Real-world effectiveness of Trastuzumab Deruxtecan in HER2-low Metastatic breast cancer: a single-center retrospective study

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Background

Clinical trials of trastuzumab deruxtecan (T-Dxd) have expanded options for HER2-low breast cancer, yet real-world patients often present with poorer prognostic features such as active brain metastases or heavy pretreatment. Robust effectiveness data in routine practice are therefore needed.

Methods and Materials

This is a retrospective real-world monocentric study conducted by 81 patients with HER2-low advanced breast cancer, who were treated with T-Dxd. Database from the Department of Breast Oncology at Peking University Cancer Hospital was reviewed, spanning March 2023 to January 2025. All patients underwent at least one radiologic response assessment.

Table 1. Study population characteristics.

	All (n=81)	HR+ (n=68)	TNBC (n=13)	*P*
Mean age (range)yr	56.1 (33.3-82.0)	56.5 (37.7-82.0)	54.0 (33.3-68.1)	0.44
Median ECOG	1 (0-3)	1 (0-3)	1 (0-2)	0.23
Visceral Metastases	70	58	12	0.50
Lines of therapy for metastatic disease				
Median no. of lines (range)	5 (2-12)	5 (2-12)	4 (2-10)	0.10
Median no. of chemotherapy	3(1-10)	3(1-8)	4(2-10)	0.05

Results

- The median progression-free survival (PFS) was 6.0 months (95%CI, 3.8-8.1).
- There were 68 HR+(83.95%) and 13 HR- (16.05%) patients included. HR+ disease showed a median PFS of 6.7 months (95%CI, 5.2-8.2) versus 3.4 months (95%CI, 2.1-4.7) in triple-negative breast cancer (TNBC), no statistical significance between these two groups (*P*=0.062). TNBC patients had a significantly shorter median overall survival (OS) (8.7 months, (95%CI, 2.2-15.2) , *P*=0.002), while mOS was not reached in HR+ group.
- Presence of visceral, liver, lung, or CNS lesions did not materially alter PFS (6.0 vs 5.9 months, *P*=0.906).
- Baseline IHC score (HER2 1+ vs 2+) did not affect PFS (5.9 vs 6.0 months, *P*=0.707). But patients whose metastatic sites showed up-regulated HER2 expression achieved longer PFS (7.0 vs 3.4 months, *P*=0.015).
- The cohort had received a median of 4 prior lines of systemic therapy, including a median of 2 chemotherapy regimens. Administering T-Dxd after more than 3 prior chemotherapy lines or after exposure to topoisomerase I/II inhibitors significantly shortened PFS (4.5 vs 7.0 months, *P*=0.018 and 3.2 vs 6.7 months, *P*=0.002, respectively).

- Of the 48 patients who underwent germline BRCA testing, 13 carried BRCA1/2 mutations and 35 were wild type. Although mPFS was numerically longer in the mutant subgroup (7.5 months) than in the wild-type subgroup (4.8 months), the difference was not statistically significant (P = 0.607).
- Among the 13 BRCA-mutated patients, 10 had previously received PARP inhibitors; their mPFS did not differ from that of PARP-naïve patients (7.5 vs 4.5 months, P = 0.989).
- PAM-pathway alterations (PIK3CA/AKT/PTEN) were evaluated in 41 patients, with 11 found to be mutant. Median PFS was similar between the PAM-mutated and wild-type groups (6.0 vs 4.2 months, P = 0.065).

Figure 1. PFS according to HR status

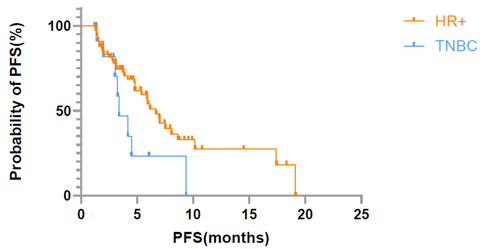
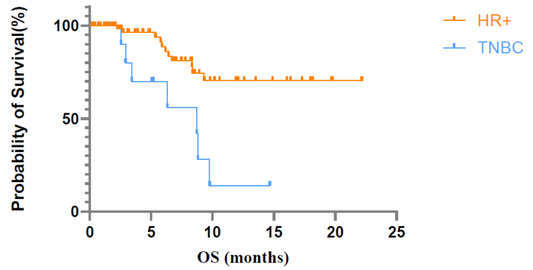


Figure 2. OS according to HR status



Conclusions

- In routine clinical practice, T-Dxd delivers meaningful disease control for heavily pre-treated HER2-low metastatic breast cancer, including patients with active brain metastases—but its effectiveness is more modest than that seen in randomized trials.
- Greatest benefit is observed when: (i) metastatic lesions up-regulate HER2 expression, and (ii) T-Dxd is introduced earlier in the chemotherapy sequence. Outcomes are less favorable in triple-negative disease and after prior topoisomerase-targeted therapy, suggesting that biomarker- and timing-guided patient selection could optimize real-world use.

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