Real-World Comparison of Trastuzumab Deruxtecan Treatment Outcomes in HER2-Positive or HER2-Low Metastatic Breast Cancer Patients With and Without Brain Metastases

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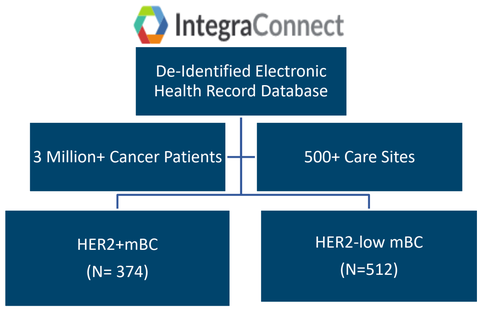
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Introduction

In the DESTINY-Breast12 trial, individuals with HER2-positive (HER2+) metastatic breast cancer (mBC) who received trastuzumab deruxtecan (T-DXd) had similar progression-free survival (PFS) regardless of the presence of brain metastases (BrM). We sought to evaluate time to treatment discontinuation or death (TTD), time to next treatment (TTNT; a surrogate for PFS), and overall survival (OS) using real-world data to assess patients (pts) outside of a clinical trial setting for both HER2+and HER2-low mBC.

Data Source



Eligibility Criteria:

- ≥ 18 years old
- HER2+ or HER2-low mBC
- ≥ 2 documented visits
- T-DXd treatment initiation between 1/1/2020-5/31/2024, with observation through 11/30/2024

Methods

- This was a retrospective, observational analysis of data from patients in the IntegraConnect PrecisionQ real-world de-identified database, enriched with information obtained by curation
- The index date was the initiation of T-DXd. Documentation of BrM was determined at or prior to index date.
- Patient data included structured data supplemented with data obtained via chart abstraction.
- TTD, TTNT, and OS by documentation of BrM were analyzed using Kaplan-Meier analysis.
- Unadjusted hazard ratios (HR) were estimated using Cox proportional hazard models.

Results

- Pts with HER2+ mBC did not have statistically significant differences in median TTD, TTNT, or OS regardless of the presence of BrM (Figures 1-3)
- Pts with HER2-low mBC without BrM had significantly longer
  - Median TTD (5.5 months vs. 3 months, logrank p=0.002)
  - Median TTNT (7.2 months vs. 5.8 months, logrank p=0.002)
  - Median OS (15.8 months vs. 10.2 months, logrank p<0.001)

Table. Real-World Time to Treatment Discontinuation (TTD), Time to Next Treatment (TTNT), and Overall Survival (OS) from Initiation of Fam-Trastuzumab Deruxtecan among individuals with HER2+ and HER2-Low Metastatic Breast Cancer by Documentation of Brain Metastases (BrM)

	HER2-Positive			HER2-Low		
	Median, months (95% CI)		HR (95% CI), P value	Median, months (95% CI)		HR (95% CI), P value
	BrM (n=94)	No BrM (n=280)		BrM (n=80)	No BrM (n=432)	
TTD	9.2 (6.4, 14.7)	12.4 (9.9, 14.7)	1.07 (0.81, 1.42), 0.64	3.0 (2.1, 4.8)	5.5 (4.6, 6.3)	1.51 (1.16, 1.97), 0.0021
TTNT	14.1 (7.9, 17.7)	15.2 (13.4, 16.5)	1.10 (0.81, 1.48), 0.55	5.8 (3.6, 6.5)	7.2 (6.5, 8.2)	1.52 (1.16, 1.97), 0.002
OS	14.1 (7.9, 17.7)	15.2 (13.4, 16.5)	1.01 (0.68, 1.49), 0.97	10.2 (6.6, 11.9)	15.8 (14.2, 18.9)	1.98 (1.46, 2.69), <0.0001

