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Real-world experience with trastuzumab deruxtecan in patients with breast cancer: 6 month-interim analysis of an all-patient postmarketing surveillance in Japan

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Objectives

- To describe patient demographics, clinical features, treatment and safety profile (particularly ILD/p [interstitial lung disease/pneumonitis]) among breast cancer patients treated with T-DXd in a real-world setting in Japan.

Conclusions

- During the first 6 months from the initial treatment, the incidence of any grade, grade ≥3, and grade 5 adjudicated drug-related ILD/p were 8.2% (n=99), 1.7% (n=20), and 0.4% (n=5), respectively.
- A final analysis, including ILD/p incidence data from the ongoing PMS, will provide further useful information and is planned for the future.

Limitations

- This interim analysis is limited in that it only includes data from the first 6 months of follow up from treatment initiation with T-DXd.
- This was a single-arm surveillance with no control group. However, it included all patients who received T-DXd during a specified time period and provides sufficient representation of the real-world patient experience.
- Because the surveillance is being conducted in Japan, the findings must be interpreted with caution when generalizing to other populations.

Introduction

- Trastuzumab deruxtecan (T-DXd) is an anti–human epidermal growth factor receptor 2 (HER2) antibody–drug conjugate.
- T-DXd has shown great efficacy against HER2-positive breast cancer, and received regulatory approval in Japan in March 2020.
- In Japan, all-patient postmarketing surveillance (PMS) is underway to evaluate the risk of ILD/p in patients with breast cancer treated with T-DXd.
- Because of the limited generalizability of results from clinical trials, there is a need for more information about ILD/p in a real-world setting.

Methods

Study design

- This is an 18-month observational, multicenter, all-patient PMS (jRCT1080225197) with a planned sample size of 1500.
- All patients treated with T-DXd for recurrent/advanced HER2-positive breast cancer were enrolled.

Patients

- Patients who started T-DXd treatment between May 2020 (the launch date of T-DXd) and May 2021 were included in the interim analysis to ensure at least 6-month observation period from treatment initiation.
- This interim analysis is based on safety data from the first 6 months of treatment of 1204 patients.

Data collection

- Baseline characteristics and incidence of ILD/p.
- All potential cases of ILD/p (identified based on the AE terms) reported by physicians were adjudicated by an independent ILD adjudication committee.
- Incidence of ILD/p was determined from data for adjudicated drug-related ILD/p.

References

1) Powell CA, et al.: *ESMO Open* 7: 100554, 2022

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=1231

Excluded n=27

Did not receive treatment with T-DXd	n=1
Duplicate registration at the same site	n=1
Could not be evaluated for safety by a physician	n=1*
Off-label use	n=8
History of prior treatment with T-DXd	n=12
Site did not agree to provide data for publication	n=4

*The patient has not visited the hospital since the first visit

Safety analysis set N=1204

2. Baseline characteristics

	Safety analysis set (N=1204)	
Sex		
Female	1198	(99.5)
Age (years)		
Median (range)	60.0	(27–87)
<65	786	(65.3)
BMI (kg/m^2)		
Median (range)	21.3	(12.9–39.8)
ECOG performance status		
0	614	(51.0)
1	485	(40.3)
2	81	(6.7)
3	23	(1.9)
4	1	(0.1)
Site(s) of metastasis or recurrence*		
Local/lymph node	735	(61.0)
Lung/pleural	640	(53.2)
Liver	428	(35.5)
Brain	262	(21.8)
Meninges/spinal fluid	9	(0.7)
Bone	523	(43.4)
Other	161	(13.4)
SpO_2 (%)		
<95	35	(2.9)
≥95	902	(74.9)
Not implemented	254	(21.1)
Unknown/missing	13	(1.1)
Time from recurrent or unresectable breast cancer diagnosis (months)		
<12	96	(8.0)
≥12 to <48	578	(48.0)
≥48	514	(42.7)
Unknown/missing	16	(1.3)
Renal function (CLCr [mL/min])		
Normal: ≥90	434	(36.0)
Mild: ≥60 to <90	531	(44.1)
Moderate: ≥30 to <60	209	(17.4)
Severe: ≥15 to <30	8	(0.7)
End-stage: <15	4	(0.3)
Unknown/missing	18	(1.5)

	Prior disease		Concomitant disease	
Respiratory disease	77	(6.4)	67	(5.6)
ILD/p	18	(1.5)	10	(0.8)
Radiation pneumonitis	33	(2.7)	23	(1.9)
COPD or emphysema	1	(0.1)	4	(0.3)
Asthma	17	(1.4)	14	(1.2)
Other respiratory disease	10	(0.8)	20	(1.7)

Data are n (%), * Multiple counts

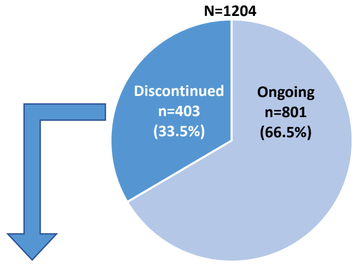
3. Prior cancer therapy for unresectable or recurrent breast cancer

