Daiichi-Sankyo

Clinical Results Summary

A clinical study to learn about the effects of DS-8201a in women with HER2-positive breast cancer previously treated with T-DM1 that has spread and/ or cannot be surgically removed

Protocol number: DS8201-A-U201

Thank You!

Daiichi Sankyo, Inc., 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 women affected with HER2-positive breast 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?

Metastatic breast cancer

Researchers were looking for a better way to treat people with unresectable and/or metastatic breast cancer. Breast cancer starts in the cells of the breasts, and is more common in women than men. These cells divide more rapidly than the normal cells, forming a lump or mass. "Metastatic" means that cancer has spread to other parts of the body, and "unresectable" means that cancer cannot be completely removed through surgery. Symptoms of metastatic breast cancer include swelling in the breast, redness of the skin near the breast area, weakness in any part of the body, difficulty in breathing, and chest pain.

At this time treatment options for breast cancer are surgery, radiation therapy, endocrine (hormone) therapy and chemotherapy. Radiation therapy is a type of cancer treatment that uses radiation to kill cancer cells. Hormone therapy is a cancer treatment that stops the growth of cancer that uses hormones to grow. Chemotherapy uses medicine 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 breast cancer are needed.

Some people with breast cancer have an increased level of a protein called HER2, which makes their cells grow and divide too fast. This is called HER2-positive breast cancer.

DS-8201a, also known as trastuzumab deruxtecan or (as used from this point) T-DXd, specifically binds to HER2-expressing cells to inhibit the cell growth and cause the death of target tumor cells.

In this study, researchers wanted to learn about the effects of T-DXd in women with HER2-positive breast cancer who were previously treated with T-DM1 (also known as trastuzumab emtansine).

Treatment given in this study

T-DXd

(Study drug)

Drug being studied for the treatment of HER2-positive unresectable and/or metastatic breast cancer in participants who were previously treated with T-DM1.

Main goal of this study

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

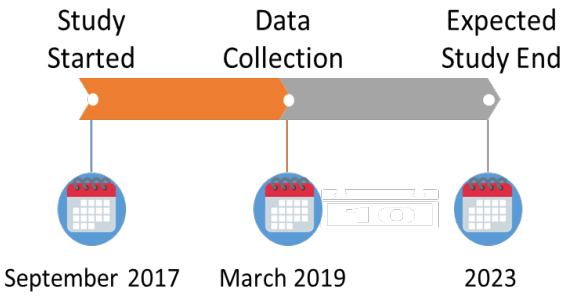
How many participants had tumors that completely disappeared or became at least 30% smaller after treatment?

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 long did participants live after first day of treatment?
- What side effects did the participants develop during the study?

How long was this study?

