Clinical Results Summary

A clinical study to learn about the safety and effects of PLX3397 when given to Asian people with advanced solid tumors

Protocol number: PL3397-A-A103

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 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

Researchers were looking for a better way to treat people with advanced solid tumors. A solid tumor is a type of cancer or other abnormal growth that starts in an organ of the body. “Advanced” means that the cancer has spread to other parts of the body. Symptoms experienced by people with advanced solid tumors include swelling that can be examined by hand, weight loss, and fever.

At this time, treatment options for solid tumors are surgery, radiation therapy, chemotherapy, or a combination of all three. Radiation therapy is a type of cancer treatment that uses X-rays to kill cancer cells. Chemotherapy uses medicine to kill cancer cells or stop them from growing and dividing. Currently, these treatment options do not show high rates of success in patients. Therefore, new methods for treating advanced solid tumors are needed.

Some people with advanced solid tumors have a change or mutation in genes such as Flt3 and KIT, which makes their cells grow and divide too fast. PLX3397 is a drug that is believed to stop these mutated genes from working. Once in the body, PLX3397 breaks down and produces other products, such as ZAAD-1006a.

Before this study, researchers had studied the safety and effects of PLX3397 in people based in regions other than Asia. In this study, researchers wanted to learn about the safety and effects of PLX3397 in Asian people with solid tumors that have spread to other parts of the body. They also measured the levels of PLX3397 and its breakdown product ZAAD-1006a in the blood of participants.

Additionally, researchers wanted to understand the effect of changing doses of PLX3397 on the levels of colony stimulating factor-1 (CSF-1) and adiponectin in the blood of participants. CSF-1 is a type of protein that plays an important role in the growth of white blood cells. Adiponectin is a protein that maintains normal glucose level in the human body. It also binds to cancer cells and stops them from growing and dividing.

Treatment given in this study

PLX3397

Study drug being studied for the treatment of advanced solid tumors. 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 goals of this study

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

How many participants had side effects during this study?

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

Other goals of this study

Other questions researchers wanted to answer in this study were:

- What were the levels of PLX3397 and its breakdown product ZAAD-1006a in the blood of participants?
- How much time did it take to reach the highest level of PLX3397 and its breakdown product ZAAD-1006a in the blood?
- How did blood levels of CSF-1 and adiponectin change with changing doses of PLX3397?

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 tumor did not get worse and they did not have serious side effects. The study started in July 2016 and is expected to end in May 2021.

The results were collected up to June 2017 and a study report was created. This summary is based on that report.
Who was in this study?

This study included 11 participants from Taiwan.

Participants could take part in this study if they:

- were 20 years or older and expected to live for at least 3 months,
- had solid tumor that came back after treatment, did not respond to standard treatment, or for which no standard treatment was available,
- had recovered from side effects of previous cancer treatment,
- had undergone surgery, radiation therapy, or chemotherapy at least 4 weeks before participating in the study,
- did not have hepatitis B, hepatitis C, or lung disease,
- had adequate blood, liver, and kidney function.

What happened during this study?

This was a Phase 1, “open label” study. Phase 1 studies are done to find out how a new study drug works in a small number participants. “Open label” means that both the researchers and the participants knew which treatment was given to which participants.

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

Participants were divided into 2 groups. Researchers started by giving 600 milligrams (mg) of PLX3397 per day to the participants in Group 1. If this dose was considered to be safe by the researchers, the next group of participants would receive a higher dose of PLX3397. However, if this dose was not considered to be safe, the next group of participants would receive a lower dose of PLX3397. 600 mg of PLX3397 was considered to be safe and so the participants in Group 2 were given 1000 mg of PLX3397 per day. After 2 weeks, this dose was reduced to 800 mg per day. For both groups, PLX3397 was given by mouth as 2 divided doses, one in the morning and one in the evening each day. For example, the 600 mg per day group received 200 mg of PLX3397 in the morning and 400 mg of PLX3397 in the evening.

The researchers identified 1000 mg as the highest dose of PLX3397 that could safely be given to the participants in the study.
The participants continued to receive treatment as long as they did not show worsening of their tumor, have serious side effects, or asked to be removed from the study.

