Poster 076

Real-World Safety of Trastuzumab Deruxtecan in HER2-Low Metastatic Breast Cancer: Insights From US Community Oncology Practices

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Objective

To describe the use and tolerability of trastuzumab deruxtecan (T-DXd) among patients with human epidermal growth factor receptor 2 (HER2)-low metastatic breast cancer (mBC) treated in a real-world community oncology setting.

Conclusions

- In this real-world cohort, rates of T-DXd discontinuation due to toxicity were consistent with those observed in DESTINY-Breast04.
- Despite higher disease burden among community oncology patients compared to clinical trial settings (e.g., older, fewer hormone receptor positive (HR+), poorer ECOG performance status, more heavily pretreated), the safety profile of T-DXd remained aligned with clinical trial data, supporting its use and tolerability in US community oncology settings.

Plain language summary

Why did we perform this research?

T-DXd is widely used for HER2-low metastatic breast cancer, but there is limited information on its side effects outside clinical trials. We wanted to see how patients in community cancer clinics tolerate T-DXd and which side effects are most common.

How did we perform this research?

We reviewed medical records from 31 community oncology practices in the ONCare Alliance. We included people with metastatic breast cancer who started T-DXd and had HER2-low disease. We looked at medical events that occurred during treatment and within 30 days after.

What were the findings of this research?

We studied 300 patients who started T-DXd from 2021 to 2025, most of whom were age 65 or older. The most common side effects were fatigue, nausea or vomiting, diarrhea, and anemia. More serious issues were uncommon, including heart-related problems, low white blood cell counts with fever, and infusion reactions. Interstitial lung disease (ILD)/pneumonitis occurred in 10% of patients; most received steroids, and many needed treatment holds or discontinuation. Overall, 15% of patients stopped T-DXd because of side effects.

What are the implications of this research?

Side effects and treatment discontinuation rates in community clinics were similar to those seen in clinical trials, even though real-world patients often have more health challenges. These findings support that T-DXd is generally well tolerated across diverse community cancer settings.

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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), an antibody–drug conjugate that delivers chemotherapy directly to HER2-expressing cells, is approved for HER2-low disease after prior chemotherapy and, more recently, for HR-positive HER2-low/ultralow disease following progression on endocrine therapy in the metastatic setting.[2]
- Clinical trials have shown meaningful antitumor activity and a well-characterized safety profile, including known frequency and severity of toxicities such as nausea, fatigue, cytopenias, and interstitial lung disease.[2]
- As T-DXd use grows rapidly in routine practice, real-world evidence describing treatment patterns, side effects, and tolerability in community oncology settings remains limited.
- This study evaluates how T-DXd is used and tolerated across US community clinics.

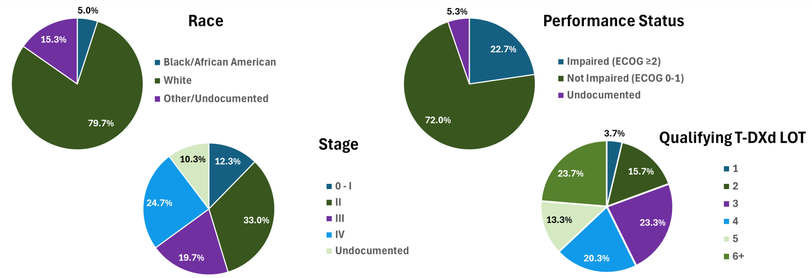
Methods

- **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 who initiated T-DXd in any progression-based 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:** Medical events of interest (MEOIs) of all grades during and up to 30 days following T-DXd initiation. Note that real-world data generally do not support specific grading of MEOIs
- **Statistical Methods:** Baseline characteristics, MEOIs, and actions taken in management of MEOIs were analyzed with descriptive statistics

Results

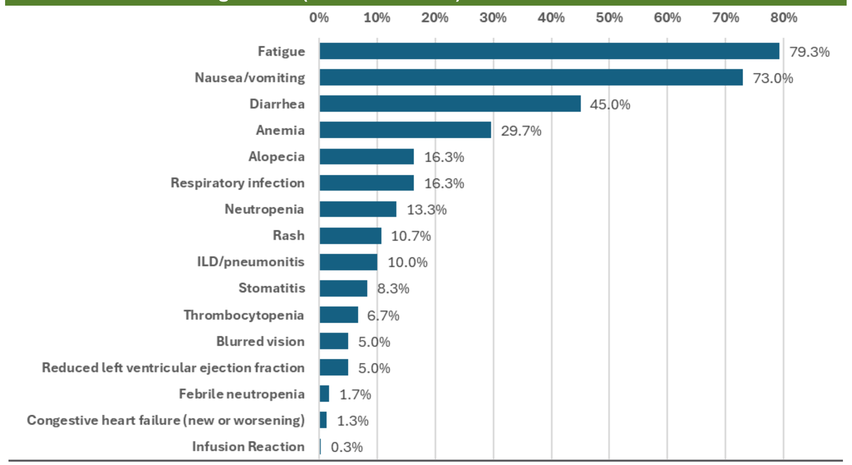
Table 1. Baseline Patient and Treatment Characteristics

