A pragmatic, hybrid observational study evaluating the effectiveness of trastuzumab deruxtecan in patients with human epidermal growth factor receptor 2 immunohistochemistry 3+ solid tumors: DESTINY-PanTumor04

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Plain language summary

Why are we performing this research?

Human epidermal growth factor receptor 2 (HER2) is a protein found at a high level in some solid tumors, known as HER2-positive immunohistochemistry (IHC) 3+, and may be associated with aggressive disease and poor outcomes.[1–5] Trastuzumab deruxtecan (T-DXd) is an antibody-drug conjugate, comprising a chemotherapy with a linker (together called deruxtecan) joined to an antibody (trastuzumab).[6,7] T-DXd is approved in more than 15 countries, including in the US as a treatment for people with HER2-positive (IHC 3+) solid tumors that cannot be removed with surgery (unresectable) or have spread to other parts of the body (advanced/metastatic), and for those who have received prior treatment and have no alternative treatment options.[8] The approval was partly based on recent clinical data showing antitumor activity and clinical benefit of T-DXd;[9] this study will evaluate how well T-DXd works in everyday healthcare settings.

How are we performing this research?

DESTINY-PanTumor04 is an ongoing study taking place at multiple locations in the US to assess the benefit of T-DXd as a treatment for people with HER2-positive (IHC 3+) solid tumors in routine clinical practice. Data will be collected using a hybrid approach, combining physician-completed case report forms as primary data and electronic health records as secondary data. This method is designed to ensure efficient data transfer while saving doctors' time.

Who will participate in this study?

To participate, people must be aged 18 years or older, have HER2-positive (IHC 3+) advanced, unresectable, or metastatic solid tumors, and their doctor must have decided to initiate treatment with T-DXd. People cannot participate if they have been diagnosed with cancer of the breast, colon, rectum, lung, gastric body, or where the stomach and food pipe meet (gastroesophageal junction), or with blood cancer.

Where can I access more information?

For more information about DESTINY-PanTumor04, please visit https://clinicaltrials.gov/study/NCT07124000. You may also speak to your doctor about clinical studies.

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Background

- Human epidermal growth factor receptor 2 (HER2) immunohistochemistry (IHC) 3+ expression is seen in a wide range of solid tumors, and may be associated with biologically aggressive tumor phenotypes, increased risk of disease recurrence, and poor clinical outcomes in advanced or metastatic settings;[1–5] HER2-directed therapies provide an opportunity to improve outcomes in patients with HER2-expressing tumors, particularly in second-line settings, where effective therapeutic options remain limited[6–8]
- Trastuzumab deruxtecan (T-DXd) is a HER2-directed antibody-drug conjugate approved in multiple countries, including in the US for patients with unresectable or metastatic HER2-positive (IHC 3+) solid tumors who have received prior treatment and have no satisfactory alternative therapies[9]
  - The approval was based, in part, on results from Part 1 of the DESTINY-PanTumor02 study, which demonstrated clinically meaningful antitumor activity of T-DXd in pretreated HER2-expressing (IHC 3+/2+) advanced or metastatic solid tumors (investigator-assessed [INV] objective response rate [ORR], 37.1%; INV median progression-free survival [mPFS], 6.9 months)[7]
  - The greatest benefit was observed in HER2 IHC 3+ solid tumors, irrespective of whether HER2 IHC status was determined by central testing (INV ORR, 61.3%; INV mPFS,11.9 months),[7] or local or central test results for study enrollment (INV ORR, 51.4%; INV mPFS, 9.7 months)[8]
- Additional studies are needed to help strengthen the evidence for T-DXd use in patients with HER2-positive (IHC 3+) solid tumors, particularly in routine clinical practice
  - Pragmatic observational studies are uniquely positioned to assess the therapeutic effectiveness in routine clinical practice, by enrolling heterogeneous patient populations using broad eligibility criteria, and by focusing on patient-centric outcomes, while capturing data reflective of real-world healthcare settings[10]

DESTINY-PanTumor04 is a pragmatic observational study designed to evaluate the real-world effectiveness of T-DXd in HER2-positive (IHC 3+) solid tumors, using a hybrid data collection approach that enhances efficiency for sites and physicians

Key inclusion criteria

- Adults aged ≥18 years
- Locally advanced, unresectable, or metastatic HER2-positive (IHC 3+) solid tumors
- HER2-positive status (IHC 3+) determined by local testing prior to study enrollment
- ≥1 prior systemic treatment and without alternative treatment options as determined by the investigator
- Clinical decision for T-DXd treatment in accordance with the US Food and Drug Administration label

