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ORIGINAL RESEARCH

Efficacy of Trastuzumab Deruxtecan in HER2-Positive and HER2-Low Metastatic Breast Cancer: A Real-World Retrospective Cohort Study in China

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Background: Limited real-world data are available on the effectiveness and safety of trastuzumab deruxtecan (T-DXd, DS8201a) in patients with HER2-positive and HER2-low metastatic breast cancer (MBC), particularly within the Chinese population.

Methods: Between 2022 and 2025, 98 patients with MBC treated with T-DXd were retrospectively enrolled at Fudan University Shanghai Cancer Center. Patients were categorized as HER2-positive and HER2-low cohort. Clinical outcomes including objective response rate (ORR), progression-free survival (PFS), disease control rate (DCR), and clinical benefit rate (CBR), were assessed and compared between cohorts. The primary endpoint of the study was PFS, which was estimated using the Kaplan–Meier method and compared using the Log rank test.

Results: Among the 98 patients, the median PFS was 15.0 months. The ORR, DCR, and CBR were 48.0%, 69.4%, and 41.8%, respectively. HER2-positive patients experienced longer PFS compared to HER2-low patients (not reached vs 9.0 months). Among HER2-low patients, liver metastases were associated with poorer outcomes. Patients with brain metastases achieved a median PFS of 15.5 months and a 1-year PFS rate of 65.3%. Grade ≥3 adverse events included neutropenia (20.4%), nausea (5.1%), anemia (4.1%), and interstitial lung disease in 6.1% of patients, leading to discontinuation in 2.0%.

Conclusion: In this real-world analysis, T-DXd demonstrated robust clinical activity in both HER2-positive and HER2-low MBC, consistent with the findings from the DESTINY-Breast clinical trials. Notably, we identified several clinically relevant prognostic factors, including HER2 status, metastatic site, treatment line, and prior therapies. These findings support the broader clinical application of T-DXd and offer insights into individualized treatment selection.

Keywords: T-DXd, prognosis, real-world, breast cancer, HER2

Introduction

Breast cancer remains the most frequently diagnosed malignant tumor in women worldwide, accounting for approximately 32% of all new cancer cases in this population and over 42,000 annual deaths.[1] Over the past decade, breast cancer has been reclassified into distinct molecular subtypes based on gene expression profiling, including luminal A, luminal B, HER2-enriched, and triple-negative subtypes.[2] Among these, the HER2-enriched subtype is characterized by amplification or overexpression of the human epidermal growth factor receptor 2 (HER2).[3] HER2 is overexpressed in approximately 20% of invasive breast cancers and is associated with increased metastatic risk and worse prognosis.[4]

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Approximately 60% of HER2-negative metastatic breast cancers exhibit low (Immunohistochemistry (IHC) 1+ or 2+ with negative in situ hybridization (ISH)) but detectable HER2 expression—a biologically distinct subgroup that has historically fallen outside the scope of traditional HER2-targeted therapies.[5] These HER2-low tumors, spanning both hormone receptor (HR)-positive and triple-negative subtypes, display heterogeneous clinical behaviors and limited responses to conventional treatments, highlighting a critical gap in therapeutic strategies for this patient population.[6] In contrast, therapeutic advancements in HER2-positive disease—including dual HER2 blockade and antibody–drug conjugate (ADC)—have markedly improved survival outcomes.[7] Nevertheless, existing agents like T-DM1 show modest efficacy in later-line settings,[8] minimal activity in HER2-low disease,[9] and suboptimal control of brain metastases,[10] underscoring the need for novel approaches capable of addressing these unmet clinical challenges.

