Daiichi-Sankyo

# Clinical Results Summary

# A clinical study to learn about the effects of Trastuzumab deruxtecan, also known as T-DXd, in combination with nivolumab in people with HER2-positive advanced breast or urinary tract cancer

**Thank You!**

Daiichi Sankyo, Inc., the sponsor of this study, would like to thank the participants who took part in this study. Each participant helped to advance medical research for people affected with HER2-positive advanced breast or urinary tract cancer. Their contribution to medicine and healthcare is greatly appreciated.

**Protocol number:** DS8201-A-U105

**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?

Researchers were looking for a better way to treat people with advanced breast cancer or urinary tract cancer.

## 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. Symptoms of advance breast cancer include swelling in the breast, redness of the skin near the breast area, nipple discharge, weakness in any part of the body, headache, pain in the bones, difficulty in breathing, and chest pain.

## Urinary tract cancer

Urinary tract cancer is a type of cancer that can start anywhere in the urinary tract, which includes the kidneys, ureters, bladder, and urethra. Symptoms of urinary tract cancer can include frequent urination, pain or burning sensation when urinating, blood in the urine and pain in the lower back or side.

**What is the role of HER2 in advanced cancer?**

Advanced cancer means that the cancer has spread to other parts of the body. 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-expressing cancer. This study included participants with cancers that expressed high levels of HER2 (HER2-positive) and participants with cancers that expressed low levels of HER2 (HER2-low).

Currently, treatment options for breast cancer and urinary tract cancer are surgery, radiation therapy, hormone therapy, chemotherapy and immunotherapy. 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 cells that use hormones to grow. Chemotherapy uses medicine to kill cancer cells or stop them from growing and dividing. Immunotherapy is a type of therapy that uses substances to modify the action of immune system. The immune system helps the body to fight cancer, infection, and other diseases. Current treatment options do not work in all patients. Therefore, new methods for treating breast and urinary tract cancer are needed.

Trastuzumab deruxtecan, also known as T-DXd, specifically binds to HER2-positive cells to inhibit the cell growth and cause the death of target cancer cells.

Nivolumab is a cancer treatment that binds to a protein on the surface of immune cells that prevents the immune system from working properly and attacking cancer cells. It helps to make your immune system find and kill cancer cells. Nivolumab is approved for the treatment of several different cancers.

In this study, researchers wanted to learn about the effects of T-DXd in combination with nivolumab in people with HER2-positive breast cancer or urinary tract cancer.

## Treatments given in this study

The treatments given in this study were:

**T-DXd**
(study drug)
Drug being studied for the treatment of HER2-positive advanced breast and urinary tract cancer.

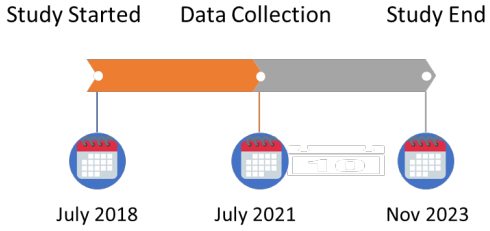
**Nivolumab**
(anti-cancer drug)
Drug being studied along with T-DXd for the treatment of HER2-positive advanced breast and urinary tract cancer.

## Main goal of this study

The main questions the researchers wanted to answer in this study were:

- What was the maximum tolerated dose of T-DXd when given in combination with nivolumab?
- How many participants had tumors that completely disappeared or became at least 30% smaller after treatment?

