Daiichi-Sankyo

Clinical Results Summary

A clinical study to learn more about the effects and safety of pexidartinib in people with tumor growth in or around the joint due to tenosynovial giant cell tumor (TGCT)

Also called: ENLIVEN

Protocol number: PLX108-10

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 tumor growth in or around the joint, a condition known as tenosynovial giant cell tumor, or TGCT. 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?

Tenosynovial giant cell tumor

Tenosynovial giant cell tumor (TGCT) is a condition in which people have tumors that grow in and around their joints. Localized TGCT is more common and usually affects small joints, such as the hands and ankles. Diffuse TGCT is less common and affects large joints, such as the hips and knees. This condition causes pain, stiffness, swelling, and a decrease in the range of movement of the joints.

At this time, the main treatment option for TGCT is surgery. However for some people, tumors can come back even after surgery. For others, doctors may not recommend surgery if the tumor has grown or has invaded the joint too much. For all of these patients, new methods of treating TGCT are needed.

Researchers think these tumors form when some cells in the joint start making too much of a protein that attracts other cells to the joint. As more and more cells reach the joint, they join together to form tumors. Pexidartinib is a treatment that may stop this protein from attracting cells. In this study, researchers wanted to see if pexidartinib could be used to shrink the tumors or stop new tumors from growing in and around the joints for people who have TGCT.

Treatments given in this study

Pexidartinib: A treatment being studied for its ability to shrink the tumor in or around the joint and to stop new tumors from forming. 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.

Placebo: A placebo looks like the study treatment and is given in the same way, but it does not have any medicine in it. Using placebo helps researchers better understand the effect of a study treatment.

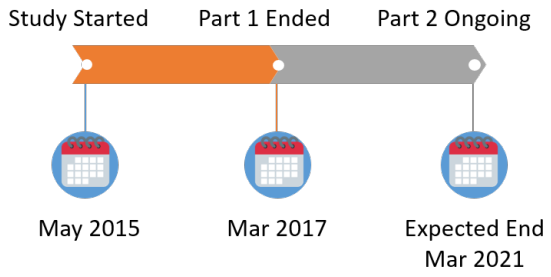
Main purpose of this study

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

How many participants had tumors that completely disappeared or became 30% smaller after about 6 months of treatment?

The researchers also wanted to learn more about the safety of pexidartinib. Additionally, they tracked participants' joint movement, stiffness, ability to perform daily activities, intensity of pain, and use of pain medication.

How long was this study?

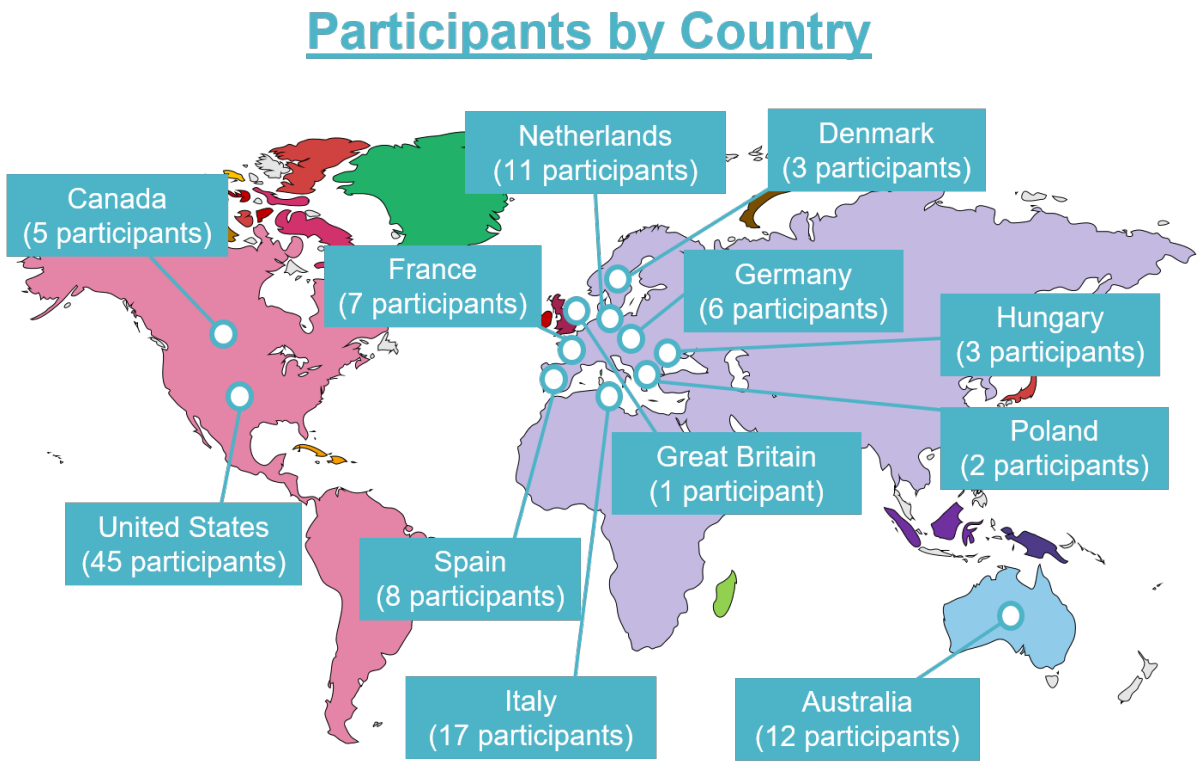


An individual participant could have stayed in Part 1 of the study for about 6 months. Depending on their treatment group in Part 1, the same participants could have stayed for Part 2 and continued treatment with pexidartinib.

