Poster PS5-08-14

DESTINY-Breast Respond HER2-low Europe: Description of first enrolled patients in the non-interventional study of T-DXd in HER2-low metastatic breast cancer

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Objective

- To report an initial snapshot of baseline characteristics and prior treatment lines from the ongoing DESTINY-Breast Respond HER2-low EUROPE study, up to April 15, 2025

Conclusions

- DESTINY-Breast Respond HER2-low represents a more diverse range of patients with HER2-low mBC treated with T-DXd versus those from the pivotal DESTINY-Breast04 trial; median age, proportion of older patients and overall health status differ
- The median number of prior treatment lines (three) in the real world was shown to be comparable to the DESTINY-Breast04 trial
- The ongoing, non-interventional DESTINY-Breast Respond HER2-low Europe study will add valuable insights on real-world effectiveness, treatment management, safety, and quality of life for patients with HER2-low mBC treated with T-DXd in the European region

Plain language summary

Why did we perform this research?

- Trastuzumab deruxtecan (T-DXd), a treatment for metastatic breast cancer that targets the HER2 protein, has been assessed in several clinical trials. The DESTINY-Breast04 trial showed that T-DXd is effective for breast cancers that have low levels of HER2 expression
- Prospective data for T-DXd in the HER2-low population is currently limited to clinical trials (e.g., DESTINY-Breast04 and -06). The current study, DESTINY-Breast Respond HER2-low Europe, aims to look at the effectiveness and safety of T-DXd in real-world practice

How did we perform this research?

- The study includes patients receiving T-DXd for HER2-low metastatic breast cancer, as well as patients receiving traditional chemotherapy to put the findings into context. Data will be collected until their disease progresses

What were the findings of this research?

- The data indicate that patients with HER2-low metastatic breast cancer treated with T-DXd in the real world are more diverse than those in the DESTINY-Breast04 trial

What are the implications of this research?

- This study will be the largest to date examining the use of T-DXd in the European region, providing valuable insight into the effectiveness and safety of this treatment as well as how it is used and how it impacts the lives of patients

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 SABCS 2025 by Valentina Guarneri. Corresponding author email address: valentina.guarneri@unipd.it.

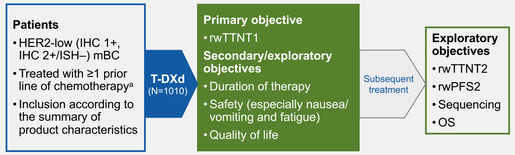
Introduction

- The DESTINY-Breast04 trial showed significantly longer PFS and OS in patients with HER2-low (IHC 1+ or IHC 2+/ISH–) mBC treated with T-DXd versus physician's choice of chemotherapy after one or two lines of chemotherapy[1]
- As such, HER2 is no longer seen as a binary classification but as a spectrum, including HER2-low as a targetable biomarker
- The ongoing, non-interventional DESTINY-Breast Respond HER2-low Europe study will evaluate real-world effectiveness and safety of T-DXd in patients with HER2-low mBC
- We report an initial snapshot of baseline characteristics and prior treatment lines

Methods

- DESTINY-Breast Respond HER2-low Europe (NCT05945732) is a multicenter, observational, prospective, non-interventional study, including patients from 206 sites across 10 European countries
  - Patients may also be included retrospectively in France, as some patients already receive T-DXd via an early access program
- The study design (**Figure 1**) has been previously published.[2] Briefly, the study is enrolling patients with HER2-low mBC who received ≥1 prior line of chemotherapy in the metastatic setting and are being treated with T-DXd or standard chemotherapy (N=1010)
- The primary objective is effectiveness of T-DXd based on rwTTNT
- Secondary objectives include:
  - Assessment of treatment patterns, baseline demographics, and clinical characteristics
  - Assessment of the safety and tolerability of T-DXd via safety events of interest and patient-reported outcomes
  - Assessment of real-world time to treatment discontinuation
  - Detailed assessment of geriatric status, nausea/vomiting, and quality of life via questionnaires
- Data cutoff for this initial snapshot analysis of baseline characteristics was April 15, 2025

Figure 1. DESTINY-Breast Respond HER2-low Europe study design



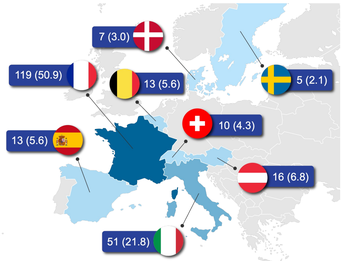
[a]Patients who have received prior chemotherapy in the metastatic setting, or patients who have developed disease recurrence during or within 6 months of completing adjuvant chemotherapy.

Results

Enrolled patients in the snapshot analysis, up to April 15, 2025

- A total of 234 patients have been enrolled from eight European countries (**Figure 2**)

Figure 2. Number (and percentage) of patients in each country included in the snapshot analysis



Sites in Portugal and Norway will also be included in the study, but were not recruiting at time of the snapshot analysis

Baseline characteristics

- The enrolled population to date includes a large proportion of older patients, patients with varying activity levels and some patients with comorbidities of interest (**Table 1**)

Biopsy and disease characteristics

- A range of different biopsy and disease characteristics are present in the enrolled population to date (**Table 2**)

Table 1. Baseline characteristics

Baseline characteristics	Total (n=234)
Median age, years (range)	**62.0 (33–89)**
<65 years, n (%)	140 (59.8)
65–74 years, n (%)	59 (25.2)
≥75 years, n (%)	35 (15.0)
ECOG PS, n (%)[a]	
0	**98 (41.9)**
1	75 (32.1)
2	13 (5.6)
3	3 (1.3)
Brain metastases, n (%)[b]	**20 (8.5)**
Stable	10 (4.3)
Active	8 (3.4)
Lung-related comorbidities, n (%)	
No	229 (97.9)
Yes	**5 (2.1)**

[a]ECOG PS for 45 patients was missing. [b]Status for two patients was unknown or not recorded.