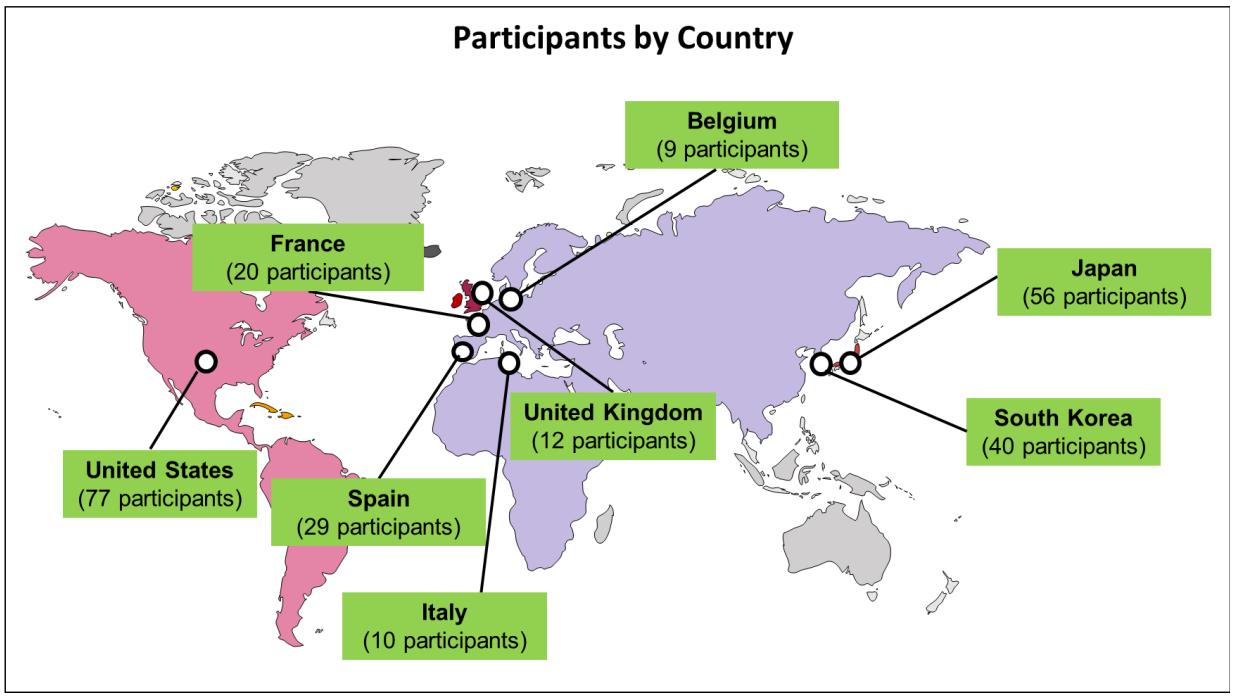


The study was designed so that participants could continue in it as long as their tumor did not get worse and they did not have serious side effects. The study started in September 2017 and is expected to end in 2023.

The results were collected up to March 2019 and a study report was created. This summary is based on that report.

Who was in this study?

This study included 253 participants from 8 countries.



Participants could take part in this study if they:

- were at least 18 years of age
- had confirmed HER2-positive breast cancer that was unresectable or metastatic
- had breast cancer that was previously treated with T-DM1

In this study

253 women took part

They had an average age of 56 years

- were either fully active OR unable to do hard physical activity but able to walk and do light housework or office work
- had adequate liver, kidney, bone marrow and blood clotting function, as measured by blood tests

What happened during this study?

This was a Phase 2 study, which means that study treatment was given to a smaller number of participants with the disease to gather information about its effects. It was open label, meaning that the researchers knew which treatment was given to which participants, and the participants knew which treatment they received.

Participants continued to receive treatment as long as they did not show worsening of cancer, have serious side effects, or ask to be removed from the study.

Part 1

Part 1 of the study was divided into 2 stages: a pharmacokinetic ('PK') stage and a dose finding stage.

PK stage: During the PK stage, researchers studied 3 different doses and based on the levels of T-DXd in participants' blood, they chose 2 dose levels that could be tested in the next stage.

Participants were randomly divided into 3 groups. In all 3 groups, T-DXd was given as an injection.

Doses of 5.4 mg/kg (low), 6.4 mg/kg (medium) and 7.4 mg/kg (high) were assessed. The researchers identified the low and medium doses as the recommended doses of T-DXd that could be given to participants in the next stage of Part 1.

