Poster 2105P

Trastuzumab deruxtecan in patients with HER2+ gastric cancer or gastroesophageal junction adenocarcinoma who received prior anti-HER2 treatment other than / in addition to trastuzumab in DESTINY-Gastric06

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Objective

- To evaluate the efficacy and safety of trastuzumab deruxtecan (T-DXd) in patients from China with human epidermal growth factor receptor 2 (HER2)-positive (+) gastric or gastroesophageal junction (GEJ) adenocarcinoma in the DESTINY-Gastric06 study, who have received prior HER2-directed treatment, other than or in addition to trastuzumab

Conclusions

- In this analysis, efficacy and safety of T-DXd in patients who received HER2-directed treatment, other than or in addition to trastuzumab, were generally consistent with results for the overall DESTINY-Gastric06 study population[1,2]
- Clinical activity was seen with T-DXd in patients from China with HER2+ gastric or GEJ adenocarcinoma who received varying types of prior HER2-directed treatment; the small sample size should be considered when interpreting these data
- These data support T-DXd (6.4 mg/kg) as a treatment option for patients from China with HER2+ gastric or GEJ adenocarcinoma after HER2-directed treatment

Plain language summary

Why did we perform this research?

Trastuzumab deruxtecan (T-DXd) is a human epidermal growth factor receptor 2 (HER2)-directed antibody-drug conjugate that kills HER2-altered cancer cells.[1,2] DESTINY-Gastric06 evaluated T-DXd in people from China with gastric or gastroesophageal junction (GEJ) adenocarcinoma (cancer in the stomach or where the stomach joins the esophagus), with the highest levels of HER2 protein (known as HER2-positive or HER2+) that had spread to nearby tissues or other parts of the body (known as advanced or metastatic). The people evaluated had received at least two prior anticancer treatments; this included different types of HER2-directed treatments.[3,4] Although benefit with T-DXd has been shown in the overall DESTINY-Gastic06 population,[3,4] it is important to determine whether similar benefit with T-DXd is observed in the subgroup of people from the study who had previously received HER2-targeting treatment, other than or in addition to trastuzumab.

How did we perform this research?

We evaluated the antitumor activity and safety profile of T-DXd in the subset of people from the DESTINY-Gastric06 study who had previously received treatment targeting HER2, other than or in addition to trastuzumab.

What were the findings of this research?

A response (reduction in the size or number of tumors) to T-DXd (confirmed by independent radiologists) was seen in seven of 22 people (32%) who had previously received treatments that target HER2, other than or in addition to trastuzumab; this was similar to the overall DESTINY-Gastric06 population (21 of 73 people [29%] had a response to T-DXd).[4] The side effects of T-DXd in this subgroup were consistent with those seen in the overall DESTINY-Gastric06 study.[4]

What are the implications of this research?

These results support T-DXd as a treatment option for people from China with HER2+ gastric or GEJ adenocarcinoma who have previously received treatment targeting HER2, other than or in addition to trastuzumab.

Where can I access more information?

For more information about DESTINY-Gastric06, please visit https://clinicaltrials.gov/study/NCT04989816. You can also speak to your doctor about this and other clinical studies.

1. Nakada T, et al. *Chem Pharm Bull (Tokyo).* 2019;67:173–185; 2. Ogitani Y, et al. *Clin Cancer Res.* 2016;22:5097–5108; 3. Shen L, et al. Abstract presented at ESMO 2023 (Abstract 172P); 4. Peng Z, et al. *EClinicalMedicine.* 2025;87:103404

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In March 2019, AstraZeneca entered into a global development and commercialization collaboration agreement with Daiichi Sankyo for trastuzumab deruxtecan (T-DXd; DS-8201).
Poster presented at ESMO 2025 by Professor Zhi Peng. Corresponding author email address: zhipeng@bjmu.edu.cn

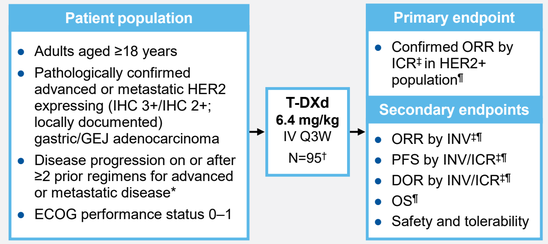
Introduction

- In DESTINY-Gastric06, T-DXd (a HER2-directed antibody-drug conjugate) showed antitumor activity and no new safety signals in pretreated patients from China with centrally confirmed HER2+ (immunohistochemistry [IHC] 3+ or IHC 2+ / in situ hybridization positive [ISH+]) advanced gastric or GEJ adenocarcinoma[1,2]
- Based in part on DESTINY-Gastric06 primary results,[1] T-DXd (6.4 mg/kg) is approved in China for advanced/metastatic HER2+ gastric or GEJ adenocarcinoma after ≥2 prior treatment regimens[3]
- The patient population of DESTINY-Gastric06 was heavily pretreated[2]
  - This included prior treatment with several different types of HER2-directed therapies
- This post-hoc analysis evaluated the efficacy and safety of T-DXd in patients from DESTINY-Gastric06 who received prior HER2-directed treatment, other than or in addition to trastuzumab

