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Real-world experience with trastuzumab deruxtecan among patients with gastric cancer: 4 month-interim analysis of an all-patient post-marketing surveillance study in Japan

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Introduction

- Trastuzumab deruxtecan (T-DXd) is an anti–human epidermal growth factor receptor 2 (HER2) antibody–drug conjugate.
- Interstitial lung disease (ILD)/pneumonitis is an important identified risk included in the Japanese risk management plan for T-DXd.
- In Japan, an all-patient post-marketing surveillance (PMS) is under way to investigate the risk of ILD among patients with gastric cancer treated with T-DXd in a real-world setting.
- We present 4 month-interim results of the large-scale all-patient PMS.

Objective

- To describe patient demographics, clinical features, treatment and safety profile (particularly ILD) among gastric cancer patients treated with T-DXd in the post-marketing setting in Japan.

Methods

Study design

- 12-month observational, multicenter (510 sites), all-patient PMS study (jRCT2001200001) focused on ILD with a planned sample size of 900.

Patients

- All patients started T-DXd treatment for HER2-positive unresectable advanced and/or recurrent gastric cancer.

Registration period

- From Sep 2020 (when T-DXd was approved for this indication in Japan) to Dec 2021.

Interim analysis

- Safety data from the first 4 months for all enrolled patients.
- All potential cases of ILD (identified based on the AE terms) reported by physicians were adjudicated by an independent ILD adjudication committee.
- The incidence of ILD was calculated using the adjudicated drug-related ILD data.

Outcomes

- Baseline characteristics, drug exposure of cancer therapy, and incidence of ILD.
- Incidence of ILD was analyzed by CTCAE grade, baseline characteristics, and time to onset.

Conclusions

- This interim analysis was conducted using data during the first 4 months of initial T-DXd treatment, among 1074 patients with gastric cancer in Japan.
- The median initial dose of T-DXd was 6.4 mg/kg (range: 3.1–6.4), and the median duration of T-DXd treatment was 4.0 months (range: 0.7–4.0).
- During the first 4 months from the initial treatment, the incidence of all-grade, grade ≥3, and grade 5 adjudicated drug-related ILD were 5.2% (n=56), 1.5% (n=16), and 0.7% (n=7), respectively.
- A final analysis, including ILD incidence data from the ongoing PMS, will provide further useful information and is planned for the future.

Limitations

- The analysis was conducted using data from only the first 4 months of the initial T-DXd treatment; the overall study period is 12 months.
- This was an observational study with no comparator group. However, it included all patients who received T-DXd during a specified time period and sufficiently represents the real-world patient experience in Japan.
- Because the surveillance is being conducted in Japan, the findings must be interpreted with caution when generalizing to other populations and countries (i.e. limited generalizability).

Disclosure

This PMS is sponsored by Daiichi Sankyo Co., Ltd. In March 2019, AstraZeneca K.K. entered into a global development and commercialization collaboration agreement with Daiichi Sankyo Co., Ltd. for Trastuzumab Deruxtecan (T-DXd; DS-8201).

Results

1. Patient disposition

Case report forms collected N=1129

Excluded n=55
- Could not be evaluated by a physician for safety * n=3
- History of prior treatment with T-DXd n=49
- Site did not agree to provide data for publication n=3