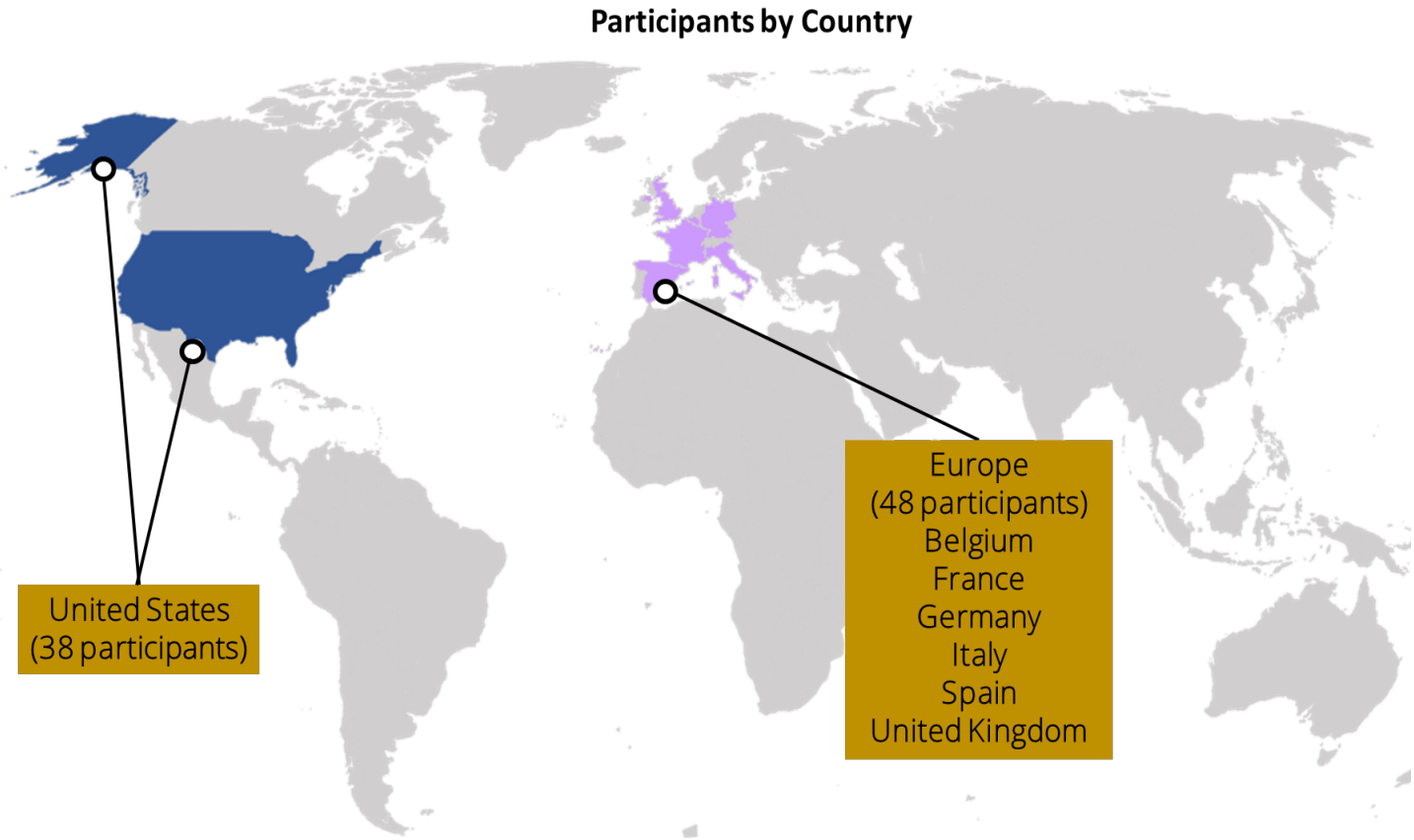
# How long was this study?




The study was designed so that participants could continue in it as long as their cancer did not get worse, participants continued to derive benefit from the treatment and did not have serious side effects. The study started in July 2018 and ended in Nov 2023. The results were collected up to Jul 2021 and a study report was created. This summary is based on that report.

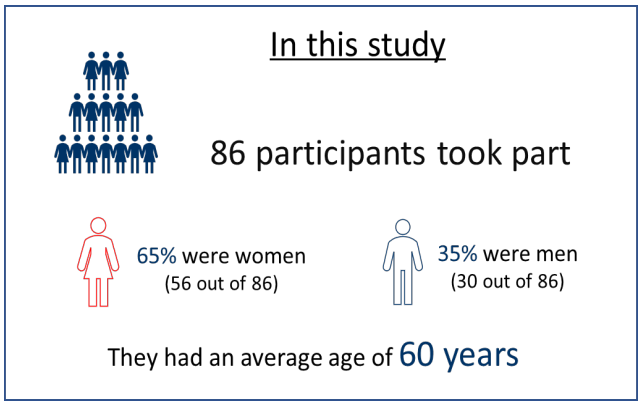
# Who participated in this study?

This study included 86 participants from the following 7 countries.



Participants could take part in this study if they:

- were at least 18 years of age.
- were either fully active OR unable to do hard physical activity but able to walk and do light housework or office work.
- had confirmed HER2-expressing breast cancer OR urinary tract cancer.
- had adequate heart, 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 a 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 and nivolumab the participants were given.

The study was divided into 2 parts, Part 1 and Part 2.

