Poster ID: 138eP

ESMO Asia, December 5-7, 2025, Singapore

Preliminary Analysis for Baseline Characteristics and Treatment Patterns of Trastuzumab Deruxtecan in Chinese Patients with HER2-positive and HER2-low Breast Cancer: First Interim Analysis of REFRESH Study

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Objective

- This preliminary analysis of REFRESH study was aimed to provide preliminary data of trastuzumab deruxtecan (T-DXd) treatment patterns and baseline characteristics in 307 Chinese patients with HER2-positive (HER2+) or HER2-low metastatic breast cancer (mBC). Demographic, clinical characteristics and T-DXd treatment patterns were described among eligible patients with HER2+ or HER2-low unresectable or metastatic BC who were newly initiating T-DXd in a real-world setting.

Conclusions

- T-DXd is emerging as a practice-changing therapy in China, now being widely used in treatment for HER2+ mBC and HR+, HER2-low mBC.

Plain language summary

Why did we perform this research?

- T-DXd has been approved in China for unresectable or metastatic pre-treated HER2+ and HER2-low BC.
- However, the real-word use and outcomes of T-DXd in Chinese patients was not well reported. This real-world study will help us to understand utilization and clinical outcomes of T-DXd.

How did we perform this research?

- This ongoing study began in January 2024 and enrolled patients diagnosed with unresectable or metastatic BC who received T-DXd in routine clinical practice.
- Throughout the study, information was collected on treatment duration, treatment patterns, patient characteristics, adverse events, and how those adverse events were managed.
- Current data reports the utilization of T-DXd in Chinese patient with HER2+ or HER2-low BC.

What were the findings of this research?

- T-DXd was used in patients with HER2+ or HER2-low BC regardless of the number of metastatic organs involved, visceral metastases status, or the presence of brain metastases.
- For HER2+ patients, T-DXd was prescribed mostly in second-line or third-line. T-DXd was used as first line therapy in patients who experience recurrence during or after adjuvant therapy
- For HER2-low patients, regardless of HR status, T-DXd was mostly used in patients who were previously treated with ≥2 lines of therapy. Over 25% patients were chemotherapy-naive in the metastatic setting.

What are the implications of this research?

- This study helps us better understand how T-DXd is used in real-world settings and the characteristics of Chinese patients who received it. T-DXd is becoming an important treatment option and is now being used in earlier lines of advanced HER2+ or HER2-low BC.

Where can I access more information?

- This study is expected to end on March 1, 2028. Information about the medicine being used in this study and the people who could participate can be found here: https://clinicaltrials.gov/study/NCT06210776.

This study was sponsored by Daiichi Sankyo. 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 Asia Congress 2025 by Xiang Huang. Corresponding author is Yongmei Yin, email address: ymyin@njmu.edu.cn.

Introduction

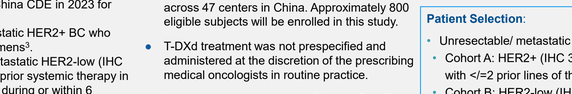
- Breast cancer (BC), the second most prevalent malignancy among Chinese women, has approximately 357,200 new cases annually[1,2].
- Trastuzumab deruxtecan (T-DXd) has been approved by China CDE in 2023 for these BC indications:
  - HER2+ mBC: Adult patients with unresectable or metastatic HER2+ BC who have received one or more prior anti-HER2-based regimens[3].
  - HER2-low mBC: adult patients with unresectable or metastatic HER2-low (IHC 1+ or IHC 2+/ISH-) breast cancer who have received a prior systemic therapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy[3].
- T-DXd is reshaping the treatment landscape for advanced BC in China. However, large scale real-world data of T-DXd utilization and outcomes in Chinese BC patients remain limited.

Methods

- REFRESH (NCT06210776) was a prospective, multi-center, two-cohort, observational study across 47 centers in China. Approximately 800 eligible subjects will be enrolled in this study.
- T-DXd treatment was not prespecified and administered at the discretion of the prescribing medical oncologists in routine practice.
- Patients were prospectively followed from T-DXd treatment initiation until death, voluntary discontinuation of study participation, loss to follow-up, or end of study.

