Daiichi-Sankyo

Clinical Results Summary

A clinical study to learn about the safety and effects of DS-8201a in participants with HER2-positive cancer that has spread and/or is difficult to treat

Protocol number: DS8201-A-A103

Thank You!

Daiichi Sankyo, the sponsor of this study, would like to thank the participants who took part in this study for trastuzumab deruxtecan, also known DS-8201a or T-DXd. Each participant helped to advance medical research for people affected with HER-2 positive cancer. 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 cancer

A tumor is an abnormal growth of cells in the body that starts in an organ, muscle, or bone. An “advanced” cancer usually means one that has spread to other parts of the body. A certain kind of protein called a ‘kinase’ helps tumor cells divide and grow. It is believed that by stopping this protein from working, the growth of the tumor cells can be stopped.

Some people with cancers have an increased level of a protein called HER2, which makes their cells grow and divide too fast. This is called a HER2-positive cancer. DS-8201a, also known as trastuzumab deruxtecan or T-DXd, specifically binds to HER2-expressing cells to inhibit the cell growth and cause the death of target tumor cells.

Participants could take part in this study if they had HER2-positive cancer of one of the following types:

- Gastric (stomach) cancer
- Gastroesophageal junction (GEJ) cancer: cancer in the area where the food pipe and stomach join together
- Breast cancer

At this time treatment options for the above mentioned cancers are:

- surgery
- radiation therapy - a treatment that uses radiation to kill cancer cells
- endocrine (hormone) therapy - a treatment that stops the growth of cancers that use hormones to grow
- chemotherapy – a treatment that uses drugs to kill cancer cells or stop them from growing and dividing

Current treatment options do not work in all patients, therefore new methods for treating these cancers are needed.

In this study, researchers wanted to learn about the safety and effects of T-DXd in participants with HER2-positive advanced cancer which is refractory. Refractory means that the cancer does not respond to or cannot be treated with available treatment options.

Treatment given in this study

T-DXd

Drug being studied for the treatment of HER2-positive advanced and/or refractory cancer

Main goal of this study

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

How many participants had side effects during the study?

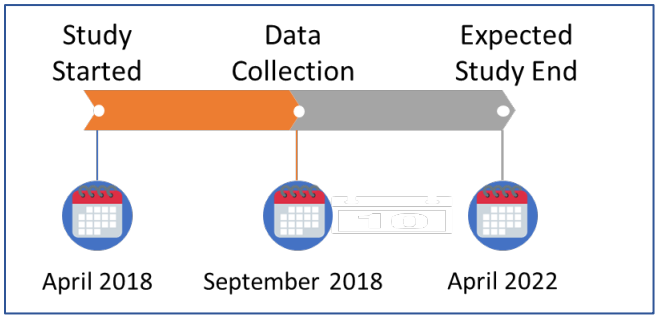
Other goals of this study

Researchers also wanted to answer the following question:

- What were the levels of T-DXd*, its breakdown product MAAA-1181a, and total anti-HER2 antibody, in the blood of participants?

*T-DXd consists of 2 components. One component is deruxtecan. The other is the HER2 targeted antibody called trastuzumab. The 2 components are designed to stay together until T-DXd binds to a cell with the HER2 marker on it. Once T-DXd binds to a HER2 positive cell, it gets activated. The 2 components then separate and a released topoisomerase I inhibitor (MAAA-1181a) kills the HER2 positive cell.

How long was this study?

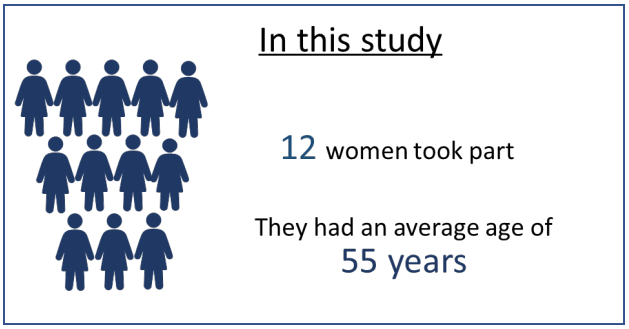


The study was designed so that participants could continue in it as long as their tumor did not get worse and they did not have serious side effects, or were asked to be removed from the study. The study started in April 2018 and is expected to end in April 2022.

The results were collected up to September 2018 and a study report was created. Once the study is completed, a full summary of results will also be made available.

Who was in this study?

This study included 12 female participants (of Chinese descent) with breast cancer.



