# Assessing Value Based Care (VBC) Metrics and Clinical Outcomes Among Patients with HER-2 Positive Breast Cancer

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## Background

- HER2-positive breast cancer accounts for approximately 15-20% of breast cancers and is associated with aggressive disease biology with historically poor outcomes in the metastatic setting[1]
- HER2 positivity is defined by an IHC score of 3+ or an IHC score of 2+ with HER2 gene amplification confirmed by in-situ hybridization (ISH)[2]
- Fam-trastuzumab deruxtecan-nxki (Enhertu®, T-DXd) is a HER2-directed antibody-drug conjugate carrying a topoisomerase I inhibitor payload and is approved for multiple HER2-positive, HER2-low, and HER2-ultralow metastatic breast cancer populations[3]
- In DESTINY-Breast03, T-DXd significantly improved median PFS2 compared with T-DM1 (45.2 vs. 23.1 months), suggesting durable benefit beyond initial treatment[4]
- HER2-positive metastatic breast cancer is associated with substantial economic burden, with first-year costs ranging from $218,000 to $320,000 per patient and cumulative 3-year costs exceeding $400,000-$770,000[5,6]
- Patients with metastatic disease incur approximately $13,000 to $34,000 higher monthly healthcare costs than those without progression[6]
- Systemic therapies account for the majority of costs (56%), driven largely by HER2-targeted agents, while inpatient hospitalizations contribute an additional 20%[7]
- Although the DESTINY trials demonstrated superior efficacy, the impact of T-DXd on real-world healthcare resource utilization, including hospitalizations, emergency department visits, supportive care needs, and subsequent treatment patterns, remains unclear
- This retrospective chart review aims to generate real-world evidence assessing whether the clinical benefits of T-DXd translate into measurable reductions in healthcare utilization and associated costs

## Objective

This project aimed to evaluate the impact of treatment selection on downstream healthcare utilization by comparing the frequency and rate of healthcare resource use among patients with HER2-positive metastatic breast cancer (mBC) treated with T-DXd versus a time-aligned cohort receiving alternative standard-of-care therapies

## Methods

- We conducted a retrospective chart review of patients with recurrent unresectable or mBC treated between May 1, 2021 and May 1, 2026 across 11 outpatient hematology/oncology clinics in Northeast Florida
- Electronic health records (EHRs) within OncoEMR® (Ratiron Health, New York, NY) were queried to identify eligible patients

**Inclusion Criteria**

- Adults ≥ 18 years of age
- Pathologically, radiographically, or clinically confirmed diagnosis of recurrent unresectable or mBC (Stage IV, M1)
- Pathologically confirmed HER2-positive disease (IHC3+ or IHC 2+/ISH+)[8]
- Presence of an ICD-10 diagnosis code for malignant neoplasm of the breast (C50.X)
- Receipt of at least one dose of T-DXd or an alternative HER2-directed therapy available within the practice
- Availability of sufficient EHR and/or claims data to capture:
  - Treatment start/end dates
  - Healthcare utilization events
  - Baseline disease characteristics
  - Minimum follow-up of 30 days from treatment initiation (unless death occurred earlier

- Patients were stratified according to demographic and disease characteristics, including: age, sex, HER2 testing methodology, hormone receptor status, treatment exposure, clinical outcomes, and value-based care (VBC) outcomes
- Descriptive analyses were performed to summarize patient demographics, disease characteristics, treatment patterns, clinical outcomes, and VBC metrics
- Categorical variables were reported as frequencies and percentages, while continuous variables were summarized using means, medians, and ranges
- Outcomes were evaluated by treatment group (T-DXd vs. Other HER2-directed therapies) and line of therapy
- Given the small sample size, analyses were exploratory, and no formal statistical comparisons were conducted

