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A multicenter, prospective, observational study of patients receiving trastuzumab deruxtecan for the treatment of HER2-positive and HER2-low unresectable and/or metastatic breast cancer: DESTINY-Breast-RESPOND

Joyce O'Shaughnessy,[1] Reva Basho,[2] Maryam B Lustberg,[3] Gary H Lyman,[4] Manoj Prahladan,[5] Gareth D James,[6] Della Varghese,[7] Flavia Lujan,[8] Hans Tesch[9]

[1]Baylor University Medical Center, Texas Oncology and The US Oncology Network, Dallas, TX, US; [2]Ellison Institute of Technology, Los Angeles, CA, US; [3]Department of Internal Medicine, Section of Medical Oncology, Yale School of Medicine, New Haven, CT, US; [4]Fred Hutchinson Cancer Center, Seattle, WA, US; [5]Global Medical Affairs, Oncology R&D, AstraZeneca, Cambridge, UK; [6]Medical Statistics Consultancy Ltd, London, UK; [7]Oncology Outcomes Research, Global Real-World Evidence Generation, Oncology Business Unit, AstraZeneca, Gaithersburg, MD, US; [8]Global Medical Affairs, Oncology Business Unit, AstraZeneca, Cambridge, UK; [9]Bethanien Hospital, Frankfurt, Germany

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Plain language summary

Why are we performing this research?

T-DXd is an antibody-drug conjugate, which is a chemotherapy with a linker (deruxtecan) joined to an antibody (trastuzumab).[1,2] Trastuzumab binds to a **protein found on cancer cells called HER2**, where it releases the chemotherapy to kill these cells.[1] Breast cancers can be defined as HER2-positive or HER2-low depending on the level of HER2 found in diagnostic tests.[3,4] T-DXd is used to treat patients with HER2-positive or HER2-low breast cancer.[5]

As well as information from clinical studies, it is important to gather **data about T-DXd from routine clinical practice**, which may include a broader population of patients than those who participate in clinical trials. This will tell us how long patients are treated with T-DXd, how treatment affects patient well-being, reasons for stopping treatment and any subsequent therapy used, and how side effects are managed by patients and doctors in the real world. Understanding this will help ensure that patients can get the maximum benefit from new treatments.

How are we performing this research?

The DESTINY-Breast-RESPOND study began in July 2023, and is collecting information about how long people with breast cancer are treated with T-DXd. Patients with HER2-positive breast cancer will be recruited from several regions, including but not limited to North America, Europe, Brazil, Singapore, and Israel. Patients with HER2-low breast cancer will be recruited from USA only. Throughout the study, patients will report health and treatment information to describe their experience with T-DXd. Side effects, and the way that doctors and patients choose to manage them, will also be recorded.

Who will participate in this study?

Adults can take part if they meet all of the following criteria:

- They have HER2-positive or HER2-low breast cancer that cannot be completely removed with surgery, or has spread to other parts of the body
- They have started treatment with T-DXd; this decision must be made by the patient and physician before agreeing to participate in the study
- The intention is to include patients similar to those included in clinical trials of T-DXd in patients with HER2-positive and HER2-low metastatic breast cancer[6,7]

Where can I access more information?

This study is expected to end on October 27, 2026. For more information about DESTINY-Breast-RESPOND, please visit https://clinicaltrials.gov/study/NCT05592483?id=NCT05592483&rank=1. You may also speak to your doctor about clinical studies.

This study is sponsored by AstraZeneca. In March 2019, AstraZeneca entered into a global development and commercialization collaboration agreement with Daiichi Sankyo for trastuzumab deruxtecan (T-DXd; DS-8201).

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Background

- Approximately 20% of breast cancer (BC) cases are human epidermal growth factor receptor 2 (HER2) positive (immunohistochemistry [IHC] 3+, IHC 2+ / in situ hybridization [ISH]+),[1,2] and up to ~50% of patients with primary or metastatic BC have HER2-low tumors (IHC 1+, IHC 2+/ISH−),[2] a new therapeutically targetable subset of BC
- Trastuzumab deruxtecan (T-DXd) is a HER2-directed antibody-drug conjugate approved in the US, EU, and other countries for the treatment of adult patients with unresectable or metastatic HER2+ BC who have received a prior anti-HER2-based regimen, or with unresectable or metastatic HER2-low BC who have received a prior chemotherapy (CTx) in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant CTx[3–5]
- T-DXd treatment in the clinical trials DESTINY-Breast03 (DB-03) (in HER2+ BC) and DESTINY-Breast04 (DB-04) (in HER2-low BC) improved median progression-free survival compared with trastuzumab emtansine (28.8 vs 6.8 months, nominal P<0.0001) and physician's choice of CTx (9.9 vs 5.1 months, P<0.001), respectively[6,7]
- The safety profile of T-DXd is acceptable and generally manageable; the most common adverse events (AEs) in T-DXd clinical trials included nausea/vomiting, neutropenia, fatigue, and alopecia, and a minority of patients experienced potentially serious AEs, including interstitial lung disease (ILD) / pneumonitis and left ventricular ejection fraction (LVEF) decrease[3]
- Given that patients who experience AEs may have a lower quality of life, which may lead to decreased adherence to therapy, it is important that suitable AE management strategies are implemented in real-world settings to ensure that patients derive the maximum possible benefit from novel targeted treatments
  - Proactive management/prevention strategies for T-DXd safety events of interest (SEIs) include use of prophylactic antiemetic medications to prevent nausea/vomiting[4] and adherence to clinical practice guidelines for management of ILD/pneumonitis (to prevent progression to Grade 4/5)[6]