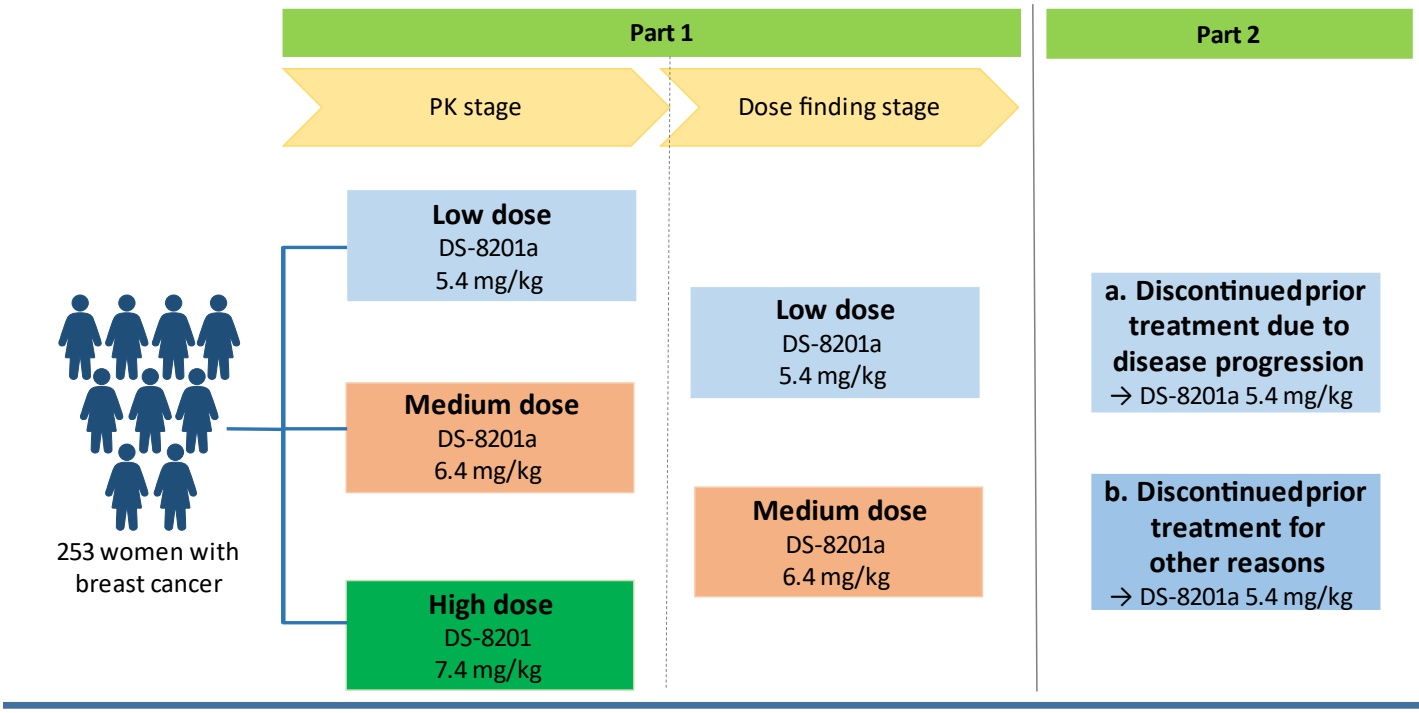
Dose finding stage:

During this stage, researchers gave the low and medium doses of T-DXd and looked at its effects and safety in the participants to find out the recommended dose for further testing during Part 2. Based on the results, the low dose was chosen as the recommended dose in the study.

Part 2

During Part 2, participants were included into 2 groups according to their response to T-DM1 before enrolling in this study. Group 2a (130 participants) comprised patients who had discontinued treatment with T-DM1 due to progression of their disease; Group 2b (4 participants) consisted of patients who had discontinued T-DM1 for other reasons. Both groups received the same low dose (5.4 mg/kg).

The following diagram shows the study stages and the different doses received by participants:

