Clinical Results Summary

A clinical study to understand the response of participants with recurring brain cancer to PLX3397 treatment

Protocol number: PLX108-04

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 who have a type of brain cancer called glioblastoma. 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 Multiforme (GBM)

Researchers were looking for a better way to treat people with a type of cancer called glioblastoma, or glioblastoma multiforme (GBM). GBM is a cancer of the brain or the spinal cord. The spinal cord is a long structure made up of nerve tissue, which extends from the brain to the lower back and helps control different functions of the body. GBM occurs due to damage to the cells that keep the brain healthy. Symptoms experienced by people who have GBM include headache, vomiting, and feeling sick to their stomach. These symptoms can get worse and lead to unconsciousness.

The main treatment for GBM is surgery followed by chemotherapy. Chemotherapy uses medicine to kill cancer cells or stop them from growing and dividing. GBM does not always respond well to treatment and is likely to come back. The participants in this study had GBM that came back after treatment. In this study, researchers wanted to understand how participants with GBM that came back after treatment respond to PLX3397.

Treatment given in this study

PLX3397
(study drug)

Drug being studied for the treatment of glioblastoma multiforme. When the study started, PLX3397 was not approved for use. This means that it could only be used in a research study such as this one.

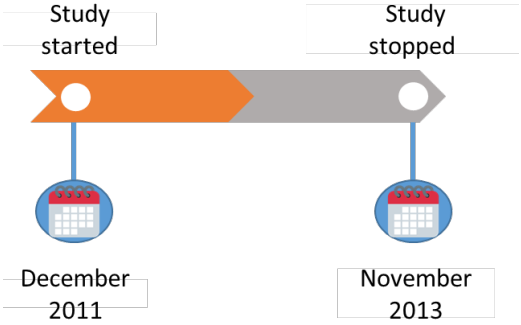
Main purpose of this study

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

- How many participants had cancer that did not get worse or lead to death for at least 6 months after the start of study drug?
- How many participants were alive at the end of the study?
- What were the levels of PLX3397 in the blood of participants?
- How much time did it take to reach the highest level of PLX3397 in the blood?

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 and they did not have serious side effects.

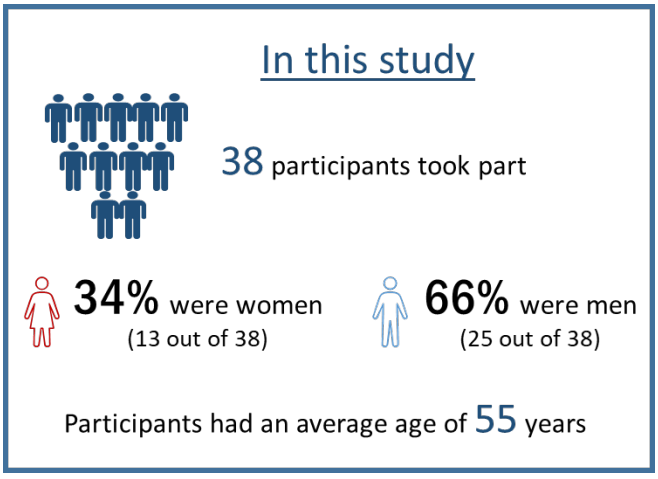
This study started in December 2011 but was stopped early, in November 2013. The study was stopped early because the treatment did not show much response in participants with GBM. Researchers believed that the main purpose of the study would not be achieved even after enrolling more participants in the study, so they stopped enrolling participants. Results were collected up to November 2013 and a study report was created. This summary is based on that report.

Who was in this study?

This study included 38 participants from the United States.

Participants could take part in this study if they:

- were 18 years or older and expected to live for at least 8 weeks
- had recurring GBM that had previously been treated
- could provide samples of their tumors as slides from any previous GBM surgery
- had recovered satisfactorily from side effects of prior treatments
- had adequate blood, liver, and kidney function



What happened during this study?

