Poster 075

Trastuzumab Deruxtecan in HER2-Low Metastatic Breast Cancer: Real-World Treatment Patterns and Outcomes From Community Oncology Settings

Marvin Nguyen PharmD[1]; Ruchit Shah PhD[1]; Anagha Gogate PhD[1]; Deepak Adhikari MS[2]; Lisa Herms PhD[2]; Heather Neuhalfen MBA[2]; Aaron Peevyhouse MSBA[2]; Scott Cole MD[2]; Sibel Blau MD[2]; Mark Walker PhD[2]

[1]Daiichi Sankyo, Basking Ridge, New Jersey, United States; [2] ONCare Alliance LLC, Tacoma, Washington, United States

Objective

Among patients with human epidermal growth factor receptor 2 (HER2)-low metastatic breast cancer (mBC) treated with trastuzumab deruxtecan (T-DXd) in the mBC setting:

- To describe the demographic and clinical characteristics of patients.
- To describe treatment patterns and sequencing.
- To assess real-world outcomes.

Conclusions

T-DXd demonstrated favorable effectiveness in real-world community oncology patients with hormone receptor positive (HR+) and negative (HR-) HER2-low mBC, despite this population appearing older, frailer, and more heavily pretreated than typical clinical trial patients.
T-DXd showed greater effectiveness in HR+ patients who were chemo-naïve than in HR+ non-chemo-naïve patients. Effectiveness was numerically similar in patients with and without brain metastases. These findings support the use of T-DXd across diverse clinical settings.

Plain language summary

Why did we perform this research?

Trastuzumab deruxtecan (T-DXd) is an important treatment for people with HER2-low metastatic breast cancer (mBC), but we still have limited information about how well it works for patients treated in everyday community cancer clinics. We wanted to better understand who is receiving T-DXd in these settings and how patients are doing after starting this medicine.

How did we perform this research?

We reviewed medical records from community oncology patients. We included people with HER2-low mBC who were treated with T-DXd and looked at how long treatment worked, how long patients lived after starting it, and how often their cancer shrank.

What were the findings of this research?

We studied 300 patients, most age 65 or older. On average, patients went more than seven months before their cancer worsened, about 62% were alive at one year, and more than half had their tumor shrink. Patients with hormone receptor–positive disease who had not received prior chemotherapy did especially well, and patients with brain metastases had similar results to those without.

What are the implications of this research?

T-DXd worked well across a wide range of real-world patients, despite patients being older or having more health problems than typical clinical trial patients. This supports its use in diverse community cancer settings.

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 43rd Annual Miami Breast Cancer Conference® by Lisa Herms, PhD. Corresponding author email address: apeevyhouse@oncarealliance.com.

Introduction

- Among the 80% to 85% of breast cancer tumors historically considered HER2-negative, those classified as immunohistochemistry (IHC) 1+ or IHC 2+ with no evidence of amplification by in situ hybridization (ISH) are now considered HER2-low. About 60% of HER2-negative tumors overall are considered HER2-low by this definition.[1]
- Trastuzumab deruxtecan (T-DXd) is an antibody–drug conjugate that targets low levels of HER2 protein on these tumors, delivering chemotherapy directly to cancer cells.[2]
- T-DXd received FDA approval based on DESTINY-Breast04 for patients with unresectable or metastatic HER2-low breast cancer (mBC) previously treated with chemotherapy, and expanded approval based on DESTINY-Breast06 for adults with unresectable or metastatic hormone receptor (HR)-positive, HER2-low or HER2-ultralow (IHC 0 with membrane staining) disease after progression on endocrine therapy in the metastatic setting.[2]
- However, real-world data regarding treatment patterns and effectiveness remains limited, particularly in community settings. This study evaluated T-DXd use and outcomes across US community oncology clinics.

Methods

- **Study Design**: Retrospective observational cohort study
- **Data Source**: Structured and unstructured electronic health record data deeply curated through human review from ONCare Alliance
- **Study Population**: 300 randomly sampled adult patients with HER2-low mBC initiating T-DXd in any progression-based line of therapy (LOT) after mBC diagnosis
- **Study Period**: Interval from mBC diagnosis through the end of follow-up, which occurred at the end of the LOT that followed the qualifying T-DXd-containing regimen, end of record, or death, whichever occurred first
- **Index Date**: Start date of the qualifying T-DXd-containing regimen following mBC diagnosis
- **Endpoints**
  - **Real-world Overall Response Rate (rwORR):** Proportion of patients with a best overall response of partial response or better
  - **Real-world Progression-free Survival (rwPFS):** Time from index to the earlier of disease progression or death
  - **Overall Survival (OS):** Time from index to death
- **Statistical Methods**
  - Baseline characteristics, ORR and time-to-event outcomes were analyzed with descriptive statistics and Kaplan-Meier methods, using log-rank and chi-square tests of group differences.
  - Results were stratified by HR status, prior chemotherapy, and presence of brain metastases (BM).