T-DXd is a next-generation HER2-targeted ADC that combines trastuzumab with a potent topoisomerase 1 (TOP1) inhibitor payload (DXd) via a cleavable tetrapeptide-based linker with a high drug-to-antibody ratio (DAR) of 8:1, developed to address these challenges.[11] The DESTINY-Breast (DB) clinical trials have redefined the therapeutic landscape for HER2-expressing tumors. In DB-01 trial, T-DXd demonstrated durable responses in heavily pretreated HER2-positive metastatic breast cancer, leading to FDA approval.[12] This milestone was subsequently validated in the Phase III DB-03 trial, where T-DXd outperformed T-DM1 with a mPFS of 28.8 months vs 6.8 months (HR: 0.28; 95% CI: 0.22–0.37) and reduced the risk of death by 36% in HER2-positive MBC.[13] The paradigm-shifting DB-04 trial extended T-DXd's utility to HER2-low MBC achieving a mPFS of 10.1 months vs 5.4 months with chemotherapy (HR: 0.51; $p<0.001$) and a median overall survival (mOS) of 23.9 vs 17.5 months (HR: 0.64; $p=0.0028$).[14] Emerging investigations like DB-06 are further exploring T-DXd's potential in HER2-ultralow populations (IHC >0<1+), with preliminary data suggesting preserved efficacy.[15] This series of trials exemplifies a strategic expansion from late-line salvage therapy to earlier-line applications and biomarker-driven patient selection, ultimately challenging the historical HER2 classification dichotomy.

These findings have catalyzed a paradigm shift in HER2 classification and therapeutic strategy. Consequently, T-DXd has been incorporated into clinical guidelines as a preferred treatment option for both HER2-positive and HER2-low advanced breast cancer. While randomized trials provide high-level evidence, their strict inclusion criteria often limit generalizability. Therefore, real-world studies are essential to validate efficacy in broader populations and to explore outcomes across heterogeneous clinical scenarios.[16] In this retrospective study, we analyzed the real-world effectiveness of T-DXd in a cohort of patients with HER2-positive and HER2-low MBC, aimed to assess survival outcomes, and identify clinicopathological factors associated with response to therapy.

Materials and Methods

Cohort Population

From January 2022 to February 2025, 98 metastatic breast cancer patients treated with T-DXd were retrospectively enrolled at Fudan University Shanghai Cancer Center. Patients who met the following criteria were enrolled in the study: pathologically diagnosed of invasive breast cancer with HER2-positive or HER2-low status determined by immunohistochemical analysis; the presence of at least one measurable metastatic lesion in accordance with RECIST version 1.1 criteria; and baseline hematologic, hepatic, renal, and electrocardiographic assessments within normal reference ranges. To reduce potential selection bias, all individuals meeting these conditions were included without further restriction. T-DXd was administered intravenously at a dose of 5.4 mg/kg every 3 weeks until disease progression or unacceptable toxicity. We collected clinical characteristics, including age, ECOG performance status, hormone receptor status (ER and PR), HER2 status, and sites of metastasis, as well as data on PFS, OS, treatment responseand adverse events. HER2 status was assessed according to the ASCO/CAP guidelines using IHC as the primary method, with FISH performed for cases scored as IHC 2+. HER2-positive was defined as IHC 3+ or IHC 2+ with ISH amplification, while HER2-low was defined as IHC 1+ or IHC 2+ without ISH amplification. In cases where HER2 expression was near the threshold between IHC 0 and 1+, an experienced breast pathologist at Fudan University Shanghai Cancer Center conducted a secondary pathological review to ensure consistency and accuracy in HER2 classification. The relevant institutional review board or ethics committee of Fudan University Shanghai Cancer Center approved the study (1907204–8 for

Fudan University Shanghai Cancer Center), which was conducted in accordance with the Declaration of Helsinki. All patients gave their signed informed consent.

Efficacy Analysis

The primary endpoint was progression-free survival (PFS), which was calculated from the beginning of treatment with T-DXd until disease progression or death from any cause. The response was evaluated according to the RECIST guideline 1.1. Secondary endpoints included overall response rate (ORR), clinical benefit rate (CBR), and disease control rate (DCR). ORR was defined as the proportion of patients who achieved either a complete or partial response (CR or PR); CBR referred to the percentage of patients who maintained disease control—defined as complete response, partial response, or sustained stable disease for at least 24 weeks (CR, PR, or SD for a minimum of 24 weeks); DCR was determined by evaluating the proportion of patients who achieved disease control (CR, PR, or SD). Duration of response (DoR) was defined as the time from the first documentation of objective response (CR or PR) to the first occurrence of disease progression or death from any cause. PFS2 was defined as the interval from the initiation of post-T-DXd therapy to the second progression or death, in patients who had experienced disease progression on T-DXd. Patients without documented progression or death were censored at the date of the last adequate tumor assessment. Adverse events were evaluated by NCI CTCAE (version 5.0).[17] PFS was estimated using the Kaplan–Meier method, with 95% confidence intervals calculated and compared with Log rank tests. Survival analyses between groups were performed using the Cox proportional hazards model. Significance was set at $p \leq 0.05$. All analyses were performed with Statistical Product and Service Solutions (SPSS) v27.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the hospital ethics committee (1907204–8 for Fudan University Shanghai Cancer Center) and all patients gave their signed informed consent.