* Patients who had not visited the hospital since their first visit

Safety analysis set N=1074

2. Demographic and clinical characteristics

	Safety analysis set N=1074
Sex	
Male	830 (77.3)
Age (years)	
Median (range)	70.0 (23–100)
≥65	770 (71.7)
BMI (kg/m^2)	
Median (range)	20.4 (13.2–36.8)
ECOG performance status	
0	462 (43.0)
1	504 (46.9)
2	89 (8.3)
3	17 (1.6)
4	2 (0.2)
Primary lesion [a)]	
Stomach	877 (81.7)
Esophagogastric junction	191 (17.8)
Other	13 (1.2)
Laurén classification	
Intestinal type	495 (46.1)
Diffuse type	204 (19.0)
Mixed type	99 (9.2)
Indeterminate type	13 (1.2)
Unknown/missing	263 (24.5)
Site(s) of metastasis or recurrence [a)]	
Lymph node	714 (66.5)
Lung/pleural	232 (21.6)
Lymphangitis carcinomatosis	11 (1.0)
Liver	515 (48.0)
Brain	23 (2.1)
Peritoneum	352 (32.8)
Bone	80 (7.4)
Other	87 (8.1)
Time from gastric cancer diagnosis (months)	
<12	194 (18.1)
≥12 to <48	726 (67.6)
≥48	143 (13.3)
Unknown/missing	11 (1.0)
SpO_2 (%)	
<95	17 (1.6)
≥95	842 (78.4)
Not implemented	207 (19.3)
Unknown/missing	8 (0.7)
Renal function (CLCr mL/min)	
Normal: ≥90	187 (17.4)
Mild: ≥60 to <90	430 (40.0)
Moderate: ≥30 to <60	406 (37.8)
Severe: ≥15 to <30	32 (3.0)
End stage: <15	3 (0.3)
Unknown/missing	16 (1.5)

	Safety analysis set N=1074	
	Prior disease	Concomitant disease
Respiratory disease	58 (5.4)	89 (8.3)
ILD	16 (1.5)	2 (0.2)
Radiation pneumonitis	3 (0.3)	2 (0.2)
Pulmonary fibrosis	0 (0.0)	2 (0.2)
COPD or emphysema	12 (1.1)	61 (5.7)
Asthma	11 (1.0)	7 (0.7)
Other	17 (1.6)	17 (1.6)

Data are reported as n (%).
a) Multiple counts.

3. Prior cancer therapy for gastric cancer

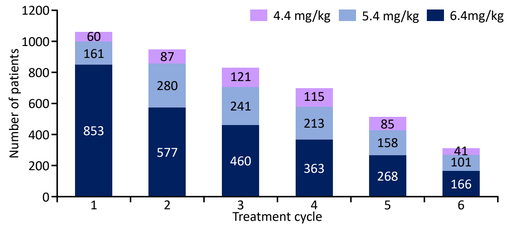
	Safety analysis set N=1074
Number of regimens	
0 (None)	0 (0.0)
1	22 (2.0)
2	470 (43.8)
3	282 (26.3)
≥4	299 (27.8)
Unknown/missing	1 (0.1)
Prior anti-HER2 therapies	
No	38 (3.5)
Yes	1035 (96.4)
Unknown/missing	1 (0.1)
Prior molecularly targeted therapies	
No	184 (17.1)
Yes	889 (82.8)
Unknown/missing	1 (0.1)
Prior immune checkpoint Inhibitors	
No	610 (56.8)
Yes	463 (43.1)
Unknown/missing	1 (0.1)
Prior chest radiation therapy	
No	1015 (94.5)
Yes	57 (5.3)
Unknown/missing	2 (0.2)

Data are n (%).

4. T-DXd Treatment status during the first 4 months

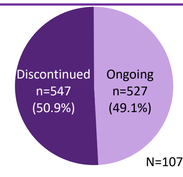
T-DXd dose (mg/kg)	Safety analysis set (N=1074) [d)] Initial dose, n (%)
4.4 [a)]	60 (5.6)
5.4 [b)]	161 (15.0)
6.4 [c)]	853 (79.4)
Median (range):	6.4 (3.1-6.4)

a) ≤4.4, b) >4.4 to ≤5.4, c) >5.4 to ≤6.4,
d) There was one case where the physician incorrectly entered ">250 mg/kg" on the case report form at cycles 3 and 4. The correct value will be reflected in the final analysis.



5. T-DXd treatment status at 4 months

Median treatment duration (months) : 4.0 (0.7–4.0)



N=1074

Reason for treatment discontinuation [a)]	Discontinued (n=547)
Progression of primary disease (including death)	390 (71.3)
Adverse Events (other than ILD)	76 (13.9)
ILD (reported by treating physician)	56 (10.2)
Untraceable (including site transfer)	13 (2.4)
Refusal or request of the patient	32 (5.9)
Other	8 (1.5)

Data are reported as n (%) a) Multiple counts.

