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Trastuzumab deruxtecan for pretreated patients in China with HER2 IHC 3+ solid tumors: DESTINY-PanTumor03 Part 1 primary analysis

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Objective

- To present the primary analysis results from DESTINY-PanTumor03 (NCT06271837) Part 1, evaluating the efficacy and safety of trastuzumab deruxtecan (T-DXd) in pretreated patients in China with human epidermal growth factor receptor 2 (HER2) immunohistochemistry (IHC) 3+, locally advanced, unresectable, or metastatic solid tumors[1]

Conclusions

- T-DXd demonstrated durable and clinically meaningful benefit in pretreated patients in China with HER2 IHC 3+ advanced or metastatic solid tumors
  - Antitumor activity was observed across a range of solid tumors, and durable responses led to clinically meaningful progression-free survival (PFS)
- Safety was generally consistent with the established T-DXd profile, with no new safety signals observed[2,3]
- Data were consistent with results from Part 1 of the DESTINY-PanTumor02 (NCT04482309) study[2]
- Overall, results from DESTINY-PanTumor03 Part 1 support T-DXd as a tumor-agnostic treatment for patients in China with HER2 IHC 3+ solid tumors

Plain language summary

Why did we perform this research?

Trastuzumab deruxtecan (T-DXd) is an antibody-drug conjugate, which is a chemotherapy with a linker (together called deruxtecan) joined to an antibody (trastuzumab). T-DXd binds to human epidermal growth factor receptor 2 (HER2) on the surface of cancer cells. Once inside the cell, it releases the chemotherapy to kill these cells.[1,2] T-DXd is a recommended treatment in multiple countries, including the US, for people with solid tumors that have the highest level of HER2 (HER2-positive, also known as immunohistochemistry [IHC] 3+ tumors) and have spread from the original site to other parts of the body (known as advanced or metastatic cancer) or cannot be completely removed with surgery, and who have received prior systemic treatment and/or have no satisfactory alternative treatment options available.[3–5] As treatment options for these individuals in China are limited, DESTINY-PanTumor03 Part 1 investigated the benefits and side effects of T-DXd in people in China with HER2 IHC 3+ solid tumors.[6]

How did we perform this research?

Part 1 of DESTINY-PanTumor03 included people with HER2 IHC 3+ advanced or metastatic solid tumors that had spread or could not be completely removed with surgery, except those with breast or stomach tumors, or those with lung cancer with a known *HER2* mutation. Participants must have received prior systemic treatment or had no satisfactory alternative treatment options available before receiving T-DXd.

What were the findings of this research?

Overall, 29 out of 50 people (58.0%) who participated in Part 1 had a complete or partial response to T-DXd. The most common side effects related to T-DXd, seen in more than 50% of people, included reduced neutrophil count, white blood cell count, and platelet count, as well as anemia, nausea, and increased aspartate aminotransferase levels. Overall, the observed side effects were generally consistent with those expected in people receiving T-DXd.[7,8]

What are the implications of this research?

Results from DESTINY-PanTumor03 Part 1 support the use of T-DXd as a treatment for people with HER2 IHC 3+ cancers that have spread or cannot be completely removed with surgery and who have received prior systemic treatment and/or have no satisfactory alternative treatment options available.[3–5]

Where can I access more information?

For information about DESTINY-PanTumor03, please visit https://www.clinicaltrials.gov/study/NCT06271837. You can also speak to your doctor about this and other clinical studies.

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Poster

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Introduction

- HER2 expression is observed in a range of tumor types (**Figure 1**)
- T-DXd (HER2-directed antibody-drug conjugate) is approved in multiple countries for HER2-positive and HER2-low/ultralow breast cancer; HER2-positive gastric or gastroesophageal junction adenocarcinoma; and *HER2*-mutant non-small cell lung cancer (NSCLC)[4–6]
- In DESTINY-PanTumor02 Part 1, T-DXd demonstrated clinically meaningful activity in pretreated advanced HER2-expressing solid tumors; the greatest benefit was observed in HER2 IHC 3+ tumors[2]
- Based in part on these data, T-DXd has been approved in over 15 countries, including the US, for adult patients with unresectable or metastatic HER2-positive (IHC 3+) solid tumors who have received prior treatment and/or have no satisfactory alternative therapies[4–6]
- As treatment options are limited for this patient population in China, DESTINY-PanTumor03 Part 1 evaluated T-DXd as a tumor-agnostic treatment for pretreated patients in China with HER2 IHC 3+ solid tumors[1]