Results

Baseline Characteristics

A total of 98 patients with MBC who received T-DXd were included in the final analysis. Table 1 displays the demographic and clinical characteristics of the patients. The median age was 51 years (range, 27–79), and 93.9% had

Table 1 Demographic and Clinical Characteristics of the Patients

Characteristic	Overall Population (n = 98)	HER2-Low (n=52)	HER2-Positive (n=46)
Age at inclusion (years)			
Median (range)	51 (31–74)	51.5 (33–74)	49 (31–74)
ECOG performance status at inclusion			
ECOG≤1	92 (93.9%)	49 (94.2%)	43 (93.5%)
ECOG=2	6 (6.1%)	3 (5.8%)	3 (6.5%)
HR status of breast cancer			
Negative	44 (44.9%)	20 (38.5%)	24 (52.2%)
Positive	54 (55.1%)	32 (61.5%)	22 (47.8%)

(*Continued*)

Table 1 (Continued).

Characteristic	Overall Population (n = 98)	HER2-Low (n=52)	HER2-Positive (n=46)
Most recent known HER2 status (on primary or metastases)			
IHC 1+	20 (20.4%)	20 (38.5%)	0
IHC 2+/ERBB2 ISH-negative	32 (32.7%)	32 (61.5%)	0
IHC 2+/ERBB2 ISH-positive	11 (11.2%)	0	11 (23.9%)
IHC 3+	35 (35.7%)	0	35 (76.1%)
Ki67 index of breast cancer			
≤20%	13 (13.3%)	10 (19.2%)	3 (6.5%)
>20%	75 (76.5%)	37 (71.2%)	38 (82.6%)
Missing	10 (10.2%)	5 (9.6%)	5 (10.9%)
Number of metastatic sites at inclusion			
1	28 (28.6%)	8 (15.4%)	20 (43.5%)
2	41 (41.8%)	14 (26.9%)	17 (37.0%)
≥3	31 (31.6%)	22 (42.3%)	9 (19.6%)
Sites of metastasis at inclusion			
Liver metastasis	41 (41.8%)	25 (48.1%)	16 (34.8%)
Lung metastasis	38 (38.8%)	23 (44.2%)	15 (32.6%)
Brain metastasis	34 (34.7%)	17 (32.7%)	17 (37.0%)
Bone metastasis	50 (51.0%)	30 (57.7%)	20 (43.5%)
Previous anti-HER2 therapy in any setting			
Yes	45 (45.9%)	0	45 (97.8%)
No	53 (54.1%)	52 (100%)	1 (2.2%)
Previous CDK4/6 inhibitor therapy			
Yes	34 (34.7%)	31 (59.6%)	3 (6.5%)
No	64 (65.3%)	21 (40.4%)	43 (93.5%)
Previous lines of treatment in any setting			
1	9 (9.2%)	2 (3.8%)	7 (15.2%)
2	19 (19.4%)	8 (15.4%)	11 (23.9%)
≥3	70 (71.4%)	42 (80.8%)	28 (60.9%)

Abbreviations: ECOG, Eastern Cooperative Oncology Group; HR, Hormone receptor; HER2, human epidermal growth factor receptor 2.

an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. Hormone receptor (HR) status was positive in 54 patients (55.1%) and negative in 44 patients (44.9%). HER2 status at the most recent assessment, either on primary or metastatic lesions, showed HER2-low expression (IHC 1+ or 2+/FISH-) in 52 patients (53.1%) and HER2-positive (IHC 3+ or 2+/FISH+) in 46 patients (46.9%). Visceral metastases were common, including liver (41.8%), lung

(38.8%), and brain (34.7%). The majority of patients (70.4%) had fewer than three metastatic sites. The median number of prior systemic therapy lines was three (range, 1–17), and 71.4% had received three or more prior lines. Additionally, 45.9% of the overall cohort had received anti-HER2 therapy before enrollment, all of whom were HER2-positive.