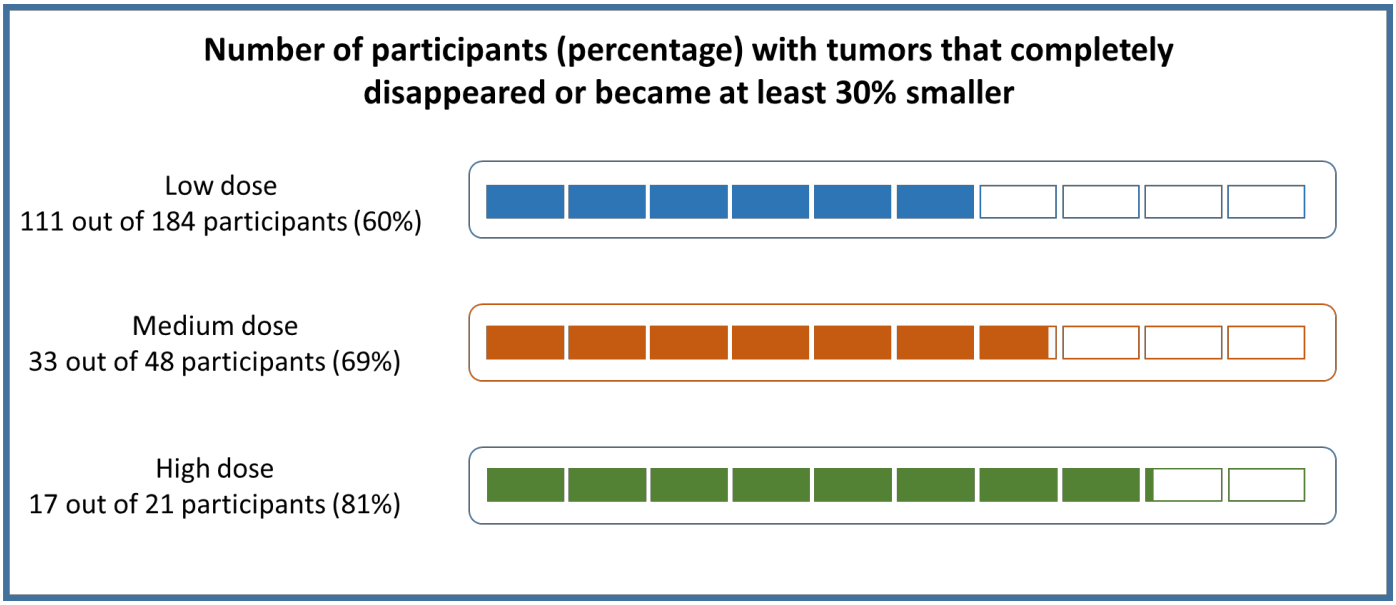


For part 2 all participants received the low dose. They were split according to why they had discontinued treatment with T-DM1 prior to enrolment on this study. Group (a) had discontinued due to progression of their disease, and group (b) had discontinued for other reasons

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 became at least 30% smaller after treatment?



What were the other results of this study?

How long did participants live with their cancer before it got worse or led to death?

The median length of time participants lived with their cancer before it got worse or led to death could not be evaluated at the time of this analysis. The cancer remained at least stable and did not worsen for the majority of participants in these groups.

Participants who received the higher dose (7.4mg/kg) in the first part of the study, lived for a median of about 9½ months before their cancer got worse or led to death, whichever occurred first.

This means that for half of the participants who were given high dose of T-DXd, it took less than 9½ months for their cancer to start getting worse and for the other half of participants, it took longer.

How long did participants live after first day of treatment?

Due to the relatively small number of participants who died during the study, the length of time participants lived since their first day of treatment could not be evaluated.

What medical problems did the study participants have?