Results

- **Patient Characteristics**: Median age among 300 randomly sampled patients (77.0% HR+; 23.0% HR-) was 65 years, and 79.7% were White. One-fourth (24.7%) had de novo mBC, 22.7% had ECOG performance status ≥2, and 39.3% had ≥1 comorbidity.
- **Treatment Patterns**: Most patients received T-DXd monotherapy (87.3%), with T-DXd starts ranging from 2021 to 2025. Baseline characteristics were similar by HR status, but HR+ patients received T-DXd in later lines (88.7% of HR+ vs. 53.6% of HR- were 3L+).
- **Clinical Outcomes**: Median rwPFS was 7.4 months (7.7 months HR+ and 4.9 HR-, *ns*). The Kaplan-Meier 12-month OS estimate was 62% (64% HR+ and 55% HR-, p=0.06). rwORR was 56.3% (56.4% HR+ and 56.0% HR-, *ns*).
- **Prior Chemotherapy**: Among HR+ patients, T-DXd showed greater effectiveness in HR+ chemo-naïve (n=41) compared to HR+ non-chemo-naïve (n=190): rwPFS was 10.2 vs. 7.4 months and 12-month OS was 74% vs. 62% (p<0.05 for both).
- **Brain Metastasis**: rwPFS was numerically similar in patients with BM (n=40) vs. those without (n=260): 6.3 vs. 7.5 months (p=0.07).

Table 1. Baseline Patient and Treatment Characteristics

	Overall (N=300)	HR+ (N=231)	HR- (N=69)	p-Value
Age at Index (years), mean (SD)	63.5 (12.1)	63.4 (11.8)	63.9 (13.3)	0.7754
Female Sex, n (%)	296 (98.7%)	227 (98.3%)	69 (100.0%)	0.5770
Race, n (%)				
Black/African American	15 (5.0%)	11 (4.8%)	4 (5.8%)	0.9253
White	239 (79.7%)	184 (79.7%)	55 (79.7%)	
Other/Undocumented	46 (15.3%)	36 (15.6%)	10 (14.5%)	
Follow-up (months), mean (SD)	12.6 (8.0)	13.2 (7.9)	10.6 (8.0)	**0.0189**
Stage at Initial Diagnosis, n (%)				
0-I	37 (12.3%)	29 (12.6%)	8 (11.6%)	0.3956
II	99 (33.0%)	78 (33.8%)	21 (30.4%)	
III	59 (19.7%)	42 (18.2%)	17 (24.6%)	
IV	74 (24.7%)	61 (26.4%)	13 (18.8%)	
Undocumented	31 (10.3%)	21 (9.1%)	10 (14.5%)	
Performance Status, n (%)				
Impaired (ECOG ≥2)	68 (22.7%)	53 (22.9%)	15 (21.7%)	0.7186
Not Impaired (ECOG 0-1)	216 (72.0%)	167 (72.3%)	49 (71.0%)	
Undocumented	16 (5.3%)	11 (4.8%)	5 (7.2%)	
≥1 Comorbidity, n (%)	118 (39.3%)	92 (39.8%)	26 (37.7%)	0.7488
T-DXd Monotherapy, n (%)	262 (87.3%)	201 (87.0%)	61 (88.4%)	**0.0220**
Number of Prior Endocrine Therapy Lines, median (Q1-Q3)	2 (1, 3)	2 (2, 3)	0 (0, 0)	**<.0001**
Line of Qualifying T-DXd, n (%)				
1	11 (3.7%)	4 (1.7%)	7 (10.1%)	**<.0001**
2	47 (15.7%)	22 (9.5%)	25 (36.2%)	
3+	242 (80.7%)	205 (88.7%)	37 (53.6%)	

Abbreviations: ECOG, Eastern Cooperative Oncology Group; HR, hormone receptor; T-DXd, trastuzumab deruxtecan

Table 2. Clinical Outcomes

	Overall (N=300)	HR+ (N=231)	HR- (N=69)	HR+ Subset	
				Chemo-naïve (N=41)	Non-chemo-naïve (N=190)
Median (95% CI) DOT, in Months	6.9 (6.0, 7.8)	6.9 (6.2, 8.1)	6.0 (2.1, 9.1)	8.3 (3.7, 11.1)	6.7 (5.8, 7.6)
Median (95% CI) rwPFS, in Months	7.4 (6.1, 8.0)	7.7 (6.6, 8.4)	4.9 (2.6, 8.3)	10.2 (5.6, 16.3)	7.4 (6.1, 8.0)
12-Month OS Rate	62.0%	64.0%	55.0%	74.0%	62.0%
rwORR[a]	56.3%	56.4%	56.0%	71.0%	53.5%

Abbreviations: CI, Brookmeyer-Crowley confidence interval; DOT, duration of therapy; HR, hormone receptor; OS, overall survival; rwORR, real-world overall response rate; rwPFS, real-world progression-free survival
[a] Amongst patients with a documented response assessment (N = 238 overall, 188 HR+, 50 HR-).