## Part 1

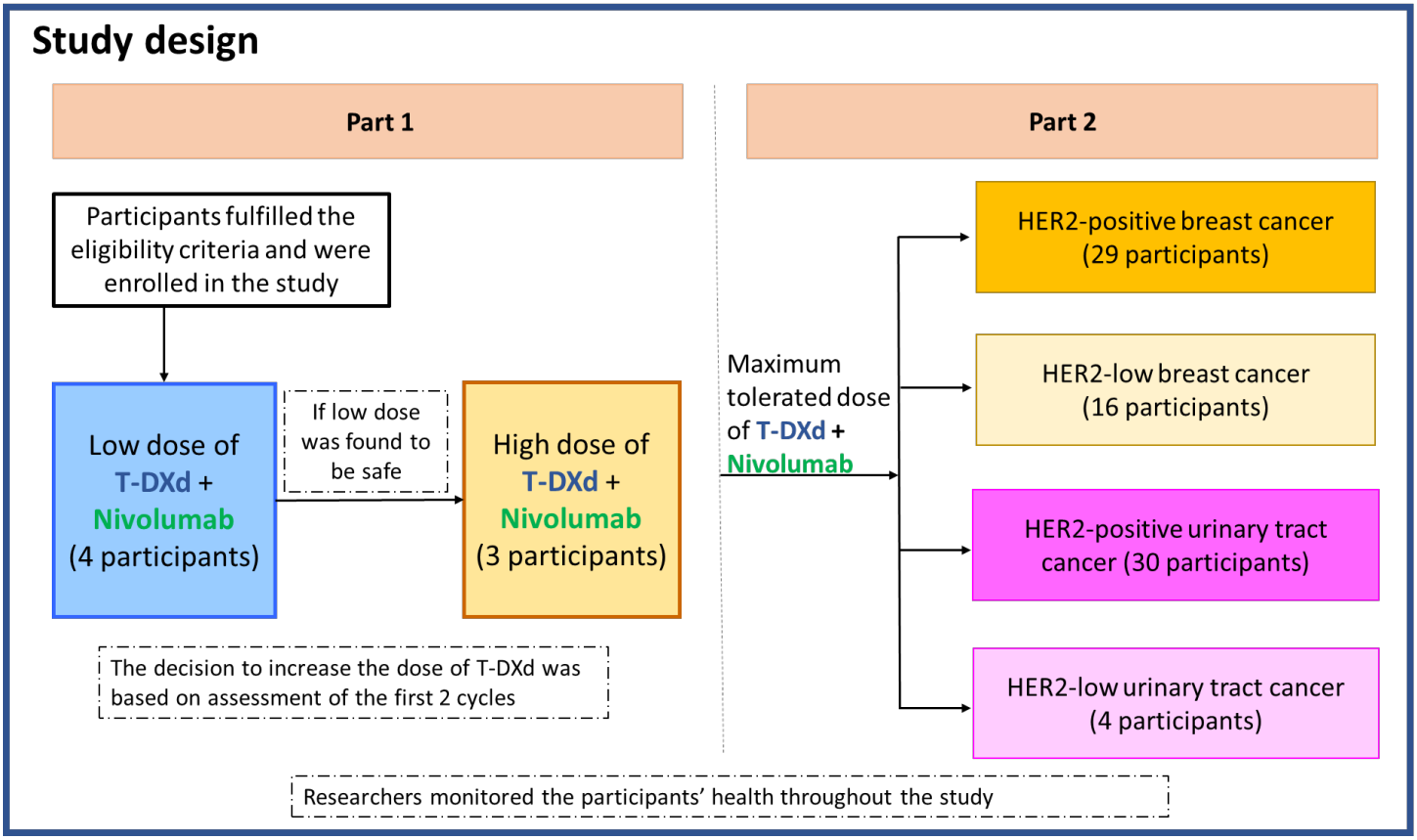
In Part 1, researchers wanted to find out the maximum dose of T-DXd which was tolerated by the participants (maximum tolerated dose). Participants received T-DXd through a drip, immediately after receiving nivolumab through a drip, once every 21 days (1 cycle). This cycle of treatment could be repeated as long as the study doctor considered it was beneficial for the participant.

The first group of participants received a low dose of T-DXd and a fixed dose of nivolumab. Once the researchers considered the low dose of T-DXd safe, the next group of participants received a higher dose of T-DXd and a fixed dose of nivolumab. The researchers assessed if the participants had any side effects which could potentially be related to the study treatment for up to 2 cycles (6 weeks) to find the maximum tolerated dose.