Clinical Outcomes

Overall, 98 patients received the recommended dose of T-DXd (5.4 mg per kilogram of body weight). In the overall cohort (n = 98), the mPFS was 15.0 months (Figure 1A). Two patients (2.0%) achieved a complete response (CR), thirty-seven (37.8%) a partial response (PR), twenty-nine (29.6%) had stable disease (SD), and thirty (30.6%) progressed (Table 2). The ORR was 48.0% (95% CI: 37.8–57.3), and the DCR was 69.4% (95% CI, 59.3–78.3). The median duration of follow-up was 6.0 months (range, 0.5 to 26). Among the 30 patients with progressive disease (PD), follow-up was continued, and 15 patients received a documented subsequent line of therapy. The median PFS2 in this subgroup was only 2.0 months (95% CI, 1.19–2.81) (Figure 1B).

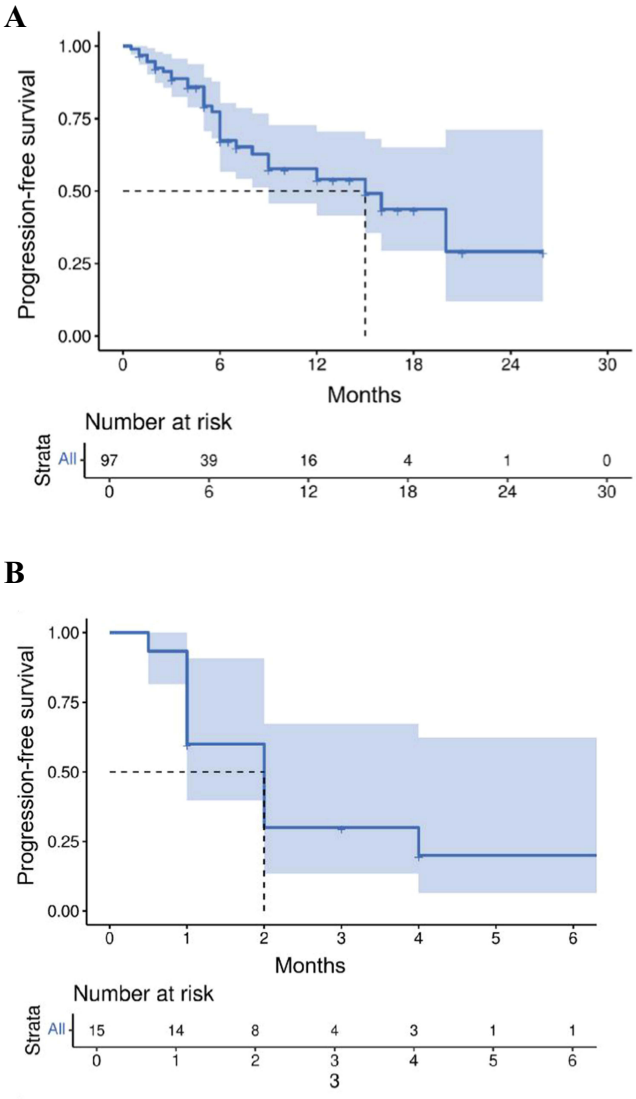

Figure 1 Progression-free survival (PFS) in patients treated with T-DXd. (**A**) Kaplan–Meier curve for PFS in the overall cohort of patients receiving T-DXd (5.4 mg/kg). (**B**) Kaplan–Meier curve for PFS2 in patients who received subsequent therapy after progression on T-DXd.

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Table 2 Response to T-DXd in 98 Metastatic Breast Cancer Patients

Response	Overall Population n (%)	HER2-Low n (%)	HER2-Positive n (%)
Complete response (CR)	2 (2.0%)	1 (1.9%)	1 (2.2%)
Partial response (PR)	37 (37.8%)	20 (38.5%)	17 (37.0%)
Stable disease (SD)	29 (29.6%)	10 (19.2%)	19 (41.3%)
Progressive disease (PD)	30 (30.6%)	21 (40.4%)	9 (19.6%)

Subgroup Analysis

In the HER2-low expression and HER2-positive expression groups, PFS was 9.0 months (95% CI, 4.73–13.27) and not reached, respectively (Figure 2A and B). Additionally, the 12-month PFS rate was markedly lower in HER2-low patients (38.1%) compared to HER2-positive patients (69.2%).

