



Daiichi-Sankyo

## Clinical Results Summary

# A clinical study to learn about the effects of pexidartinib in people with newly diagnosed brain cancer when combined with radiation therapy and temozolomide

Protocol number: PLX108-08

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 newly diagnosed with a condition known as glioblastoma, which is a type of brain cancer. 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?

## Glioblastoma

Glioblastoma is a type of brain cancer that makes up 12% to 15% of all brain cancers. The symptoms experienced by people with glioblastoma are not specific, which means that they can be experienced by people with many different conditions. These symptoms include headache, feeling sick to your stomach, and sudden change in appearance, actions, or feelings.

At this time, there is no cure for glioblastoma. Surgery, followed by radiation therapy and chemotherapy, is the primary treatment given to people with this condition. Radiation therapy is a type of cancer treatment that uses X-rays to kill cancer cells. Chemotherapy is the use of anti-cancer medicine, such as temozolomide, for cancer treatment. Currently, this combination treatment does not show high rates of success in patients. Therefore, new methods of treating glioblastoma are needed.

PLX3397, also known as pexidartinib, is a study treatment that is being tested for its ability to reduce the growth of cancer cells. In this study, researchers wanted to see if giving pexidartinib to participants in addition to their standard treatment for glioblastoma would increase the amount of time participants lived with their cancer before it got worse. Researchers also wanted to compare the results of this study with a study performed in the past using standard treatment for the same type of cancer.

The participants in this study were newly diagnosed with glioblastoma and had recovered from recent surgery performed to remove the cancer.

## Treatments given in this study



### **Pexidartinib** (Study treatment)

Drug being studied for the treatment of glioblastoma. 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.

### **Standard treatment** (Approved treatment)

**Radiation therapy:** Treatment that uses X-rays to kill cancer cells

**Temozolomide:** Approved drug for treatment of glioblastoma



## Main goals of this study

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

How long did participants live with their cancer before it got worse?

How did participants' results compare with a study performed in the past for this same condition?

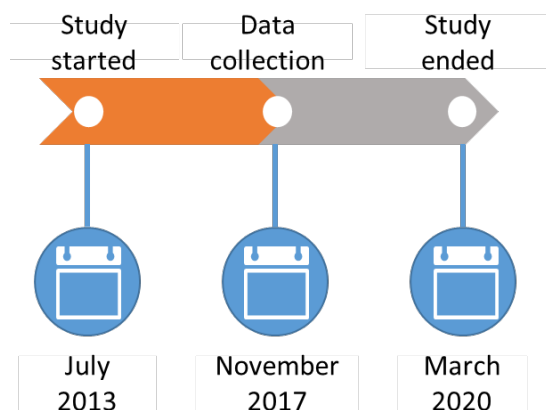
## Other goals of this study

Other questions researchers wanted to answer in this study were:

- How long did participants live after their first day of treatment?
- Was there a difference in how long participants lived after treatment started in this study compared with a study performed in the past for this same condition?

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

## How long was this study?



The study was designed in such a way that the participants could continue in it as long as their cancer did not get worse or they did not have serious side effects. The study started in July 2013 and ended in March 2020.

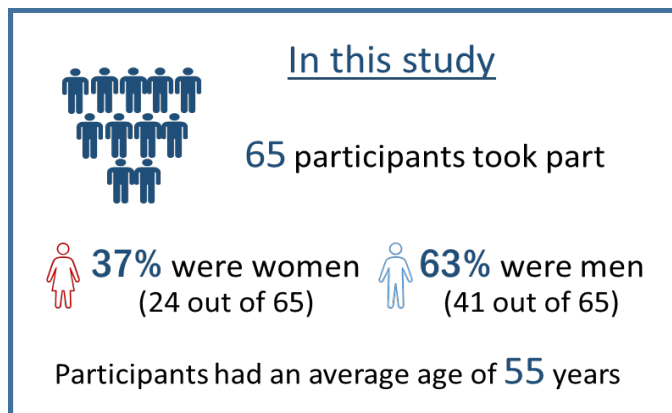
The first set of results were collected up to November 2017 and a study report was created. This summary is based on that report. Now that the study has been completed, a full summary of results will also be made available.

## Who was in this study?

This study included 65 participants from the United States.

Participants could take part in this study if they:

- were 18 years of age or older
- had newly diagnosed glioblastoma
- had recovered from recent cancer-related surgery
- had normal blood, liver, and kidney function
- did not have hepatitis B or C



## What happened during this study?

This was an open-label study, which means that both the researchers and the participants knew what treatment was given to each participant. This study was divided into 2 parts. The first part was called Phase 1b. Phase 1b studies are sometimes done to find the highest dose of a drug that can be safely given to participants who are receiving other therapy. The second part was called Phase 2. Phase 2 studies are done to better understand if a drug can treat the condition it has been developed for.

