Poster 2175P

Risk of HBV reactivation in patients with past or resolved HBV or inactive chronic HBV infection treated with trastuzumab deruxtecan in DESTINY-Gastric06

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Objectives

- To evaluate hepatitis B virus (HBV) reactivation in patients with past or resolved HBV or inactive chronic HBV infection who received trastuzumab deruxtecan (T-DXd) 6.4 mg/kg monotherapy in the DESTINY-Gastric06 study
- To assess the safety of T-DXd in patients enrolled in DESTINY-Gastric06 who had past or resolved HBV or inactive chronic HBV infection

Conclusions

- Despite the short median duration of T-DXd treatment and the limited number of patients enrolled in DESTINY-Gastric06, this analysis suggests that T-DXd 6.4 mg/kg may be administered to patients with both human epidermal growth factor receptor 2–positive (HER2+) gastric or gastroesophageal junction (GEJ) adenocarcinoma and past or resolved HBV or inactive chronic HBV infection
- The safety of T-DXd in patients with past or resolved HBV or inactive chronic HBV infection was consistent with results for the overall population of the DESTINY-Gastric06 study[1]
- Overall, these data provide preliminary evidence of a low risk of HBV reactivation among patients with HER2+ gastric or GEJ adenocarcinoma treated with T-DXd

Plain language summary

Why did we perform this research?

In China, long-term infection with hepatitis B virus (HBV) is associated with an increased risk of death.[1] In people with cancer, HBV reactivation (defined as the sudden increase in the amount of HBV in the body) can occur in those receiving treatments that suppress the immune system, such as chemotherapy.[2,3] In some cases, HBV reactivation can lead to serious clinical complications.[3] As such, people with cancer who have active or previous HBV infection are often excluded from clinical studies.[4,5] DESTINY-Gastric06 evaluated trastuzumab deruxtecan (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 the human epidermal growth factor receptor 2 (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 in the study had received two or more prior anticancer treatments; results showed the benefit and safety of T-DXd in this population.[6]

How did we perform this research?

We evaluated HBV reactivation in people with past or resolved HBV (known as hepatitis B surface antigen [HBsAg]–negative) or inactive chronic HBV (known as HBsAg-positive) infection who received T-DXd in the DESTINY-Gastric06 study. The safety profile of T-DXd was also assessed in this population.

What were the findings of this research?

Among the 19 people with past or resolved HBV or inactive chronic HBV infection, no HBV reactivation with or without hepatic flare was observed during and after the study treatment period. Side effects of T-DXd were consistent with those observed in the overall population in the DESTINY-Gastric06 study.[6]

What are the implications of this research?

This analysis suggests that people with both HER2+ gastric or GEJ adenocarcinoma and past or resolved HBV or inactive chronic HBV infection can be treated with T-DXd, with a low likelihood of HBV reactivation.

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. Si J, et al. *BMJ Open*. 2019;9:e027696; 2. Loomba R, Liang TJ. *Gastroenterology*. 2017;152:1297–1309; 3. Pattullo V. *Clin Mol Hepatol*. 2016;22:219–237; 4. Cohen EB, et al. *Drug Saf*. 2024;47:321–332; 5. Mustafayev K, et al. *J Immunother Precis Oncol*. 2024;7:111–121; 6. Peng Z, et al. *EClinicalMedicine*. 2025;87:103404

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Introduction

- Gastric cancer cases in China account for over 44% of the global disease burden[2]
- In China, chronic HBV infections are a major cause of morbidity and mortality, and represent a high proportion of global HBV cases[3]
  - In patients with cancer, HBV reactivation can occur in those with chronic HBV infections who receive cytotoxic chemotherapy or immunosuppressive therapy and may lead to poor survival outcomes[4,5]
  - Patients with cancer who have active HBV infection are often excluded from clinical trials; however, recent consensus guidelines recommend broadening eligibility criteria to include patients at low risk of HBV reactivation[6,7]
- In DESTINY-Gastric06, T-DXd showed durable clinical benefit, with no new safety signals identified, in pretreated patients from China with advanced HER2+ gastric or GEJ adenocarcinoma[1]
  - Based on findings from the primary analysis of DESTINY-Gastric06,[8] T-DXd has received conditional approval in China for pretreated patients with locally advanced HER2+ gastric cancers[9]
- This analysis of DESTINY-Gastric06 evaluated HBV reactivation in patients with past or resolved HBV or inactive chronic HBV infection. The safety of T-DXd was also assessed in this subgroup

Methods

- DESTINY-Gastric06 (NCT04989816) was a Phase 2, multicenter, open-label study in which patients from China with HER2 immunohistochemistry (IHC) 3+/IHC 2+ locally advanced unresectable or metastatic gastric or GEJ adenocarcinoma with ≥2 prior treatments received T-DXd 6.4 mg/kg by intravenous infusion every 3 weeks[1,10]
- Patients with past or resolved HBV or inactive chronic HBV infection were included if they met all HBV-specific eligibility criteria

