



Daiichi-Sankyo

## Clinical Results Summary

**A clinical study of DS-8201a to learn about its effects on heart activity and how it is absorbed, distributed and removed from the body in participants with HER2-positive cancer that had spread and/or could not be surgically removed**

**Protocol number:** DS8201-A-J102

**Thank You!**



Daiichi Sankyo, Inc., the sponsor of this study, would like to thank the participants who took part in this study for DS-8201a also known Trastuzumab Deruxtecan (T-DXd). Each participant helped to advance medical research for people 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?

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

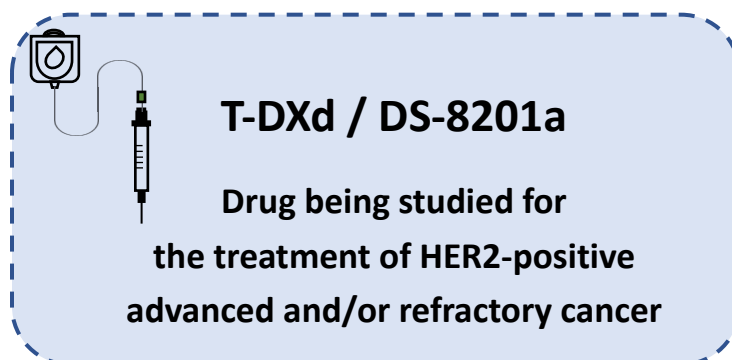
At this time treatment options for HER2-positive cancers are:

- surgery
- radiation therapy - a treatment that uses radiation to kill cancer cells
- endocrine (hormone) therapy - a treatment that stops the growth of cancer cells 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 effects of DS-8201a on the activity of the heart as measured by electrocardiogram (ECG) tests, and how it is processed by the body after multiple doses in participants with HER2-positive advanced cancer.

### Treatment given in this study



## Main goals of this study

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



**What was the effect of DS-8201a on heart rhythm and activity?**

This was measured using an electrocardiogram (ECG) test.



**What were the levels of DS-8201a, its breakdown product MAAA-1181a, and total anti-HER2 antibody in the blood of participants?**

\*DS-8201a 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 DS-8201a binds to a cell with the HER2 marker on it. Once DS-8201a 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.

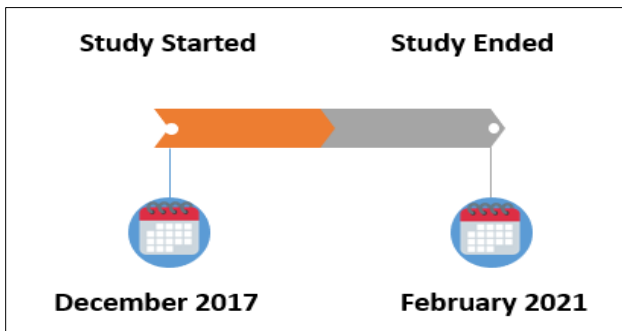
## Other goals of this study

Researchers also wanted to answer the following question:



**How many participants had side effects 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, or were asked to be removed from the study. An individual participant could have been in this study for 3 Years and 2 months. The study started in December 2017 and ended in February 2021.

## Who was in this study?

This study included 51 female participants from Japan. Participants could take part in this study if they:

- had breast cancer with the presence of HER2 protein that came back after standard treatment, or could not be treated by standard treatment, or for which no standard treatment was available
- had at least 50% of total blood pumped out with each heart beat from the left side of the heart
- were either fully active or able to walk and do light work, but unable to do a hard physical activity
- Had adequate organ function (for example liver, kidneys)
- were expected to live for at least 3 months