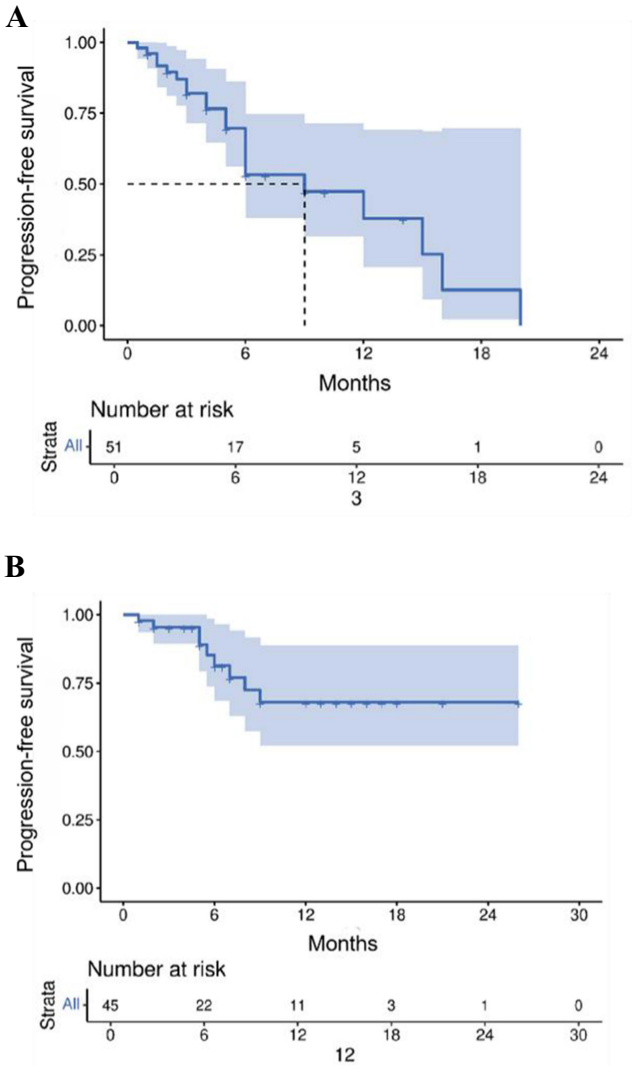

Figure 2 Efficacy of T-DXd and median PFS in HER2-low and HER2-positive patients. (**A**) Kaplan–Meier curve for PFS in patients with HER2-low expression treated with T-DXd. (**B**) Kaplan–Meier curve for PFS in patients with HER2-positive expression treated with T-DXd.

The Log rank test results showed that, in the HER2-low cohort, liver metastasis (p = 0.003) were significantly associated with the effectiveness of T-DXd, whereas age, brain metastasis, bone metastasis, and lines of previous treatment did not show a significant impact. In contrast, within the HER2-positive cohort, none of the evaluated factors—including age, liver metastasis, brain metastasis, bone metastasis, lung metastasis, prior anti-HER2 therapy, or lines of previous treatment—were significantly associated with T-DXd efficacy (Table 3).

In the HER2-low cohort, patients without liver metastases exhibited significantly longer PFS than those with liver metastases (15.0 months vs 6.0 months, p = 0.003) (Figure 3A). In the cohort of HER2-positive patients (n=46), 45 patients had received anti-HER2 therapy before T-DXd. When stratified by the number of prior anti-HER2 treatment lines, those who had received <3 lines demonstrated significantly better PFS compared to those with ≥3 lines (log-rank p = 0.034; HR = 0.026, 95% CI: 0.000–8.841) (Figure 3B). This suggests that earlier-line use of T-DXd may confer superior clinical benefit, even within the HER2-positive population. In 11 patients previously treated with T-DM1, T-DXd achieved an ORR of 36.4% and DCR of 90.9%. The 12-month PFS rate was 88.9%, suggesting preserved efficacy despite prior ADC exposure.