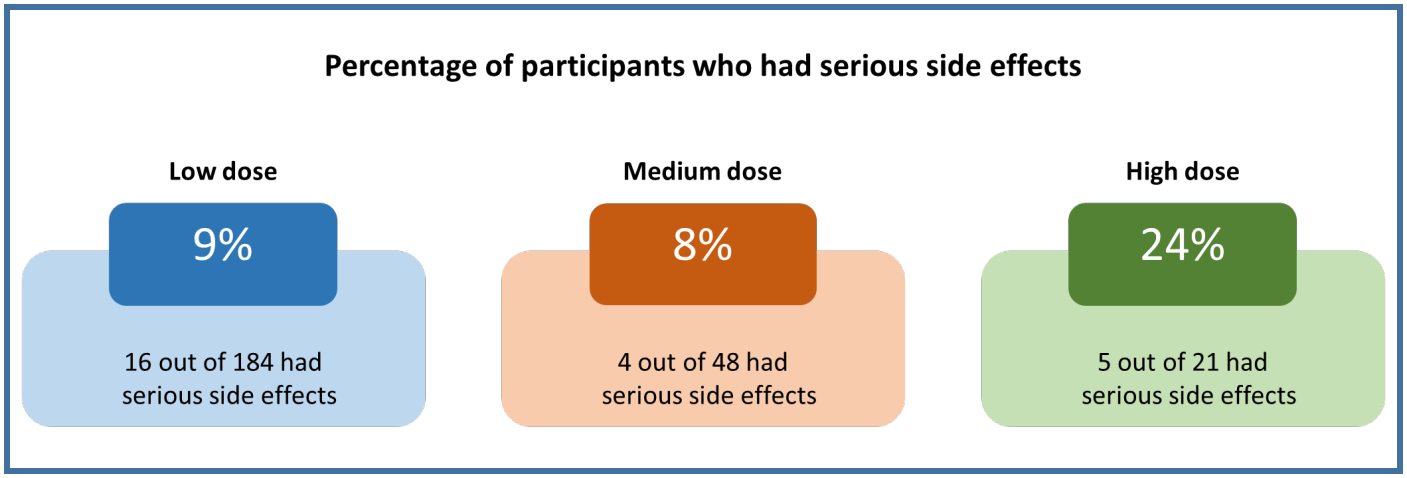
Side effects are medical problems (such as a feeling tired) that happened during the study which the study doctor thought could be related to the treatments in the study.

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

Side effects that are related to the study treatment (T-DXd) are reported here. For more information on medical problems, please visit the websites listed at the end of this summary.

How many participants had serious side effects?

During the study, 25 out of 253 participants (10%) had serious side effects.



The serious side effects that occurred in at least 5% (5 out of 100) of participants in any group were:

Serious side effects	Low dose (out of 184 participants)	Medium dose (out of 48 participants)	High dose (out of 21 participants)
Lung infection	0	0	5% (1 out of 21)
Swelling in the lungs	1% (1 out of 184)	0	5% (1 out of 21)
Lung damage	1% (1 out of 184)	4% (2 out of 48)	5% (1 out of 21)
Skin infection	0	0	5% (1 out of 21)
Fever in patients with low neutrophils[a]	0	0	5% (1 out of 21)
Low sodium level in blood	0	0	5% (1 out of 21)
A certain form of damage to lung tissue	0	2% (1 out of 48)	5% (1 out of 21)
General pain	0	0	5% (1 out of 21)
Water between the lungs and chest wall	0	0	5% (1 out of 21)
Increase in liver test value of aspartate aminotransferase in the blood[b]	0	0	5% (1 out of 21)
Increase in liver test value of alanine aminotransferase in the blood[b]	0	0	5% (1 out of 21)

[a] Neutrophils are a type of white blood cells that fight bacteria.

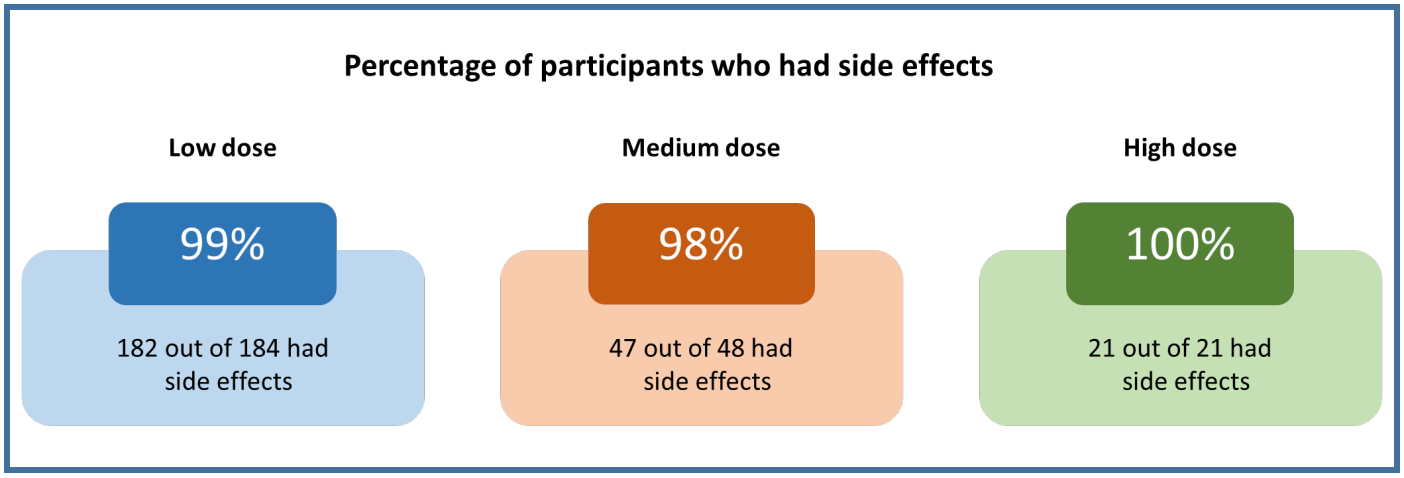
[b] An increase in blood levels of aspartate aminotransferase and alanine aminotransferase indicates damage to the liver.