Figure 1. Time to Treatment Discontinuation or Death: HER2+

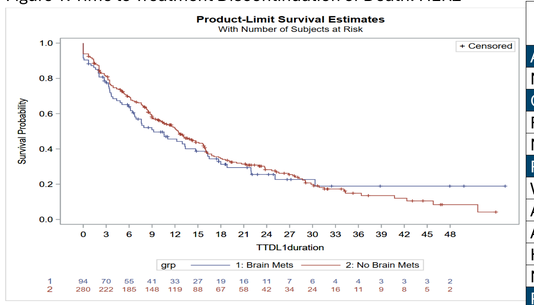


Figure 2. Time to Next Treatment or Death: HER2+

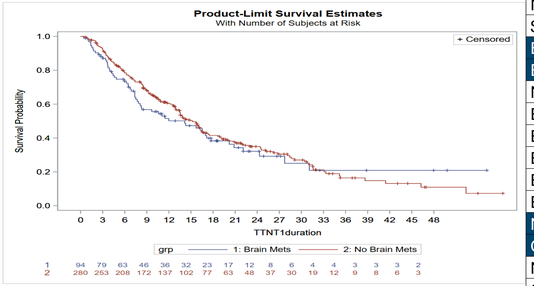


Figure 3. Overall Survival: HER2+

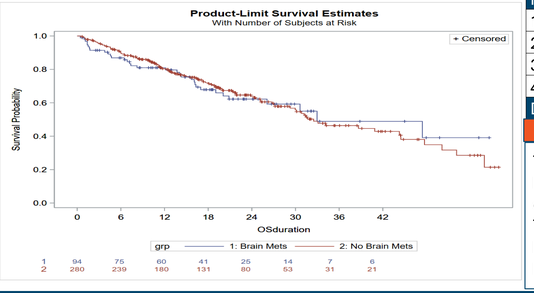


Table: Baseline demographics and Clinical characteristics of HER2+ Patients

	Overall (N=374)	Brain Mets (N=94)	No Brain Mets (N=280)
Age at Treatment, Median (IQR)	62.5 (54, 71)	59.5 (51, 66)	64 (54, 73)
Median (IQR)			
Gender (n, %)	373 (99.7)	94 (100)	279 (99.6)
Female	0 (0.0)	0 (0.0)	0 (0.0)
Male	1 (0.3)	0 (0.0)	1 (0.4)
Race/Ethnicity (n, %)	269 (71.9)	70 (74.5)	199 (71.1)
White	42 (11.2)	8 (8.5)	34 (12.1)
African/American	11 (2.9)	3 (3.2)	8 (2.9)
Asian	52 (13.9)	13 (13.8)	39 (13.9)
Hispanic	263 (70.3)	73 (77.7)	190 (67.9)
Not Hispanic	87 (23.3)	14 (14.9)	73 (26.1)
Payer Type	89 (23.8)	17 (18.1)	72 (25.7)
Commercial	124 (33.2)	34 (36.2)	90 (32.1)
Medicare/Medicaid	161 (43)	43 (45.7)	118 (42.1)
Self Pay/Other			
BMI at Treatment, Median (IQR)	55 (14.7)	18 (19.1)	37 (13.2)
ECOG status at Treatment (n, %)	40 (10.7)	9 (9.6)	31 (11.1)
No. of PTs with missing data (n, %)	113 (33.8)	21 (24.7)	92 (36.9)
ECOG 0	172 (51.5)	46 (54.1)	126 (50.6)
ECOG 1	40 (12)	14 (16.5)	26 (10.4)
ECOG 2	7 (2.1)	3 (3.5)	4 (1.6)
ECOG 3	2 (0.6)	1 (1.2)	1 (0.4)
ECOG 4			
No. of Metastatic Sites, Median (IQR)	3 (2, 4)	3 (2, 4)	3 (2, 3)
Charlson Comorbidity Index	0.3 (0.8)	0.3 (1.0)	0.2 (0.7)
Mean (Std)	48 (12.8)	14 (14.9)	34 (12.1)
CI > 0 (n, %)			
Metastatic LoT	31 (8.3)	8 (8.5)	23 (8.2)
1	116 (31)	24 (25.5)	92 (32.9)
2	91 (24.3)	25 (26.6)	66 (23.6)
3	136 (36.4)	37 (39.4)	99 (35.4)
4+			
Duration of Follow-Up, Median (IQR)	16.6 (9.5,	16.3 (7.2,	16.6 (9.8,

Discussion & Conclusions

This real-world comparison of T-DXd treatment reaffirmed findings from DESTINY-Breast12 in which PFS did not differ among HER2+ mBC pts based on the presence of BrM. While this study showed significantly longer median TTD, TTNT, and OS in HER2-low mBC pts without BrM compared to those with BrM, further research and larger samples sizes are needed to understand how the line of therapy for T-DXd impacts these findings.

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References

1. Harbeck, N., Ciruelos, E., Jerusalem, G., et al. (2024). Trastuzumab deruxtecan in HER2-positive advanced breast cancer with or without brain metastases: a phase 3b/4 trial. *Nature Medicine*. Published online 13 September 2024

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