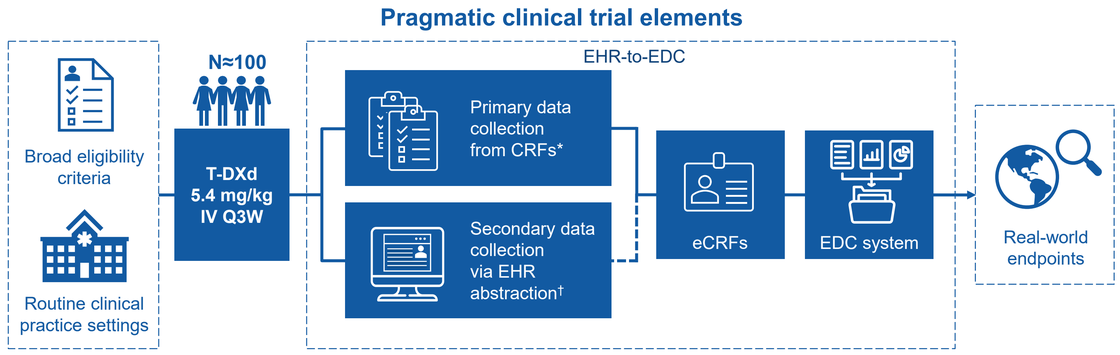
Key exclusion criteria

- Primary diagnosis of breast cancer, colorectal cancer, non-small cell lung cancer, gastric or gastroesophageal junction cancers, or hematologic malignancies
- Previously treated with T-DXd
- Participation in a concurrent interventional study

Study design

DESTINY-PanTumor04 (NCT07124000) is a multicenter, pragmatic observational real-world study in the US assessing the efficacy of T-DXd (5.4 mg/kg) in HER2-positive (IHC 3+) solid tumors[11]

- Approximately 100 patients will be recruited from ~30 sites across the US, including community oncology practices, hospital systems, and academic medical centers[11]
- Data will be collected using a hybrid approach, combining primary and secondary sources, with participating sites utilizing technology-enabled patient identification and data abstraction[11]
  - This innovative hybrid collection approach will increase participating site efficiency while enabling timely and efficient collection and reporting of patient data[11,12]



- ✓ Simplified patient identification and enrollment
- ✓ Technology integration that reduces site burden
- ✓ Decreased treating physician's time
- ✓ Improved data accuracy and completeness

For more information about DESTINY-PanTumor04, please visit https://clinicaltrials.gov/study/NCT07124000

*Baseline tumor burden, comorbidities, ECOG performance status, treatment response, and survival; †all other data
CRF, case report form; eCRF, electronic case report form; ECOG, Eastern Cooperative Oncology Group; EDC, electronic data capture; EHR, electronic health record; IV, intravenous; Q3W, every 3 weeks; T-DXd, trastuzumab deruxtecan

Enrollment start: September 18, 2025 | Currently recruiting

Participating study sites in the US

Birmingham (Alabama), Bullhead City (Arizona), Casa Grande (Arizona), San Diego (California), Boulder (Colorado), Coral Springs (Florida), St. Petersburg (Florida), West Palm Beach (Florida), Decatur (Illinois), Topeka (Kansas), Durham (North Carolina), Wilson (North Carolina), Canton (Ohio), Maumee (Ohio), Philadelphia (Pennsylvania), Nashville (Tennessee), Dallas (Texas)

Key study endpoints

1° Primary endpoints

- **Real-world objective response rate**,* defined as the proportion of patients with a complete response or partial response
- **Real-world duration of response**,* defined as the time from the first objective response (complete response or partial response) to disease progression, or death, whichever occurs first

2° Secondary endpoints

- **Real-world time to treatment discontinuation**, defined as the time from the first administration of T-DXd to treatment discontinuation per clinician's decision, or death, whichever occurs first
- **Real-world time to next treatment**, defined as the time from the first administration of T-DXd to the first administration of the next line of treatment, or death, whichever occurs first

*As assessed by the clinician per the criteria used in routine clinical practice

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Disclosures

Bradley J Monk reports consulting/advisory roles for AbbVie, Alkermes, AstraZeneca, BioNTech, Corcept Therapeutics, Daiichi Sankyo, Eisai, Genmab/Seagen, GOG Foundation, Gradalis, ImmunoGen, Incyte, Karyopharm Therapeutics, Lilly, Merck, Mersana, Myriad Pharmaceuticals, Natera, Novartis, Novocure, OncoC4, Panavance Therapeutics, pharma&, ProfoundBio, Regeneron, Roche/Genentech, Sutro Biopharma, Tubulis GmbH, Verastem, Zentalis, and Zymeworks; being an invited speaker for AstraZeneca, Eisai, ImmunoGen/AbbVie, Lilly, Merck, and GSK; honoraria from AbbVie, AstraZeneca, BioNTech, Corcept Therapeutics, Daiichi Sankyo, Eisai, Genmab, Genmab/Seagen, GOG Foundation, GSK, ImmunoGen, Incyte, Karyopharm Therapeutics, Lilly, Merck, Mersana, Mural Oncology, Myriad Genetics, Natera, Novartis, Novocure, OncoC4, Panavance Therapeutics, pharma&, ProfoundBio, Regeneron, Roche/Genentech, Sutro Biopharma, Tubulis GmbH, Verastem, Zentalis, and Zymeworks; institutional research funding from Advaxis, Amgen, Array BioPharma, AstraZeneca, Genentech, GSK, ImmunoGen, Janssen, Lilly, Morphotek, Novartis, NuCana, Pfizer, and Regeneron.

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Poster

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DESTINY PanTumor04

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