- DESTINY-Breast-RESPOND will characterize the real-world tolerability and effectiveness of T-DXd, as well as patient experience and treatment strategies for management/prevention of AEs, in patients with HER2+ or HER2-low unresectable and/or metastatic BC

Study design

Patient population

- Patients with unresectable and/or metastatic BC (HER2+ or HER2-low) who initiate T-DXd treatment* (N≈1000)
- Recruitment not limited by hormone receptor status
- The intention is to recruit patients similar to those from DB-03 (HER2+) and DB-04 (HER2-low)
- Patients will be enrolled in two cohorts
- For the HER2+ cohort, patients will be enrolled into the study across several regions globally (n≈750), including, but not limited to, North America, Europe, Brazil, Singapore, and Israel
- For the HER2-low cohort, patients will be enrolled into the study from USA only (n≈250)

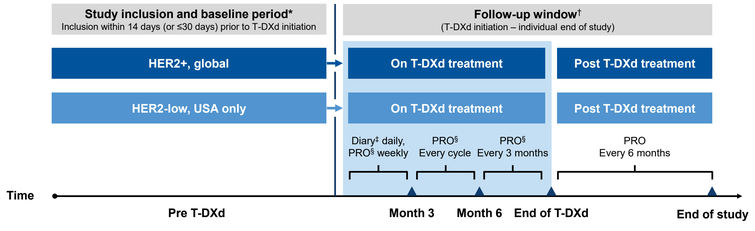
T-DXd
5.4 mg/kg
every 3 weeks*

Study design

- Multicenter, multicountry study, with enrollment planned across 120 sites, with 29 currently active
- Data collected via chart abstraction and patient-reported outcome questionnaires
- Patients observed until the end of the study period, withdrawal from study, death, or loss to follow up, whichever occurs first
- For each cohort, the study will end when ~60% of patients from that cohort have received their next line of anticancer treatment or have died

*The decision to initiate T-DXd will be made by the physician and patient prior to, and independently of, participation in this study and in accordance with marketing authorization; the recommended dose is 5.4 mg/kg intravenous infusion every 3 weeks until disease progression or unacceptable toxicity

Study schema



- The final analysis will be conducted separately for each cohort, when ~60% of patients have received their next line of anticancer treatment or have died

*Baseline data include patient characteristics, tumor characteristics, treatment history, metastases, PROs, and other data. Documentation of some information collected at baseline (eg on prior medication, prior SEIs, comorbidities) refers to a time period of 6 months prior to index date
†Follow-up data include predefined SEIs, SEI management strategies, other safety data including death (includes evaluation of SUSARs, AEs, and/or SAEs that lead to a dose interruption, reduction, or discontinuation), PROs including daily symptom diary, T-DXd administration, discontinuation and interruptions, concomitant medication, and subsequent lines of therapy
‡Select gastrointestinal toxicities of interest, including nausea/vomiting, will be assessed via daily diaries
§PROs will be measured via validated questionnaires: overall SEIs (single-item PGI-TT assessment), physical function (EORTC IL19), select symptomatic SEIs (symptom items from the NCI PRO-CTCAE and EORTC Item Library)

AE, adverse event; EORTC, European Organisation for Research and Treatment of Cancer; EORTC IL19, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Physical Functioning Scale; HER2, human epidermal growth factor receptor 2; NCI PRO-CTCAE, National Cancer Institute Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events; PGI-TT, Patient's Global Impression of Treatment Tolerability; PRO, patient-reported outcome; SAE, serious adverse event; SEI, safety event of interest; SUSAR, suspected unexpected serious adverse reaction; T-DXd, trastuzumab deruxtecan

Key inclusion criteria

- Age ≥18 years at the time of informed consent
- Diagnosis of unresectable and/or metastatic BC confirmed by histology or cytology
- Documented HER2 status by validated method
- Decision to newly initiate monotherapy (T-DXd) per standard of care*

*For patients with unresectable or metastatic **HER2+ BC***

- Received prior treatment with anti-HER2-based regimen in the metastatic setting, or in the neoadjuvant or adjuvant setting and developed disease recurrence during or within 6 months of completing therapy*

*For patients with unresectable or metastatic **HER2-low BC***

- Received prior treatment with CTx (metastatic setting) or disease recurrence during or within 6 months of completing adjuvant CTx*

*Therapies that are paused for a period of time and then restarted, including at reduced dose without disease progression having occurred, will be considered as part of the same line rather than a new line. Cohort allocation will be at investigator's discretion in compliance with the label (taking into consideration prior BC treatment patients have received)

Key exclusion criteria

- Pregnancy/breastfeeding
- History of other primary malignancies in the 2 years prior to unresectable and/or metastatic BC diagnosis
- Participation in other interventional studies

Key study endpoints

1° Primary endpoints

- Real-world time to next treatment from T-DXd initiation
- Treatment patterns (HER2+ cohort only; secondary endpoint for HER2-low cohort)

2° Secondary endpoints

- Physician-reported SEIs (nausea/vomiting, fatigue, alopecia, ILD/pneumonitis, LVEF decrease)
- Evaluation of prophylactic and reactive treatments for SEI management
- Real-world time to treatment discontinuation
- Patient-reported tolerability (Patient's Global Impression of Treatment Tolerability, National Cancer Institute Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events, symptom diary)

Exploratory endpoints

- Real-world progression-free survival from index date
- Hospital-related resource utilization
- Overall survival from index date

Please scan this quick response (QR) code with your smartphone camera or app to obtain a copy of this poster. Alternatively, access at: https://bit.ly/3s2lIEn

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Disclosures

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