HBV-specific eligibility criteria

For patients with hepatitis B surface antigen (HBsAg)–negative or –positive status at baseline:

- HBV core total antibody (anti-HBc)–positive, HBV DNA <2000 IU/mL, and alanine aminotransferase (ALT) less than or equal to the upper limit of normal
- Normal liver architecture (absence of any liver pathology including cirrhosis, fibrosis, and liver metastases)
- Access to a local hepatitis B expert during and after the study
- No current / history of hepatitis C virus coinfection
- Started receiving prophylactic antiviral treatment at least 7 days prior to receiving T-DXd for patients with HBsAg-positive status, and for those with HBsAg-negative status and detectable HBV DNA at baseline

For patients with HBsAg-positive status only at baseline:

- Hepatitis B e-antigen (HBeAg)–negative
- No presence / family history of hepatocellular carcinoma / cirrhosis, no extrahepatic manifestations (eg arthritis or polyarteritis nodosa)

Patents were monitored for HBV reactivation throughout the treatment and follow-up periods. Those who discontinued T-DXd continued to be monitored at least every 3 months for a minimum of 12 months

HBV reactivation definition

If HBsAg-negative or -positive status at baseline:

- HBV DNA >2 log (100×) baseline or HBV DNA becomes detectable (if undetectable at baseline)
- With or without a hepatitis flare (defined as ALT increase to ≥3× baseline level and >100 U/L)

If only HBsAg-negative status at baseline:

- Reverse HBsAg seroconversion (reappearance of HBsAg positivity)

If HBV reactivation confirmed

Interrupt T-DXd and start antiviral therapy (for those not already receiving antiviral therapy)

↓

Restart T-DXd after consultation with study physician and the supervising local hepatitis B expert

↓

Continue antiviral therapy for ≥12 months after last dose of T-DXd

↓

Safety follow up until HBV reactivation resolution

Results

Patient population

- At data cutoff (February 28, 2024), 95 patients with advanced HER2 IHC 3+/IHC 2+ gastric or GEJ adenocarcinoma were included in the intent-to-treat population[1]
  - In total, 19 patients (20.0%) had past or resolved HBV (17.9%) or inactive chronic HBV infection (2.1%) at baseline (**Table 1**)

Table 1. HBV status at baseline

n (%)	N=95*[1]
HBsAg-negative, anti-HBc–positive, and HBV DNA <2000 IU/mL	17 (17.9)
HBsAg-positive, anti-HBc–positive, HBeAg-negative, and HBV DNA <2000 IU/mL	2 (2.1)

*Intent-to-treat population: all patients enrolled in the study
anti-HBc, hepatitis B virus core total antibody; HBeAg, hepatitis B e-antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus

- In the subgroup of patients with past or resolved HBV or inactive chronic HBV infection, the median age was 65.0 years; the majority of patients were male (n=14; 73.7%) (**Table 2**)
- All patients with past or resolved HBV or inactive chronic HBV infection were of Asian race

Table 2. Patient demographics

	n=19
Median (range) age, years	65 (39–75)
Age group, years, n (%)	
<50	1 (5.3)
≥50 to <75	17 (89.5)
≥75	1 (5.3)
Sex, n (%)	
Female	5 (26.3)
Male	14 (73.7)
Race, n (%)	
Asian	19 (100)

Incidence of HBV reactivation or hepatic flare

- Among patients with past or resolved HBV or inactive chronic HBV infection (n=19), no HBV reactivation with or without hepatic flare was reported during the treatment or follow-up periods

Safety and tolerability

- The median (range) T-DXd treatment duration was 2.8 (1.3–16.2) months in the HBV subgroup and 3.4 (0.4–22.3) months in the overall population[1] (**Table 3**)
  - Most patients in the HBV subgroup (52.6%) and the overall population (45.3%) received T-DXd treatment for ≤3 months

Table 3. Exposure to T-DXd

	n=19	N=95*[1]
Median (range) T-DXd treatment duration, months	2.8 (1.3–16.2)	3.4 (0.4–22.3)
Duration of T-DXd exposure, months, n (%)		
≤3	10 (52.6)	43 (45.3)
>3 to ≤6	5 (26.3)	29 (30.5)
>6	4 (21.1)	23 (24.2)
Median (range) relative dose intensity, %	99.0 (58.2–101.1)	97.7 (52.2–102.5)

*Safety analysis set: all patients who received at least one dose of T-DXd
T-DXd, trastuzumab deruxtecan

