Daiichi-Sankyo

Clinical Results Summary

A clinical study to learn about the safety and effects of PLX3397 when given in addition to vemurafenib to people with a type of skin cancer called metastatic melanoma

Protocol number: PLX108-09

Thank You!

Daiichi Sankyo, Inc., the sponsor of this study, would like to thank the participants who took part in this study for PLX3397. Each participant helped to advance medical research for people affected with a type of skin cancer called metastatic melanoma. 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?

Metastatic or unresectable melanoma

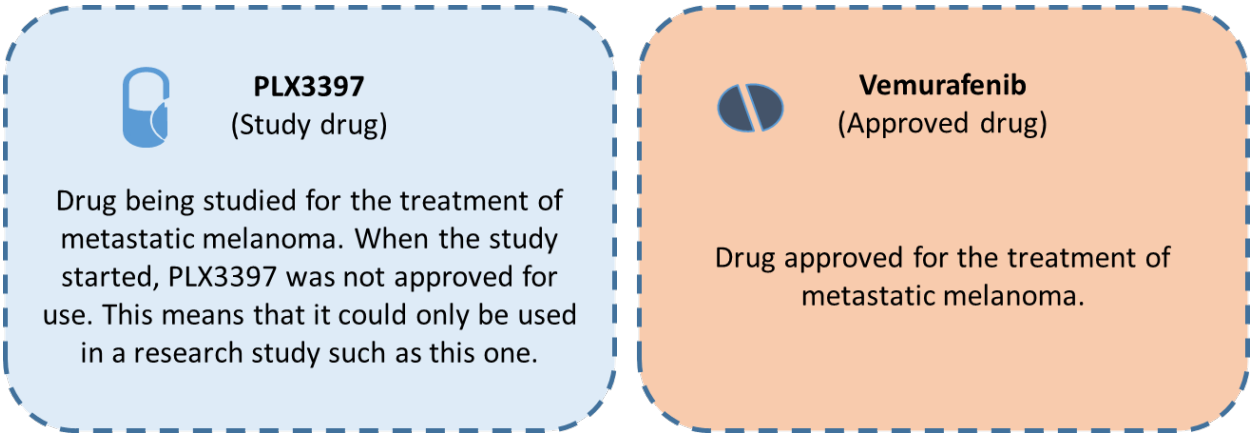
Melanoma is a type of skin cancer in which tumors form when there is damage to melanin-producing cells. Melanin is a natural skin pigment that gives a dark color to skin, hair, and eyes. As more and more melanin cells get damaged, they join to form tumors. Melanomas can develop anywhere on the body. They most often develop in the areas of back, legs, arms, and face. When the tumor spreads to other parts of the body, the cancer is considered “metastatic,” or advanced. People who have melanoma often have symptoms such as itchiness, swelling under the skin, headache, weight loss, and feeling of tiredness.

At this time, the main treatment option for metastatic melanoma is surgery followed by chemotherapy. Chemotherapy uses medicines to kill cancer cells or to stop them from growing and dividing. Surgery alone can be used if the cancer has not spread to other parts of the body. However, if the cancer has spread, doctors may not recommend surgery. If the cancer cannot be removed by surgery, it is considered “unresectable”. For unresectable melanoma new methods of treatment are needed. Some people with metastatic melanoma have a change or mutation in their BRAF gene, which makes their cells grow and divide too fast. Vemurafenib is a chemotherapy drug that stops this gene from working.

PLX3397 is a study drug that is being tested for its ability to reduce the growth of cancer cells. In this study, researchers wanted to understand the safety and effects of PLX3397 given in addition to vemurafenib to people with metastatic melanoma that could not be treated by surgery.

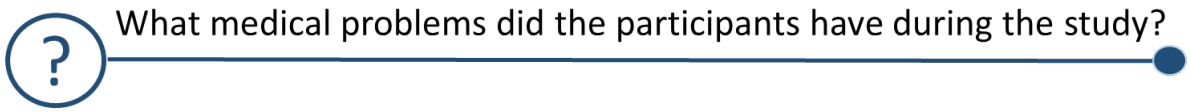
Treatments given in this study

The treatments given in this study were:

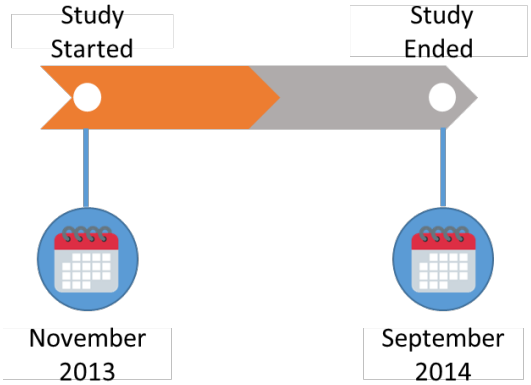


Main goal of this study

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



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 and they did not have serious side effects.