Among the study cohort, 34 patients (34.7%) had brain metastases (BM) at the time of T-DXd initiation. In this subgroup, the median progression-free survival (PFS) was 15.5 months, and the 12-month PFS rate reached 65.3%. A further stratified analysis of patients who had received ≤2 prior lines of therapy in HER2-positive patients—a population similar to that enrolled in the DESTINY-Breast12 (DB-12) trial—showed that the median PFS in patients with BM was not reached, and the 12-month PFS rate reached 88.9%.

In addition, five patients in our cohort presented with leptomeningeal metastasis (LM), of whom three had concurrent parenchymal brain metastases. Four out of five LM patients (80.0%) achieved disease control under T-DXd treatment, including one patient who attained a PFS of 9 months.

In our retrospective study, we analyzed survival and response data of patients treated with T-DXd according to age and compared the findings to the outcomes reported in the DB-01, DB-02 and DB-03 studies (Table 4). Among patients aged <65 years, the median PFS was 20.0 months (95% CI, 4.8–35.2), and 15.0 months (95% CI, 3.8–26.2) in those aged ≥65 years. Response rates were also numerically lower than those reported in clinical trials: ORR was 46.9% (<65 years) and 52.9% (≥65 years), while DCRs were 70.4% and 64.7%, respectively. These differences may reflect more advanced disease, greater treatment burden, and shorter follow-up in the real-world setting. Furthermore, the relatively shorter follow-up period in our study might also contribute to lower recorded survival outcomes and response rates.

Table 3 Log-Rank Analysis of Factors Associated with T-DXd PFS

Characteristic	Log-Rank Analysis p-value	
	HER2-Low	HER2-Positive
Age (≥50 vs < 50)	0.373	0.355
Brain metastasis (yes vs no)	0.506	0.058
Liver metastasis (yes vs no)	0.003	0.447
Bone metastasis (yes vs no)	0.623	0.481
CDK4/6 inhibitor therapy (yes vs no)	0.346	
Previous anti-HER2 therapy in any setting		0.830
Lines of previous treatment (<3 vs ≥3)	0.273	0.572

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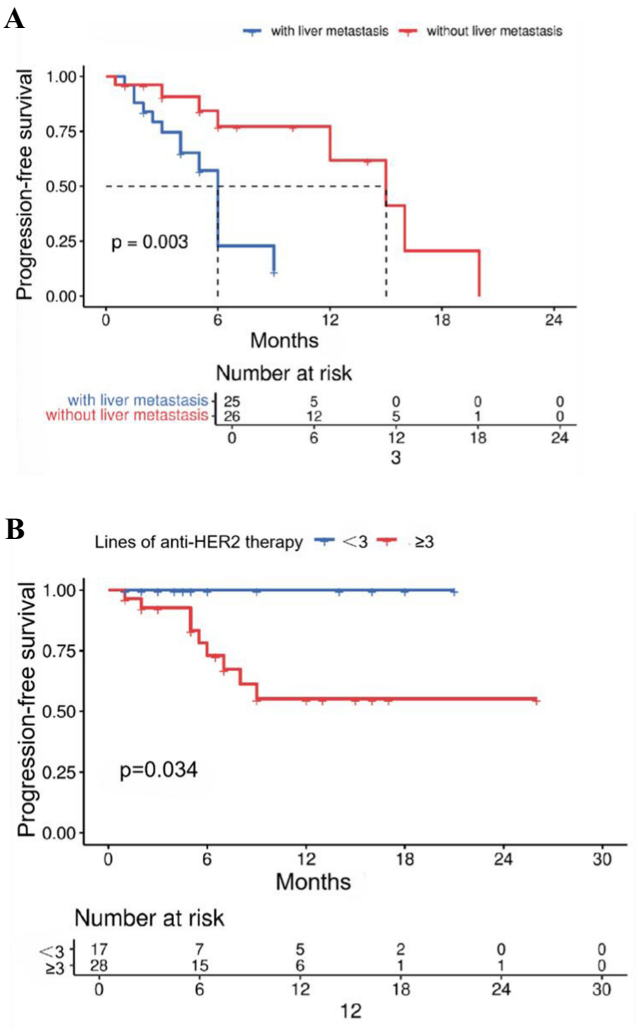