- All-causality adverse events (AEs) occurred in all 19 patients
  - The most common events (≥50%) were anemia (n=16; 84.2%), white blood cell count decreased (n=12; 63.2%), neutrophil count decreased (n=11; 57.9%), and hypoalbuminemia (n=10; 52.6%)
  - DESTINY-Gastric06 was conducted during the peak of the coronavirus disease 2019 (COVID-19) pandemic; COVID-19–associated events occurred in seven patients (36.8%)
  - Hepatobiliary disorder-associated AEs occurred in two patients (10.5%) overall (hyperbilirubinemia, n=1; cholestatic jaundice, n=1; liver injury, n=1)
- In total, 16 patients (84.2%) had all-causality Grade ≥3 AEs and ten patients (52.6%) had serious AEs
- Drug-related AEs occurred in 18 patients (94.7%) in the HBV subgroup and in 94 patients (98.9%) in the overall population[1] (**Table 4**)
  - The most common drug-related events (≥15%) in the HBV subgroup are shown in **Figure 1**
  - Grade ≥3 drug-related AEs were reported for nine of 19 patients (47.4%); the most common events (≥15%) were neutrophil count decreased (n=5; 26.3%), anemia (n=3; 15.8%), and platelet count decreased (n=3; 15.8%)

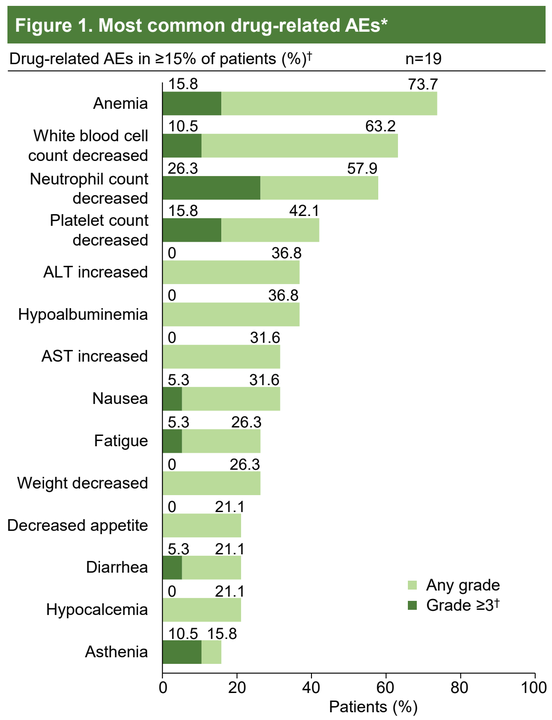
Table 4. Overall summary of drug-related AEs*

n (%)	n=19	N=95†[1]
AEs	18 (94.7)	94 (98.9)
Grade ≥3 AEs	9 (47.4)	64 (67.4)
SAEs	4 (21.1)	22 (23.2)
SAEs leading to death	1 (5.3)	2 (2.1)
AEs leading to dose interruption	5 (26.3)	26 (27.4)
AEs leading to dose reduction	5 (26.3)	25 (26.3)
AEs leading to discontinuation	1 (5.3)	3 (3.2)

Includes all AEs with an onset date on or after the date of the first T-DXd dose up to and including 47 days following the date of the last dose or until initiation of the first subsequent anticancer therapy following discontinuation of study treatment (whichever was earlier). AEs with an onset prior to dosing that worsened during this period were also included. Patients with multiple occurrences in the same category are counted once per category regardless of the number of occurrences. *Drug-related events assessed by the investigator as possibly related to treatment; †safety analysis set: all patients who received at least one dose of T-DXd
AE, adverse event; SAE, serious adverse event; T-DXd, trastuzumab deruxtecan

- In total, four patients (21.1%) had drug-related serious AEs
  - Drug-related serious AEs (all n=1 [5.3%]) included thrombocytopenia, decreased appetite, pulmonary embolism, asthenia, fatigue, neutrophil count decreased, platelet count decreased, and white blood cell count decreased
  - One patient (5.3%) died due to a drug-related serious AE of pulmonary embolism
- Adjudicated drug-related interstitial lung disease / pneumonitis occurred in one patient (5.3%; Grade 1 event) and led to discontinuation of T-DXd
- Among the two patients with HBsAg-positive, anti-HBc–positive, HBeAg-negative status, and HBV DNA <2000 IU/mL at baseline, no hepatobiliary-associated AEs occurred; both patients had all-causality Grade 3 AEs, none of which were associated with any liver injury or toxicity
  - One patient had a Grade 3 event of organic mental disorder, with no evidence of hepatic encephalopathy
  - The other patient had Grade 3 events of neutrophil count decreased and COVID-19

Figure 1. Most common drug-related AEs*



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AE, adverse event; ALT, alanine transferase; AST, aspartate aminotransferase; T-DXd, trastuzumab deruxtecan

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Disclosures

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DESTINY Gastric06