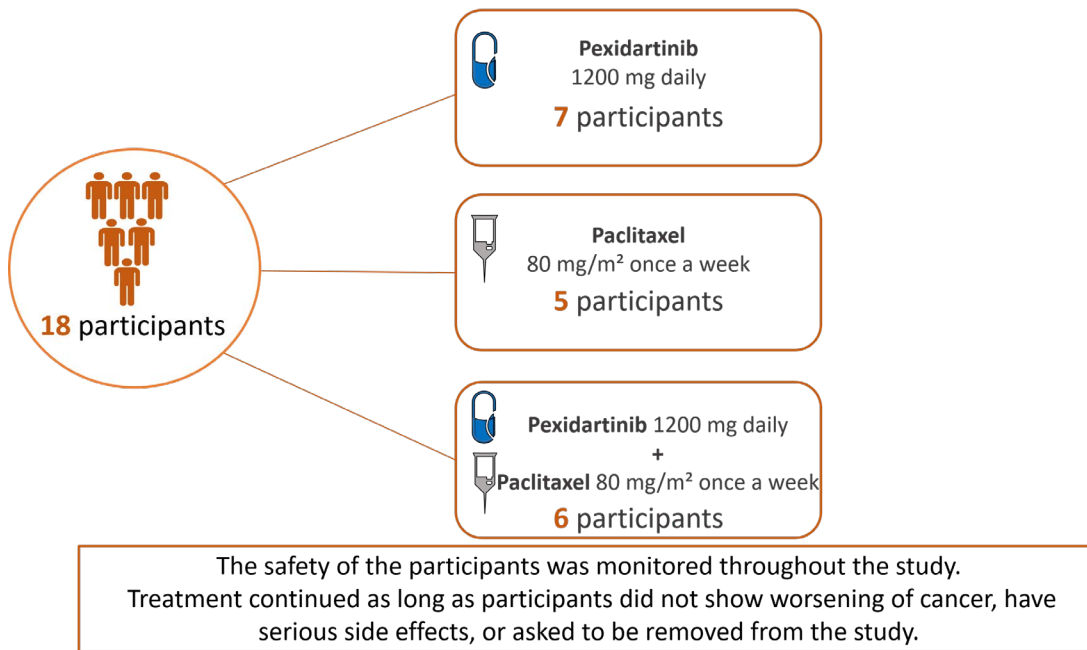


### Part 3

Part 3 included participants with epithelial ovarian cancer, primary peritoneal cancer, or fallopian tube cancer who were receiving other treatment for cancer but either did not respond to treatment or whose cancer had come back after treatment. Participants were assigned to 1 of 3 treatment groups, as shown in the figure below, which could last from 28 to 35 days.

## What happened in this study

### Part 3



## Changes to the study plan

Researchers found that the initial results of Part 3 for participants given pexidartinib in addition to paclitaxel were not as beneficial as the effect of giving participants paclitaxel alone. After careful consideration, it was decided that no additional participants should be enrolled in Part 3 after 02 March 2017. At that time, only 18 participants were in Part 3, and they were allowed to continue in 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 website listed at the end of this summary.

### Parts 1 and 2

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

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

In this study, side effects were monitored for 54 participants in [Parts 1 and 2](#). Out of 54 participants, 51 participants (94%) reported side effects related to pexidartinib.

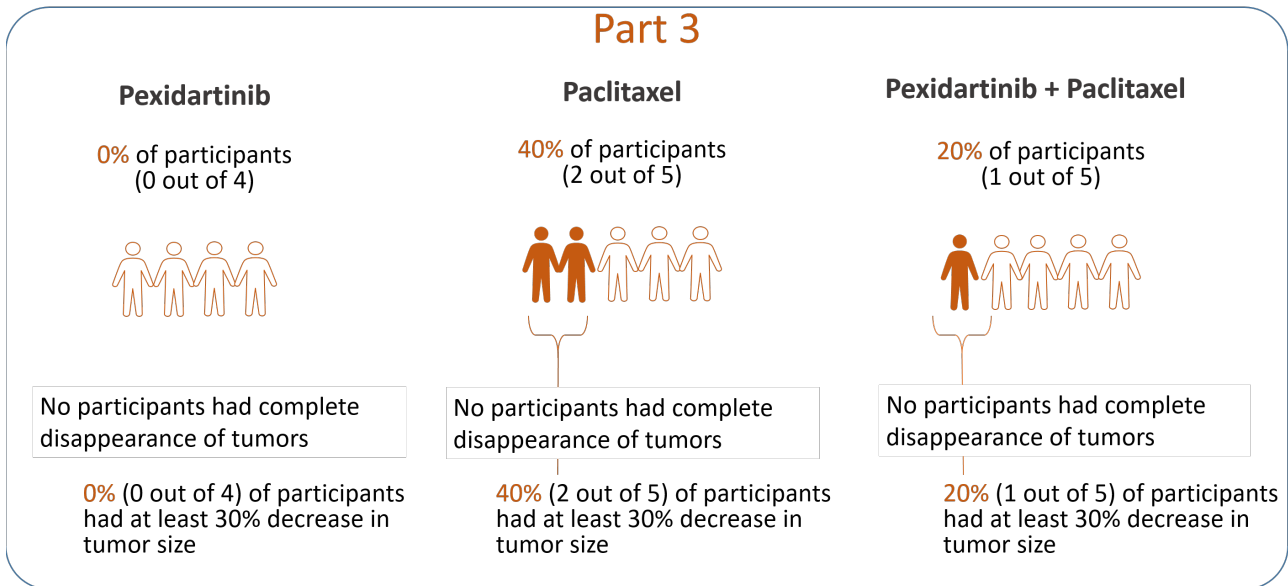
More detailed information about the side effects reported by participants is given below in the "Medical Problems" section of this summary.