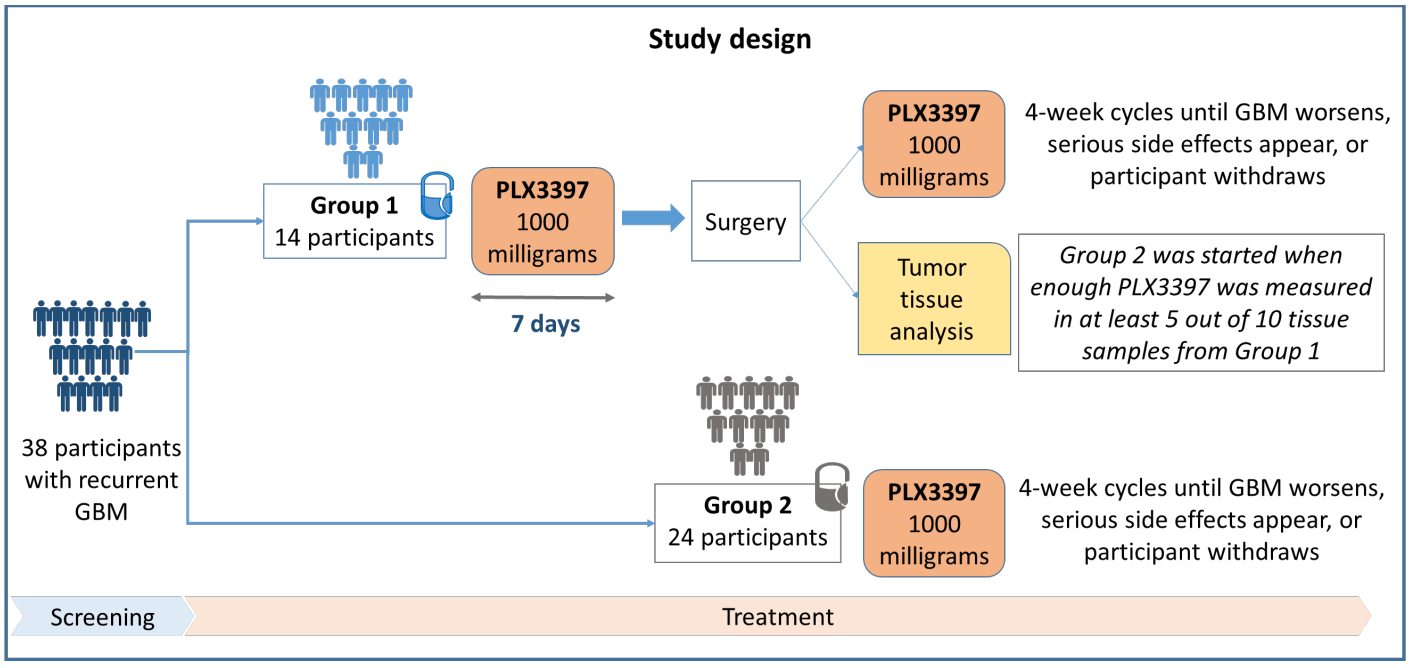
This Phase 2 study was an open label study. This means both the participants and researchers knew which treatment was given to which participants. In Phase 2 studies, the study drug is given to a small number of participants with the disease condition to gather information about the effects of the study drug in patients and to find the best dose.

Participants first completed a screening period to find out if they could be a part of the study. The researchers then assigned the participants to 2 groups: Group 1 and Group 2.

Participants who needed surgery to remove the tumor were assigned to Group 1. In this group, participants took PLX3397 by mouth twice a day for 7 days before surgery. After surgery, participants continued to take PLX3397 twice a day in 4-week cycles. When sufficient levels of PLX3397 were found in the tumor tissue samples of at least 5 out of 10 participants in Group 1, researchers started treatment for Group 2.

Participants who did not need surgery to remove the tumor were assigned to Group 2. In this group, participants took PLX3397 by mouth twice a day in 4-week cycles.