## Conclusion and Discussion

- In this real-world cohort of patients with recurrent unresectable or metastatic HER2-positive breast cancer, T-DXd (Enhertu®) was associated with longer rwPFS and lower treatment discontinuation rates compared with other standard HER2-directed therapies when used in both second- and third-line settings
- From a VBC perspective, patients treated with T-DXd generally experienced a longer interval before their first downstream healthcare utilization, potentially reflecting prolonged disease control and delayed need for additional healthcare resources
  - Practices participating in VBC programs should consider a potential increased incidence of inpatient admissions in 2L when evaluating VBC episodes
- Although healthcare utilization outcomes were mixed and should be interpreted cautiously due to a small sample size, the observed improvements in rwPFS coupled with delayed downstream utilizations suggest that T-DXd may offer value beyond clinical efficacy alone by potentially reducing disease-related burden and supporting more efficient resource utilization
- Importantly, the substantial improvement in real-world progression-free survival observed with T-DXd in later-line settings may provide additional real-world rationale for considering earlier use of T-DXd in the treatment sequence
- While this study was not designed to evaluate first-line therapy and cannot establish first-line efficacy, the observed clinical benefit may serve as supportive evidence when discussing the potential value of moving T-DXd earlier in the treatment paradigm, alongside emerging prospective clinical trial data
- Given the retrospective design, limited sample size, and non-randomized nature of analysis, these findings should be considered **hypothesis-generating only** and interpreted in conjunction with clinical trial evidence and current treatment guidelines

## Results

**Baseline Demographics and Clinical Characteristics (n=30):**

Median Age: 60.2 (46.75-75) years old
Female Gender: 30 (100%)
Histology:
- IDC: 26 (86.7%)
- ILC: 2 (6.7%)
- Metaplastic: 1 (3.3%)
- Unknown: 1 (3.3%)

HER2-Positive Expression Status:
- IHC3+ or IHC 2+/FISH+: 28 (93.3%)
- FISH+ only: 2 (6.7%)

Tumor Grade:
- G1: 1 (3.3%)
- G2: 5 (16.7%)
- G3: 14 (46.7%)
- G2/3, GX, Unknown: 10 (33.3%)

HR Status:
- ER+/PR+: 11 (36.7%)
- ER+/PR-: 6 (20.0%)
- ER-/PR-: 12 (40.0%)
- Unknown: 1 (3.3%)

**Table 1. HER2-Directed Treatment by Line of Therapy**

| Line of Therapy | Patients (n) | Most Common Regimens (n, %) |
|---|---|---|
| 1L | 20 | Taxane + HP-containing regimens (19, 95%) |
| 2L | 18 | T-DXd (11, 61%) |
| 3L | 6 | T-DXd (4, 67%) |
| 4L | 5 | Capecitabine + Tucatinib + Trastuzumab (4, 80%) |
| 5L | 1 | Gemcitabine + Trastuzumab (1, 100%) |

**Table 2. Second-Line (2L) Outcomes**

| Outcome | T-DXd (n=10) * | Other Therapies (n=7) |
|---|---|---|
| Discontinuation Rate | 60% (6/10) | 100% (7/7) |
| Median rwPFS (range) | 438 days (112-676) | 91 days (63-934) |
| Median Time to First Healthcare Utilization (range) | 61 days (0-350) | 0.5 days (0-153) |
| Total Inpatient Admissions | 10 | 0 |
| Median ED Visits (range) | 0 (0-2) | 1 (0-1) |
| Median Unscheduled OP Visits (range) | 1 (0-3) | 1 (0-1) |
| New Metastatic Sites | 50% (5/10) | 14% (1/7) |

*not included: 1 patient who switched 2L (patient choice)

**Table 3. Third-Line (3L) Outcomes**

| Outcome | T-DXd (n=3)* | Other Therapies (n=2) |
|---|---|---|
| Discontinuation Rate | 67% (2/3) | 100% (2/2) |
| Median rwPFS (range) | 269.5 days (52-487) | 112 days (91-133) |
| Median Time to First Healthcare Utilization (range) | 0 days (0-43) | 12 days (0-24) |
| Total Inpatient Admissions | 0 | 0 |
| Median ED Visits (range) | 0 (0-3) | 0 (0) |
| Median Unscheduled OP Visits | 0 (0) | 0.5 (0-1) |
| New Metastatic Sites | 0% (0/3) | 100% (2/2) |

*not included: 1 patient who switched 3L due to copay

**Abbreviations:** Invasive ductal carcinoma of no special subtype (IDC); invasive lobular carcinoma (ILC); immunohistochemistry (IHC); fluorescence in situ hybridization (FISH); estrogen/progestogen receptor (ER/PR); real-world progression free survival (rwPFS); emergency department (ED); outpatient (OP); Herceptin® and Perjeta® - containing (HP); progression free survival (PFS)

## Disclosures/References

The authors have no financial or professional disclosures to report.

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