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Trastuzumab Deruxtecan Versus Trastuzumab Emtansine for Breast Cancer: A Plain Language Summary of the DESTINY-Breast03 Study

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Plain Language Summary of Publication

Trastuzumab deruxtecan versus trastuzumab emtansine for breast cancer: a plain language summary of the DESTINY-Breast03 study

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Summary

What is this summary about?

This is a summary of a publication about the DESTINY-Breast03 study, which was published in the *New England Journal of Medicine* in March 2022. The study included 524 adults with advanced breast cancer that is HER2-positive, which means it has high levels of a protein called HER2. All of the participants in this study had their cancer worsen after previously receiving treatment. The treatment that was previously given to participants was a combination of a drug called trastuzumab with a type of chemotherapy called a taxane. The researchers wanted to know whether a drug called trastuzumab deruxtecan (T-DXd) could improve participants' cancer more than the standard treatment. The standard treatment is a drug called trastuzumab emtansine (T-DM1). The researchers looked at the results of this study before it was finished. This is a summary of those results.

How to say (double click sound icon to play sound)...

- **Trastuzumab:** tras-TOO-zoo-mab
- **Deruxtecan:** der-UHX-teh-can
- **Emtansine:** em-TAN-seen
- **Interstitial:** in-ter-STIH-shull
- **Pneumonitis:** nuh-moe-NITE-iss

What were the results?

Researchers in this study found that the risk of dying or the participants' cancer getting worse was reduced by 72% in the T-DXd group compared with the T-DM1 group. This is also called progression-free survival.

79.7% of participants in the T-DXd group had their tumors shrink significantly or disappear, compared to 34.2% of those in the T-DM1 group.

During the study, 10.9% of participants who received T-DXd had serious drug-related medical problems, compared to 6.1% who received T-DM1.

Of the participants who received T-DXd, 10.5% experienced drug-related interstitial lung disease (ILD) or pneumonitis, compared to 1.9% of those who received T-DM1. ILD and pneumonitis are potentially serious lung problems.

When the researchers first looked at the results, they could not yet be certain that T-DXd helped participants survive longer overall than T-DM1. But, when they looked at the results later in the study, they found that T-DXd did help participants to survive longer overall than T-DM1. These newer results were published separately and are not part of this summary. A link to more information about the newer results can be found at the end of this summary.

What do the results mean?

T-DXd gave participants a meaningful benefit overall compared to T-DM1. T-DXd could be a treatment option for people with advanced HER2-positive breast cancer that has been previously treated.

Who should read this article?

This summary may be helpful for patients with HER2-positive breast cancer, their family members, and caregivers. It may also be helpful for patient advocates and healthcare professionals, including those who are looking for treatment options for patients with HER2-positive breast cancer.

Future Medicine part of fsg

Where can I find the original article on which this summary is based?

The full title of the original publication in the *New England Journal of Medicine* is: Trastuzumab deruxtecan versus trastuzumab emtansine for breast cancer.

You can read the original publication for free at: https://www.nejm.org/doi/full/10.1056/NEJMoa2115022

Who sponsored this clinical study?

Daiichi Sankyo Co., Ltd, and AstraZeneca funded this study. The study was designed and led by Daiichi Sankyo Co., Ltd, for data collection and analysis, and was approved by the institutional review board at each partnering site. In March 2019, AstraZeneca entered into a collaboration agreement with Daiichi Sankyo Co., Ltd, for trastuzumab deruxtecan (T-DXd). All authors and sponsors assisted in data interpretation, writing the report, reviewing the manuscript, and provided final approval to submit the manuscript for publication.

What is advanced HER2-positive breast cancer?

In people with **breast cancer**, the body is not able to control the growth of abnormal cells in the breast. These extra cells can form tumors that can spread to other parts of the body.

HER2 is a type of protein found on the surface of some cells. Breast cancer with high levels of HER2 is called **HER2-positive breast cancer**.

HER2-positive breast cancer cells often grow quickly and spread to other parts of the body. When this happens, it is called **advanced HER2-positive breast cancer**.

How are people who have advanced HER2-positive breast cancer normally treated?

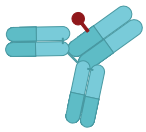
Currently, chemotherapy drugs that kill cancer cells are used to treat people with advanced HER2-positive breast cancer.

There are also approved treatments that are not chemotherapy that are specifically for people with HER2-positive breast cancer. One of these treatments is called trastuzumab. Trastuzumab is a manmade antibody that attaches to HER2 proteins and blocks the tumors from growing. Trastuzumab emtansine (T-DM1) is another treatment that is commonly used for treating HER2-positive breast cancer. T-DM1 contains trastuzumab as well as a chemotherapy drug.