Methods

- DESTINY-Gastric06 (NCT04989816) was a Phase 2, single-arm, multicenter, open-label study conducted in China for previously treated patients with HER2-expressing (IHC 3+ or IHC 2+) locally advanced or metastatic gastric or GEJ adenocarcinoma[1,2,4]
- Patients had to have received ≥2 prior treatments for advanced or metastatic disease, including a fluoropyrimidine agent and a platinum agent[1,2,4]
- Patients received T-DXd (6.4 mg/kg) by intravenous infusion once every 3 weeks until disease progression according to Response Evaluation Criteria in Solid Tumours 1.1, unacceptable toxicity, withdrawal of consent, or any other criterion for discontinuation[1,2]
- Additional details on the patient population, and key study endpoints are shown in **Figure 1**
- All patients who had received a prior HER2-directed treatment other than or in addition to trastuzumab (henceforth referred to as 'prior HER2-directed treatment subgroup') were included in this post-hoc analysis

Figure 1. DESTINY-Gastric06 study design[4]



*Prior systemic therapy must have included a fluoropyrimidine agent and a platinum agent; †ITT population included all patients enrolled in the study; ‡per RECIST 1.1; ¶analysis performed in the centrally confirmed HER2+ population; HER2+ defined as IHC 3+ or IHC 2+/ISH+
DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; GEJ, gastroesophageal junction; HER2, human epidermal growth factor receptor 2; HER2+, HER2-positive; ICR, independent central review; IHC, immunohistochemistry; INV, investigator assessment; ISH+, in situ hybridization positive; ITT, intent-to-treat; IV, intravenous; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumours; T-DXd, trastuzumab deruxtecan

Results

Patient population

- At data cutoff (February 28, 2024), 95 patients had locally confirmed HER2-expressing (IHC 3+ or IHC 2+) advanced gastric or GEJ adenocarcinoma and were included in the intent-to-treat (ITT) population[2]
  - In total, 73 patients in the ITT population had centrally confirmed HER2+ tumors (IHC 3+ or IHC 2+/ISH+) and comprised the full analysis set (FAS)[2]
  - Of patients in the FAS, 22 had received prior HER2-directed treatment and were included in this analysis
- The baseline characteristics of the subgroup were generally consistent with those of the DESTINY-Gastric06 FAS (**Table 1**)
  - Patients in the prior HER2-directed treatment subgroup had a numerically higher number of prior lines of therapy than the FAS (72.7% and 49.3% with ≥3 previous lines of treatment, respectively)

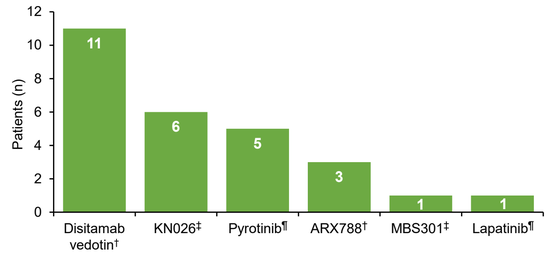
Table 1. Patient demographics

	Prior HER2-directed treatment subgroup n=22*	FAS n=73†[2]
Age, years		
Median (range)	60 (43–73)	60 (28–77)
Sex, n (%)		
Female	6 (27.3)	18 (24.7)
ECOG performance status, n (%)		
0	5 (22.7)	27 (37.0)
1	17 (77.3)	46 (63.0)
Tumor/cancer location, n (%)		
Gastric	14 (63.6)	51 (69.9)
GEJ	8 (36.4)	22 (30.1)
HER2 status by central testing, n (%)		
IHC 3+	15 (68.2)	53 (72.6)
IHC 2+/ISH+	7 (31.8)	20 (27.4)
Number of metastatic sites, n (%)		
<2	5 (22.7)	15 (20.5)
≥2	17 (77.3)	58 (79.5)
Number of previous lines of therapy, n (%)		
2	6 (27.3)	37 (50.7)
3	7 (31.8)	21 (28.8)
4	3 (13.6)	8 (11.0)
≥5	6 (27.3)	7 (9.6)
Sum of diameters of measurable tumors at baseline,‡ n (%)		
<10 cm	20 (90.9)	59 (80.8)
≥10 cm	2 (9.1)	14 (19.2)

*The subgroup included patients in the FAS who had received prior HER2-directed treatment, other than or in addition to trastuzumab; †FAS: 73 patients with centrally confirmed HER2+ status (IHC 3+ or IHC 2+/ISH+); ‡assessed by ICR at baseline
ECOG, Eastern Cooperative Oncology Group; FAS, final analysis set; GEJ, gastroesophageal junction; HER2, human epidermal growth factor receptor 2; HER2+, HER2-positive; ICR, independent central review; IHC, immunohistochemistry; ISH+, in situ hybridization positive

- In the prior HER2-directed treatment subgroup, 21 of 22 patients also received trastuzumab
- The most commonly received prior HER2-directed treatment other than trastuzumab was disitamab vedotin (n=11), followed by KN026 (n=6) and pyrotinib (n=5) (**Figure 2**)