Part 1 and Part 2 results were evaluated up to 31 January 2018 and a study report was created. This summary is based on that report. Once Part 2 of the study is completed, a full summary of results will also be made available to all participants.

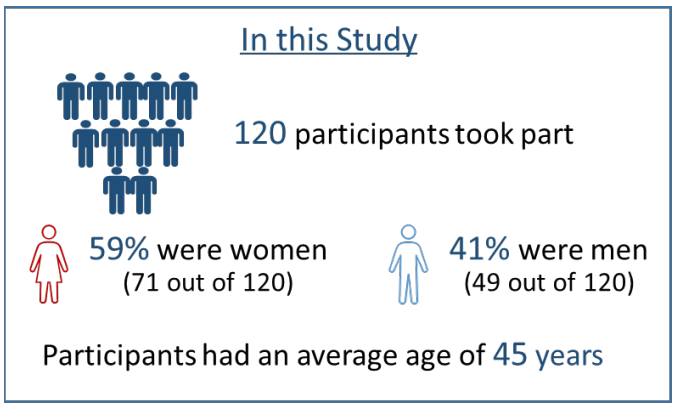
Who was in this study?

This study included 120 participants from the following countries:



Participants could take part in this study if they:

- were over 18 years of age,
- had TGCT and doctors considered that surgery could have caused more harm than good,
- had normal blood, liver, and kidney function,
- suffered from pain and stiffness that interfered with their daily activities, and
- did not have any other type of active cancer that needed treatment, aside from a few exceptions.



What happened during this study?

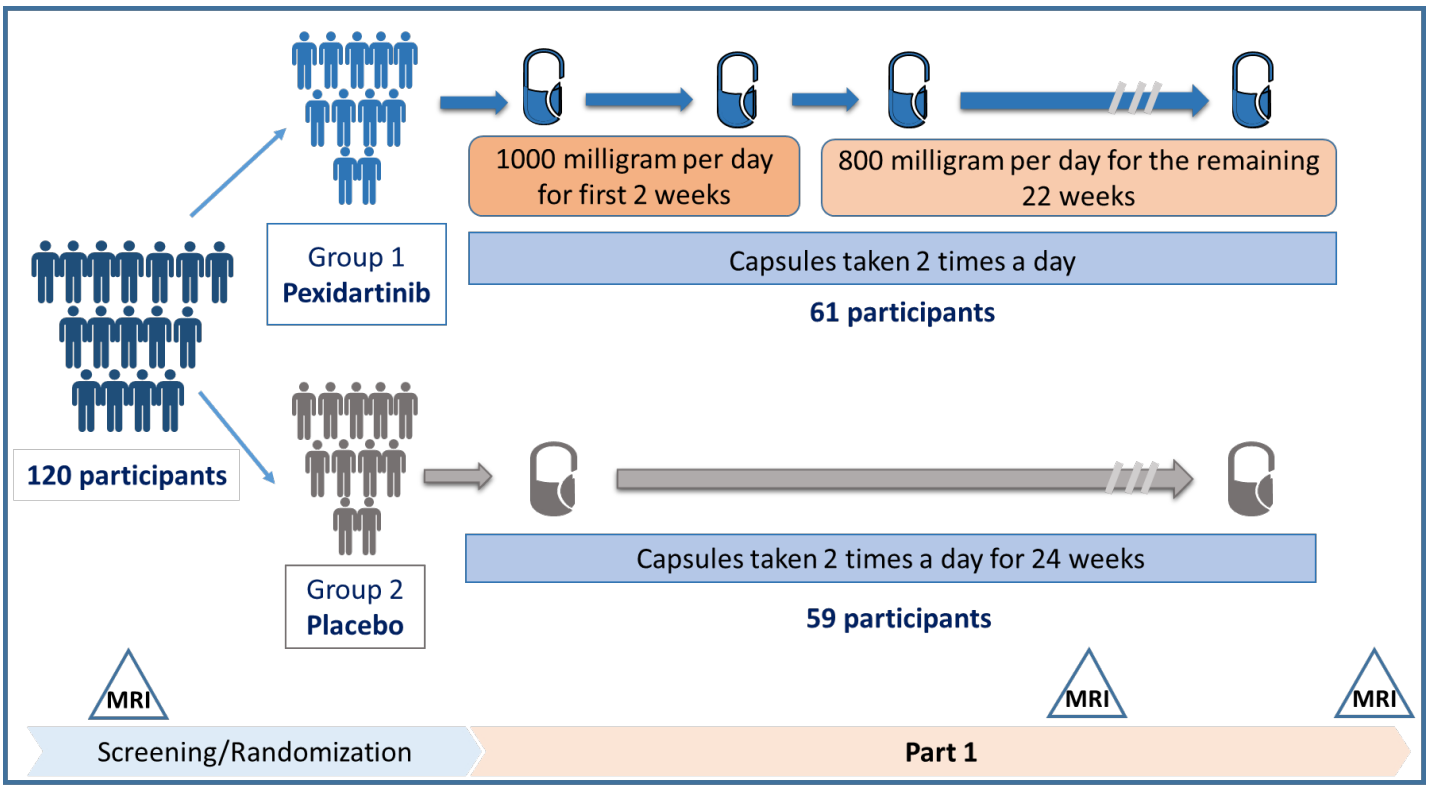
This was a large, global, Phase 3 study that compared the effects and safety of pexidartinib with placebo in participants with TGCT who had tumor growth in or around their joints. Participants in Part 1 had the option to continue on to Part 2.