## Part 2

In Part 2, researchers wanted to find out how well the treatment combination of T-DXd and nivolumab worked. They also checked the safety and tolerability of the treatment during this part. Participants were divided into 4 groups depending on the type of cancer. Participants in all the 4 groups received the same dose (maximum tolerated dose from Part 1) of T-DXd in combination with the fixed dose of nivolumab. The participants continued to receive the treatment in 21-day cycles as long as they did not show worsening of cancer, have serious side effects, or ask to be removed from the study.

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



# 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.

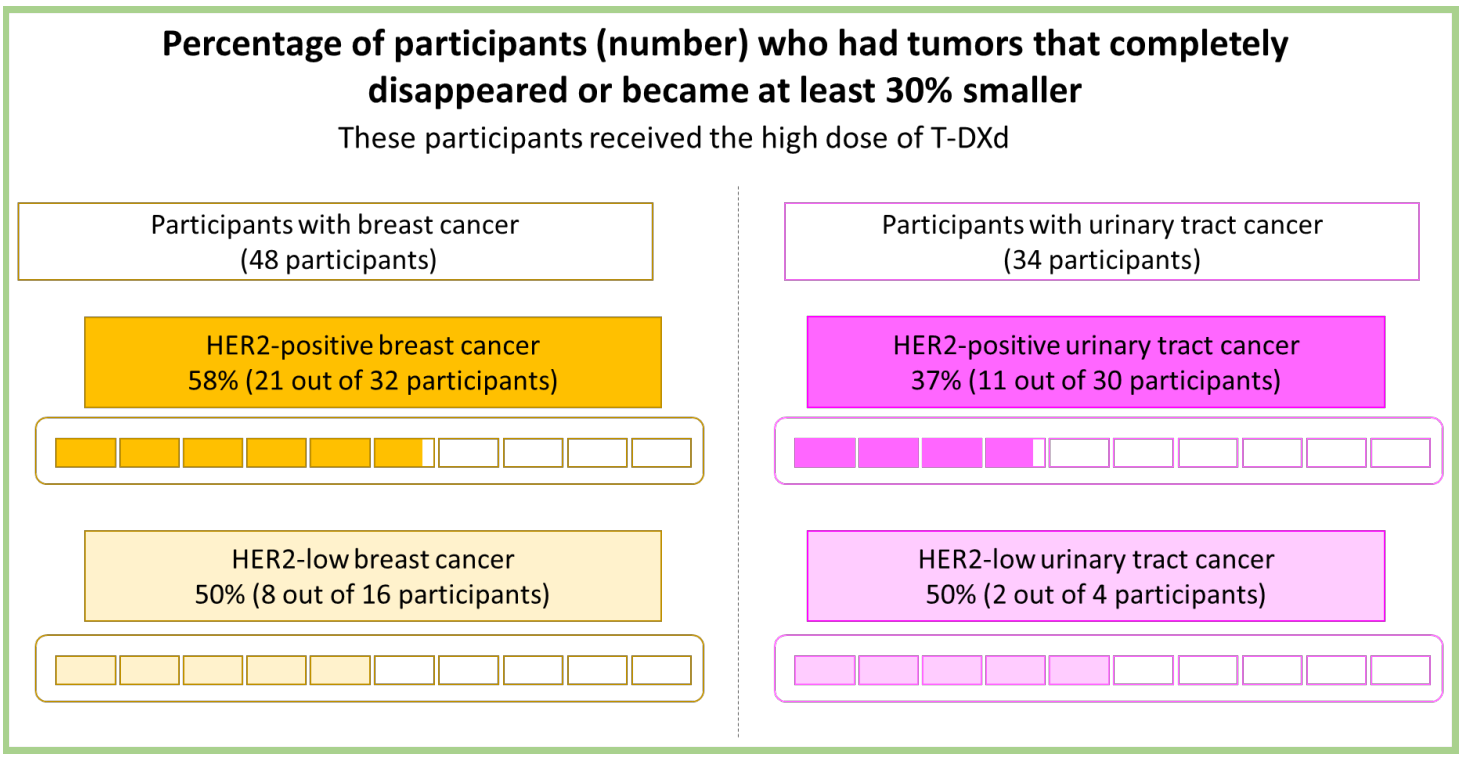
## What was the maximum dose of T-DXd which was tolerated by the participants when given with nivolumab?

To answer this question, in Part 1 of the study, researchers assessed if the participants had any side effects which were not related to their cancer after receiving 2 cycles of treatment. No participants had side effects during Part 1 which were not related to their cancer.

> The high tested dose of T-DXd was confirmed as the maximum dose of T-DXd which was tolerated by the participants when given with nivolumab.