Despite treatment with these drugs, the cancer often returns meaning researchers are looking at new drugs that may offer better ways to treat advanced HER2-positive breast cancer.

What is trastuzumab emtansine (T-DM1)?

T-DM1 is:



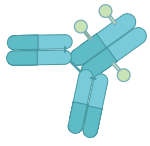
a drug made up of 2 parts. One part is trastuzumab, which attaches to HER2 proteins found on the surface of tumor cells. The other part is a chemotherapy drug. When T-DM1 enters the body, the trastuzumab part sticks to the tumor cells, which helps T-DM1 deliver a dose of chemotherapy directly to the cells and kill them.

given as an intravenous infusion.

T-DM1 was already approved for patients to receive in certain countries when this study happened. At the beginning of this study, T-DM1 was the standard treatment for patients whose cancer returned after the first treatment that they received.

What is trastuzumab deruxtecan (T-DXd)?

The study drug, T-DXd, is:

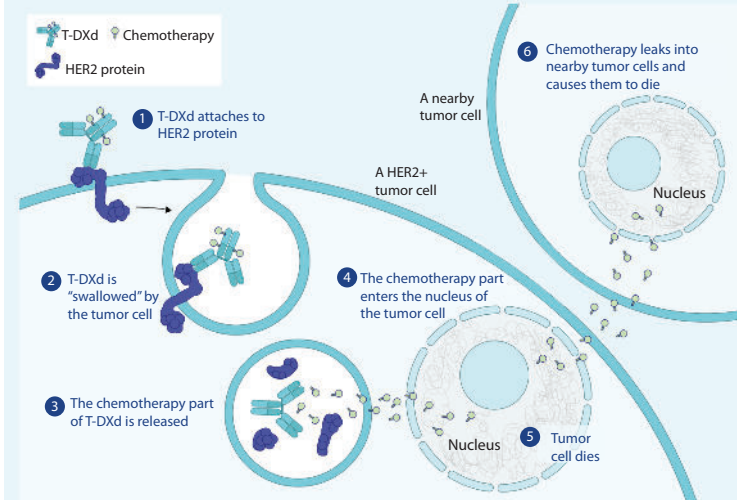


made up of 2 parts: trastuzumab, and a chemotherapy drug. **T-DXd** is similar to **T-DM1**, except it has a different chemotherapy drug, and a higher amount of the chemotherapy drug, in each dose.

given as an intravenous infusion.

Researchers wanted to learn how well T-DXd works compared to T-DM1, and how safe it is.

How T-DXd is designed to work?



More detailed information on how T-DXd is designed to work can accessed at: https://www.futuremedicine.com/doi/10.2217/fon-2023-0245.

About the DESTINY-Breast03 study

Goals of the study

- To learn if T-DXd works better than T-DM1 in people with advanced HER2-positive breast cancer
- To learn if T-DXd is safe in people with advanced HER2-positive breast cancer

- Ongoing, started July 2018
- Results analyzed May 2021

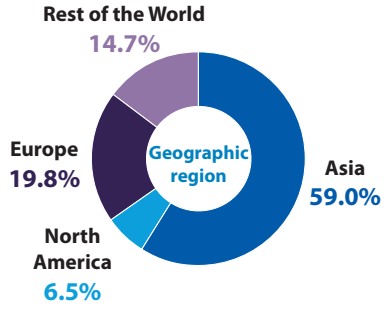
524 participants

This study was an open label study. This term means that all of the participants, researchers, and doctors knew what treatment each participant was given.

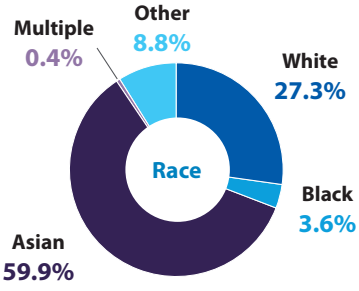
About the DESTINY-Breast03 study participants

The participants in this study were:

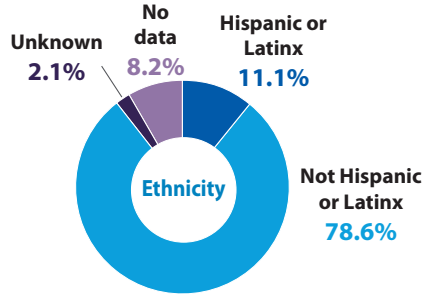
20–83
age range



Geographic region is where in the world participants live.



Race describes groups of people with certain physical traits that have social meaning.



Ethnicity describes groups of people that share a common culture and heritage.