Part 1

Participants completed a screening period to find out if they could be a part of the study. The researchers then used a computer program to randomly assign participants into 2 groups, Group 1 and Group 2, a process called randomization. This means that each person had an equal chance of being in any group. Participants in Group 1 received pexidartinib as capsules 2 times a day, for 24 weeks. Participants in Group 2 received placebo as capsules 2 times a day, for 24 weeks. This part was double-blinded, meaning neither the participants nor the study doctors knew who took which treatment.

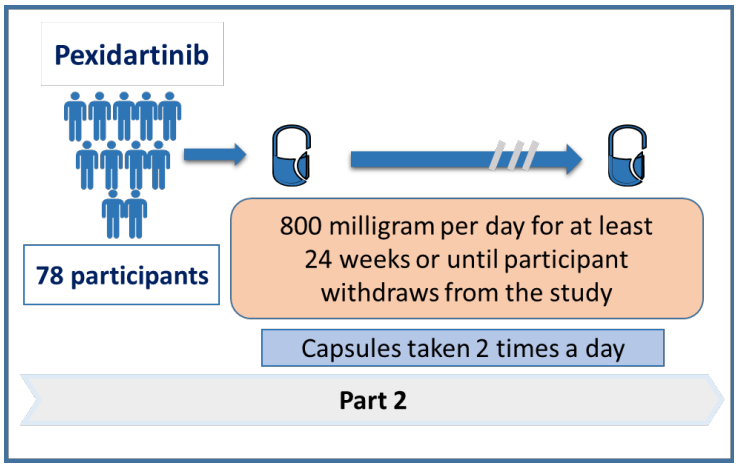
The researchers used a special scan, called magnetic resonance imaging or MRI, to measure the participants' tumor size during the study at different times.

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



Part 2

Part 2 was an open-label study, which means that both the researchers and the participants knew what treatment was given. All participants in Part 2 received 800 mg pexidartinib as capsules 2 times a day. The study was designed so that all participants who completed Part 1 (Group 1 and Group 2) could advance to Part 2.



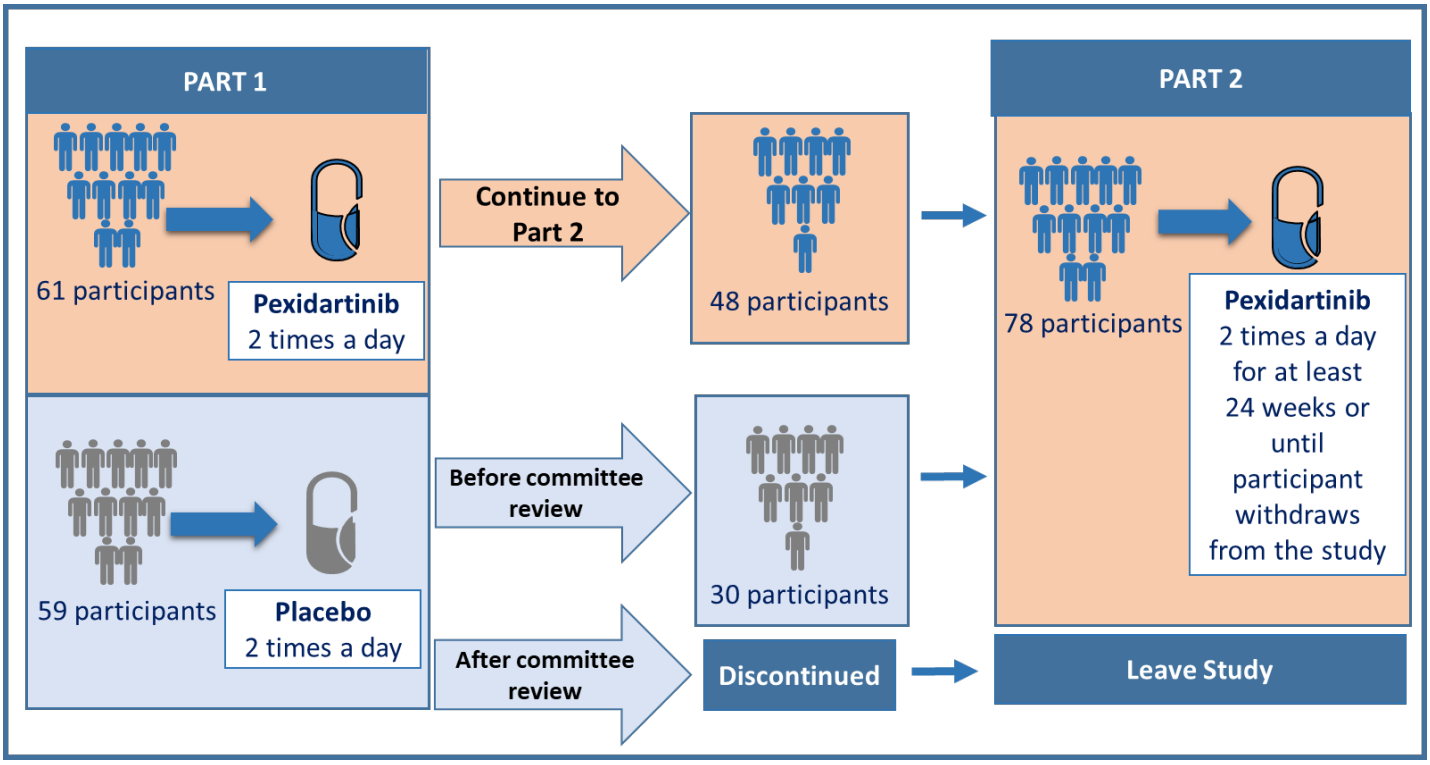
Changes to the study plan

In the early stages of the study, an independent committee was asked to monitor the overall health of all participants. During the study, there were 2 participants who showed signs of serious liver problems. One of these participants required hospitalization and 2 liver dialysis procedures. Study treatment was discontinued

for both participants. On 29 September 2016, the independent monitoring committee carefully reviewed the health data. After review, to ensure the safety of all participants in the study, the sponsor made the following changes to the study design:

- Researchers did more liver tests more often to monitor participants' liver function and overall health.
- Only participants who were in the pexidartinib group of Part 1 could advance to Part 2.
- Participants in the placebo group could no longer advance to Part 2 after they completed Part 1.
- No new participants were allowed to start the study.