Table 2. Biopsy and disease characteristics

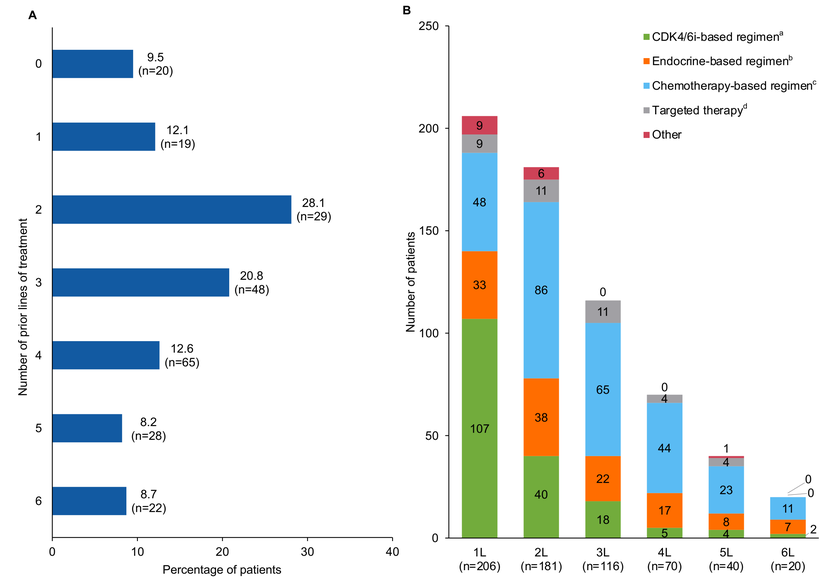
Biopsy or disease characteristics, n (%)	Total (n=234)
Sample used for most recent HER2 status testing[a]	
Archival tissue	85 (36.3)
Newly obtained tissue	**144 (61.5)**
Biopsy tissue type[b]	
Primary tumor	82 (35.0)
Metastasis	**146 (62.4)**
HR status[c]	
HR+	**183 (78.2)**
HR–	44 (18.8)
IHC score[d,e]	
0	27 (11.5)
1+	**113 (48.3)**
2+	**82 (35.0)**
3+	3 (1.3)

[a]Type of sample used for HER2 status testing was missing for 5 patients. [b]Biopsy tissue type was unknown or missing for 6 patients. [c]HR status for seven patients was unknown or missing. [d]All patients had a history of HER2-low disease as determined by IHC for inclusion in the study. [e]Status for nine patients was unknown, not recorded, or missing.

Prior treatment received

- Patients received a median of 3 prior lines of therapy (range: 1–6 lines) in the metastatic setting before initiation of the study (**Figure 3A**). Patients receiving T-DXd were most commonly treated with CDK4/6i-based regimens in 1L (52%), whereas chemotherapy-based regimens were the most common treatments in 2L and beyond (54%; **Figure 3B**)
  - The most common chemotherapy used was capecitabine (35.6%)

Figure 3. Number of prior lines of treatment in the metastatic setting (A), and most common treatments for each prior line of treatment (B)



[a]Includes CDK4/6i monotherapy and combinations that contain endocrine therapy, chemotherapy, targeted therapy, and other. [b]Excludes combinations that contain CDK4/6i therapy. [c]Excludes combinations that contain CDK4/6i and endocrine therapies. [d]Excludes combinations that contain CDK4/6i therapy, endocrine therapy, and chemotherapy.

Abbreviations

1/2L, first/second line; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; IHC, immunohistochemistry; ISH, *in situ* hybridization; mBC, metastatic breast cancer; OS, overall survival; (rw)PFS, (real-world) progression-free survival; rwTTNT, real-world time to next treatment; T-DXd, trastuzumab deruxtecan.

Acknowledgments

Under the guidance of the authors and in accordance with Good Publication Practice 2022 guidelines, medical writing and editorial support were provided by Kezia Pittaway of Springer Health+, Springer Healthcare Ltd., UK, and was funded by Daiichi Sankyo.

Disclosures

VG has received personal fees for advisory board membership for AstraZeneca, Daiichi Sankyo, Eisai, Eli Lilly, Exact Sciences, Gilead, Merck Serono, MSD, Novartis, Olema Oncology, and Pfizer; personal fees as an invited speaker for AstraZeneca, Daiichi Sankyo, Eli Lilly, Exact Sciences, Gilead, GSK, Menarini Steamline, Novartis, and Roche; personal fees for expert testimony for Eli Lilly; and institutional funding as a local principal investigator for AstraZeneca, BMS, Daiichi Sankyo, Eli Lilly, GSK, Merck, MSD, Nerviano, Novartis, Pfizer, Roche, Seagen, and Synton Biopharmaceutical.

References

1. Modi S, et al. N Engl J Med. 2022;387:9–20.
2. Guarneri V, et al. Future Oncol. 2024;20:1237–50.

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