Figure 1. Study design

Patient Selection:
- Unresectable/ metastatic BC
- Cohort A: HER2+ (IHC 3+ or IHC 2+/ISH+) with </=2 prior lines of therapy
- Cohort B: HER2-low (IHC 1+ or IHC 2+/ISH-) with </= 2 prior lines of CT
- Decision to receive T-DXd before enrollment



Sample Size: Approx. N=800, **47** sites

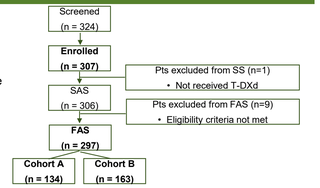
Outcomes:
- Primary outcomes: real-world time to next treatment (rwTTNT)
- Secondary outcomes: T-DXd treatment patterns, T-DXd dosing, Duration of Treatment (DOT) and dose amendment, safety events of interest (SEI) and management, real-world time to treatment discontinuation (rwTTD)

Interim Analysis 1

- This first interim analysis was planned after about 300 patients enrolled, to report baseline characteristics and treatment patterns.
- Data cut-off date: Feb 07, 2025

Results

Figure 2. Patient Disposition



- Between January 15, 2024, and February 7, 2025, 307 patients were enrolled, 297 patients (134 HER2+, 163 HER2-low) were included in full analysis set.

Table 1. Demographics and Baseline Characteristics

	HER2+ Cohort (N=134)	HER2-low Cohort (N=163)	Total (N=297)
Age, median (range), years	54 (32-88)	53 (31-77)	53 (31-88)
Sex, n (%)			
Male	0	1 (0.6)	1 (0.3)
Female	134 (100)	162 (99.4)	296 (99.7)
Region, n (%)			
Asia	134 (100)	163 (100)	297 (100)
Race, n (%)			
Asian	134 (100)	163 (100)	297 (100)
Weight, median (range), kg	57.9 (35.5-87.0)	59.0 (38.6-109.8)	58.0 (35.5-109.8)
ECOG PS, n (%)			
0	25 (18.7)	28 (17.2)	53 (17.8)
1	79 (59.0)	106 (65.0)	185 (62.3)
2	13 (9.7)	7 (4.3)	20 (6.7)
3	0	1 (0.6)	1 (0.3)
4	0	1 (0.6)	1 (0.3)
Unknown	17 (12.7)	20 (12.3)	37 (12.5)
HER2 status, n (%)			
IHC 1+	NA	74 (45.4)	74 (24.9)
IHC 2+/ISH-	NA	89 (54.6)	89 (30.0)
IHC 2+/ISH+	35 (26.1)	NA	35 (11.8)
IHC 3+	99 (73.9)	NA	99 (33.3)
HR status, n (%)			
Positive	63 (47.0)	137 (84.0)	200 (67.3)
Negative	70 (52.2)	26 (16.0)	96 (32.3)
Unknown	1 (0.7)	0	1 (0.3)
Disease history at initial diagnosis, n (%)			
De novo mBC	42 (31.3)	36 (22.1)	78 (26.3)
Recurrent mBC	92 (68.7)	127 (77.9)	219 (73.7)

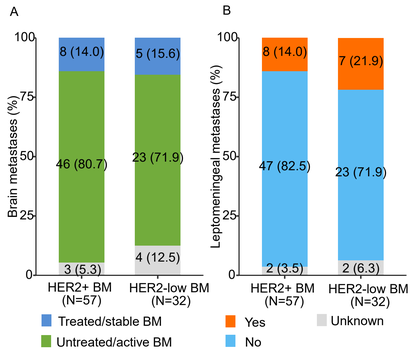
Baseline Characteristics of Patients Who Received T-DXd

- Median age was 53 years (range, 32-88). ECOG PS of 0, 1, 2-4 were recorded in 17.8%, 62.3%, 7.3% of all patients.
- At baseline, 236 patients (79.5%) were diagnosed with visceral metastases, and 125 patients (42.1%) had metastases involving ≥3 organs.
- Brain metastases (BM) were identified in 42.5% of HER2+ patients and 19.6% of HER2-low patients, respectively.
- Among BM patients, 80.7% of HER2+ and 71.9% of HER2-low patients had untreated/active BM, and 14.0% of HER2+ and 21.9% of HER2-low patients had leptomeningeal metastases, respectively.

Table 1. continued

	HER2+ Cohort (N=134)	HER2-low Cohort (N=163)	Total (N=297)
Number of metastatic organs, n (%)			
<3	81 (60.4)	91 (55.8)	172 (57.9)
≥3	53 (39.6)	72 (44.2)	125 (42.1)
Visceral metastases, n (%)			
Yes	103 (76.9)	133 (81.6)	236 (79.5)
No	31 (23.1)	30 (18.4)	61 (20.5)
Baseline brain metastases, n (%)			
Yes	57 (42.5)	32 (19.6)	89 (30.0)
No	77 (57.5)	131 (80.4)	208 (70.0)