Figure 2. Prior HER2-directed treatments*



*Prior HER2-directed treatments received, other than or in addition to trastuzumab. Patients may have received more than one type of prior HER2-directed treatment; †antibody-drug conjugate; ‡bispecific antibody; ¶tyrosine kinase inhibitor
HER2, human epidermal growth factor receptor 2

Efficacy

- The median (range) duration of follow up was 14.5 (0.4–23.4) months in the prior HER2-directed treatment subgroup and 10.2 (0.4–27.9) months in the FAS[2]
- Efficacy in the prior HER2-directed treatment subgroup and FAS is shown in **Table 2**
  - In the prior HER2-directed treatment subgroup, the objective response rate (ORR) by independent central review and investigator assessment was 31.8% and 45.5%, respectively
  - In the FAS, the confirmed ORR was 28.8% by independent central review and 37.0% by investigator assessment[2]

Table 2. Efficacy

	Prior HER2-directed treatment subgroup n=22*		FAS n=73†[2]	
	ICR	INV	ICR	INV
Confirmed ORR,‡ % (n)	**31.8 (7)**	**45.5 (10)**	**28.8 (21)**	**37.0 (27)**
95% CI	13.9, 54.9	24.4, 67.8	18.8, 40.6	26.0, 49.1
mDOR,‡ months	**5.6**	**6.0**	**6.7**	**6.0**
95% CI	2.5, 7.9	2.9, 9.4	4.6, 8.8	4.4, 8.6
mPFS,‡ months	**5.9**	**5.7**	**5.7**	**5.7**
95% CI	2.7, 8.6	3.1, 7.4	4.0, 6.8	4.3, 7.0
mOS, months (95% CI)	**14.5** (6.9, 17.5)		**11.1** (7.7, 13.7)	

*The subgroup included patients in the FAS who had received prior HER2-directed treatment, other than or in addition to trastuzumab; †FAS: patients with centrally confirmed HER2+ status (IHC 3+ or IHC 2+/ISH+); ‡per RECIST 1.1
CI, confidence interval; FAS, full analysis set; HER2, human epidermal growth factor receptor 2; HER2+, HER2-positive; ICR, independent central review; IHC, immunohistochemistry; INV, investigator assessment; ISH+, in situ hybridization positive; mDOR, median duration of response; mOS, median overall survival; mPFS, median progression-free survival; ORR, objective response rate; RECIST, Response Evaluation Criteria in Solid Tumours

Safety

- The median (range) duration of exposure to T-DXd was 4.0 (0.4–17.4) months for the prior HER2-directed treatment subgroup and 3.4 (0.4–22.3) months for the safety analysis set[2] (SAS; all patients in the ITT population who received at least one dose of T-DXd)
- A summary of safety data is shown in **Table 3**; no new safety signals were identified
- In the prior HER2-directed treatment subgroup, there were no cases of adjudicated drug-related interstitial lung disease / pneumonitis
  - In the SAS, there were three cases of adjudicated drug-related interstitial lung disease / pneumonitis (two cases, Grade 1; one case, Grade 2)[2]

Table 3. Overall summary of AEs

Safety analyses, n (%)	Prior HER2-directed treatment subgroup n=22*	SAS N=95†[2]
All-causality AEs	22 (100)	95 (100)
Drug-related AEs‡	22 (100)	94 (98.9)
All-causality Grade ≥3 AEs	17 (77.3)	71 (74.7)
Drug-related Grade ≥3 AEs‡	16 (72.7)	64 (67.4)
Most common (≥20%) drug-related Grade ≥3 AEs‡§		
Neutrophil count decreased	6 (27.3)	24 (25.3)
Anemia	6 (27.3)	23 (24.2)
White blood cell count decreased	5 (22.7)	17 (17.9)
Platelet count decreased	4 (18.2)	19 (20.0)
Drug-related AEs leading to discontinuation‡	0 (0)	3 (3.2)
Drug-related AEs leading to dose reduction‡	7 (31.8)	25 (26.3)
Drug-related AEs leading to dose interruption‡	11 (50.0)	26 (27.4)
SAEs	7 (31.8)	40 (42.1)
Drug-related SAEs‡	3 (13.6)	22 (23.2)
Drug-related SAEs leading to death‡	1 (4.5)¶	2 (2.1)‖

*The subgroup included patients in the FAS who had received prior HER2-directed treatment, other than or in addition to trastuzumab; †SAS: all patients in the ITT population who received at least one dose of T-DXd; ‡drug-related AEs: events assessed by the investigator as possibly related to study treatment; §incidence of ≥20% in either the prior HER2-directed treatment subgroup or the SAS; ¶death caused by pneumonia; ‖deaths caused by pneumonia (n=1) and pulmonary embolism (n=1)
AE, adverse event; FAS, full analysis set; HER2, human epidermal growth factor receptor 2; ITT, intent-to-treat; SAE, serious adverse event; SAS, safety analysis set; T-DXd, trastuzumab deruxtecan

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Disclosures

Professor Zhi Peng reports consulting for AstraZeneca and BeiGene.

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DESTINY Gastric06