There were 5 deaths that were reported as possibly related to T-DXd:

- 1 participant in the high dose group died due to swelling in the lungs.
- 4 participants in the low dose group died due to infection of the lymphatic vessels, swelling in the lungs, loss of ability to breathe adequately or supply enough oxygen to the blood and organs, and sudden loss of ability to breathe adequately or supply enough oxygen to the blood and organs.

How many participants had side effects?

All side effects, both serious and non-serious, are presented in this section.



The most common side effects that occurred in at least 15% (15 out of 100) of participants in any group were:

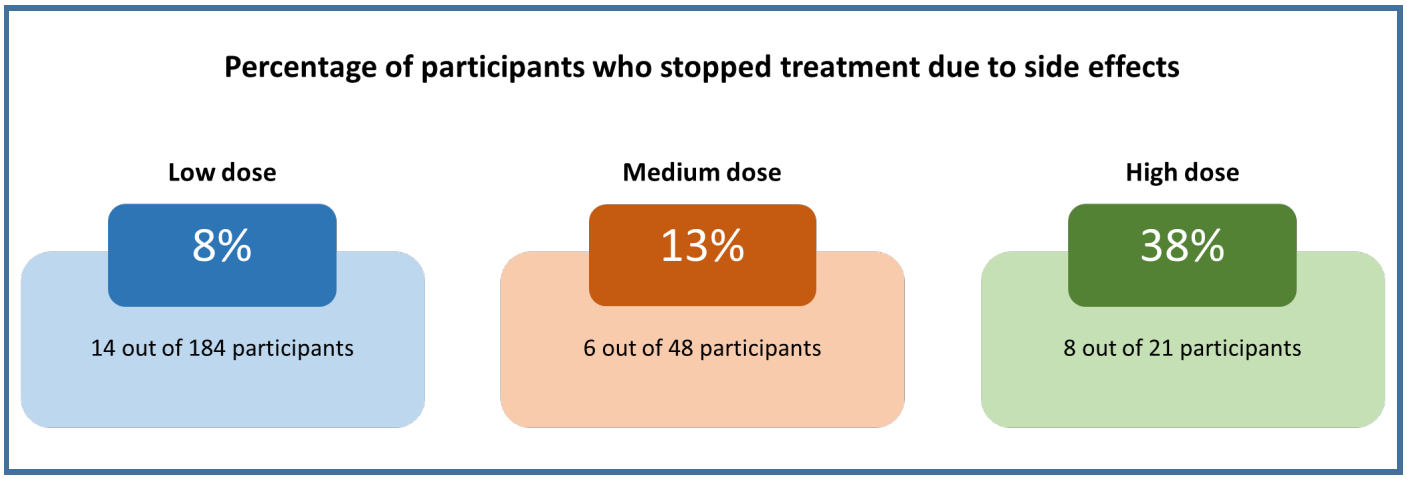
Side effects	Low dose (184 participants)	Medium dose (48 participants)	High dose (21 participants)
Decreased neutrophil* count below normal level	11% (20 out of 184)	13% (6 out of 48)	19% (4 out of 21)
Feeling tired	44% (81 out of 184)	48% (23 out of 48)	52% (11 out of 21)
Decreased red blood cell count	21% (39 out of 184)	38% (18 out of 48)	48% (10 out of 21)
Nausea	76% (140 out of 184)	81% (39 out of 48)	62% (13 out of 21)
Decrease in white blood cell count	17% (32 out of 184)	31% (15 out of 48)	62% (13 out of 21)