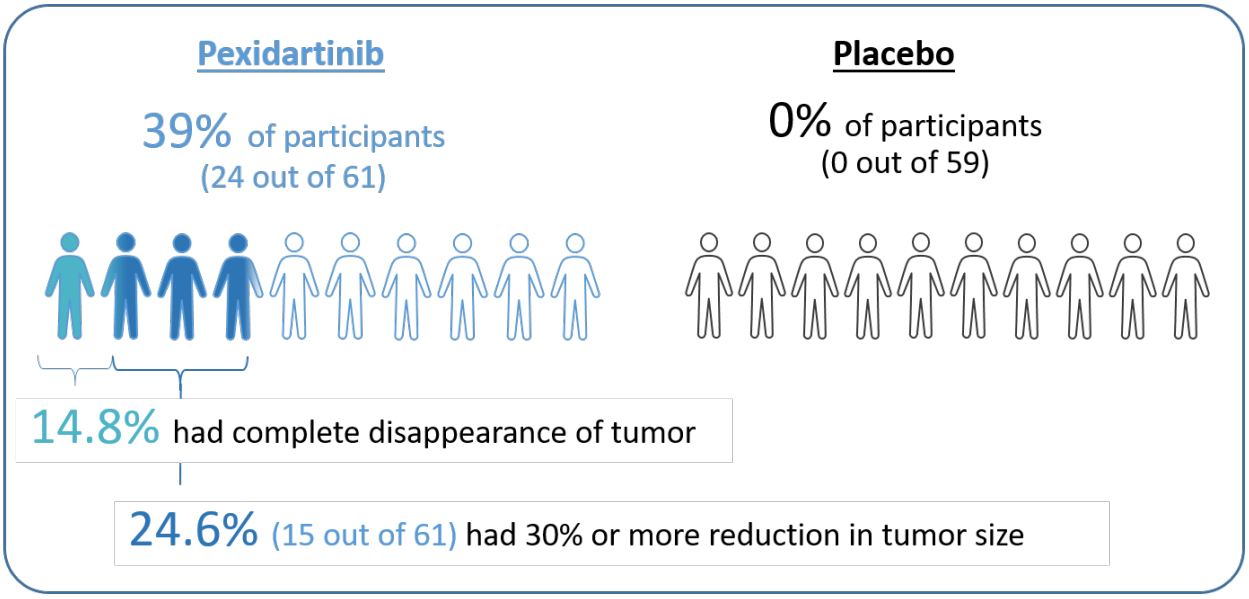
Overview of study after committee review



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 websites listed at the end of this summary.

How many participants had tumors that completely disappeared or had tumors that became 30% smaller after about 6 months of treatment?



What were the other results of this study?

Participants taking pexidartinib showed greater improvement in range of motion of the joints, tumor-related stiffness of affected joints, and ability to perform daily activities. Participants in pexidartinib group who responded to pexidartinib maintained the response to treatment.

More participants who took pexidartinib reported a decrease in pain and use of pain medication. However, this decrease may have been due to chance and not caused by the study treatment.

What medical problems did the study participants have?

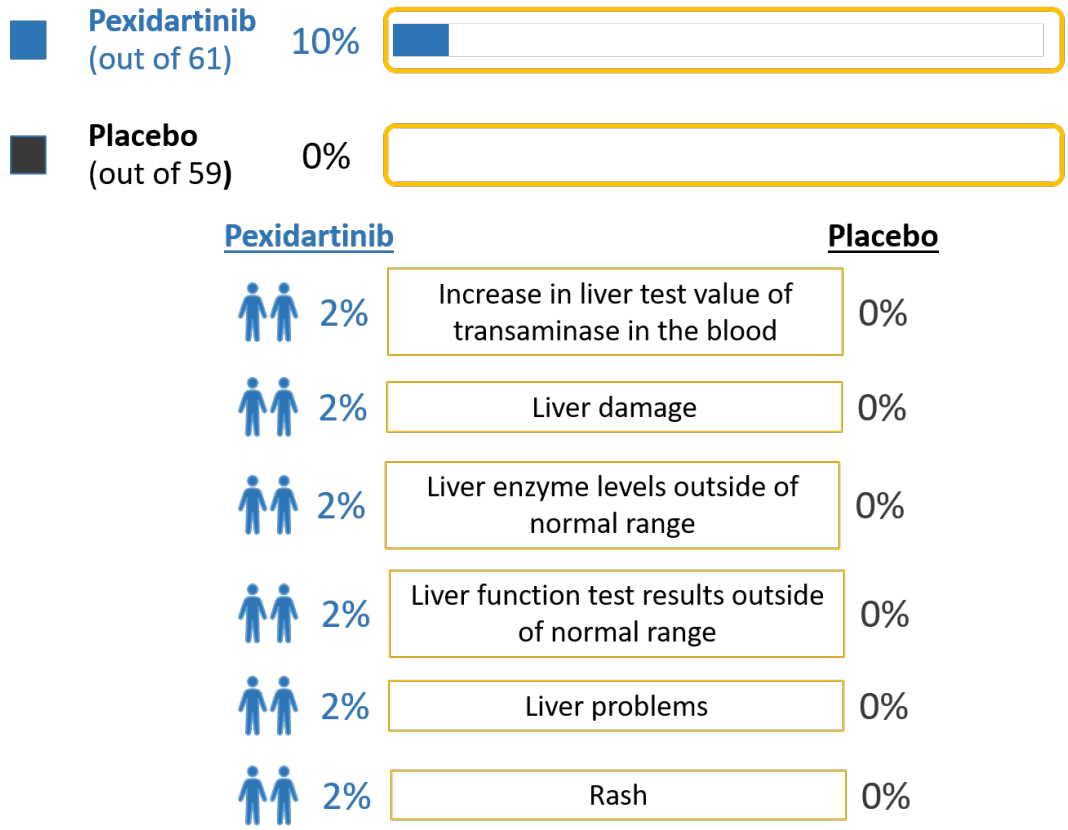
Side effects are medical problems (such as feeling tired) that happened during the study which the study doctor thought could be related to the treatments in the study.