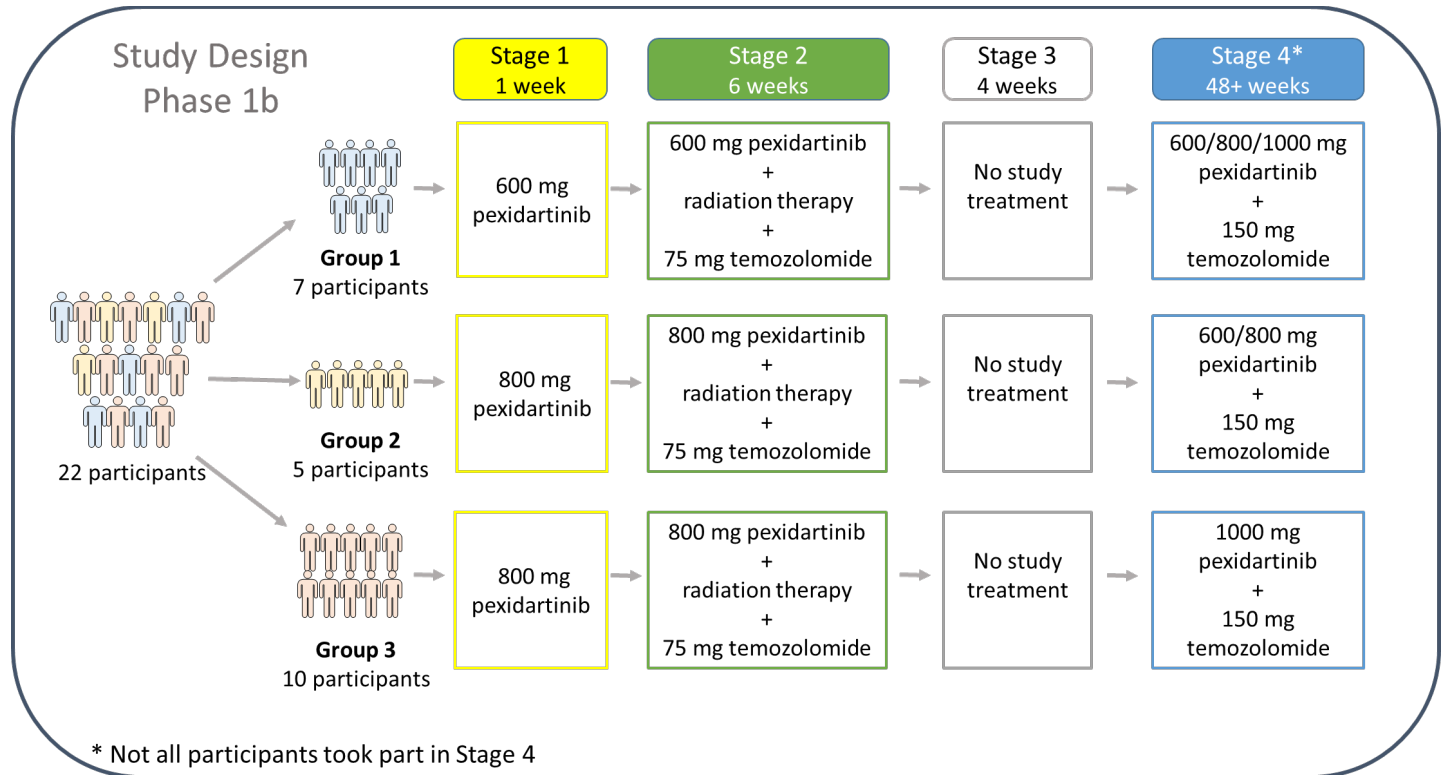
Participants first completed a screening period to find out if they could take part in the study.

In both the Phase 1b and Phase 2 parts of the study, there were 4 stages:

1. Stage 1: participants were given pexidartinib for 1 week
2. Stage 2: participants were given pexidartinib in combination with standard treatment of radiation therapy and 75 mg temozolomide for 6 weeks
3. Stage 3: no study treatment was given to participants for 4 weeks
4. Stage 4: participants were given pexidartinib and 150 mg temozolomide for 48 weeks or more, as long as there was no toxicity unacceptable enough to harm the participants and their cancer did not get worse. Not all participants were given this additional stage of treatment.