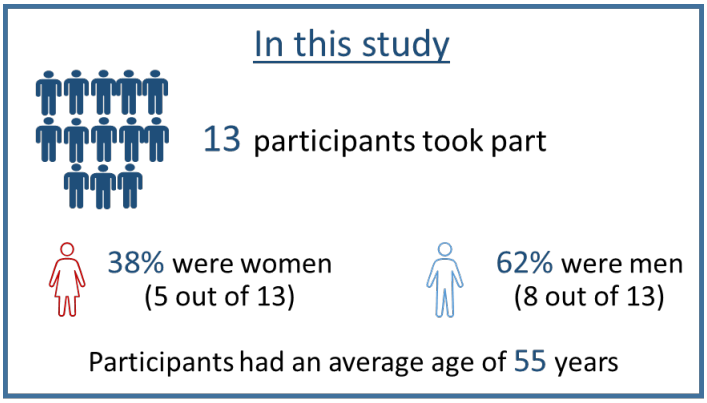
The study started in November 2013 and was stopped early in September 2014. The study was stopped because the study drug did not show much response in participants with metastatic melanoma. Researchers believed that the main purpose of the study would not be achieved even after enrolling more participants in the study, so no additional participants were enrolled. The results were collected up to September 2014 and a study report was created. This summary is based on that report.

Who was in this study?

This study included 13 participants from France, Germany, and the United States.

Participants could take part in this study if they:

- were 18 years of age or older
- had Stage 3 or 4 metastatic melanoma that could not be treated by surgery
- were expected to live for at least 3 months
- tested positive for a mutation of the BRAF gene
- had not previously been treated with a drug that targeted the BRAF gene
- had recovered from the effects of any major surgery at least 14 days before the start of the study



What happened during this study?

This was a Phase 1b study, which is sometimes done to find the highest dose of a drug that can safely be given to participants. This was also an open-label study, which means that both the researchers and the participants knew which drug was given to which participant.