Side effects are considered serious if they cause death, are life-threatening, cause lasting problems, or require hospitalization. Some participants stopped study treatment because of side effects.

How many participants had serious side effects during Part 1?

In this study, side effects were monitored for 61 participants who took pexidartinib and 59 participants who took placebo.

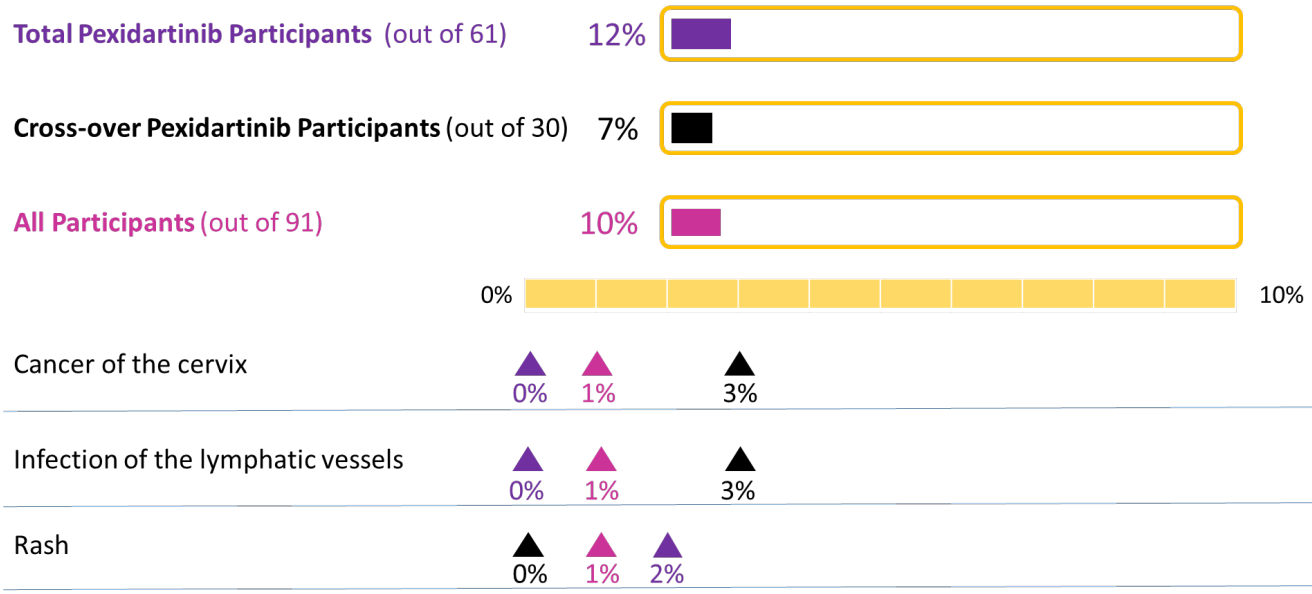
Percentage of Participants who had Serious Side Effects During Part 1



How many participants had serious side effects while taking pexidartinib during the study?

The first row labeled 'Total Pexidartinib Participants' shows total percentage of serious side effects reported by participants who received pexidartinib during Part 1 and 2. The second row labeled 'Cross-over Pexidartinib Participants' shows serious side effects in participants who crossed over to receive pexidartinib in Part 2 after receiving placebo in Part 1. The third row labeled 'All Participants', shows the serious side effects reported by all the participants who received pexidartinib either in Part 1 or Part 2.

Percentage of Participants who had Serious Side Effects While Taking Pexidartinib



There was one participant's death reported.