All of the study participants:

- Had **locally advanced** or **metastatic**, HER2-positive breast cancer
- Had their cancer get worse after receiving one or both of 2 different treatments: trastuzumab, and a type of chemotherapy called a taxane

None of the study participants:

- Had previously received a type of treatment for their advanced cancer that is similar to T-DXd or T-DM1
  - *This type of treatment is called an antibody-drug conjugate*
- Previously needed steroids to treat noninfectious **pneumonitis** or **interstitial lung disease (ILD)**
- Were suspected to have ILD or pneumonitis when they entered the study
- Had a tumor in the brain that had symptoms or needed treatment

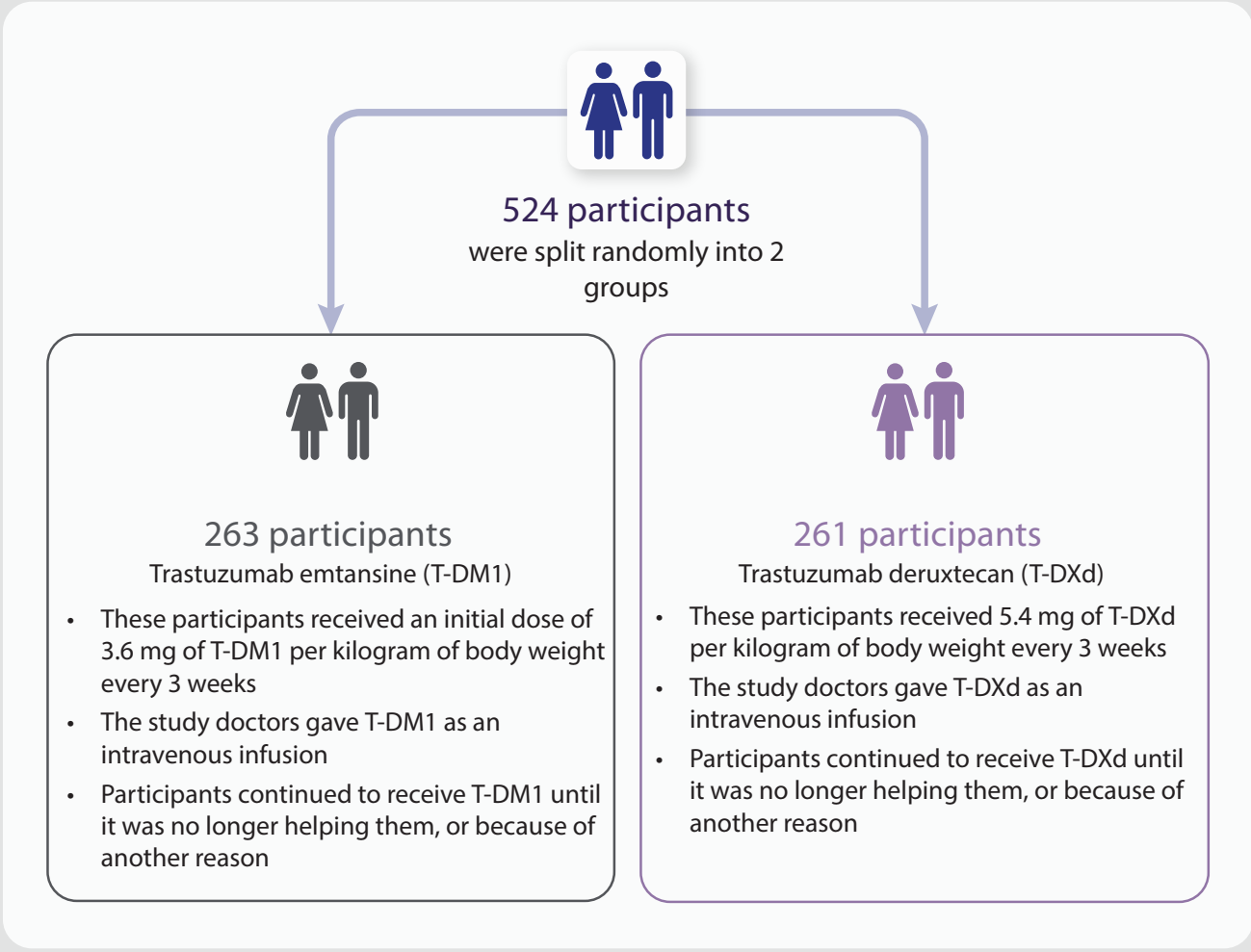
Locally advanced: the cancer has spread to nearby parts of the body from the organ where it started.

Metastatic: the cancer has spread to distant parts of the body.