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

To answer this question, in Part 2 of the study, researchers measured the tumors from imaging (scans). The results were available for 82 participants who received the high tested dose of T-DXd. The results for the 3 participants who received the high tested dose of T-DXd in Part 1 were combined with the results of the 79 participants who received the high tested dose of T-DXd in Part 2 of the study.




# What side effects 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. The website listed at the end of this summary has more information about the side effects that happened in this study.

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

## How many participants had serious side effects?

During Part 1:

The number of participants in Part 1 was very small. **25% (1 out of 4)** of the participants had a serious side effect of swelling in the lungs which the study doctor thought could be related to the low tested dose of T-DXd. No participants had serious side effects which the study doctor thought could be related to nivolumab. The researchers found that the combination was well tolerated by the 4 participants who received the lower dose.

During Part 2:

**10% (8 out of 82)** of the participants had serious side effects reported as related to the high tested dose of T-DXd. **10% (8 out of 82)** had serious side effects reported as related to nivolumab. The most common serious side effect was swelling in the lungs, which occurred in at least 2 participants. It was reported as related to the high tested dose of T-DXd and nivolumab. All other serious side effects each occurred in 1 participant.

There were 2 deaths that were reported as possibly related to the high tested dose of T-DXd and nivolumab. The deaths were caused by swelling in the lungs and inability to breathe enough oxygen.

## How many participants had side effects?

During Part 1:

**50% (2 out of 4)** of the participants had side effects that were reported as related to the low tested dose of T-DXd. **25% (1 out of 4)** of the participants had side effects that were reported as related to nivolumab. The number of participants in Part 1 was very small. Nausea occurred in 2 participants and was reported as related to T-DXd. Constipation, dry eye, dry mouth, swelling in the lungs and vomiting occurred in 1 participant, and were reported as related to nivolumab. Nausea and vomiting occurred in 1 participant and were reported as related to nivolumab.

During Part 2:

**93% (76 out of 82)** of the participants who received high tested dose of T-DXd and **85% (70 out of 82)** of the participants who received nivolumab had side effects.

The most common side effects that occurred in at least 10% (10 out of 100) of participants receiving high tested dose of T-DXd and nivolumab are presented below:

| Side effects | Percentage (%) (out of 82 participants) |
|---|---|
| **Related to T-DXd** | |
| Nausea | 54% (44) |
| Feeling tired | 40% (33) |
| Vomiting | 32% (26) |
| Loss of appetite | 27% (22) |
| Hair loss | 27% (22) |
| Decreased red blood cell count | 18% (15) |
| Diarrhea | 18% (15) |
| Constipation | 13% (11) |
| Weakness | 12% (10) |
| Swelling in the lungs | 11% (9) |
| Dry mouth | 5% (4) |
| **Related to Nivolumab** | |
| Nausea | 40% (33) |
| Feeling tired | 39% (32) |
| Loss of appetite | 22% (18) |
| Vomiting | 17% (14) |
| Diarrhea | 15% (12) |
| Decreased production of thyroid hormone | 12% (10) |
| Hair loss | 12% (10) |
| Constipation | 11% (9) |
| Increase in the liver test value of aspartate aminotransferase in the blood* | 11% (9) |

* Indicates damage to the liver

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

**25% (1 out of 4)** of the participants in Part 1 stopped treatment early because of side effects related to low tested dose of T-DXd.

**19% (16 out of 82)** of the participants stopped treatment because of side effects related to high tested dose of T-DXd in Part 2 of the study.

**21% (17 out of 82)** of the participants stopped treatment early because of side effects related to nivolumab in Part 2 of the study.

The most common side effects that led to participants stopping study treatment were 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 about the maximum dose of T-DXd which was tolerated by the participants when given with nivolumab and also to understand if the treatment can decrease the growth of tumor cells in participants with breast and urinary tract cancer. This study also helped researchers learn about the safety and other effects of T-DXd in combination with nivolumab when given to participants with HER2-expressing advanced breast and urinary tract cancer. Findings from this study may be used in other studies to learn whether patients with HER2-expressing advanced breast and urinary tract cancer are helped by this treatment.

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 NCT03523572 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 1B, Multicenter, Two-Part, Open-Label Study of Trastuzumab Deruxtecan, an Anti-Human Epidermal Growth Factor Receptor-2 (HER2)-Antibody-Drug Conjugate (ADC), in Combination with Nivolumab, an Anti-PD-1 Antibody, for Subjects with HER2-Expressing Advanced Breast and Urothelial Cancer

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