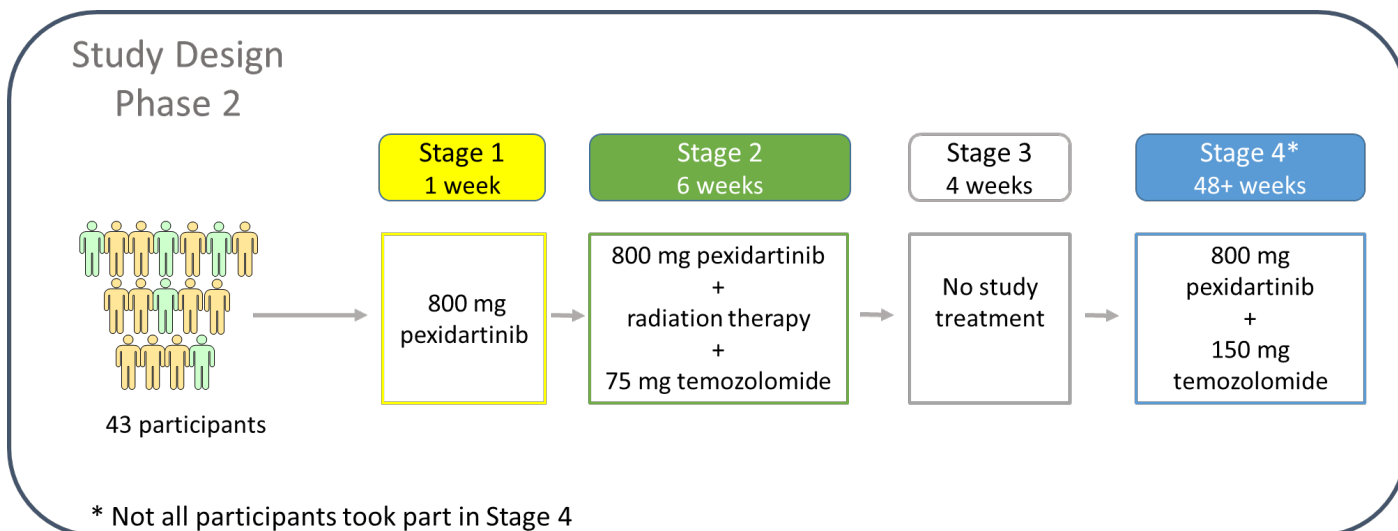
## Phase 1b

All participants were given pexidartinib as capsules that were taken by mouth twice a day. In Stages 1 and 2, pexidartinib was given either 5 or 7 days a week. In Stage 4, pexidartinib was given 7 days a week.



## Phase 2

All participants in Phase 2 were also given pexidartinib as capsules that were to be taken twice a day. Participants received 800 mg pexidartinib 5 days a week during Stages 1 and 2. Participants who took part in Stage 4 received 800 mg pexidartinib with 150 mg temozolomide 7 days a week during Stage 4.



## 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.

### How long did participants live with their cancer before it got worse?

Participants lived for a median of about **6.7 months** before their cancer got worse or led to death, whichever occurred first.

This means that for half of the participants, it took less than 6.7 months for their cancer to start getting worse and for the other half of participants, it took more time.

### How did participants' results compare with a study performed in the past for this same condition?

The amount of time participants in this study lived with their cancer before it got worse or led to death was similar to the time reported by participants in a past study for this same condition.

## What were the other results of this study?

### **How long did participants live after their first day of treatment?**

Participants lived for a median of about **13.1 months** since their first day of treatment.

About half of the participants in the study lived for less than 13.1 months and the other half lived for more than this amount of time.

### **Was there a difference in how long participants lived after treatment started in this study compared with a study performed in the past for this same condition?**

The amount of time participants in this study lived after treatment was similar to the amount of time reported for participants in a past study for this same condition.

## 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 thought could be related to the treatments in the study. This section provides a summary of side effects related to the study treatment 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?**

In this study, side effects were monitored for all 22 participants who participated in Phase 1b and all 43 participants who participated in Phase 2 of the study. A total of 23% (15 out of 65) of participants had serious side effects related to pexidartinib. There were no deaths reported in this study that were considered to be related to the study treatment.

## Phase 1b

**Percentage of participants who had serious side effects in Phase 1b**  
Percentage (number of participants)

Stage 1 pexidartinib dose	Group 1 600 mg				Group 2 800 mg			Group 3 800 mg	
Stage 4 pexidartinib dose	■ *	600 mg	800 mg	1000 mg	■ *	600 mg	800 mg	■ *	1000 mg
Number of participants	2	3	1	1	3	1	1	5	5
Decreased platelet count	0	0	0	0	33 % (1)	0	0	20 % (1)	20 % (1)
Decreased neutrophil count	0	0	0	0	67 % (2)	0	0	0	20 % (1)
Fever due to decreased neutrophil count	0	0	0	0	0	0	0	0	20 % (1)

\*Not all participants took part in Stage 4

Neutrophils are a type of white blood cell that help fight infections.