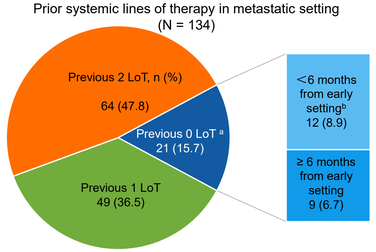
Figure 3. Type of Brain Metastasis



T-DXd Treatment patterns

- **HER2+ cohort:**
  - 15.7%, 36.5%, 47.8% patients previously received 0, 1, 2 LoT in metastatic setting.
  - 95.5%, 72.4%, 67.2% patients previously received trastuzumab, pertuzumab, anti-HER2 TKI, respectively.
- **HER2-low cohort:**
  - 66.3% patients received >/=2 prior lines of treatment, 25.8% patients were chemo-naïve in metastatic setting.
  - HR+/HER2-low: T-DXd was initiated in 25.8% HR+ patients who were chemo-naïve in metastatic setting, and in 48.9% patients following 1 line of chemotherapy. 89.6% of HR+ patients previously received CDK4/6i in metastatic setting.
  - HR-/HER2-low: T-DXd was initiated following 1-2 lines of chemotherapy in more than 70% patients.

Figure 4. T-DXd Treatment Patterns in HER2+ Cohort



[a] All patients were recurrent from early breast cancer and initiated T-DXd based on China label. [b] patients progressed during neoadjuvant/adjuvant treatment or within 6 months after completion of adjuvant treatment

Table 3. T-DXd Treatment Patterns in HER2-low Cohort

	HR+ (N=137)	HR- (N=26)	Total (N=163)
Prior systemic lines of therapy in metastatic setting, n (%)			
0	3 (2.2)	3 (11.5)	6 (3.7)
1	43 (31.4)	6 (23.1)	49 (30.1)
≥2	91 (66.4)	17 (65.4)	108 (66.3)
Prior lines of chemotherapy in metastatic setting, n (%)			
0	39 (28.5)	3 (11.5)	42 (25.8)
1	67 (48.9)	12 (46.2)	79 (48.5)
2	31 (22.6)	11 (42.3)	42 (25.8)

Table 2. Prior Therapies in HER2+ Cohort

Any previous systemic therapy, n (%)	N=134
Trastuzumab	128 (95.5)
Pertuzumab	97 (72.4)
anti-HER2 TKI [c]	90 (67.2)
anti-HER2 ADC [d]	10 (7.5)

Previous systemic therapy in metastatic setting, n (%)	N=113
Trastuzumab	80 (70.8)
Pertuzumab	56 (49.6)
anti-HER2 TKI [c]	79 (69.9)
anti-HER2 ADC [d]	7 (6.2)

[c] Anti-HER2 TKI included pyrotinib, neratinib, lapatinib. [d] Anti-HER2 ADC included Trastuzumab Emtansine, Disitamab Vedotin, BB-1701, DP303c, MRG002 for both data set.

Table 4. Prior Therapies in HER2-low Cohort

Any prior therapy, n (%)	HR+ (N=137)	HR- (N=26)	Total (N=163)
Endocrine therapy	129 (94.2)	13 (50.0)	142 (87.1)
CDK4/6i	123 (89.8)	10 (38.5)	133 (81.6)
Anthracycline	88 (64.2)	22 (84.6)	110 (67.5)
Taxane	111 (81.0)	23 (88.5)	134 (82.2)
Capecitabine	42 (31.3)	14 (60.9)	56 (35.7)
Platinum-based	25 (18.2)	6 (23.1)	31 (19.0)

Prior therapy in metastatic setting, n (%)	HR+ (N=134)	HR- (N=23)	Total (N=157)
Endocrine therapy	120 (89.6)	8 (34.8)	128 (81.5)
CDK4/6i	120 (89.6)	8 (34.8)	128 (78.5)
Taxane	68 (50.7)	9 (39.1)	77 (49.0)
Capecitabine	39 (29.1)	10 (43.5)	49 (31.2)
Anthracycline	22 (16.4)	3 (13.0)	25 (15.9)
Platinum-based	18 (13.4)	5 (21.7)	23 (14.6)

Abbreviations

BC, breast cancer; T-DXd, trastuzumab deruxtecan; HER2+, HER2-positive; mBC, metastatic breast cancer; LoT, lines of therapy; CDE, center for drug evaluation; ECOG PS, eastern cooperative oncology group performance status; BM, brain metastases; HR+, hormone receptor-positive; HR−, hormone receptor-negative.

Acknowledgments

Medical writing support, under the direction of the authors, was provided by Lishun Zhang, PhD, of Daiichi-Sankyo China Holding, Co. LTD., in accordance with Good Practice guidelines (http://www.ismpp.org/gpp-2022)

Disclosures

All authors declare no competing interests.

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