Real-World Comparison of Time to Next Treatment for Patients With HR-Positive, HER2-Low Metastatic Breast Cancer Treated With Either Chemotherapy or Trastuzumab Deruxtecan in the Second-Line

R. Mahtani[1], R. Choksi[2], F. Kudrik[3], D. Patt[4], S. Reddy[5], S. Reganti[5], S. Rosenfeld[6], S. W. Champaloux[7], D. Parris[7], A. Rui[7], A. Sharma[7], M. Gart[7], C. Wall[7], B. Wang[7], P. Varughese[7], J. Donegan[7], L. Morere[7], R. Geller[7], J. Scott[7], V. Gorantla[2]

[1]Medical Oncology, Miami Cancer Institute, Baptist Health South Florida, Miami, FL, [2]Medical Oncology, University of Pittsburgh Medical Center (UPMC), Pittsburgh, PA, [3]Medical Oncology, South Carolina Oncology Associates, Columbia, SC, [4]Medical Oncology, Texas Oncology, Austin, TX, [5]Medical Oncology, Cancer Care Specialists, Reno, NV, [6]Medical Oncology, Highlands Oncology Group (HOG), Fayetteville, AR, [7]PrecisionQ, IntegraConnect, West Palm Beach, FL

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Introduction

In the DESTINY-Breast06 trial, patients (pts) with HR-positive (HR+)/HER2-low or ultra-low metastatic breast cancer (mBC) who received trastuzumab deruxtecan (T-Dxd) following ≥1 line of endocrine therapy (ET) experienced improved progression-free survival (PFS) compared to those who received chemotherapy (chemo). To assess whether similar benefits are seen in a real-world setting, we evaluated overall survival (OS) and time to next treatment (TTNT), which is a surrogate measure for PFS.

Methods and Materials

- This was a retrospective, observational analysis of data from patients in the Integra PrecisionQ real-world de-identified database.
- Eligible pts included adults with a confirmed diagnosis of HR+/HER2-low mBC who had ≥2 documented visits and a CDK4/6 inhibitor(i) ± ET in the first-line metastatic setting.
- Pts with T-Dxd or chemo after ET were identified and observed between 6-1-2022 and 4-30-2025.
- TTNT was defined as time from the treatment start to either the initiation of a subsequent line of therapy or death. We did not assess for the reason pts discontinued (e.g., toxicity or disease progression).
- TTNT and OS were analyzed using Kaplan-Meier analysis. Hazard ratios (HR) adjusting for age at treatment and race were estimated using Cox proportional hazard models.

Results

Table 1. Baseline Demographic and Clinical Characteristics

	Overall (N=340)	T-DXd (n=82)	Chemo (n=248)
Median (IQR) age at mBC diagnosis, yr	60.0 (50.0, 66.0)	60.0 (49.2, 65.7)	60.0 (50.7, 67.0)
Median (IQR) age at treatment, yr	64.0 (55.2, 70.0)	63.0 (54.2, 68.0)	64.0 (56.0, 70.2)
Race, n (%)			
White	231 (70.0)	49 (59.8)	182 (73.4)
Other	58 (17.6)	20 (24.4)	38 (15.3)
Black/African American	35 (10.6)	10 (12.2)	25 (10.1)
Asian	6 (1.8)	3 (3.7)	3 (1.2)
Ethnicity, n (%)			
Not Hispanic	247 (74.8)	60 (73.2)	187 (75.4)
Other	64 (19.4)	18 (22.0)	46 (18.5)
Hispanic	19 (5.8)	4 (4.9)	15 (6.0)
Payer type, n (%)			
Commercial	61 (18.5)	20 (24.4)	41 (16.5)
Medicare/Medicaid	125 (37.9)	24 (29.3)	101 (40.7)
Other	144 (43.6)	38 (46.3)	106 (42.7)

	Overall (N=340)	T-DXd (n=82)	Chemo (n=248)
ECOG status at treatment, n (%)			
Pts missing data	29 (8.5)	3 (3.6)	26 (10.4)
ECOG 0	134 (43.1)	27 (34.1)	107 (48.2)
ECOG 1	143 (45.9)	43 (54.4)	100 (40.4)
ECOG 2	28 (9.1)	7 (8.9)	21 (9.5)
ECOG 3	6 (1.9)	2 (2.6)	4 (1.9)
Median lines (IQR), n	2 (2, 3)	2 (2, 3)	2 (2, 3)
Median (IQR) follow-up, mo	14.6 (7.3, 21.4)	13.5 (4.6, 21.7)	14.9 (7.6, 21.4)

- The chemo group had a higher percentage of patients identified as White compared with the T-DXd group (73.4% vs 59.8%)
- Overall, most pts (89%) had an ECOG of 0-1 at treatment initiation

Results, Continued

- The HR is adjusted for race and age at diagnosis, and chemotherapy is the reference group.
- The median TTNT was significantly longer for the T-DXd group compared with the chemo group (10.1 vs. 6.0 months; adjusted HR 0.45 (95% confidence interval [CI] 0.30, 0.66) (Table 1, Figure 1).
- The median OS was similar for the T-DXd and chemo groups (21.0 months for both groups; adjusted HR 1.16 (95% CI 0.79, 1.69) (Table 2, Figure 2).