Platelets are tiny blood cells that help the body form blood clots to stop bleeding.



## Phase 2

**Percentage of participants who had serious side effects in Phase 2**  
Percentage (number of participants)

Stage 1 pexidartinib dose	Group 1 800 mg	Group 2 800 mg	Stage 1 pexidartinib dose	Group 1 800 mg	Group 2 800 mg
Stage 4 pexidartinib dose	■ *	800 mg	Stage 4 pexidartinib dose	■ *	800 mg
Number of participants	16	27	Number of participants	16	27
Decreased platelet count	13% (2)	0	Feeling very tired	0	4% (1)
Decreased neutrophil count	6% (1)	4% (1)	Swelling in the brain	6% (1)	0
Increase in liver test value of alanine aminotransferase	6% (1)	0	Decreased white blood cell count	13% (2)	0
Increase in liver test value of aspartate aminotransferase	6% (1)	0	Decreased lymphocyte count	6% (1)	0
Death of CNS cells	0	4% (1)	Mental status changes	0	4% (1)
Decreased flow of bile from the liver	6% (1)	0	Blockage in a lung artery	0	4% (1)
Blood clot in vein deep inside body	0	4% (1)	Fever	6% (1)	0
			Life-threatening reaction to a drug	6% (1)	0

\*Not all participants took part in Stage 4

CNS = central nervous system

Bile is a fluid produced by the liver which helps with digestion.

Leukocytes, lymphocytes, and neutrophils are types of white blood cells that help fight infections.

Platelets are tiny blood cells that help the body form blood clots to stop bleeding.

## What were the most common side effects?

The most common side effects related to pexidartinib, both serious and non-serious, that occurred in at least 15% (15 out of 100) of participants in any group are reported below.

## Phase 1b

**Most common side effects in Phase 1b**  
Percentage (number of participants)

Stage 1 pexidartinib dose	Group 1 600 mg				Group 2 800 mg			Group 3 800 mg	
Stage 4 pexidartinib dose	■ *	600 mg	800 mg	1000 mg	■ *	600 mg	800 mg	■ *	1000 mg
Number of participants	2	3	1	1	3	1	1	5	5
Feeling very tired	50 % (1)	0	0	0	67 % (2)	0	100 % (1)	100 % (5)	40 % (2)
Reduced hunger	0	0	100 % (1)	100 % (1)	33 % (1)	0	0	20 % (1)	40 % (2)
Feeling sick to your stomach	0	33 % (1)	0	0	0	0	0	40 % (2)	40 % (2)
Decreased platelet count	0	33 % (1)	100 % (1)	0	33 % (1)	0	100 % (1)	20 % (1)	20 % (1)
Change in sense of taste	0	0	0	0	33 % (1)	0	0	40 % (2)	40 % (2)
Itching	0	33 % (1)	0	0	0	0	0	40 % (2)	20 % (1)
Decreased neutrophil count	0	0	100 % (1)	0	33 % (1)	0	0	20 % (1)	20 % (1)

\*Not all participants took part in Stage 4

Neutrophils are a type of white blood cell that help fight infections.

Platelets are tiny blood cells that help the body form blood clots to stop bleeding.

## Phase 2

Most common side effects in Phase 2		
Percentage (number of participants)		
Stage 1 pexidartinib dose	Group 1 800 mg	Group 2 800 mg
Stage 4 pexidartinib dose	■ *	800 mg
Number of participants	16	27
Feeling very tired	31 % (5)	59 % (16)
Reduced hunger	25 % (4)	30 % (8)
Feeling sick to your stomach	50 % (8)	33 % (9)
Decreased neutrophil count	6 % (1)	22 % (6)
Rash	6 % (1)	26 % (7)

\*Not all participants took part in Stage 4  
Neutrophils are a type of white blood cell that help fight infections.

## How many participants had to stop treatment because of side effects while taking pexidartinib during the study?



The most common side effects that caused participants to stop pexidartinib treatment were rashes, decreased platelet count, and decreased white blood cell count.


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

This study helped researchers learn about how well pexidartinib is able to help participants with a type of brain cancer called glioblastoma. 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 NCT01790503 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 Phase 1b/2 Study of Orally Administered PLX3397 in Combination with Radiation Therapy and Temozolomide in Patients with Newly Diagnosed Glioblastoma

**Sponsor:** Daiichi Sankyo, Inc.

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This summary was prepared by Kinapse Ltd, a Syneos Health company.