Figure 1. HER2 IHC 3+ prevalence by tumor type[7–37]

Biliary tract	1–19%
Bladder	4–31%
Colorectal	1–6%
Cervical	8–14%
Endometrial	4–17%
Ovarian	4–6%
NSCLC	1–5%

HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; NSCLC, non-small cell lung cancer

Methods

Patient population

- Adults with histologically confirmed locally advanced, unresectable, or metastatic solid tumors
  - Patients with breast, gastric, or gastroesophageal junction tumors, or NSCLC with a known *HER2* mutation, were excluded
- HER2 IHC 3+ expression by central testing and scored using current American Society of Clinical Oncology / College of American Pathology (ASCO/CAP) guidelines for scoring HER2 in gastric cancer[38]
- Disease progression following ≥1 prior systemic treatment for advanced or metastatic disease, or without alternative treatment options
  - Prior HER2-directed therapy was allowed
- Eastern Cooperative Oncology Group performance status of 0 or 1
- Measurable target disease by Response Evaluation Criteria in Solid Tumours 1.1

Study type

Open-label, multicenter, Phase 2

Treatment

T-DXd 5.4 mg/kg IV Q3W

Trial registration

NCT06271837

Data cutoff

November 28, 2025

Endpoints

Primary:
- Confirmed ORR (ICR)*

Secondary:
- Confirmed ORR (INV)*
- DOR, DCR, PFS (ICR and INV)*
- Overall survival
- Frequency of AEs, serious AEs, and AEs of special interest

*Per RECIST 1.1. AE, adverse event; DCR, disease control rate; DOR, duration of response; ICR, independent central review; INV, investigator assessed; IV, intravenous; ORR, objective response rate; PFS, progression-free survival; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumours; T-DXd, trastuzumab deruxtecan

Results

- At primary data cutoff (November 28, 2025), 50 patients with biliary tract (n=11), colorectal (n=6), cervical (n=10), endometrial (n=7), ovarian (n=5), non-small cell lung (n=7), or other cancers (parotid gland, n=3; bladder, n=1) had received T-DXd
- Nineteen (38.0%) patients were receiving ongoing treatment at data cutoff; the most common reason for treatment discontinuation was objective disease progression (n=15, 30.0%; **Table 1**)
- Median (range) follow up for all patients was 9.9 (1.1–18.3) months
- Median (range) number of prior treatment regimens among patients was 2 (1–10); 38.0% of all patients had received at least three prior lines of therapy (**Table 2**)

Table 1. Patient disposition

	All patients (N=50)
Received T-DXd, n	50
Ongoing treatment at DCO, n (%)	19 (38.0)
Discontinued treatment, n (%)	31 (62.0)
Objective disease progression	15 (30.0)
Adverse event	6 (12.0)
Patient decision	4 (8.0)
Death*	3 (6.0)
Subjective disease progression	2 (4.0)
Investigator decision	1 (2.0)
Median follow up, months (range)	9.9 (1.1–18.3)

*Included discontinuation of treatment which was caused by death
DCO, data cutoff; T-DXd, trastuzumab deruxtecan

Table 2. Baseline demographics and clinical characteristics

		All patients (N=50)
Age, median (range), years		59 (28–77)
Female, n (%)		36 (72.0)
Asian, n (%)		50 (100)
Number of prior treatment regimens	Median (range)	2 (1–10)
	1, n (%)	13 (26.0)
	2, n (%)	18 (36.0)
	3, n (%)	9 (18.0)
	4, n (%)	3 (6.0)
	≥5, n (%)	7 (14.0)
Prior anti-HER2 therapy, n (%)*		15 (30.0)
Prior radiotherapy, n (%)		21 (42.0)
ECOG PS, n (%)	0	7 (14.0)
	1	43 (86.0)

*Included monoclonal antibody and antibody-drug conjugate therapies
ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2

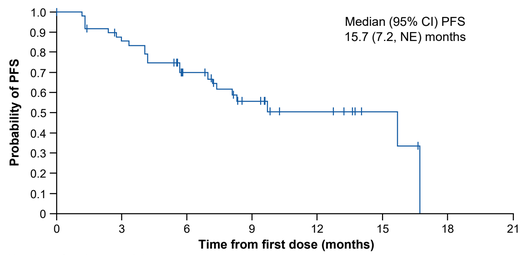
Table 3. Efficacy outcomes by ICR and INV