Table 2. OS and TTNT in 2L Therapy for T-DXd Compared to Chemo

	T-Dxd (n=82)	Chemo (n=248)	Adjusted HR[a] (95% CI)
Median OS (95% CI), mo	21.0 (15.1, 25.6)	21.0 (18.3, 27.7)	1.16 (0.79, 1.69)
Probability of OS at 6 mo, % (95% CI)	81.1 (70.2, 88.4)	85.1 (79.4, 88.7)	
Probability of OS at 12 mo, % (95% CI)	72.9 (59.2, 80.9)	68.4 (61.6, 74,3)	
Median TTNT, mo (95% CI)	10.1 (7.8, 13.1)	6.0 (5.1, 6.5)	**0.45 (0.30, 0.66)**
Probability of continuing therapy at 6 mo, % (95% CI)	70.0 (57.9, 79.0)	49.2 (42.3, 55.2)	
Probability of continuing therapy at 12 mo, % (95% CI)	39.4 (26.1, 50.1)	19.7 (14.4, 25.2)	

Bold indicates statistical significance.
2L, second line; chemo, chemotherapy; CI, confidence interval; HR, hazard ratio; OS, overall survival, T-DXd, trastuzumab deruxtecan; TTNT, time to next treatment

Conclusions

- Consistent with findings from a subset of the DESTINY-Breast06 trial,[1] pts with HR+/HER2-low mBC previously treated with a CDK4/6i who then utilized T-DXd had a significantly improved TTNT compared to chemo.
- OS was not statistically different between T-DXd and chemo.
- Treatment crossover occurred in both cohorts: 28% of pts in the chemo group utilized T-DXd in a later line of therapy, and 19% of pts in the T-Dxd group utilized chemo in a later line of therapy.
- These results may be impacted by unmeasured factors such as, tumor burden, endocrine resistance, and access to care. Further studies are needed to confirm the optimal sequencing of TDxd in the real-world setting.

Figure 1. Time to Next Treatment or Death (TTNTD)

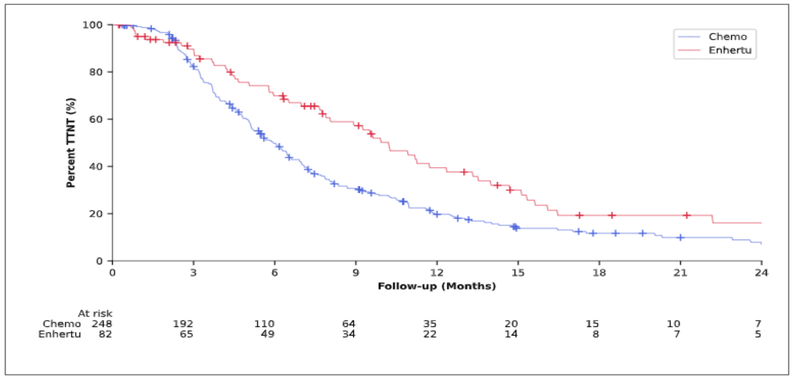
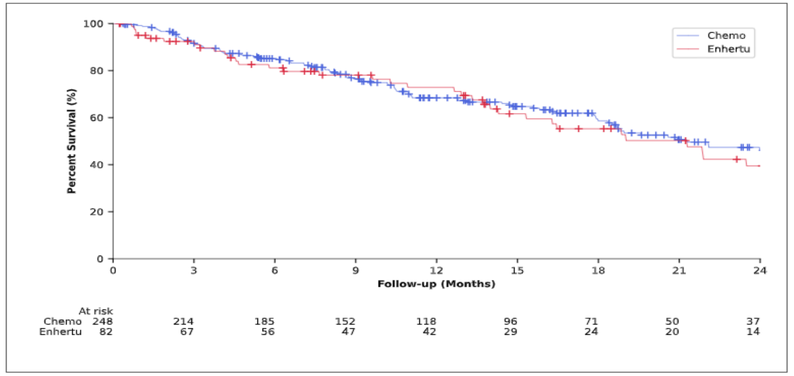


Figure 2. Overall Survival



Contact

Cecelia Wall
IntegraConnect
Email: cecelia.wall@integraconnect.com

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