What happened during this study

Group 1
- 3 participants
- PLX3397 600 milligrams per day
- 28-day cycles, could be repeated as long as participants benefitted from treatment without any serious side effects or asked to be removed from the study

Group 2
- 8 participants
- PLX3397 1000 milligrams per day
- PLX3397 800 milligrams per day
- First 2 weeks
- Remaining time
- 28-day cycles, could be repeated as long as participants benefitted from treatment without any serious side effects or asked to be removed from the study

Screening → Treatment Period

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 side effects during this 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 treatment in the study.

In this study, side effects were monitored for all 11 participants in the study. Out of 11 participants, 9 participants (82%) reported side effects related to PLX3397.

More detailed information about the side effects reported by participants is given below in the “medical problems” section of this summary.

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

1 out of 3 (33%) participants with tenosynovial-giant cell tumor (TGCT) in Group 1 had at least a 30% decrease in tumor size.

What were the other results of this study?

What were the levels of PLX3397 and its breakdown product ZAAD-1006a in the blood of participants?

The levels of PLX3397 in the blood increased with increasing doses of PLX3397 taken by the participants. PLX3397 levels in the blood reached a stable state after about 8 days of treatment. The blood levels of ZAAD-1006a also increased with increasing doses of PLX3397.
How much time did it take to reach the highest level of PLX3397 and its breakdown product ZAAD-1006a in the blood?

The highest level of PLX3397 in the blood was reached after about 1 hour of taking study drug. The highest level of ZAAD-1006a in the blood was reached after about 1.5 hours of taking study drug.

How did blood levels of CSF-1 and adiponectin change with changing doses of PLX3397?

The levels of CSF-1 and adiponectin in the blood of participants increased as the dose of PLX3397 was increased. Further studies may be needed to learn more about this effect of PLX3397.

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 during this study?

One participant in Group 1 had serious side effects of an increase in liver test values of alanine aminotransferase, alkaline phosphatase, aspartate aminotransferase, and bilirubin. None of the participants in Group 2 had serious side effects. There were no deaths that were considered to be related to the study treatment.
How many participants had the most common side effects?

The most common side effects, both serious and non-serious, that occurred in at least 20% (20 out of 100) of participants in any group are presented below.

### Most common side effects while taking PLX3397

<table>
<thead>
<tr>
<th>Group 1 3 participants</th>
<th>Group 2 8 participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage (number of participants)</td>
<td>Percentage (number of participants)</td>
</tr>
<tr>
<td><strong>Side effects</strong></td>
<td>75% (6)</td>
</tr>
<tr>
<td>100% (3)</td>
<td></td>
</tr>
<tr>
<td>33% (1)</td>
<td>Changes in hair color</td>
</tr>
<tr>
<td>0%</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>33% (1)</td>
<td>Feeling very tired</td>
</tr>
<tr>
<td>33% (1)</td>
<td>Increase in level of cholesterol in the blood</td>
</tr>
<tr>
<td>33% (1)</td>
<td>Increase in level of protein in the urine</td>
</tr>
<tr>
<td>33% (1)</td>
<td>Increase in liver test value of alanine aminotransferase</td>
</tr>
<tr>
<td>33% (1)</td>
<td>Increase in liver test value of alkaline phosphatase</td>
</tr>
<tr>
<td>67% (2)</td>
<td>Increase in liver test value of aspartate aminotransferase</td>
</tr>
<tr>
<td>33% (1)</td>
<td>Increase in liver test value of bilirubin in the blood</td>
</tr>
<tr>
<td>0%</td>
<td>Increase in liver test value of gamma-glutamyltransferase</td>
</tr>
<tr>
<td>33% (1)</td>
<td>Rash</td>
</tr>
<tr>
<td>33% (1)</td>
<td>Skin rashes</td>
</tr>
</tbody>
</table>

*An increase in the level of protein in the urine indicates damage to the kidney.*
How many participants had to stop treatment because of side effects?

None of the participants in the study stopped the study treatment early because of side effects.

How was this study useful for patients and researchers?

This study helped researchers learn about the safety and effects of PLX3397 in Asian people with advanced solid tumors. 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:


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 1 Study of Single Agent Pexidartinib in Asian Subjects With Advanced Solid Tumors

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