	Overall (N=300)
Age at Index (years), mean (SD)	63.5 (12.1)
Female Sex, n (%)	296 (98.7%)
Hormone Receptor Positive Status, n (%)	231 (77.0%)
Follow-up (months), mean (SD)	12.6 (8.0)
≥1 Comorbidity, n (%)	118 (39.3%)
Number of Prior Endocrine Therapy Lines, median (Q1-Q3)	2 (1, 3)
T-DXd Monotherapy, n (%)	262 (87.3%)



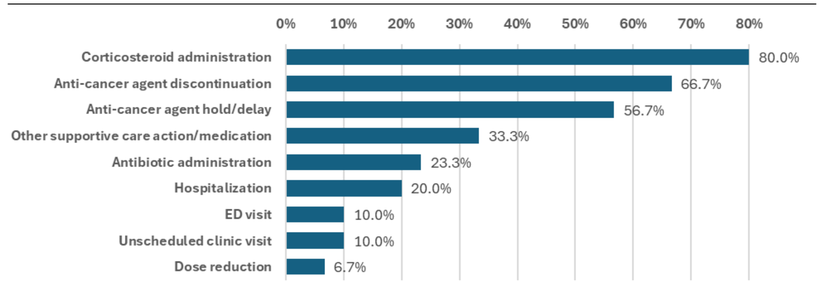
Abbreviations: ECOG, Eastern Cooperative Oncology Group; LOT, line of therapy; T-DXd, trastuzumab deruxtecan

Table 2. MEOIs during T-DXd (Overall N = 300)



Abbreviations: ILD, interstitial lung disease; MEOI, medical events of interest; T-DXd, trastuzumab deruxtecan

Table 3. Management Actions for ILD/Pneumonitis (Overall N = 30)



Abbreviations: ED, emergency department; HR, hormone receptor; ILD, interstitial lung disease

Table 4. Management Actions per Toxicity

	T-DXd Discontinuation	T-DXd Hold/Delay	T-DXd Dose Reduction
Fatigue (N=238)	5 (2.1%)	10 (4.2%)	12 (5.0%)
Nausea/vomiting (N=219)	3 (1.4%)	11 (5.0%)	13 (5.9%)
Diarrhea (N=135)	3 (2.2%)	9 (6.7%)	7 (5.2%)
Anemia (N=89)	4 (4.5%)	8 (9.0%)	7 (7.9%)
Alopecia (N=49)	0	0	0
Respiratory infection (N=49)	1 (2.0%)	6 (12.2%)	1 (2.0%)
Neutropenia (N=40)	1 (2.5%)	11 (27.5%)	14 (35.0%)
Rash (N=32)	1 (3.1%)	1 (3.1%)	0
ILD/pneumonitis (N=30)	20 (66.7%)	17 (56.7%)	2 (6.7%)
Stomatitis (N=25)	2 (8.0%)	0	0
Thrombocytopenia (N=20)	1 (5.0%)	7 (35.0%)	4 (20.0%)
Blurred vision (N=15)	0	0	1 (6.7%)
Reduced left ventricular ejection fraction (N=15)	5 (33.3%)	8 (53.3%)	0
Febrile neutropenia (N=5)	2 (40.0%)	0	0
Congestive heart failure (N=4)	0	0	0
Infusion Reaction (N=1)	0	0	0

Abbreviations: ILD, interstitial lung disease; T-DXd, trastuzumab deruxtecan
Note: Percentages taken of patients with the toxicity.

Results Summary

- **Patient Characteristics**: Among 300 study patients, 77.0% were HR+ and 23.0% were HR-. Baseline characteristics were similar by HR status; mean age was 63.5 years and 79.7% were White. One-fourth (24.7%, n=74) were de novo metastatic, and 22.7% (n=68) had ECOG ≥2 at T-DXd start. Comorbid disease burden was modest (≥1 condition: 39.3%, n=118).
- **Treatment Patterns**: T-DXd starts ranged from 2021 to 2025, with most initiating in 2022 (n=98) or 2023 (n=176). Most patients (80.7%, n=242) received T-DXd in 3L+.
- **MEOIs**: The most common MEOIs were fatigue, reported in 79.3% of patients, nausea/vomiting in 73.0%, diarrhea in 45.0%, and anemia in 29.7%. Serious MEOIs occurred in ≤5% and included congestive heart failure (n=4, 1.3%), febrile neutropenia (n=5, 1.7%), infusion reactions (n=1, 0.3%), and reduced ejection fraction (n=15, 5%). ILD/pneumonitis was reported in 10.0% (n=30) of patients.
- **Management Actions**: Among those with ILD/pneumonitis, 80.0% (n=24) received corticosteroids, 56.7% (n=17) received hold/delay, and 66.7% (n=20) discontinued T-DXd. Prophylactic intent with supportive care medications was not assessed. Toxicity-related discontinuation occurred in an additional 8.3% of patients for reasons other than ILD/pneumonitis (n=25). Discontinuations with attribution to other MEOIs included fatigue (n=5), reduced ejection fraction (n=5), anemia (n=4), diarrhea (n=3) and nausea/vomiting (n=3). Total discontinuations due to toxicity was n = 45 (15%), comparable to the 16.2% reported in DESTINY-Breast04.[3]

References

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