

Trastuzumab Emtansine (T-DM1) and Survival Outcomes in HER2-Positive Metastatic Breast Cancer: A Single-Center Experience

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Abstract

Aim: To describe real-world outcomes of trastuzumab emtansine (T-DM1) in patients with HER2-positive metastatic breast cancer and to explore clinical factors associated with survival.

Methods: This retrospective single-center cohort included women with HER2-positive metastatic breast cancer who received at least one cycle of T-DM1 between March 2020 and January 2025 at Adana City Training and Research Hospital. Demographic, clinicopathologic and treatment-related data were collected from electronic health records. Progression-free survival (PFS) and overall survival (OS) were estimated using the Kaplan-Meier method, and prespecified subgroups were compared using two-sided log-rank tests.

Results: Sixty-one patients were included; median age at T-DM1 initiation was 52 years (range, 34–82). All had received prior trastuzumab-based therapy, most had been treated with taxanes and pertuzumab, and T-DM1 was used predominantly as second-line treatment. Median PFS was 8.1 months (95% CI, 6.9–9.2) and median OS was 24.5 months (95% CI, 22.7–26.3). The objective response rate was 55.7%, with stable disease in 8.2%. ECOG performance status was the strongest prognostic factor. Patients with ECOG 0–1 had longer PFS (10.9 vs 5.9 months) and OS (30.3 vs 10.5 months) than those with ECOG 2. Median OS was shorter in patients with brain/CNS metastases than in those without (8.9 vs 25.1 months), while PFS did not differ meaningfully between these groups.

Conclusions: In this real-world cohort, T-DM1 provided PFS, OS and response rates comparable to those reported in clinical trials, in a population previously treated with trastuzumab- and pertuzumab-based first-line therapy and receiving T-DM1 predominantly as second-line treatment. Performance status and brain/CNS involvement were key determinants of outcome. These findings emphasize the prognostic role of performance status and the continuing need for more effective approaches in patients with brain/CNS metastases.

Keywords: T-DM1; HER2-positive breast cancer; metastatic breast cancer

1. Introduction

Breast cancer (BC) is the most commonly diagnosed cancer in women worldwide and remains one of the leading causes of cancer-related death among women¹. It is a heterogeneous disease, broadly defined by hormone receptor and human epidermal growth factor receptor 2 (HER2) status, with distinct patterns of clinical behavior and response to systemic therapy. HER2-positive tumors account for approximately 15–20% of all breast cancers and were historically associated with a poorer prognosis before the introduction of HER2-targeted therapies²⁻⁴.

Trastuzumab emtansine (T-DM1) is an antibody–drug conjugate that links trastuzumab to the microtubule inhibitor DM1, enabling targeted delivery of cytotoxic therapy to HER2-overexpressing tumor cells while preserving the anti-HER2 properties of the antibody⁵⁻⁷. Phase III trials such as EMILIA and TH3RESA have shown that T-DM1 improves progression-free and overall survival com-

pared with capecitabine plus lapatinib or physician's choice in previously treated HER2-positive metastatic breast cancer, with a more favorable toxicity profile^{5,7,8}.

Despite these results, trial populations do not fully reflect routine practice, where many patients are older, have comorbidities and receive T-DM1 in later lines after multiple HER2-directed regimens. Real-world data on the effectiveness and tolerability of T-DM1, particularly from our region, remain limited. In this retrospective single-center study, we aimed to describe the clinical characteristics, treatment patterns, tumor response, progression-free survival (PFS) and overall survival (OS) of patients with HER2-positive metastatic breast cancer treated with T-DM1, and to explore clinical and treatment-related factors associated with survival outcomes.

2. Materials and Methods

2.1. Study Design and Setting

This retrospective cohort study was carried out in the Medical Oncology Clinic of Adana City Training and Research Hospital.

2.2. Patient Selection

This retrospective cohort comprised consecutive patients who started trastuzumab emtansine (T-DM1) for metastatic HER2-positive breast cancer at Adana City Training and Research Hospital between March 2020 and January 2025. During this interval, all patients who newly initiated T-DM1 in routine clinical practice were identified. Because the intention was to include the entire eligible population rather than a predefined sample, no formal sample size calculation was performed and all analyses were considered exploratory. After approval by the Institutional Review Board of Adana City Training and Research Hospital, clinical and outcome data were retrieved from the electronic health records. In total, 61 consecutive patients who received at least one dose of T-DM1 and had available follow-up information were included in the analysis.

2.2.1 Inclusion Criteria

- (I) Age ≥ 18 years
- (II) Histopathologically confirmed HER2-positive breast carcinoma
- (III) Metastatic disease
- (IV) At least one prior line of systemic therapy for metastatic disease, including HER2-targeted treatment, followed by initiation of T-DM1

2.2.2 Exclusion Criteria

- (I) Missing key clinical data or insufficient follow-up precluding outcome assessment
- (II) Patients who received T-DM1 only in the adjuvant setting without metastatic disease
- (III) Diagnosis of a second concomitant primary invasive malignancy

2.3. Clinical, Demographic, and Treatment Data Collection

Demographic, clinicopathologic, and treatment-related variables including age, menopausal status, hormone receptor status, Ki-67 index, histologic subtype, sites of metastasis, disease stage at initial diagnosis, Eastern Cooperative Oncology Group (ECOG) performance status, prior systemic and HER2-targeted therapies, T-DM1 treatment line and start date, best radiologic response, and dates of progression, death, or last follow-up were retrospectively extracted from the hospital's electronic health records and patient files.