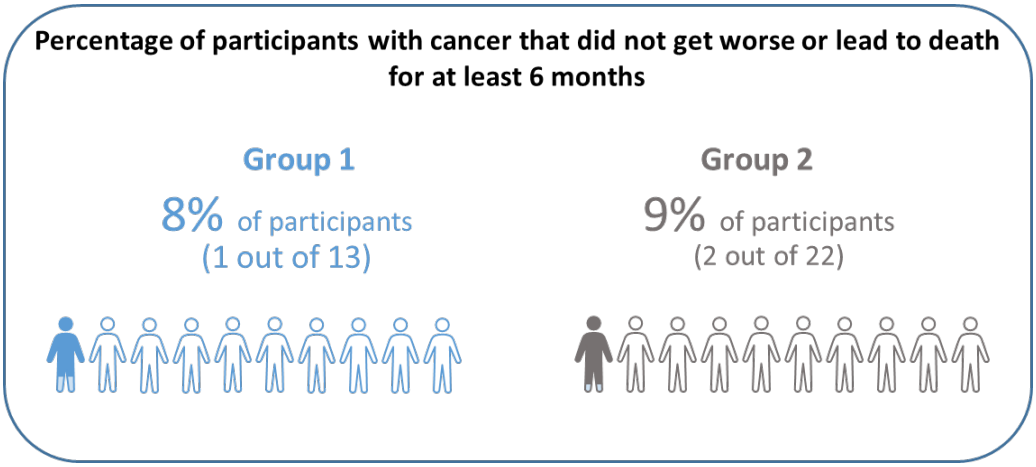
Treatment in both groups could be continued for as long as participants did not show worsening of cancer, did not have serious side effects, or asked to be removed from the study. The researchers used a scan called magnetic resonance imaging, or MRI, to measure the participants' tumor size every 8 weeks. They also took blood samples throughout the study to measure the levels of PLX3397 in the blood.



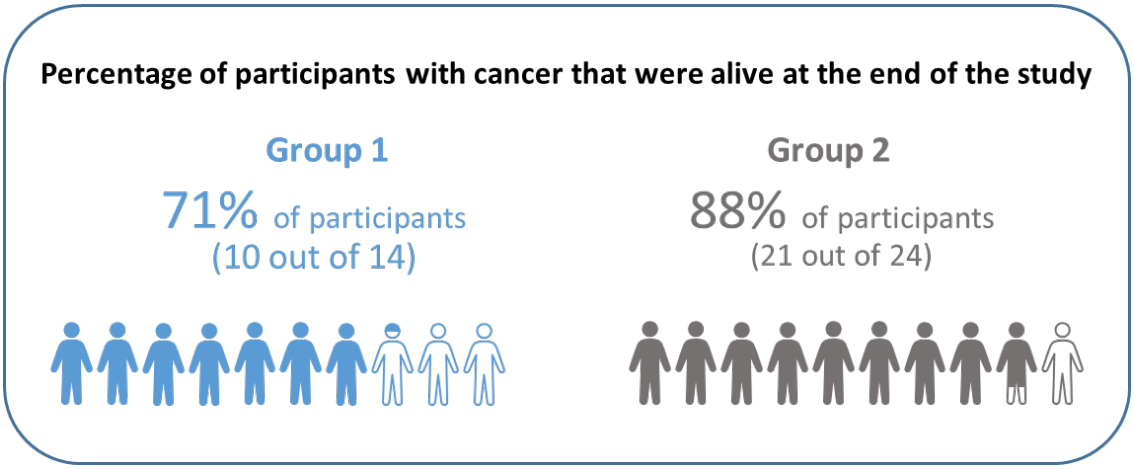
What were the key results of this study?

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 many participants had cancer that did not get worse or lead to death for at least 6 months after the start of study drug?



How many participants were alive at the end of the study?



What were the levels of PLX3397 in the blood of participants?

To answer this question, researchers measured the following:

- Total level of PLX3397 in the participants' blood 4 hours after PLX3397 was taken.
- Total level of PLX3397 in the participants' blood 6 hours after PLX3397 was taken.
- Highest level of PLX3397 in the participants' blood after treatment.