Figure 2A-B. Kaplan-Meier Survival Analysis of rwPFS and OS by HR Status

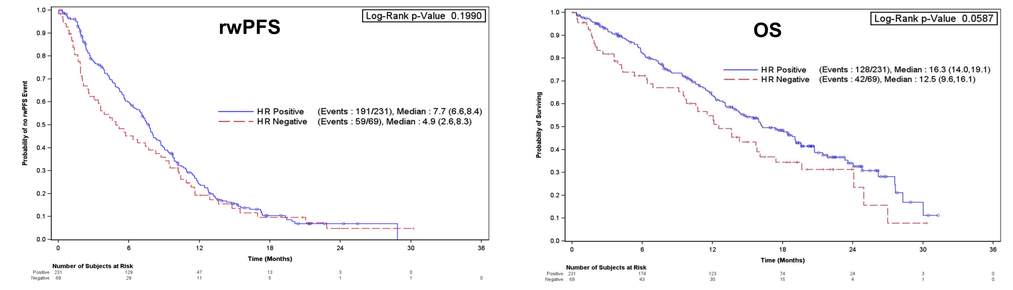


Figure 3A-B. Kaplan-Meier Survival Analysis of rwPFS and OS by Prior Chemotherapy for HR+ Subset

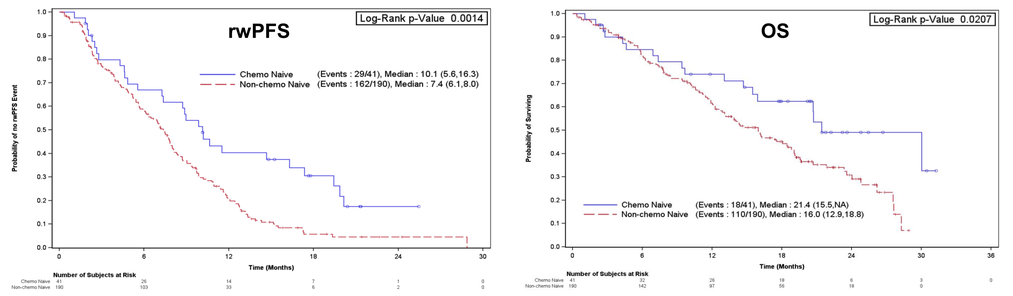


Figure 3. Patient-Level rwORR by HR Status

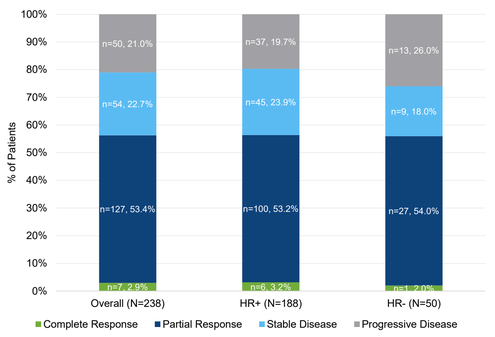
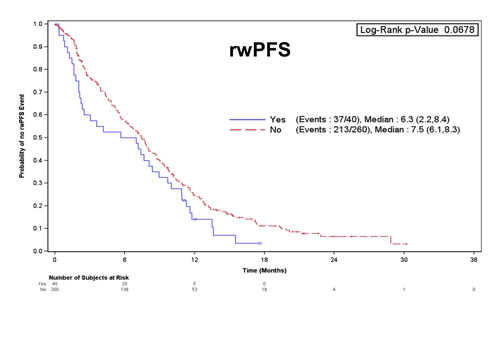


Figure 4. rwPFS by Brain Metastasis



References

1. Schettini F, Chic N, Braso-Maristany F, Pare L, Pascual T, Conte B, et al. Clinical, pathological, and PAM50 gene expression features of HER2-low breast cancer. NPJ Breast Cancer 2021;7(1):1.
2. Daiichi Sankyo I. Drug Label for Enhertu. Daiichi Sankyo, Inc., accessed October 15, 2024.