6. Incidence of adjudicated drug-related ILD during the first 4 months

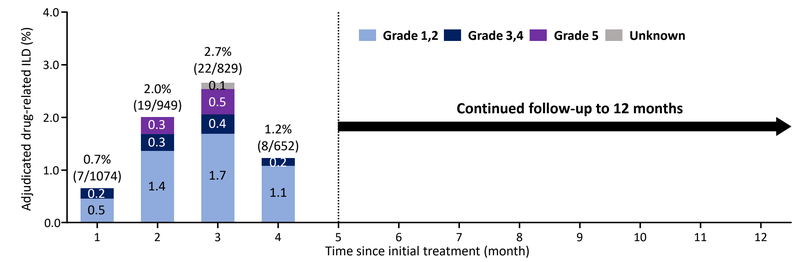
- **Adjudicated drug-related ILD n=56 (5.2%)***

***Note : The presented incidence of adjudicated drug-related ILD at 4 months may change in the final analysis (with longer observation period of 12 months.)**

- Adjudicated drug-related ILD was defined as an event that has been adjudicated by the independent ILD adjudication committee to be a case of ILD and is related to T-DXd treatment.
- The adjudication committee retrospectively reviewed all potential ILD reported by treating physicians (there was no pending case with potential ILD for adjudication).

Safety analysis set N	CTCAE grade at worst: Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)	Unknown n (%)	Total n (%)
1074	15 (1.4)	24 (2.2)	8 (0.7)	1 (0.1)	7 (0.7)	1 (0.1)	56 (5.2)

7. Adjudicated drug-related ILD incidence by time since treatment initiation



8. Treatment Status for adjudicated drug-related ILD and outcome

T-DXd treatment status	Adjudicated drug-related ILD (n=56)
Maintained on the same dose	0 (0.0)
Reduced	0 (0.0)
Discontinued	54 (96.4)
Interrupted	1 (1.8)
Onset after end of treatment	1 (1.8)

Data are reported as n (%).

Outcome	Adjudicated drug-related ILD (n=56)
Recovered	27 (48.2)
Recovering	8 (14.3)
Recovered with sequelae	2 (3.6)
Not recovered	9 (16.1)
Fatal	7 (12.5)
Unknown/missing	3 (5.4)

*Worst grade 3 (8 patients): Recovered (2), Recovering (4), Recovered with sequelae (1), Not recovered (1)
Worst grade 4 (1 patient): Recovered with sequelae (1)

9. Incidence of adjudicated drug-related ILD stratified by potential risk factors for ILD

Potential risk factor [1)]	N	Adjudicated drug-related ILD: n	% [95% CI]
All	1074	56	5.2 [4.0, 6.7]
Age (years)			
<65	304	14	4.6 [2.5, 7.6]
≥65	770	42	5.5 [4.0, 7.3]
Time from gastric cancer diagnosis (months)			
<48	920	46	5.0 [3.7, 6.6]
≥48	143	10	7.0 [3.4, 12.5]
Prior and/or current lung comorbidities			
ILD/radiation pneumonitis			
No	1051	52	4.9 [3.7, 6.4]
Yes	23	4	17.4 [5.0, 38.8]
ILD/radiation pneumonitis/COPD/emphysema/Asthma			
No	962	47	4.9 [3.6, 6.4]
Yes	112	9	8.0 [3.7, 14.7]
Baseline SpO_2 (%)			
<95	17	0	0.0 [0.0, 19.5]
≥95	842	46	5.5 [4.0, 7.2]
Baseline renal function (mL/min)			
Normal (CLCr ≥90)	187	11	5.9 [3.0, 10.3]
Mild (CLCr ≥60 to <90)	430	24	5.6 [3.6, 8.2]
Moderate/Severe (CLCr <60)	441	21	4.8 [3.0, 7.2]

1) Powell CA, et al.: ESMO Open7: 100554, 2022
95% CI, 95% confidence interval; CLCr, creatinine clearance calculated using the Cockcroft–Gault equation

A risk factor analysis for adjudicated drug-related ILD will be performed in the final analysis