Pneumonitis: inflammation of the lung tissue.

Interstitial lung disease (ILD): a group of non-infectious lung diseases that can cause scarring and stiffness of the lungs.

How was the study carried out?



What were the results?

To compare how well T-DXd and T-DM1 worked, the researchers needed to answer several questions.

One question was if the drugs caused the participants' tumors to shrink or disappear. To measure this, they used a set of rules called the Response Evaluation Criteria in Solid Tumors (RECIST). RECIST helped categorize how each tumor responded to treatment. The categories were:

- Complete response: the tumor disappeared fully
- Partial response: the tumor shrunk by at least 30%
- Stable disease: the tumor stayed the same size and did not get worse
- Progressive disease: the tumor grew larger and got worse

Did T-DXd help participants live longer without their cancer getting worse?

YES

T-DXd reduced the risk of dying or participants' cancer getting worse by **72%** compared to T-DM1.

75.8% of participants in the T-DXd group were still alive without their cancer getting worse after 12 months.

34.1% of participants in the T-DM1 group were still alive without their cancer getting worse after 12 months.

To answer this question, researchers calculated **progression-free survival**. This means how long participants lived without their cancer getting worse after receiving treatment.

Did more participants completely or partially respond to T-DXd?

YES

79.7% of participants completely or partially responded to T-DXd.

34.2% of participants completely or partially responded to T-DM1.

To answer this question, the researchers calculated the **overall response**. This means the number of participants whose tumors responded to treatment during the study. The researchers did this by analyzing scans of the participants' tumors.

Did T-DXd help participants live longer?

When the results were analyzed, the researchers could not yet be certain that T-DXd helped participants survive longer.

94.1% of participants in the T-DXd group were still alive after 12 months.

85.9% of participants in the T-DM1 group were still alive after 12 months.

To answer this question, the researchers calculated **overall survival**. This means how long participants lived after receiving either T-DXd or T-DM1.

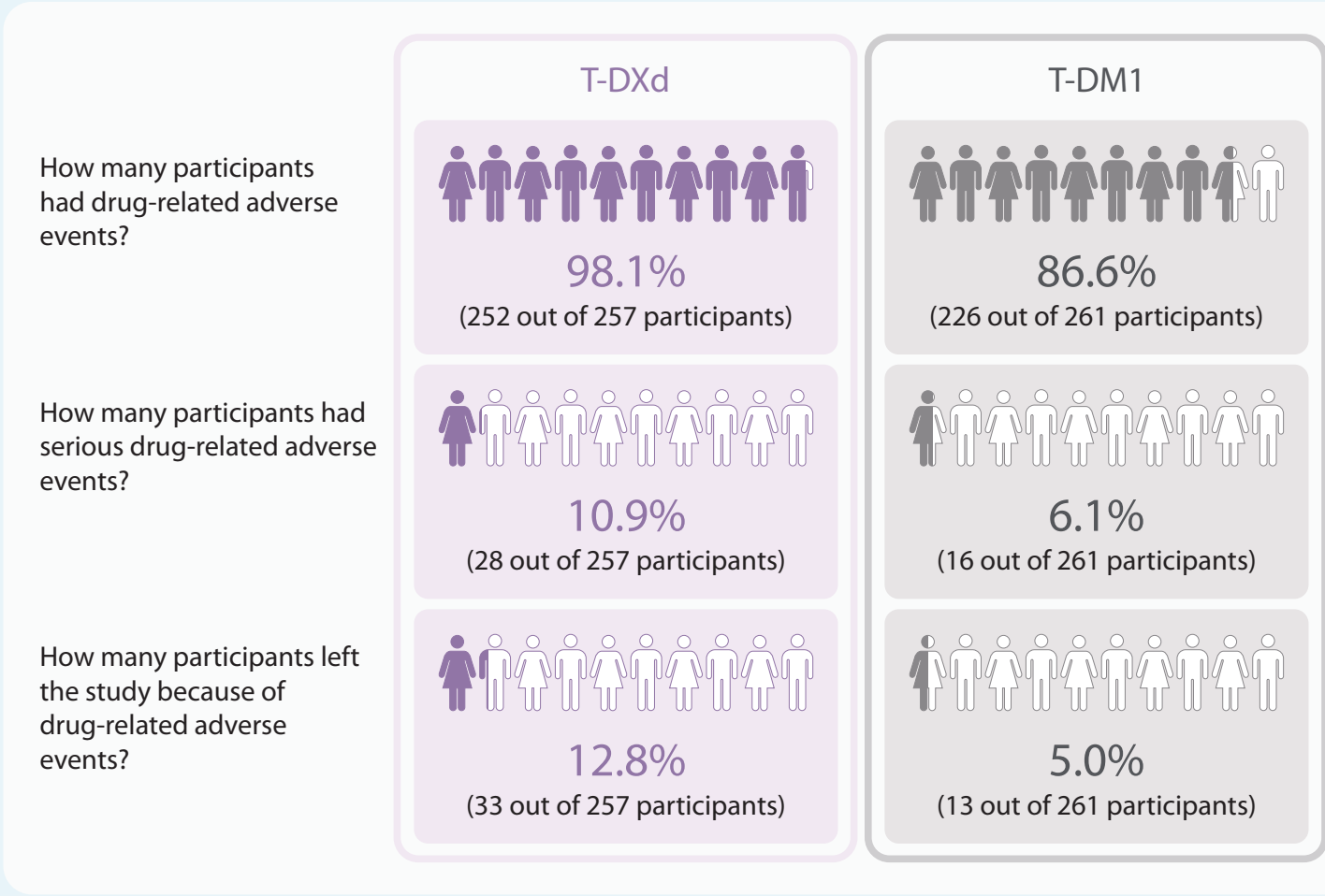
When the researchers looked at the results later in the study, they found that T-DXd did help participants to survive longer overall than T-DM1. These newer results were published separately and are not part of this summary. A link to more information about the newer results can be found the end of this summary.