Figure 3 Subgroup analysis of factors associated with PFS in HER2-low and HER2-positive cohorts. (**A**) Kaplan–Meier curve comparing PFS in HER2-low patients with and without liver metastases. Patients without liver metastases showed significantly longer PFS (15.0 months vs 6.0 months, p = 0.003). (**B**) Kaplan–Meier curve for PFS in HER2-positive patients stratified by the number of prior anti-HER2 treatment lines (<3 vs ≥3 lines). Patients receiving fewer than three prior lines demonstrated significantly improved PFS (log-rank p = 0.034).

Safety

Grade ≥3 adverse events included neutropenia (20.4%), nausea (5.1%), and anemia (4.1%). Drug-related interstitial lung disease (ILD) occurred in 6.1% of patients, and 2.0% of patients discontinued medication due to ILD. Permanent discontinuation due to adverse events occurred in three patients (2.0%), including two cases of ILD and one case of renal impairment, indicating that the regimen was generally well tolerated.

Table 4 Comparative Analysis of PFS, ORR, and DCR According to Age in Patients Receiving T-DXd

	DB-01		DB-02		DB-03		Present Study	
	<65 (n=140)	**≥65 (n=44)**	**<65 (n=321)**	**≥65 (n=85)**	**<65 (n=212)**	**≥65 (n=49)**	**<65 (n=81)**	**≥65 (n=17)**
mPFS, (95% CI)	18.1 (13.8-NE)	19.4 (12.4-NE)	17.9 (14.1–20.8)	16.8 (12.7-NE)	30.4 (22.4-NE)	25.1 (14.1–37.3)	20.0 (4.8–35.2)	15.0 (3.8–26.2)
ORR, (95% CI)	62.1 (53.6–70.2)	61.4 (45.5–75.6)	70.7 (65.4–75.6)	65.9 (54.8–75.8)	78.8 (72.6–84.1)	77.6 (63.4–88.2)	46.9 (35.7–58.3)	52.9 (27.8–77.0)
DCR, n (%)	136 (97.1)	43 (97.7)	296 (92.2)	82 (96.5)	205 (96.7)	47 (95.9)	57 (70.4)	11 (64.7)

Discussion

T-DXd has redefined the treatment landscape for HER2-expressing metastatic breast cancer, with clinical trial data supporting its use in both HER2-positive and HER2-low populations. In this real-world cohort, we observed meaningful clinical activity of T-DXd in heavily pretreated patients, consistent with results from the series of DB trials.

In the overall cohort, the mPFS of 15.0 months and ORR of 37.0% were numerically lower than those observed in the DB-03 (mPFS: 28.8 months; ORR: 78.8%) and DB-04 (mPFS: 10.1 months; ORR: 52.6%) trials. This discrepancy likely reflects real-world complexity, including a higher burden of disease (eg, 44% with liver metastases), more extensive prior therapy (median of 3 lines), and inclusion of patients with poor prognostic features. Notably, patients with HER2-low tumors derived clinical benefit from T-DXd, with a median PFS of 9.0 months—comparable to the DB-04 population (10.1 months). However, outcomes remained inferior to those in HER2-positive patients, supporting the hypothesis that HER2 expression level continues to influence T-DXd efficacy.

HER2 expression plays a critical role in predicting the efficacy of T-DXd, making accurate and reproducible HER2 assessment indispensable in clinical practice. Currently, pathological evaluation of HER2 status relies predominantly on IHC and FISH, even though the original purpose of IHC was to distinguish HER2 IHC 3+ from lower levels of expression.[18] This methodology, however, has limitations in reliably differentiating between HER2-low and ultra-low expression.[19] "Microscope magnification rule" along with secondary reviews when results fall near the threshold between IHC 0 and 1+, is critical for achieving reproducibility across different institutions.[20] In our study, nearly all enrolled patients had pathology slides re-reviewed and interpreted by experienced breast pathologists at our center, ensuring consistency and reliability in HER2 status assignments.