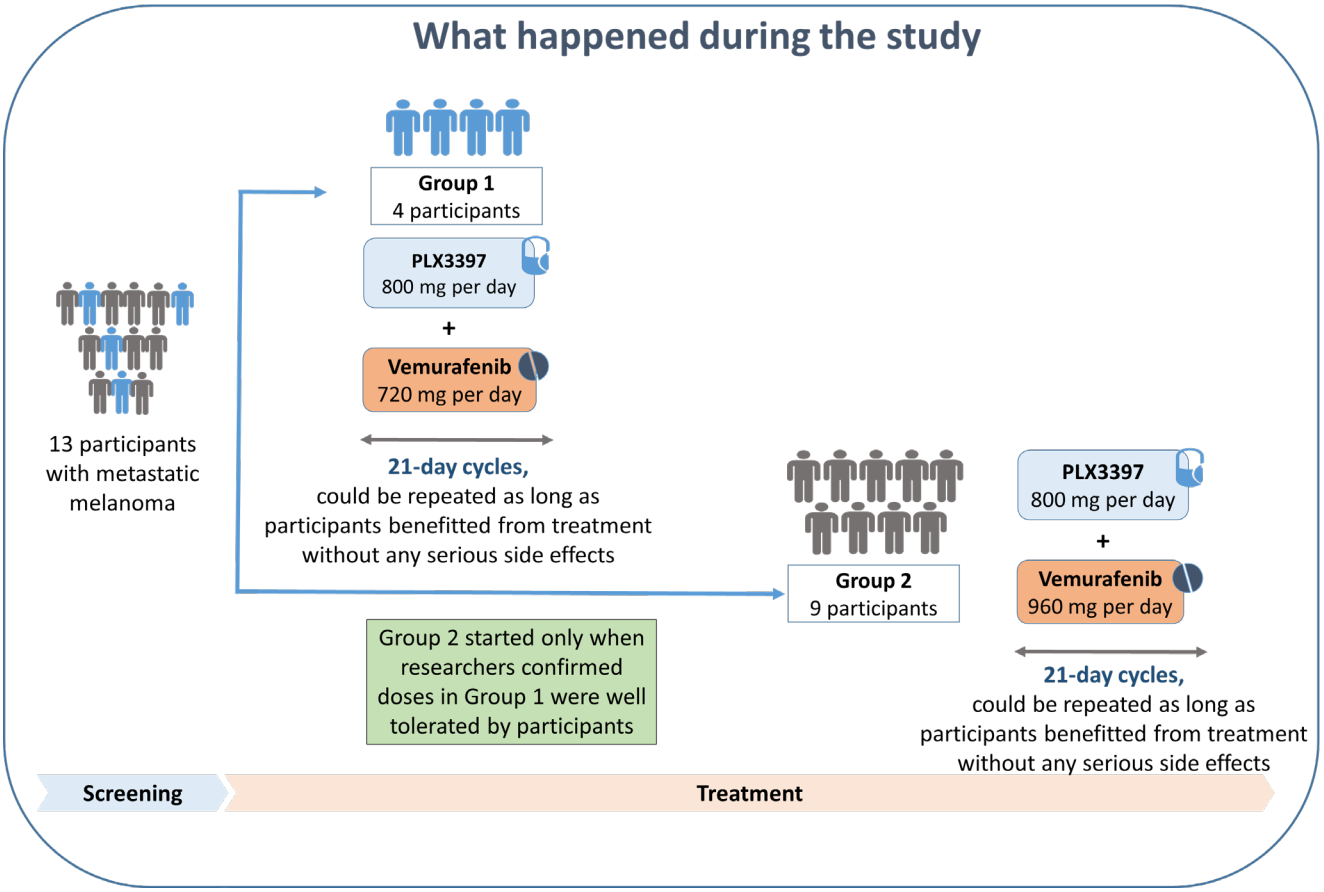
This study was divided into 2 parts. In Part 1, researchers wanted to find the highest dose of both PLX3397 and vemurafenib that could safely be given to participants. In Part 2, researchers planned to give the highest recommended dose of both PLX3397 and vemurafenib to participants with metastatic melanoma to understand if this combination was beneficial for them. However, the study was stopped early when the researchers saw no effect of the combination of study drugs on the tumors of participants in Part 1. The researchers were also concerned that a third type of drug, called a MEK inhibitor, should have been given to participants in addition to PLX3397 and vemurafenib to be consistent with a new standard of treatment for metastatic melanoma.

Part 1

Participants completed a screening period to find out if they could be a part of the study. At the start of Part 1, a small group of participants were given 800 milligrams (mg) of PLX3397 and 720 mg of vemurafenib, both of which were taken by mouth daily as 2 divided doses. For example, the 800 mg per day dose was given as 400 mg of PLX3397, 2 times in a day. If these doses were considered to be safe by the researchers, the next group of participants were given a higher dose. If these doses were not considered to be safe by the researchers, the next group of participants received a lower dose.

The researchers used scans to measure the participants' tumor size during the study. The researchers also monitored the health of participants throughout the study.

Since this study was stopped early, participants were only enrolled in 2 groups in Part 1 and the highest safe dose could not be determined.



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.

Since the researchers stopped the study after Part 1, no results were collected for Part 2.

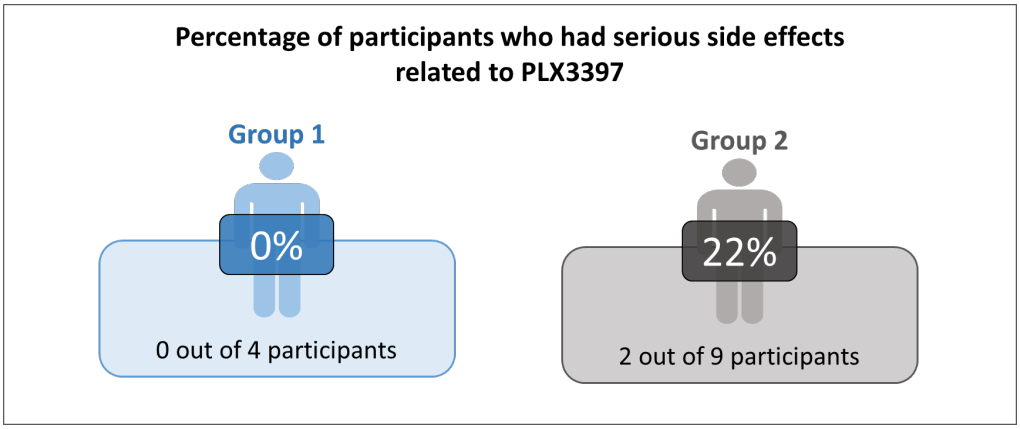
What medical problems did the participants have during the study?

