

Real-world Clinical Outcomes of Trastuzumab Deruxtecan Among HER2+ Metastatic Breast Cancer Patients with and without Brain Metastases: Data from U.S. Community Oncology Practices

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Objective

- To assess real-world clinical outcomes of T-DXd in HER2+ mBC patients, with and without active or stable brain metastasis, treated in community oncology settings.

Conclusions

- This study is among the largest real-world analyses of T-DXd effectiveness in HER2+ mBC patients with and without brain metastasis.
- Results support the clinical benefit of T-DXd in patients with brain metastasis, including those with active or stable disease.
- No significant differences in outcomes were observed between patients with active vs. stable brain metastasis.
- Consistent with the findings of DESTINY-Breast12, these results reinforce the value of T-DXd in improving long-term outcomes for HER2+ mBC patients, regardless of brain metastasis status.

Plain language summary



Why did we perform this research?

We studied how well T-DXd works for HER2+ metastatic breast cancer patients treated in community clinics, especially those with brain metastases. Brain metastases are common in advanced breast cancer and can make treatment more complex and outcomes harder to predict. Real-world data on T-DXd's effectiveness in these patients is limited, so this study helps fill that gap.



How did we perform this research?

We reviewed electronic medical records from U.S. community oncology practices in the ONCare Alliance network. The study included 300 adults with HER2+ metastatic breast cancer who received T-DXd in the second-line or later setting between January 2020 and August 2024. We compared patient characteristics and treatment outcomes, including time to treatment failure and progression-free survival, between patients with and without brain metastases. Among patients with brain metastases, we further stratified outcomes by active vs. stable.



What were the findings of this research?

Among 300 patients, 95 had brain metastases (68 active, 27 stable) when starting T-DXd. Treatment outcomes were similar for patients with and without brain metastases: median time until cancer worsened or treatment stopped was 10 vs. 11.1 months and median time until cancer worsened or patients died was 12.1 vs. 13.5 months, respectively. Outcomes were also similar between active vs. stable brain metastases, showing no meaningful differences.



What are the implications of this research?

Similar outcomes for patients with and without brain metastases—and for active vs. stable brain metastases—suggest T-DXd is an effective option across these groups. These findings support using T-DXd broadly to improve outcomes for patients, regardless of brain involvement.

Introduction

- Trastuzumab deruxtecan (T-DXd) is a HER2-directed antibody-drug conjugate approved for the treatment of adult patients with unresectable or metastatic HER2-positive (IHC 3+ or ISH positive) breast cancer who have received a prior anti-HER2-based regimen either in the metastatic setting or in the neoadjuvant or adjuvant setting and have developed disease recurrence during or within six months of completing therapy.¹
- The DESTINY-Breast12 trial demonstrated substantial and durable activity of T-DXd in patients with active (new or worsening) and stable (stable or improving) brain metastasis (BM).² However, limited data exists regarding the intracranial activity and real-world clinical benefit associated with T-DXd in this patient population.

Methods

- Study Design:** Retrospective observational cohort study
- Data Source:** Human-reviewed structured & unstructured electronic medical record (EMR) data from practices affiliated with ONCare Alliance, a national network of 31 community oncology practices that represents more than 3 million patients
- Population:** 300 randomly selected adult patients with a HER2+ mBC who received T-DXd in the second-line (2L) or later setting anytime from 01/2020 to 08/2024
- Study Periods**
 - Index date:* start date of the qualifying T-DXd-containing regimen following mBC diagnosis.
 - Study period:* interval from mBC diagnosis through the end of the line of therapy that followed the qualifying T-DXd-containing regimen, end of record, or death, whichever occurred first. However, date of death at any point was collected, if available.

Endpoints

- Real-world time to treatment failure (rwTTF):* time from index to the earlier of death, disease progression, or discontinuation of T-DXd
- Real-world progression-free survival (rwPFS):* time from index to the earlier of death or disease progression

Statistical Methods

- Patient characteristics were assessed descriptively and compared with chi-square or Fisher exact tests.
- Clinical outcomes were assessed using Kaplan-Meier median and confidence interval estimates.
- All analyses were stratified by BM vs. no BM status and active (new or worsening) vs. stable (unchanged or improving) BM status at start of T-DXd.

Results

Table 1. Baseline Demographic Characteristics

Characteristics	Overall	BM Status at Index		Type of BM at Index			p-Value
		BM	No BM	p-Value	Active BM	Stable BM	
No. of Patients	300	95	205		68	27	
Female, n (%)	297 (99.0)	95 (100)	202 (98.5)	0.5541	68 (100)	27 (100)	N/A
Age at Index (Years), Mean (SD)	59.3 (12.6)	54.0 (11.1)	61.7 (12.6)	<.0001	53.4 (11.5)	55.4 (9.8)	0.4115
Race, n (%)				0.4097			0.2746
Black	24 (8.0)	6 (6.3)	18 (8.8)		4 (5.9)	2 (7.4)	
White	247 (82.3)	77 (81.1)	170 (82.9)		53 (77.9)	24 (88.9)	
Other*	29 (9.7)	12 (12.6)	17 (8.3)		11 (16.2)	1 (3.7)	
Region, n (%)				0.7659			0.0200
Midwest	97 (32.3)	32 (33.7)	65 (31.7)		23 (33.8)	9 (33.3)	
South	100 (33.3)	28 (29.5)	72 (35.1)		16 (23.5)	12 (44.4)	
West	56 (18.7)	18 (18.9)	38 (18.5)		12 (17.6)	6 (22.2)	
Northeast	47 (15.7)	17 (17.9)	30 (14.6)		17 (25.0)	0	