Participants could take part in this study if they:

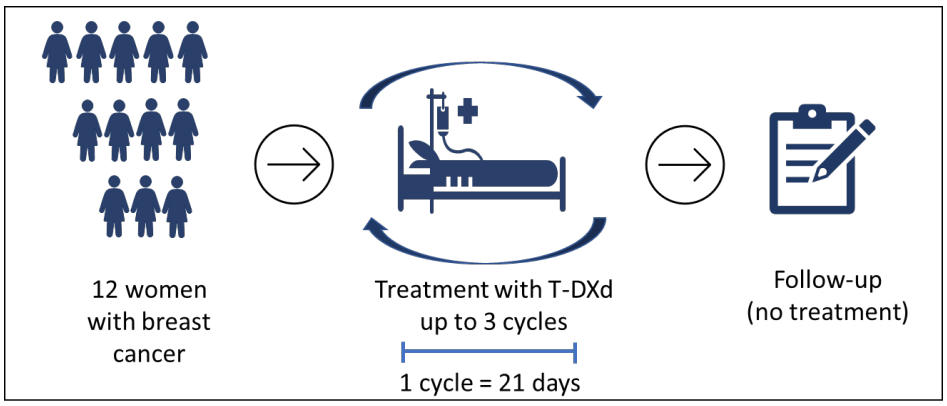
- were either fully active or able to walk and do light work but unable to do a hard physical activity,
- were expected to live for at least 3 months,
- had breast cancer that came back after standard treatment or could not be treated by standard treatment or for which no standard treatment was available,
- had adequate liver, kidney, bone marrow and blood clotting function, as measured by blood tests.

What happened during this study?

This was a Phase 1 study. Phase 1 studies are done to find out how new study treatment works in a small number of participants. This helps researchers understand what happens to the study treatment in the body, and if there are any side effects.

This study was “open label”. This means that both the researchers and the participants knew what dose of T-DXd the participants were given.

Participants received 6.4 milligram/kilogram (mg/kg) of T-DXd through a drip over 90 minutes on the first day of each cycle for a minimum of 3 cycles. Each cycle lasted 3 weeks.



Researchers took blood samples from participants at defined time points. Researchers monitored the participants' health throughout the study.

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 the study?

During this study, all the participants (12 out of 12, 100%) had at least 1 side effect.

Detailed information about side effects reported by participants is presented in the section 'What medical problems did the participants have?

What were the levels of T-DXd, its breakdown product MAAA-1181a, and total anti-HER2 antibody, in the blood of participants?

To answer this question, the researchers measured the total levels of T-DXd, MAAA-1181a and anti-HER2 antibody in the participant's blood samples during Cycle 1 and Cycle 3.

The average results of these measurements are presented below. Total levels of T-DXd, MAAA-1181a, and anti-HER2 antibody in the participants' blood is measured in d × ng hr/mL*.

Researchers found that the levels of T-DXd, MAAA-1181a, and anti-HER2 antibody in the participants' blood increased from Cycle 1 to Cycle 3.

	Cycle 1	Cycle 3
T-DXd		
Total level during dosing interval (d × ng·hr/mL)	631	991
MAAA-1181a		
Total level during dosing interval (d × ng·hr/mL)	36	41
Anti-HER2 antibody		
Total level during dosing interval (d × ng·hr/mL)	821	1180

*This means the total levels of T-DXd, MAAA-1181a, and total anti-HER2 antibody in nanograms (one thousand-millionth of a gram) found in each milliliter of blood within the dosing period.

What medical problems did the study participants have?

Side effects are medical problems (such as a feeling tired) that happened during the study which the study doctor thought could be related to T-Dxd. This section provides a summary of such side effects. 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.

How many participants had serious side effects?

In this study, 1 out of 12 participants (8%) had a serious side effect of abnormally low levels of neutrophils (a type of white blood cell that fights bacteria) accompanied with fever.

How many participants had side effects?

All side effects, both serious and non-serious, are presented in this section. All the participants (12 out of 12, 100%) had at least 1 side effect.

The most common side effects that occurred in at least 25% of participants (3 out of 12) were:

Side Effects	T-DXd (6.4 mg/kg) (out of 12 participants)
Decrease in platelet count [a]	58% (7 participants)
Increase in liver test value of aspartate aminotransferase (AST) in the blood [b]	42% (5 participants)
Decrease in white blood cells count [c]	42% (5 participants)
Nausea	58% (7 participants)
Decrease in red blood cells count	25% (3 participants)
Decrease in appetite	33% (4 participants)
Feeling tired	25% (3 participants)

[a] platelets are a type of blood cell that helps in preventing / stopping bleeding
[b] an increase in AST may indicate a liver problems
[c] white blood cells help protect your body from infection
[d] red blood cells help carry oxygen around the body

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

No participant had to stop T-Dxd treatment because of side effects.

How was this study useful for patients and researchers?

This study also helped researchers learn about the safety and other effects of T-DXd when given to participants with HER2-positive advanced/refractory breast cancer. Other studies of T-DXd are ongoing.

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 NCT03368196 in the search field.

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: Phase 1, Multicenter, Open-Label Study of DS-8201a to Assess Safety and Pharmacokinetics in Subjects with HER2-Positive Advanced and/or Refractory Gastric, Gastroesophageal Junction Adenocarcinoma, or Breast Cancer

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