Real-world patterns of trastuzumab deruxtecan (T-DXd) discontinuation in metastatic breast cancer: insights from a single-center experience

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KEY FINDINGS & CONCLUSIONS

- In this real-world study, 82.4% of pts permanently discontinued T-DXd due to disease progression
- AE-related discontinuations were less common (14.3%) and primarily driven by ILD (11%)
- Discontinuations from other AEs or pt choice were rare and occurred less often than in clinical trials
- The rate of discontinuations for reasons other than disease progression is lower than that reported in clinical trials, suggesting that optimal T-DXd management may improve adherence
- The retrospective nature of this study does not allow us to determine which factors contributed most to the improved adherence

Poster: PS5-04-18
Presented at: SABCS 2025. Dec 09th - 12th, 2025; San Antonio, TX, USA

BACKGROUND AND AIM

- T-DXd is an approved standard-of-care treatment for pts with both HER2+ and HER2-low, previously treated metastatic breast cancer (MBC)
- Clinical trials have shown that a substantial proportion of pts (~ 30-50%) discontinue treatment for reasons other than disease progression, most commonly due to adverse events (AEs) or patient choice [1-6]
- Early discontinuation may negatively impact overall treatment efficacy in clinical practice, and discontinuation rates may be influenced by physician and institutional experience with T-DXd management
- This study aimed to evaluate the reasons for T-DXd discontinuation at a single institution with established experience in T-DXd management

METHODS

- We conducted a retrospective observational study using the electronic health records of pts with MBC who received T-DXd at San Raffaele Hospital between Jul 2018 and Sep 2025
- Only pts who permanently discontinued treatment for any reason were included
- Tumors were categorized as HER2+ (IHC 3+ or 2+ ISH amplified) or HER2-low (IHC 1+ or 2+ ISH not amplified) based on at least one biopsy prior to T-DXd initiation, or HER2-0 if all biopsies showed IHC 0
- Reasons for discontinuation: clinical or radiological progressive disease (PD; including death due to progression), AEs (including death due to AE), patient decision, or other causes
- Duration of treatment (DoT): time from T-DXd initiation to permanent discontinuation
- Rates and reasons for dose reductions in this population were also analyzed

RESULTS

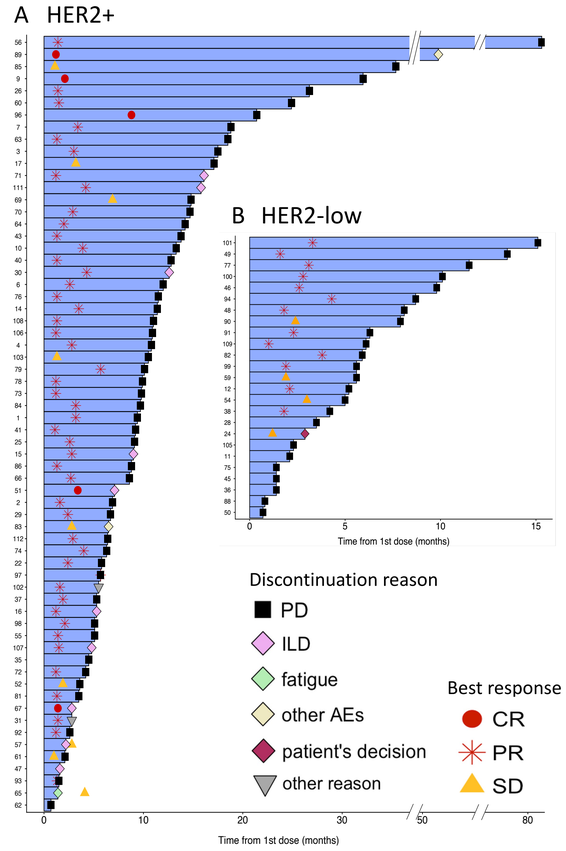
- A total of 91 pts permanently discontinued T-DXd up to November 2025. Patient and disease characteristics are showed in **Table 1**

Table 1. Patient and Disease Characteristics

Characteristics	N = 91 (%)
Age	
Range	24-85
Median	57.4
Sex	
Female	91 (100)
Tumor subtype	
HER2+	64 (70.3)
HER2-low	25 (27.5)
HER2-0	2 (2.2)
N° of prior lines for metastatic disease	
Range	0-13
0	5 (5.5)
1	16 (17.6)
2	29 (31.9)
≥3	41 (45.0)
Visceral metastases	
no	23 (25.3)
yes	68 (74.7)
History of SNC metastases	
no	65 (71.4)
yes	26 (28.6)

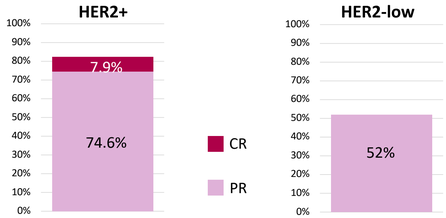
- The median DoT among pts who discontinued T-DXd was 7.1 months [range 0.7–81.4] overall: 9.6 months [0.7–81.4] in HER2+, 5.6 months [0.7–15.1] in HER2-low, and 3.9 months [2.6–5.1] in HER2-0 tumors **(Figure 1)**
- Reasons for discontinuation were PD in 82.4% (n=75), AEs in 14.3% (n=13), patient decision in 1.1% (n=1), and non–treatment-related causes in 2.2% (n=2; one COVID pneumonia and one polytrauma) **(Figure 1)**

Figure 1. Swimmer plot showing individual patient data of treatment duration, best response and discontinuation reasons. A) HER2+ (n=64). B) HER2-low (n=25).



- Overall response rates were 82.5% in HER2+ and 52% in HER2-low **(Figure 2)**. No responses were observed in the two pts with HER2-0 tumors

Figure 2. Overall Response Rates



- AEs leading to discontinuation included ILD in 11% (n=10), fatigue (n=1), liver function test (LFT) increase (n=1), and persistent neutropenia (n=1) **(Figure 1)**
- Among the 10 ILD cases, 4 were Grade 1, 1 Grade 2, 2 Grade 3, and 3 Grade 5. Including only pts who discontinued T-DXd likely enriched the ILD cohort with higher-grade cases
- The three pts with G5 ILD were managed at facilities near their homes, since they lived far from our center. In one patient, a concomitant opportunistic aspergillus infection was documented
- Dose reductions were implemented in 20.9% (n=19) of pts before permanent discontinuation, mainly due to fatigue (8.8%, n=8), LFT increase (6.6%, n=6), and nausea (4.4%, n=4)

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ACKNOWLEDGMENTS This work has been supported in part by Fondazione AIRC per la Ricerca sul Cancro (IG 2018 - ID21787 to G. Bianchini and IG 2024 – ID30919 to G. Bianchini).