* Includes other values as well as undocumented

Figure 1A-B. rwTTF and rwPFS by Brain Metastasis Status (N=300)

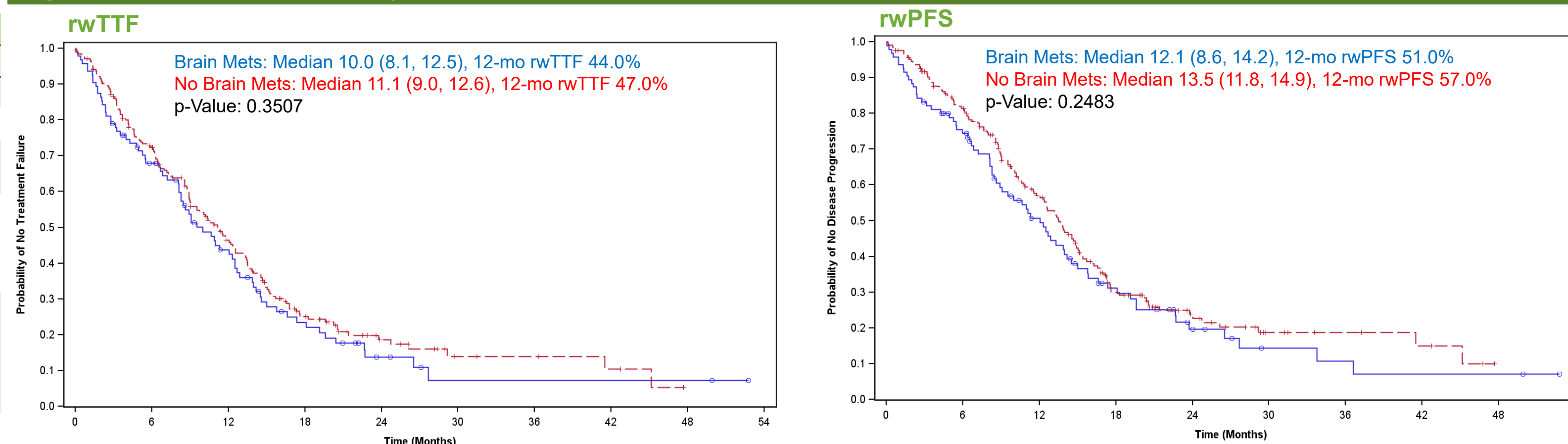


Table 2. Baseline Clinical Characteristics

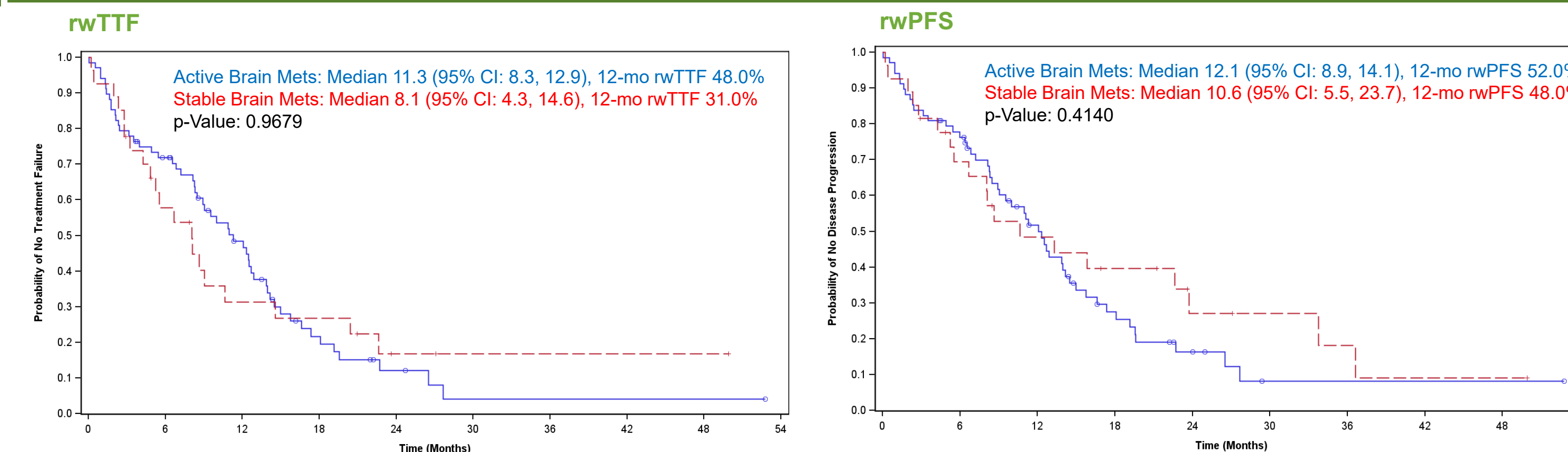
Characteristics	Overall	BM Status at Index		Type of BM at Index			p-Value
		BM	No BM	p-Value	Active BM	Stable BM	
No. of Patients	300	95	205		68	27	
Initial Stage, n (%)				0.7938			0.6011
0-I	42 (14.0)	15 (15.8)	27 (13.2)		11 (16.2)	4 (14.8)	
II	70 (23.3)	24 (25.3)	46 (22.4)		17 (25.0)	7 (25.9)	
III	55 (18.3)	19 (20.0)	36 (17.6)		15 (22.1)	4 (14.8)	
IV	116 (38.7)	32 (33.7)	84 (41.0)		23 (33.8)	9 (33.3)	
Undocumented	17 (5.7)	5 (5.3)	12 (5.9)		2 (2.9)	3 (11.1)	
Invasive ductal carcinoma, n (%)	258 (86.0)	80 (84.2)	178 (86.8)	0.5431	54 (79.4)	26 (96.3)	0.0592
T-DXd Setting*, n (%)				0.0004			0.2725
2L	70 (23.3)	10 (14.3)	60 (85.7)		9 (90.0)	1 (10.0)	
3L+	230 (76.7)	85 (37.0)	145 (63.0)		59 (69.4)	26 (30.6)	
Post-menopausal, n (%)	229 (76.3)	70 (73.7)	159 (77.6)	0.5416	49 (72.1)	21 (77.8)	0.9307
ECOG, n (%)				0.2869			1.0000
Impaired (≥2)	43 (14.3)	17 (17.9)	26 (12.7)		12 (17.6)	5 (18.5)	
Not Impaired (0-1)	241 (80.3)	75 (78.9)	166 (81.0)		54 (79.4)	21 (77.8)	
Undocumented	16 (5.3)	3 (3.2)	13 (6.3)		2 (2.9)	1 (3.7)	
HR Positive, n (%)	193 (64.3)	53 (55.8)	140 (68.3)	0.0355	38 (55.9)	15 (55.6)	0.9769
Comorbidity Index, Mean (SD)	0.6 (1.0)	0.3 (0.6)	0.7 (1.2)	<.0001	0.3 (0.6)	0.2 (0.5)	0.1139
Metastatic Sites at mBC Diagnosis, n (%)				0.0048			0.3280
Bone Only	50 (16.7)	8 (8.4)	42 (20.5)		6 (8.8)	2 (7.4)	
Visceral Only	130 (43.3)	38 (40.0)	92 (44.9)		24 (35.3)	14 (51.9)	
Bone & Visceral	120 (40.0)	49 (51.6)	71 (34.6)		38 (55.9)	11 (40.7)	
Follow-up (Months), Mean (SD)	15.0 (12.5)	18.0 (12.1)	19.4 (12.7)	0.3490	17.2 (11.1)	19.9 (14.3)	0.5663