Side effects are medical problems (such as feeling tired) that happened during the study which the study doctor thought could be related to the treatments in the study. This section provides a summary of side effects related to the study drug PLX3397. The website listed at the end of this summary has more information about all 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 treatment because of side effects.

How many participants had serious side effects?

In this study, side effects were monitored for all 13 participants who took part in this study. There were no deaths reported related to PLX3397.

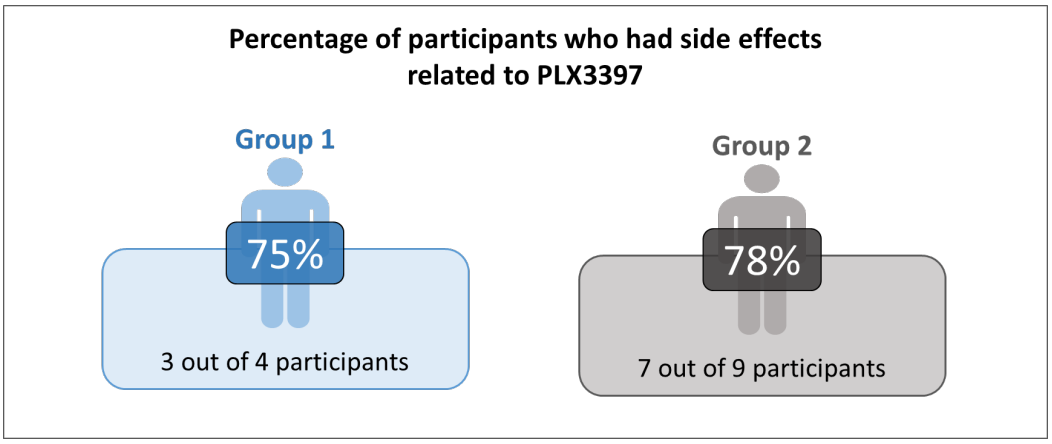


In Group 1, no participants reported serious side effects.

In Group 2, 1 participant experienced serious side effects of increase in liver test values of alanine aminotransferase and aspartate aminotransferase. Another participant experienced serious side effects of decrease in neutrophil count, increase in alkaline phosphatase levels in the blood, and increase in liver test values of alanine aminotransferase and aspartate aminotransferase. Neutrophils are a type of white blood cell that help fight infections. Increased levels of alkaline phosphatase in the blood indicate problems with the liver.

How many participants had the most common side effects?

Most common side effects reported by participants, both serious and non-serious, are presented in this section.



The most common side effects that occurred in at least 22% (22 out of 100) of participants in any group are presented below.

Most common side effects related to PLX3397

Group 1 Percentage (number) of participants	Side effects	Group 2 Percentage (number) of participants
0%	Acid reflux	22% (2)
25% (1)	Changes in hair color	11% (1)
0%	Diarrhea	22% (2)
25% (1)	Feeling sick to your stomach	11% (1)
0%	Feeling very tired	22% (2)
0%	Increase in liver test value of aspartate aminotransferase	22% (2)
25% (1)	Low number of red blood cells	11% (1)
0%	Reduced hunger	22% (2)

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

In Group 1, 1 participant stopped treatment due to increase in liver test values of alanine aminotransferase and aspartate aminotransferase.

In Group 2, 3 participants stopped treatment due to the side effects listed below.

- Increase in liver test values of alanine aminotransferase and aspartate aminotransferase.
- Reduced hunger, swelling of the stomach lining, and feeling sick to the stomach.
- Decrease in neutrophil count, increase in alkaline phosphatase levels in the blood, and increase in liver test value of aspartate aminotransferase. Neutrophils are a type of white blood cell that help fight infections. Increased levels of alkaline phosphatase in the blood indicate problems with the liver.

How was this study useful for patients and researchers?

This study helped researchers learn if PLX3397 was safe and effective when given in addition to vemurafenib to people with metastatic melanoma that could not be treated by surgery. The study was stopped early because treatment with PLX3397 in addition to vemurafenib was not benefitting participants with metastatic melanoma. Therefore, no more participants were enrolled in this study.

Findings from this study may be used in other studies with PLX3397. Other studies of PLX3397 are still 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 Use the NCT identifier NCT01826448 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 Open Label, Dose Escalation Study to Assess Safety, Pharmacokinetics, Pharmacodynamics, and Antitumor Activity of PLX3397 in Combination with Vemurafenib in V600-mutated BRAF Unresectable or Metastatic Melanoma

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