How many participants had drug-related adverse events?

In this summary, medical problems that happened during the study are referred to as "adverse events". An adverse event is considered "serious" when it is life-threatening, causes lasting problems, or the participant needs hospital care.

Below are the adverse events that the doctors reported as being possibly related to the study treatments. These are known as "drug-related adverse events". It takes a lot of research to know for sure if an adverse event is actually related to a study drug.

The medical problems shown below are only from participants who received at least one dose of study treatment. This includes 257 participants who received T-DXd, and 261 participants who received T-DM1.



No participants in this study died due to drug-related adverse events.

What were the most common drug-related adverse events?

Below are the most common drug-related adverse events. There were other drug-related adverse events, but those happened in fewer participants. Some participants may have had more than one drug-related adverse event.

What adverse events of special interest did the participants have?

In this study, researchers wanted to look at whether participants experienced the same adverse events that had been shown in previous research on T-DXd. These events were called 'adverse events of special interest'.

One adverse event of special interest is interstitial lung disease (ILD), which causes scarring of the lungs. This makes it difficult to breathe and to get enough oxygen into the blood stream. Pneumonitis is another adverse event of special interest and is when the lungs become swollen or irritated.

If participants showed either of these symptoms during the study, including a fever, cough, or shortness of breath, they stopped receiving T-DXd straight away. If the symptoms were moderate or worse, participants stopped receiving T-DXd permanently and started taking steroids.

None of the participants had life-threatening ILD or died from ILD.

What do the results mean?

- T-DXd reduced the risk of dying or participants' cancer getting worse by 72% compared to T-DM1
- More participants in the T-DXd group (79.7%) had their cancer completely or partially respond compared with participants in the T-DM1 group (34.2%)
- When the researchers first looked at the results, they could not yet be certain that T-DXd helped participants survive longer overall than T-DM1. But, when they looked at the results later in the study, they found that T-DXd did help participants to survive longer overall than T-DM1. These newer results were published separately and are not part of this summary. A link to more information about the newer results can be found at the end of this summary
- Overall, 10.9% of participants who received T-DXd had serious drug-related adverse events, compared to 6.1% who received T-DM1
- T-DXd may increase the risk of ILD. Patients and their doctors should carefully monitor for signs and symptoms of ILD and be open to discussing these so it can be found early and treated
- T-DXd could be a treatment option for people with advanced HER2-positive breast cancer

Where can readers find more information?

The full title of the original publication in the *New England Journal of Medicine* is: Trastuzumab Deruxtecan versus Trastuzumab Emtansine for Breast Cancer.

You can read the original publication at: https://www.nejm.org/doi/full/10.1056/NEJMoa2115022

A newer publication about the DESTINY-Breast03 study was published in the journal *The Lancet* in January 2023. This publication contains results that are not included in this summary. This includes results showing that T-DXd helped participants survive longer overall than T-DM1.

You can read this publication at: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)02420-5/fulltext

You can read more about the DESTINY-Breast03 study on the following websites:
- Enter the study number NCT03529110 into the "Other terms" search field at www.clinicaltrials.gov.
- Enter the EudraCT identifier 2018-000222-61 into the search field at www.clinicaltrialsregister.eu.

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 center.

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Financial & competing interests disclosure

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