	Safety analysis set (N=1204)	
No. of regimens		
0 (None)	3	(0.2)
1	30	(2.5)
2	252	(20.9)
3	247	(20.5)
≥4	660	(54.8)
Unknown/missing	12	(1.0)
Anti-HER2 therapies		
No	5	(0.4)
Yes	1194	(99.2)
Unknown/missing	5	(0.4)
Molecularly targeted therapies		
No	1027	(85.3)
Yes	172	(14.3)
Unknown/missing	5	(0.4)
Immune checkpoint inhibitors		
No	1198	(99.5)
Yes	1	(0.1)
Unknown/missing	5	(0.4)
Prior chest radiation therapy		
No	628	(52.2)
Yes	559	(46.4)
Unknown/missing	17	(1.4)

Data are n (%), * Multiple counts

4. T-DXd treatment status at 6 months

T-DXd treatment duration (months): Median 5.98 (0.7-6.0)



Reason for treatment discontinuation*	Discontinued (n=403)	
Progression of primary disease (including death)	232	(57.6)
Adverse events (other than ILD/p)	36	(8.9)
ILD/p (reported by treating physician)	97	(24.1)
Untraceable (including site transfer)	6	(1.5)
Refusal or request of the patient	32	(7.9)
Other	14	(3.5)

Data are n (%), * Multiple counts

	Safety analysis set (N=1204)	
Initial dose (mg/kg)		
3.2 [a)]	19	(1.6)
4.4 [b)]	122	(10.1)
5.4 [c)]	1063	(88.3)
Average dose (mg/kg) *		
3.2 [a)]	20	(1.7)
4.4 [b)]	147	(12.2)
5.4 [c)]	1036	(86.0)

Data are n (%); a) ≤3.2; b) >3.2 to ≤4.4; c) >4.4 to ≤5.4
* There was one patient in whom the physician incorrectly entered "210mg/kg" on the case report form at Cycle 7 of treatment. It will be the correct value in the final analysis.

5. Incidence of adjudicated drug-related ILD/p during the first 6 months

Adjudicated drug-related ILD/p n=99 (8.2%)*

*Note:
The presented incidence of adjudicated drug-related ILD/p at 6 months will change in the final analysis with observation period of 18 months.

- An adjudicated drug-related ILD/p is defined as an event that has been adjudicated as a case of ILD/p by the independent ILD adjudication committee and is related to T-DXd.
- The adjudication committee retrospectively reviews all potential ILD/p which is reported by treating physician using imaging and case report forms.

-Stratification by the CTCAE Grade at onset / worst-

		All	Worst grade 1	2	3	4	5
Grade at onset	**All**	99	44	35	14	1	5
	1	60	44	13	3	0	0
	2	26	–	22	3	0	1
	3	12	–	–	8	0	4
	4	1	–	–	–	1	0
	5	0	–	–	–	–	0

Data are n

-Treatment Status for adjudicated drug-related ILD/p, and outcome-

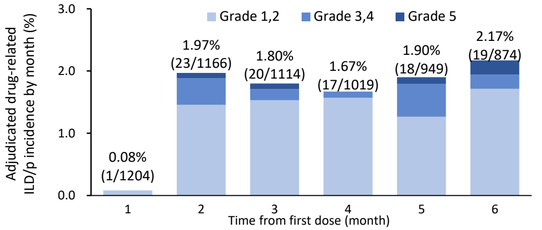
T-DXd treatment status	n=99
Continued on the same dose	2
Reduced	0
Discontinued	96
Suspended	0
Onset after end of treatment	1
Unknown/missing	0

Data are n

Outcome	n=99
Recovered	42
Recovering	29
Recovered with sequelae	8
Not recovered	13
Fatal	5
Unknown/missing	2

Data are n

6. Incidence of adjudicated drug-related ILD/p stratified by month



7. Incidence of adjudicated drug-related ILD/p stratified by baseline characteristics identified as potential risk factors for adjudicated drug-related ILD/p

Potential risk factor [1)]	Patients N	ILD/p cases n	% (95% CI)
All	1204	99	8.2 (6.7–9.9)
Age (years)			
<65	786	54	6.9 (5.2–8.9)
≥65	418	45	10.8 (8.0–14.1)
Prior and/or current lung comorbidities*			
No	1097	87	7.9 (6.4–9.7)
Yes	107	12	11.2 (5.9–18.8)
Baseline renal function (CLCr[mL/min])			
Normal (≥90)	434	28	6.5 (4.3–9.2)
Mild decrease (60 ≤ to <90)	531	45	8.5 (6.2–11.2)
Moderate/severe decrease (<60)	221	25	11.3 (7.5–16.2)
Time since disease diagnosis			
<48 months	674	55	8.2 (6.2–10.5)
≥48 months	514	43	8.4 (6.1–11.1)
Baseline SpO_2			
<95%	35	3	8.6 (1.8–23.1)
≥95%	902	80	8.9 (7.1–10.9)

* Including ILD/p, pulmonary fibrosis, radiation pneumonitis, chronic obstructive pulmonary disease (COPD), emphysema, and asthma. 95% CI, 95% confidence interval; CLCr, creatinine clearance calculated using the Cockcroft–Gault equation

Risk factor analysis for adjudicated drug-related ILD/p will be performed at final analysis