* Percentages for each grouping use the number of patients with 2L and 3L+ as the denominators, as opposed to the column total.

References

- Daiichi Sankyo, Inc. Enhertu (fam-trastuzumab deruxtecan-nxki) [prescribing information]. U.S. Food and Drug Administration. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761139s028lbl.pdf. Accessed October 30, 2025.
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Figure 2A-B. rwTTF and rwPFS by Type of Brain Metastasis (N=95)



Key Findings

- Among 300 patients, 95 had BM (68 active, 27 stable) at the start of T-DXd.
- Baseline characteristics were similar between patients with and without BMs, except for age, HR status, metastatic sites, and comorbidity index (p<0.05). (Table 1, 2)
- No statistically significant differences in baseline characteristics were observed between patients with active vs. stable BMs, except for census region (p = 0.02) (Table 1, 2)
- Clinical outcomes were similar between patients with vs. without BMs: median rwTTF was 10.0 vs. 11.1 months, p = 0.3507; and median rwPFS was 12.1 months vs. 13.5 months, p = 0.2483. (Figure 1)
- No significant differences in outcomes were observed between active vs. stable BM cohorts: median rwTTF was 11.3 months vs. 8.1 months, p = 0.9679; and median rwPFS was 12.1 months vs. 10.6 months, p = 0.4140. (Figure 2)

Abbreviations

2L, second-line; 3L+, third-line or later; BM, brain metastasis; ECOG, Eastern Cooperative Oncology Group Performance Status; HR, hormone receptor; IQR, interquartile range; mBC, metastatic breast cancer; rwPFS, real-world progression-free survival; rwTTF, real-world time to treatment failure; SD, standard deviation; T-DXd, trastuzumab deruxtecan