### Part 3

## How many participants had tumors that completely disappeared or became at least 30% smaller after treatment?

The 14 participants in **Part 3** were divided into 3 treatment groups, as shown below. Overall, 3 out of 14 (21%) of participants had tumors that completely disappeared or became at least 30% smaller after treatment.



## What were the other results of this study?

### Parts 1 and 2

## How many participants had tumors that completely disappeared or became at least 30% smaller after treatment?

Overall, 6 out of 44 (16%) participants had tumors that completely disappeared or became at least 30% smaller after treatment. 1 participant (3%) had complete disappearance of tumors and 5 participants (13%) had at least 30% reduction in tumor size.

## **For participants whose tumors completely disappeared or became at least 30% smaller, how long did the effect of treatment last?**

The participants who responded to treatment maintained the response for an average of about **14 weeks**.

### **Part 3**

## **For participants whose tumors completely disappeared or became at least 30% smaller, how long did the effect of treatment last?**

The participants who responded to treatment maintained the response for an average of about **17 weeks**.

## **How long did participants live with their cancer before it got worse or led to death?**

About half the participants lived for at least **8 weeks** before their cancer got worse or led to death, whichever occurred first.

## **What medical problems did the study participants have?**

This section provides a summary of side effects related to the study treatment. 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?

In this study, side effects were monitored for all 54 participants in [Parts 1 and 2](#) and for all 18 participants in [Part 3](#). There were no deaths reported in this study that were considered to be related to the study treatment. Serious side effects related to pexidartinib are presented below.

### Parts 1 and 2

- Abnormally low number of neutrophils accompanied with fever
- Fast heartbeat
- Feeling sick to the stomach
- Increase in liver test value of bilirubin in the blood
- Increase in liver test value of transaminase in the blood
- Irregular heartbeat
- Loss of fluid from the body
- Skin infection
- Swelling and irritation of the large intestine caused by *Clostridium difficile* infection
- Tooth infection

Increase in level of bilirubin and transaminase in the blood means there may be liver problems. Neutrophils are a type of white blood cells that help fight infections.

### Part 3

- Decrease in lymphocyte count
- Decrease in neutrophil count
- Drug induced liver injury
- Feeling very tired
- Increase in liver test value of alanine aminotransferase in the blood
- Increase in liver test value of aspartate aminotransferase in the blood
- Increase in liver test value of bilirubin in the blood
- Low red blood cell count
- Kidney damage
- Weakness

Increase in level of aspartate and alanine aminotransferase in the blood means there is damage to the liver. Lymphocytes are a type of white blood cells that help fight infections.

## What were the most common side effects?

The most common side effects, both serious and non-serious, reported by at least 15% (15 out of 100) of participants, are presented below.

### Most common side effects while taking pexidartinib Parts 1 and 2

Side effects	Percentage (number of participants)	
Feeling very tired	59% (32 out of 54)	
Feeling sick to stomach	35% (19 out of 54)	
Increase in liver test value of aspartate aminotransferase in the blood	35% (19 out of 54)	
Low red blood cell count	33% (18 out of 54)	
Increase in protein called creatine phosphokinase in the blood	31% (17 out of 54)	
Decrease in appetite	30% (16 out of 54)	
Decreased white blood cell count	30% (16 out of 54)	
Diarrhea	30% (16 out of 54)	
Change in sense of taste	26% (14 out of 54)	
Vomiting	26% (14 out of 54)	
High blood pressure	24% (13 out of 54)	
Rash	20% (11 out of 54)	
Increase in liver test value of alanine aminotransferase in the blood	19% (10 out of 54)	
Decrease in neutrophil count	17% (9 out of 54)	
Increase in liver test value of alkaline phosphatase in the blood	17% (9 out of 54)	
Low level of phosphate in the blood	15% (8 out of 54)	

- An increase in level of alkaline phosphatase and aminotransferase in the blood means there is damage to the liver.
- Neutrophils are a type of white blood cells that help fight infections.

## Most common side effects while taking pexidartinib

### Part 3

Side effects	Percentage (number of participants)	
Feeling very tired	50% (9 out of 18)	
Bald patches on scalp	44% (8 out of 18)	
Diarrhea	44% (8 out of 18)	
Feeling sick to stomach	44% (8 out of 18)	
Change in sense of taste	33% (6 out of 18)	
Decrease in appetite	33% (6 out of 18)	
Weakness or numbness in hands and feet	28% (5 out of 18)	
Low red blood cell count	22% (4 out of 18)	
Chills	17% (3 out of 18)	
Increase in liver test value of alanine aminotransferase in the blood	17% (3 out of 18)	
Increase in liver test value of aspartate aminotransferase in the blood	17% (3 out of 18)	
Inflammation of mouth and lips	17% (3 out of 18)	
Itchy skin	17% (3 out of 18)	

- An increase in level of aminotransferase in the blood means there is damage to the liver.


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

This study helped researchers learn about the effects of pexidartinib in people with advanced solid tumors when given in addition to paclitaxel. Findings from this study may be used in other studies of pexidartinib. Other studies of 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 NCT01525602 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:** A Phase 1b Study to Assess the Safety of PLX3397 and Paclitaxel in Patients with Advanced Solid Tumors.

**Sponsor:** Daiichi Sankyo, Inc.

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