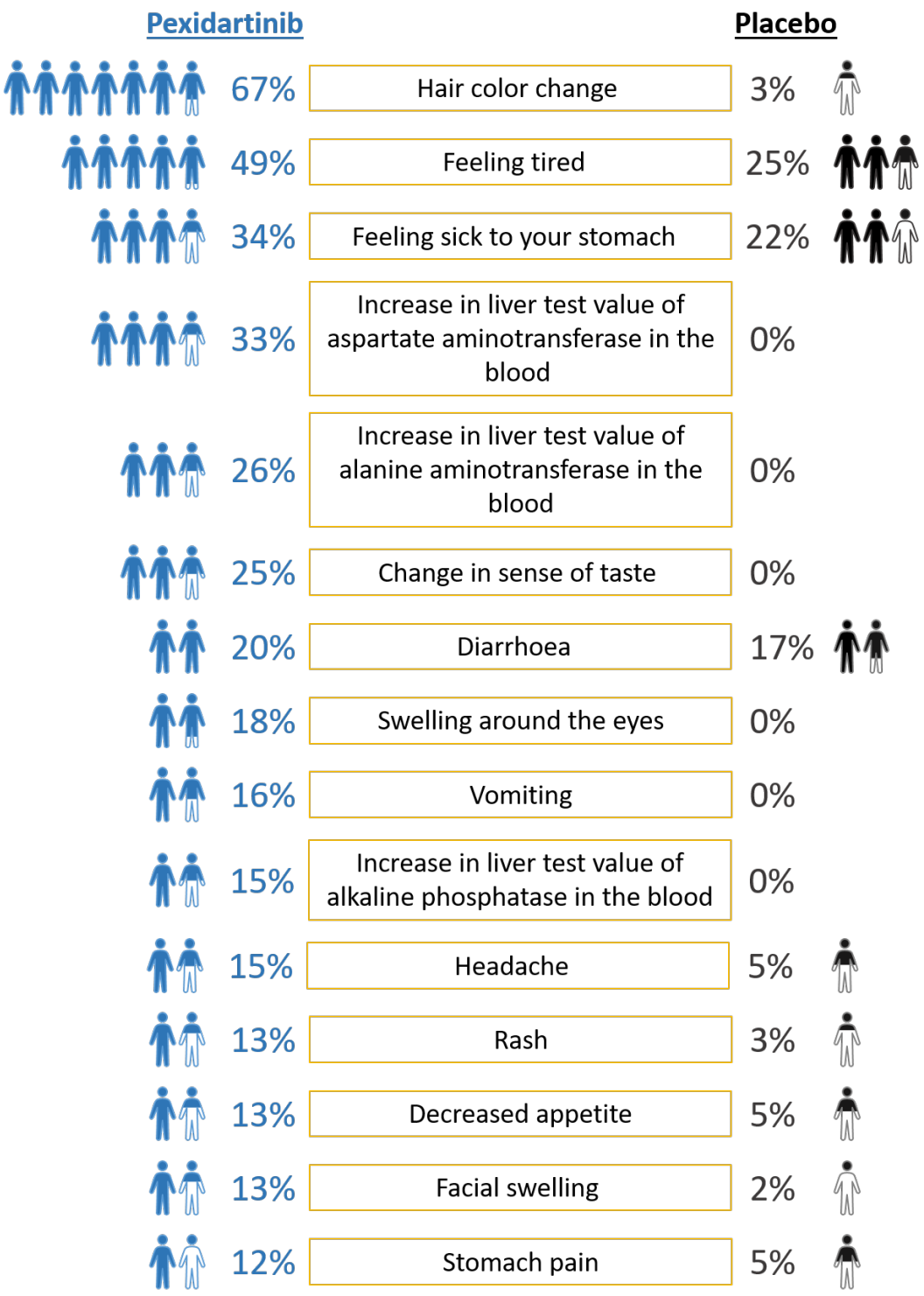
The cause of death was not related to study treatment.

What were the most common side effects during Part 1?

Side effects reported in Part 1, both serious and non-serious, are presented in this section.

Total Percentage of Participants with Side Effects During Part 1

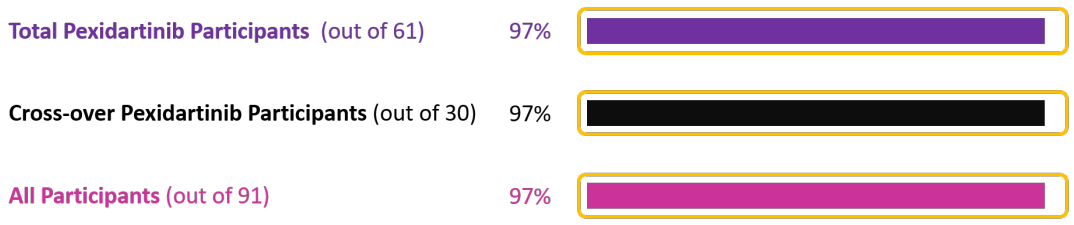
The most common side effects that occurred in at least 10% (10 out of 100) of participants in any group are presented below:



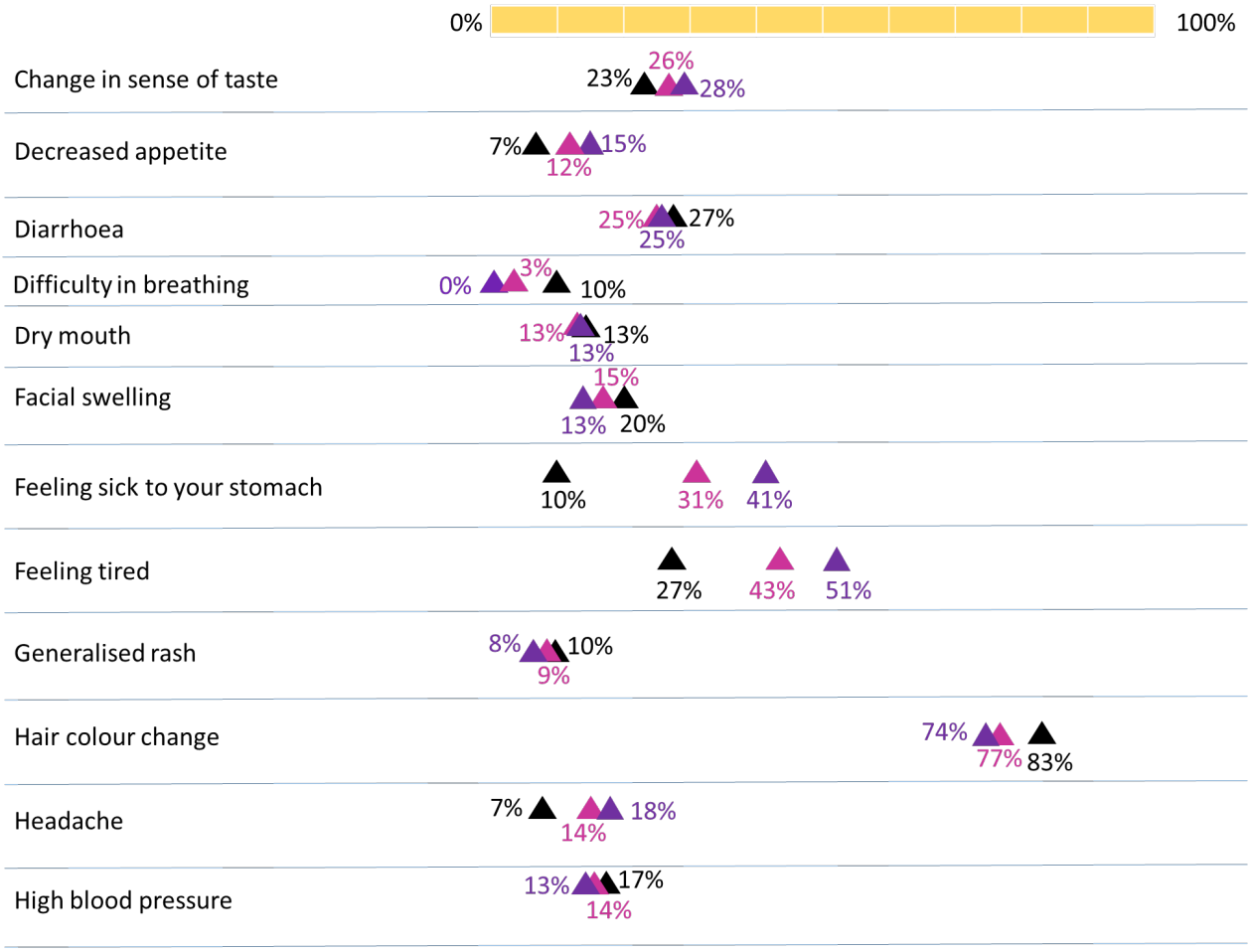
What were the most common side effects while taking pexidartinib during the study?

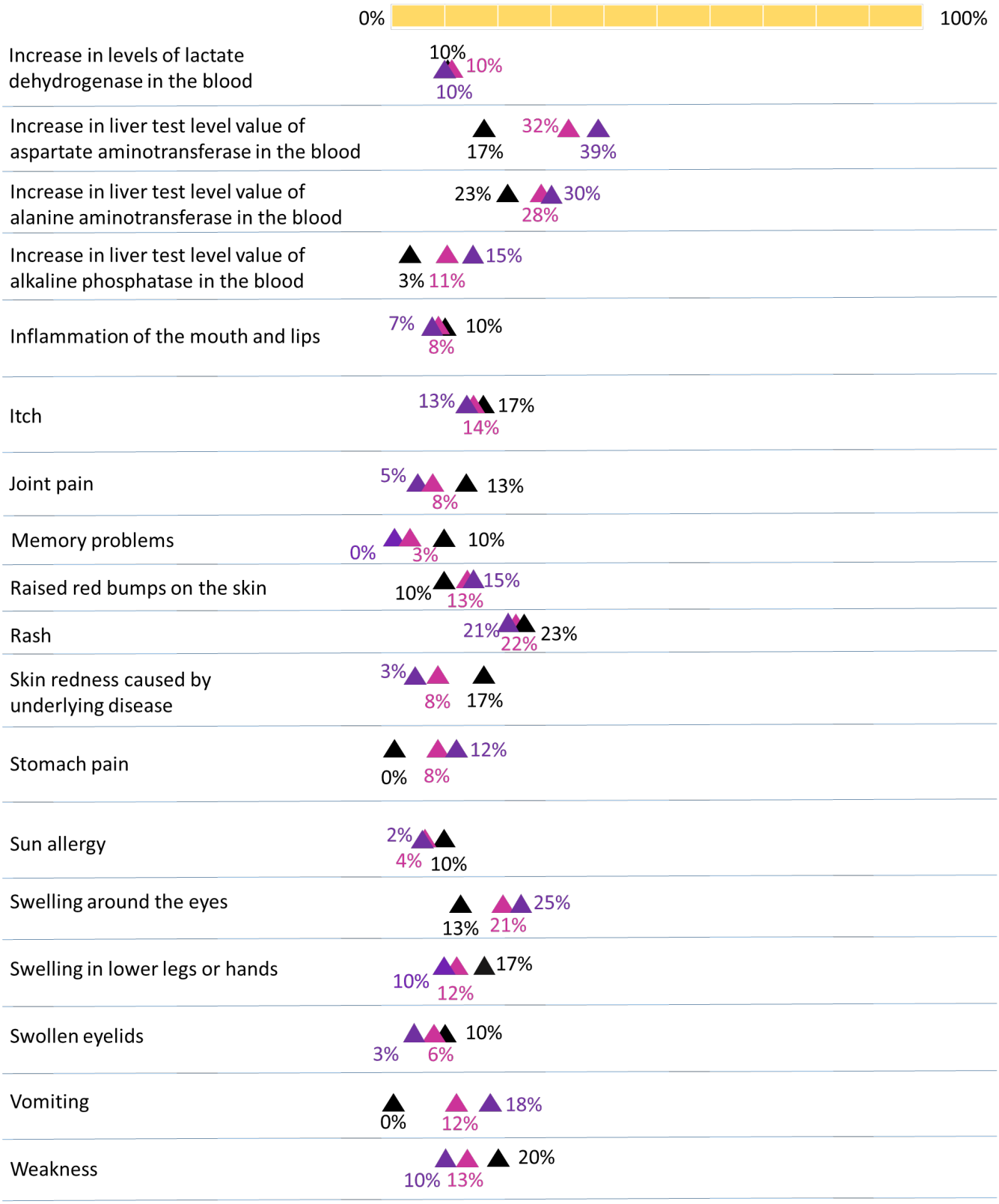
Side effects reported by participants taking pexidartinib, both serious and non-serious, are presented in this section.