**In this Study**

**51 women took part**

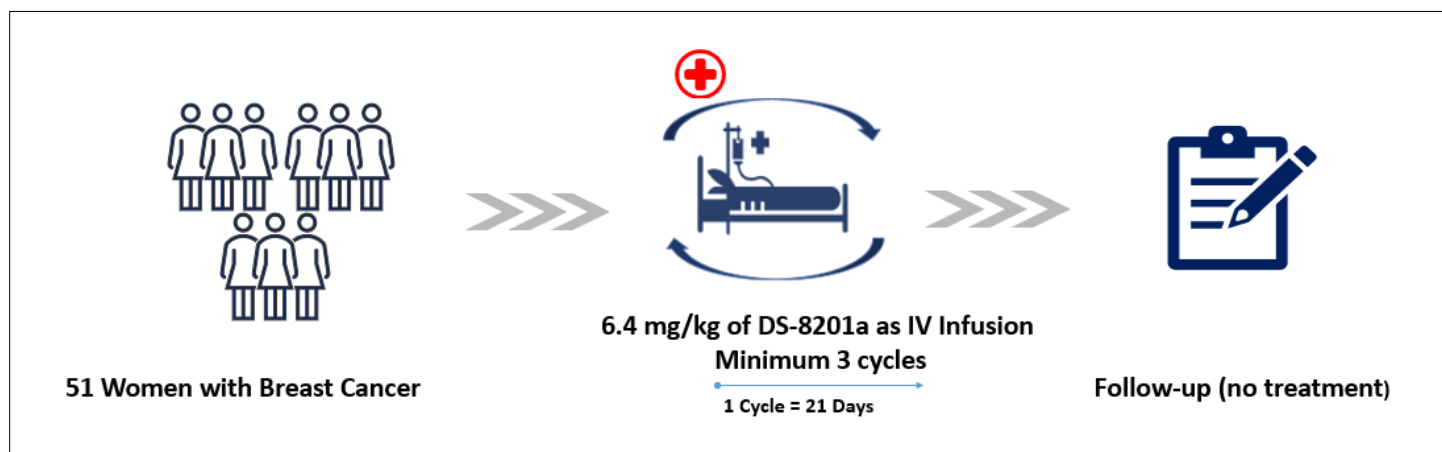
They had an average age of **56 years**

## 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 treatment was given to which participants.

51 participants received 6.4 milligram/kilogram (mg/kg) of DS-8201a through a drip over 90 minutes on the first day of each cycle, for a minimum of 3 cycles until their tumor did not get worse and they did not have serious side effects, or were asked to be removed from the study. Each cycle lasted 3 weeks.



## 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.

## What was the effect of DS-8201a on heart rhythm and activity?

The heart is a muscle that contracts and relaxes to pump blood around the body. Researchers found that drug DS-8201a at 6.4 mg/kg dosing was not associated with a meaningful change in heart muscle.

## What were the levels of DS-8201a, 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 DS-8201a, MAAA-1181a and anti-HER2 antibody in the participants' blood samples during Cycle 1 and Cycle 3.

Researchers found that the levels of DS-8201a, MAAA-1181a, and anti-HER2 antibody in the participants' blood increased from Cycle 1 to Cycle 3.

The average results of these measurements are presented below. Total levels of DS-8201a and anti-HER2 antibody in the participants' blood within the dosing period are measured in  $\mu\text{g}\cdot\text{d}/\text{mL}$ , which means micrograms (millionths of a gram) found in each milliliter of blood over 1 day. MAAA-1181a is measured in  $\text{ng}\cdot\text{d}/\text{mL}$ , which means nanograms (one thousand millionths of a gram) found in each milliliter of blood over 1 day.

	Cycle 1	Cycle 3
<b>DS-8201a:</b>		
Total level during dosing interval ( $\mu\text{g}\cdot\text{d}/\text{mL}$ )	677	905
<b>MAAA-1181a</b>		
Total level during dosing interval ( $\text{ng}\cdot\text{d}/\text{mL}$ )	39	42
<b>Anti-HER2 antibody</b>		
Total level during dosing interval ( $\mu\text{g}\cdot\text{d}/\text{mL}$ )	752	1030

## What were the other results of this study?

### How many participants had side effects during the study?

During this study, all the participants (51 out of 51, 100%) had at least 1 side effect. Detailed information about side effects reported by participants is presented in the section below: 'What medical problems did the study participants have?'

### 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 study treatment. 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. Some participants stop study treatment because of side effects.

### How many participants had serious side effects?

In this study, 1 out of 51 participants (2%) had a serious side effect of nausea.

No participants taking DS-8201a died during this study.

## How many people had the most common side effects?

In this study, side effects were monitored for 51 participants given DS-8201a. All participants who were given DS-8201a reported at least 1 side effect.

The most common side effects, which happened in at least 25% of participants in any group are presented below.

Side Effects	DS-8201a (6.4 mg/kg) Out of 51 Participants
Decrease in red blood cells count <sup>a</sup>	57% (29 participants)
Decrease in appetite	31% (16 participants)
Nausea	82% (42 participants)
Vomiting	39% (20 participants)
Inflammation of mouth and lips	31% (16 participants)
Diarrhea	28% (14 participants)
Constipation	26% (13 participants)
Bald patches on scalp	41% (21 participants)
Decrease in neutrophil count <sup>b</sup>	71% (36 participants)
White blood cell count decreased <sup>c</sup>	61% (31 participants)
Platelet count decreased <sup>d</sup>	39% (20 participants)
Lymphocyte count decreased <sup>e</sup>	26% (13 participants)

<sup>a</sup> red blood cells carry oxygen around the body

<sup>b</sup> neutrophils are white blood cells that help protect from infection

<sup>c</sup> white blood cells help protect your body from infection

<sup>d</sup> platelets are a type of blood cell that helps in preventing / stopping bleeding

<sup>e</sup> lymphocytes are white blood cells, that protect from infection

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

28% (14 out of 51) of participants given DS-8201a had stopped treatment early because of side effects. The most common side effects that led to participants stopping study treatment were heart problems, multiple lung infection, and pneumonia.


## How was this study useful for patients and researchers?

This study helped researchers learn about the effects of DS-8201a on the heart rhythm and activity in participants with HER2-positive advanced cancer.

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](http://www.clinicaltrials.gov): Use the NCT identifier **NCT03366428** in the search field.

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 1, Multicenter, Open-label, Multiple-Dose Study of DS-8201a to Assess the Effect on the QT Interval and Pharmacokinetics in Subjects with HER2-expressing Metastatic and/or Unresectable Breast Cancer

**Sponsor:** Daiichi Sankyo, Inc.

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**Date of this summary:** 18 August 2022

This summary was prepared by Syneos Health®.