Clinical Results Summary

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

Protocol number: PLX108-13

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 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 but if it has, doctors may not recommend surgery. If the cancer cannot be removed by surgery, it is considered “unresectable”. For these patients, new methods of treating metastatic melanoma are needed. Some people with metastatic melanoma have a change or mutation in their KIT gene, which makes their cells grow and divide too fast. PLX3397, also known as pexidartinib, is a drug that is thought to stop the mutated KIT gene from working.

PLX3397 is a study treatment that is being tested for its ability to reduce the growth of cancer cells. In this study, researchers wanted to understand the effect of PLX3397 in participants with metastatic melanoma with a mutation in the KIT gene who could not be treated by surgery.

Treatment given in this study

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

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:

• How long did participants live with their cancer before it got worse or led to death?
• How many participants were alive until the end of the study?

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, they did not have serious side effects, and they did not ask to be removed from the study. The study started in January 2017 and is expected to end in March 2021.

The results were collected up to August 2018 and a study report was created. This summary is based on that report.

Who was in this study?

This study included 6 participants from China.

Participants could take part in this study if they:

• were 18 years or older and expected to live for at least 3 months
• had Stage 3 or 4 melanoma with a mutation in KIT gene that was not resistant to treatment with PLX3397. Stage 3 means that cancer has spread to the nearby lymph nodes and vessels. Stage 4 means that cancer has spread to other parts of the body.
• had measurable tissue or organ damage due to tumor
• had no prior treatment with chemotherapy
• had adequate organ and bone marrow function
• did not have any long-term liver disease

<table>
<thead>
<tr>
<th>In this study</th>
</tr>
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<tbody>
<tr>
<td>6 participants took part</td>
</tr>
<tr>
<td>67% were women (4 out of 6)</td>
</tr>
<tr>
<td>33% were men (2 out of 6)</td>
</tr>
<tr>
<td>Participants had an average age of 57 years</td>
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</table>
What happened during this study?

This was an open label study, which means that both the researchers and the participants knew which treatment was given to which participant.

This study was divided into 2 parts.

- The first part was a Phase 1 study, called the Pilot Phase. Phase 1 studies are done to find the appropriate dose of a drug that can be safely given to participants.
- The second part was called Phase 2. In Phase 2 studies, the study treatment is given to a small number of participants with the disease condition to gather information about the effects of the study treatment in patients.

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

**Pilot Phase**

At the start of the Pilot Phase, a small group of participants were given 1000 milligrams (mg) of PLX3397, which was taken by mouth daily. If this dose was considered to be safe by the researchers, more participants could be enrolled in the study and Phase 2 could be started. If this dose was not considered to be safe by the researchers, the next group of participants received a lower dose of PLX3397 and the process was repeated. This was planned to find the highest dose of PLX3397 that could be safely given to participants in Phase 2. The researchers used a special scan, called computed tomography (CT), to measure the participants’ tumor size during the study at different times.
Changes to the study plan
During the Pilot Phase, there were 3 participants who showed worsening of cancer and 1 participant who had liver damage. On 31 August 2018, researchers carefully reviewed the data and to ensure the safety of the participants, decided not to enroll any participants in Phase 2 of this study. The remaining 2 participants in the Pilot Phase continued treatment with PLX3397.

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 tumors that completely disappeared or became at least 30% smaller after treatment?
1 out of 6 (17%) participants had at least a 30% decrease in tumor size.

17% of participants had at least 30% decrease in tumor size
No participants had tumors that completely disappeared

What were the other results of this study?
How long did participants live with their cancer before it got worse or led to death?
Participants lived for a median of about 10 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 10 months for their cancer to start getting worse and for the other half of participants, it took more time.

**How many participants were alive until the end of the study?**
Out of a total of 6 participants, 5 participants were alive at the end of the study. 1 participant died during the study due to worsening of cancer.

**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 treatment in the study. This section provides a summary of side effects related to the study treatment PLX3397. 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?**
33% (2 out of 6) of participants reported serious side effects of liver damage.

**How many participants had the most common side effects?**
Side effects, both serious and non-serious, occurred in all 6 participants during the study.

The most common side effects, both serious and non-serious, that were reported by at least 50% of participants are presented below.
### Most common side effects while taking PLX3397

<table>
<thead>
<tr>
<th>Side effects</th>
<th>Percentage (number of participants)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased white blood cell count</td>
<td>100% (6)</td>
</tr>
<tr>
<td>Increase in liver test value of aspartate aminotransferase</td>
<td>100% (6)</td>
</tr>
<tr>
<td>Decreased red blood cell count</td>
<td>83% (5)</td>
</tr>
<tr>
<td>Swelling of the face</td>
<td>83% (5)</td>
</tr>
<tr>
<td>Change in hair color</td>
<td>67% (4)</td>
</tr>
<tr>
<td>Decreased neutrophil count</td>
<td>67% (4)</td>
</tr>
<tr>
<td>Increase in liver test value of alanine aminotransferase</td>
<td>67% (4)</td>
</tr>
<tr>
<td>Increase in liver test value of bilirubin</td>
<td>67% (4)</td>
</tr>
<tr>
<td>Increase in liver test value of gamma-glutamyltransferase</td>
<td>67% (4)</td>
</tr>
<tr>
<td>Increase in level of lactate dehydrogenase</td>
<td>50% (3)</td>
</tr>
<tr>
<td>Increase in liver test value of alkaline phosphatase</td>
<td>50% (3)</td>
</tr>
<tr>
<td>Increase in liver test value of bile acids</td>
<td>50% (3)</td>
</tr>
<tr>
<td>Increase in liver test value of conjugated bilirubin</td>
<td>50% (3)</td>
</tr>
<tr>
<td>Lung damage</td>
<td>50% (3)</td>
</tr>
</tbody>
</table>

- An increase in level of lactate dehydrogenase means there is tissue damage in the body.
- An increase in level of bilirubin, gamma-glutamyltransferase, alkaline phosphatase, bile acids, and conjugated bilirubin means there is damage to the liver.
- Neutrophils are a type of white blood cell that help fight infections.
How many participants had to stop treatment because of side effects?
One participant stopped PLX3397 treatment due to a side effect related to liver damage.

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 skin cancer called metastatic melanoma. 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: Phase I/II Open Label, Multicenter Study of PLX3397 in Patients with Unresectable or Metastatic KIT-mutated Melanoma.

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