Percentage of Participants who had Side Effects While Taking Pexidartinib

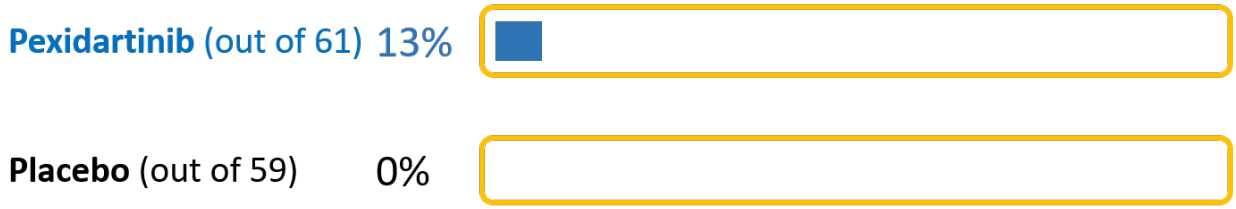


The most common side effects that occurred in at least 10% (10 out of 100) of participants in any group are reported below:



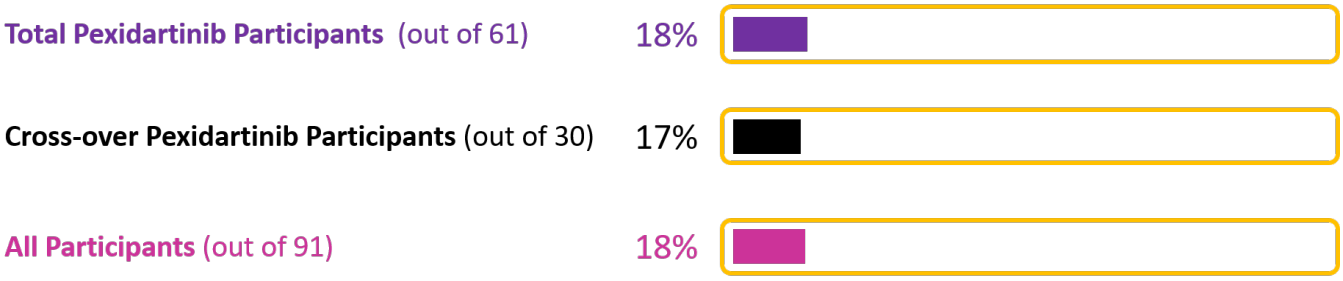

0%
100%
Increase in levels of lactate dehydrogenase in the blood
10%
10%
10%
Increase in liver test level value of aspartate aminotransferase in the blood
17%
32%
39%
Increase in liver test level value of alanine aminotransferase in the blood
23%
30%
28%
Increase in liver test level value of alkaline phosphatase in the blood
15%
3%
11%
Inflammation of the mouth and lips
7%
10%
8%
Itch
13%
17%
14%
Joint pain
5%
13%
8%
Memory problems
0%
3%
10%
Raised red bumps on the skin
10%
15%
13%
Rash
21%
23%
22%
Skin redness caused by underlying disease
3%
8%
17%
Stomach pain
12%
0%
8%
Sun allergy
2%
4%
10%
Swelling around the eyes
25%
13%
21%
Swelling in lower legs or hands
17%
10%
12%
Swollen eyelids
10%
3%
6%
Vomiting
0%
12%
18%
Weakness
20%
10%
13%

How many participants had to stop treatment because of side effects during Part 1?



The most common side effects that caused participants to stop the study treatment in Part 1 were related to liver problems. Liver problems were in line with side effects usually reported in other studies of this kind.

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



How was this study useful for patients and researchers?

This study helped researchers learn about how well pexidartinib is able to remove or reduce the size of tumors in people with TGCT who have tumor growth in or around their joints.

Findings from this study may be used to seek approval to use study treatment in patients with tumor growth in or around their joints. Other studies of pexidartinib are ongoing.

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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.

Where can I learn more about this study?

You can find more information about this study on the following websites:

- www.clinicaltrials.gov: Use the NCT identifier NCT02371369 in the search field.
- www.clinicaltrialsregister.eu: Use the EudraCT identifier 2014-000148-14 in the search field.
- https://www.nccn.org/professionals/physician_gls/default.aspx: The National Comprehensive Cancer Network® (NCCN) clinical practice guidelines in oncology: soft tissue sarcoma—v4.2019.

Please remember that the results on these websites 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 Double-blind, Randomized, Placebo-controlled Phase 3 Study of Orally Administered PLX3397 in Subjects with Pigmented Villonodular Synovitis or Giant Cell Tumor of the Tendon Sheath (ENLIVEN)

Sponsor: Daiichi Sankyo, Inc.

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