	All patients (N=50)	
	ICR*	INV*
Confirmed ORR, % (95% CI)	58.0 (43.2, 71.8)	56.0 (41.3, 70.0)
Median DOR, months (95% CI)	15.4 (12.5, NE)	12.3 (8.3, NE)
DCR at Week 6, % (95% CI)	88.0 (75.7, 95.5)	90.0 (78.2, 96.7)
DCR at Week 12, % (95% CI)	82.0 (68.6, 91.4)	86.0 (73.3, 94.2)
Median PFS, months (95% CI)	15.7 (7.2, NE)	10.8 (8.3, 13.8)
Median overall survival	Not reached	

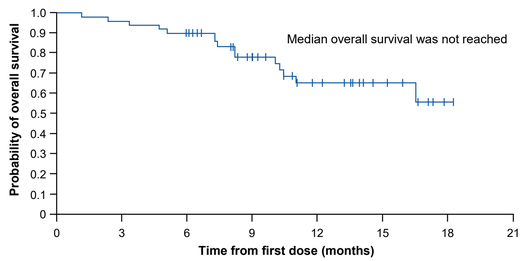
Primary endpoint: confirmed ORR by ICR. *Per RECIST 1.1. CI, confidence interval; DCR, disease control rate; DOR, duration of response; ICR, independent central review; INV, investigator assessed; NE, not evaluable; ORR, objective response rate; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumours

Figure 2. Survival outcomes

PFS by ICR



Overall survival



Vertical lines indicate a censored observation. For the PFS analysis, patients who were alive and whose disease had not progressed, as well as patients who had died or whose disease had progressed after two or more missed visits at the time of analysis, were censored at the latest evaluable RECIST 1.1 assessment, or at Day 1. For the overall survival analysis, patients who were alive at the time of analysis were censored at the last recorded date they were known to be alive
CI, confidence interval; ICR, independent central review; NE, not evaluable; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumours

Efficacy

- The primary endpoint of confirmed objective response rate by independent central review (ICR) was 58.0%; efficacy outcomes by ICR and investigator assessment (INV) are presented in **Table 3**
  - Median duration of response by ICR was 15.4 months and by INV was 12.3 months (**Table 3**)
  - Disease control rates were maintained above 80% from Week 6 through Week 12 (**Table 3**)
  - Median PFS by ICR was 15.7 months; median overall survival was not reached (**Table 3** and **Figure 2**)

Safety

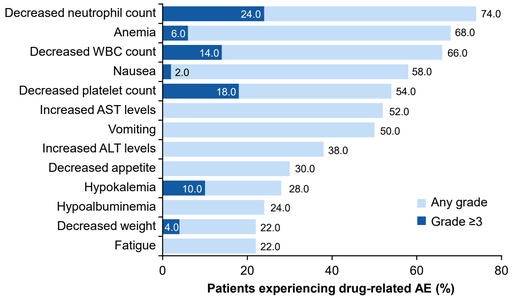
- Drug-related adverse events (AEs; any grade) occurred in 49 (98.0%) patients, and Grade ≥3 drug-related AEs occurred in 31 (62.0%) patients (**Table 4**)
  - The most common drug-related AEs included decreased neutrophil (74.0%) and white blood cell (66.0%) count, and anemia (68.0%; **Figure 3**)
- Adjudicated drug-related interstitial lung disease / pneumonitis occurred in four (8.0%) patients; three cases were Grade 2, and one case was Grade 3

Table 4. Safety

AE category, n (%)	All patients (N=50)
Any	50 (100)
Grade ≥3	34 (68.0)
Associated with death	0
Drug-related	49 (98.0)
Grade ≥3	31 (62.0)
Serious	14 (28.0)
Associated with dose reduction	11 (22.0)
Associated with dose interruption	12 (24.0)
Associated with dose discontinuation	6 (12.0)

Analyses include all patients who received ≥1 dose of T-DXd (n=50). Median (range) duration of treatment was 8.1 (0.7–17.8) months. Multiple occurrences in the same category were counted once per category regardless of the number of occurrences AE, adverse event; T-DXd, trastuzumab deruxtecan

Figure 3. Most common drug-related AEs



'Most common' was defined as occurring in >20% of patients. Analyses include all patients who received ≥1 dose of T-DXd (n=50). Multiple occurrences in the same category were counted once per category regardless of the number of occurrences AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; WBC, white blood cell

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Disclosures

Professor Xiaohua Wu declares no conflicts of interest.

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