At the 2024 ESMO Congress, the DB-12 trial presented the first prospective data focusing on the management of brain metastases in patients with HER2-positive breast cancer following ≤2 prior lines of therapy.[21] In the cohort with BM at baseline, the reported median PFS was 17.3 months, and the 12-month PFS rate reached 61.6%. In our retrospective study, among the overall population with concurrent BM, the median PFS reached 20.0 months, and the 12-month PFS rate was 65.3%, suggesting that real-world outcomes may be comparable to or even slightly exceed those reported in DB-12. Among the subgroup aligns with the inclusion criteria of the DB-12 study, those with BM exhibited a 12-month PFS rate of 88.9%. These findings indicate that the presence of BM may still be associated with an inferior prognosis in earlier-line settings, despite the promising activity of T-DXd. Collectively, our results underscore the clinical potential of T-DXd in managing HER2-positive breast cancer with BM.

Leptomeningeal metastasis (LM) from breast cancer is a highly invasive and clinically devastating complication that occurs in approximately 5–15% of advanced breast cancer patients, associated with significant neurological morbidity and poor prognosis.[22] T-DXd has demonstrated intracranial efficacy in the Phase II DEBBRAH trial, seven patients with cytologically confirmed LM achieved a median overall survival (OS) of 13.3 months and PFS of 8.9 months, with 71.4% achieving prolonged disease control.[23] Consistent with signals from the phase II DEBBRAH trial, our small but clinically informative cohort (n = 5) exhibited an 80% disease control rate. While these numbers should be interpreted cautiously due to sample size limitations, they further support the CNS activity of T-DXd and underscore its potential in addressing an area of high unmet need.

Post–T-DXd progression remains a therapeutic challenge. In our study, PFS2 after T-DXd failure was short (median, 2.0 months), reflecting either intrinsic resistance or aggressive disease biology. Notably, a multicenter retrospective study involving 84 patients with HER2-low metastatic breast cancer reported a m PFS2 of 4.4 months with sequential T-DXd and SG treatment, suggesting that PFS2 may exceed 2 months in broader populations.[24] The shorter PFS2 observed in our cohort may be attributed to the small sample size and differences in patient characteristics and subsequent therapies. With the expanding use of T-DXd and the advent of the post–T–DXd era, further investigation into resistance mechanisms is essential to optimize clinical outcomes.

This study has limitations inherent to retrospective, single-institution analyses. Additionally, follow-up duration was modest, and survival data are immature. Ongoing studies and longer follow-up will further elucidate the long-term outcomes, explore mechanisms underlying resistance in HER2-low disease, and evaluate combinatorial strategies to enhance T-DXd efficacy in high-risk subgroups including liver metastases and other clinically aggressive disease phenotypes. Furthermore, our findings highlight the importance of multidisciplinary team (MDT) approaches in optimizing individualized treatment

strategies, particularly for patients presenting with risk factors such as brain or liver metastases. In addition, proactive monitoring and management of interstitial lung disease (ILD), a known adverse event associated with T-DXd, remains critical to ensuring treatment safety and maximizing clinical benefit. These insights provide a framework for future clinical practice and research aimed at refining patient selection, sequencing therapies, and implementing comprehensive care models in the management of HER2-expressing metastatic breast cancer.

In conclusion, T-DXd demonstrated robust efficacy in both HER2-positive and HER2-low metastatic breast cancer patients, with an excellent safety and tolerability profile. The results support its use in routine clinical practice and underscore the need for optimized patient selection and post-progression strategies.

Abbreviations

ADC, Antibody-drug conjugate; AE, Adverse event; BM, Brain metastasis; CI, Confidence interval; CR, Complete response; DCR, Disease control rate; HER2, Human epidermal growth factor receptor 2; HR, Hormone-receptor; HR, Hazard ratio; ILD, Interstitial lung disease; ISH, In situ hybridization; LM, Leptomeningeal metastasis; mPFS, Median progression-free survival; ORR, Objective response rate; PD, Progressive disease; PFS, Progression-free survival; PR, Partial response; RECIST, Response evaluation criteria in solid tumors; SD, Stable disease; T-DM1, Trastuzumab emtansine; T-DXd, Trastuzumab deruxtecan.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that there is no conflict of interest in this work.

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