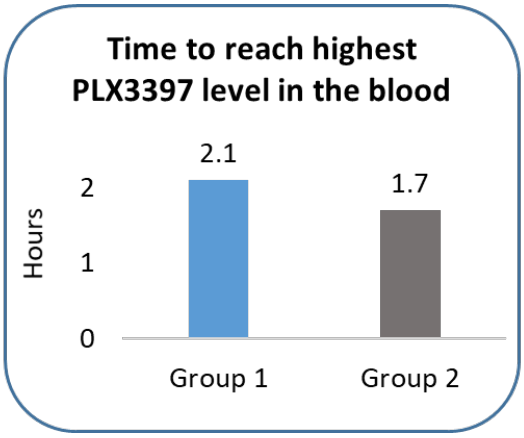
The average results of these measurements are presented below. Total level of PLX3397 in the participants' blood is measured in ng*hr/mL. Total level of PLX3397 in the participants' blood after 4 hours means how much of PLX3397 in nanogram (one thousand-millionth of a gram) was found in each milliliter of blood after 4 hours of taking PLX3397 capsule.

Levels of PLX3397 in the blood

	Group 1	Group 2
Total level after 4 hours (ng * hr/mL)	24900	26100
Total level after 6 hours (ng * hr/mL)	36100	36900
Highest level (ng/mL)	7760	8030

How much time did it take to reach the highest level of PLX3397 in the blood?

It took about 2 hours for PLX3397 to reach the highest level in the blood in both Group 1 and Group 2.



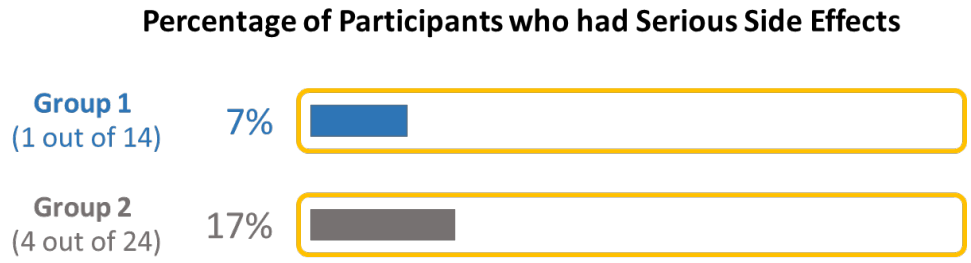
What medical problems did the study participants have?

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 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. No deaths were reported due to side effects. No participant discontinued from this study due to a side effect.

How many participants had serious side effects?

In this study, side effects were monitored for 38 participants who took PLX3397. 5 participants experienced serious side effects related to the study drug.



In Group 1, 1 participant had a lung infection. In Group 2, 4 participants experienced the serious side effects listed below.

- Decreased white blood cell count
- Increase in liver test values of aspartate aminotransferase and alanine aminotransferase in the blood and increase in INR. INR is 'international normalized ratio', which measures how much time it takes for the blood to clot. A high INR value means that a participant's blood is taking a longer time to clot than normal.
- Decreased red blood cell count and sodium levels in the blood, as well as dehydration.
- Abnormally low number of neutrophils accompanied with fever. Neutrophils are a type of white blood cells that help fight infections.

How many participants had the most common side effects?

The most common side effects, both serious and non-serious, that occurred in at least 10% of participants are reported below.

Group 1 (86%) 12 out of 14		Group 2 (92%) 22 out of 24
14%	Changes in hair color	17%
21%	Constipation	4%
14%	Decreased lymphocyte count	0%
0%	Decreased neutrophil count	13%
14%	Dry mouth	0%
7%	Feeling sick to your stomach	13%
43%	Feeling tired	58%
14%	Fever	4%
7%	Headache	13%
14%	High blood pressure	0%
14%	Increase in liver test value of alanine aminotransferase in the blood	13%
21%	Increase in liver test value of aspartate aminotransferase in the blood	13%
14%	Increased lactate dehydrogenase in the blood	4%
21%	Reduced hunger	13%
14%	Skin rash	4%

Neutrophils and lymphocytes are types of white blood cells that help fight infections.
Increase in lactate dehydrogenase means there is some type of tissue damage or disease.

How was this study useful for patients and researchers?

This study helped researchers learn if PLX3397 was safe and if it was effective in helping participants with a type of brain cancer called GBM that had returned after treatment. The study was stopped early because treatment with PLX3397 did not provide much benefit to the participants with GBM. Therefore, the researchers decided not to enroll more participants in the 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 NCT01349036 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 2 Study Of Orally Administered PLX3397 In Patients With Recurrent Glioblastoma

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