Side effects	Low dose (184 participants)	Medium dose (48 participants)	High dose (21 participants)
Decrease in appetite	28% (52 out of 184)	42% (20 out of 48)	24% (5 out of 21)
Vomiting	42% (78 out of 184)	33% (16 out of 48)	29% (6 out of 21)
Diarrhea	22% (40 out of 184)	23% (11 out of 48)	10% (2 out of 21)
Constipation	18% (33 out of 184)	29% (14 out of 48)	38% (8 out of 21)
Headache	10% (19 out of 184)	17% (8 out of 48)	5% (1 out of 21)
Inflammation of the mouth and lips	12% (22 out of 184)	27% (13 out of 48)	19% (4 out of 21)
Hair loss	46% (85 out of 184)	54% (26 out of 48)	38% (8 out of 21)
General discomfort	3% (5 out of 184)	6% (3 out of 48)	24% (5 out of 21)
Decreased neutrophil* count	20% (36 out of 184)	35% (17 out of 48)	57% (12 out of 21)
Decreased platelet** count	13% (23 out of 184)	23% (11 out of 184)	33% (7 out of 21)
Increase in liver test value of aspartate aminotransferase in the blood	10% (19 out of 184)	8% (4 out of 48)	29% (6 out of 21)
Increase in the liver test value of bilirubin in the blood	4% (8 out of 184)	4% (2 out of 48)	19% (4 out of 21)
Increase in liver test value of alkaline phosphatase in the blood	2% (4 out of 184)	4% (2 out of 48)	24% (5 out of 21)
Increase in liver test value of alanine aminotransferase in the blood	8% (14 out of 184)	8% (4 out of 48)	29% (6 out of 21)
A certain form of damage to lung tissue	3% (5 out of 184)	6% (3 out of 48)	24% (5 out of 21)

*Neutrophils are a type of white blood cell that fight bacteria.
**Platelets are a type of blood cell that prevent or stop bleeding.

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

11% of participants (28 out of 253) stopped treatment early because of side effects.



The most common side effects that led to participants stopping study treatment were lung infection, inability of the adrenal glands to produce enough hormones, swelling in the lungs, and a certain form of damage to lung tissue.

How was this study useful for participants and researchers?

This study helped researchers learn if T-DXd can reduce the growth of tumor cells in participants who either did not respond to, or whose cancer came back after, treatment with T-DM1. This study also helped researchers learn about the safety and other effects of T-DXd when given to participants with HER2 positive metastatic and/or unresectable 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 websites:

- www.clinicaltrials.gov: Use the NCT identifier NCT03248492 in the search field.
- www.clinicaltrialsregister.eu/ctr-search/search: Use the EudraCT identifier 2016-004986-18 in the search field.
- https://www.clinicaltrials.jp: Use the identifier JapicCTI-173693 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: A Phase 2 Multicenter, Open-label Study of DS-8201a, an Anti-HER2-Antibody Drug Conjugate (ADC) for HER2-positive, Unresectable and/or Metastatic Breast Cancer Subjects Previously Treated with T-DM1

Sponsor: Daiichi Sankyo, Inc.

Sponsor contact information:
211 Mount Airy Road, Basking Ridge, NJ 07920
Email: CTRInfo@dsi.com
Phone number: 1-908-992-6640

Date of this summary: 03 December 2021

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