2.4. Outcome Measures and Definitions

Index date: The date of T-DM1 initiation.

Progression-free survival (PFS): Interval from the index date to the first documentation of radiologic or clinical disease progression, or death from any cause, whichever occurred earlier; patients with no event were censored at the date of last follow-up.

Overall survival (OS): Interval from the index date to death from any cause; patients who were alive at last contact were censored at the date of last follow-up.

2.5. Statistical Analysis

Overall survival (OS) and progression-free survival (PFS) were calculated as defined above. Survival curves were estimated using the Kaplan–Meier method with 95% confidence intervals (CIs). Between-group differences were evaluated with two-sided log-rank tests ($p < 0.05$) for the following prespecified factors: hormone receptor status (positive vs negative), de novo stage IV versus recurrent metastatic disease, presence of visceral metastases (yes vs no), presence of brain metastases (yes vs no), Eastern Cooperative Oncology Group (ECOG) performance status (0–1 vs ≥ 2), and T-DM1

treatment line (second vs third or later). Given the limited sample size and number of events, formal multivariable Cox modeling was not planned in order to minimize the risk of overfitting. All statistical analyses were performed using IBM SPSS Statistics, version 25.0 (IBM Corp., Armonk, NY, USA).

3. Results

3.1. Patient Characteristics

A total of 61 women with metastatic HER2-positive breast cancer who received T-DM1 were included. The median age at T-DM1 initiation was 52 years (range 34–82). Twenty-eight patients (45.9%) were premenopausal and 33 (54.1%) postmenopausal. Most tumors were hormone receptor-positive (42 patients, 68.9%), and a high proliferative index (Ki-67 $\geq 20\%$) was observed in 40 patients (65.6%). At initial diagnosis, 33 patients (54.1%) had de novo metastatic disease, 21 (34.4%) had locally advanced disease, and 7 (11.5%) had early-stage disease that later relapsed. Bone metastases were present in 42 patients (68.9%), visceral metastases in 43 (70.5%), and brain/CNS metastases in 12 (19.7%). ECOG performance status was 0–1 in 43 patients (70.5%) and ≥ 2 in 18 (29.5%).

Table 1

Baseline patient characteristics (N=61)

Sex (female), n (%)	61 (100)
Age (years), Median (range)	52 (34-82)
ECOG, n (%)	
• 0	9 (14.8)
• 1	34 (55.7)
• 2	18 (29.5)
Menopausal status, n (%)	
• Premenopausal	28 (45.9)
• Postmenopausal	33 (54.1)
Hormone receptor status, n (%)	
• Positive	42 (68.9)
• Negative	19 (31.1)
Ki67 index, n (%)	
• $< 20\%$	21 (34.4)
• $\geq 20\%$	40 (65.6)
Disease stage at initial diagnosis, n (%)	
• De novo metastatic	33 (54.1)
• Locally advanced	21 (34.4)
• Early stage	7 (11.5)
Metastatic sites, n (%)	
• Bone metastases	42 (68.9)
• Visceral metastases	43 (70.5)
• Brain/CNS metastases	12 (19.7)
Line of T-DM1 for metastatic disease, n (%)	
• Second line	55 (90.2)
• Third line	6 (9.8)
Prior systemic/HER2-targeted therapies, n (%)	
• Trastuzumab-based therapy	61 (100)
• Taxane	56 (91.8)
• Pertuzumab	54 (88.5)
• Capecitabine–lapatinib	6 (9.8)
• Vinorelbine	5 (8.2)

All patients had previously received trastuzumab-based therapy. Taxanes had been used in 56 patients (91.8%) and pertuzumab in 54 (88.5%), whereas capecitabine–lapatinib and vinorelbine had been administered in 6 (9.8%) and 5 (8.2%) patients, respectively. T-DM1 was given predominantly as second-line therapy for metastatic disease (55 patients, 90.2%), while 6 patients (9.8%) received T-DM1 in the third or later line. Patient characteristics and demographic data are summarized in Table 1.

3.2. Efficacy Outcomes

At the data cutoff date, 91.8% of patients had experienced disease progression or death. Median progression-free survival (PFS) was 8.1 months (95% CI, 6.9–9.2; Figure 1). Overall, 52 deaths (85.2%) were recorded, and median overall survival (OS) was 24.5 months (95% CI, 22.7–26.3; Figure 2). According to RECIST v1.1, an objective response (complete or partial response) was achieved in 55.7% of patients, stable disease in 8.2%, and progressive disease as best overall response in 36.1%.

3.3. Prognostic Factors and Subgroup Analyses

In univariable analyses, ECOG performance status was the strongest determinant of outcome. Patients with ECOG 0–1 had a median PFS of 10.9 months, compared with 5.9 months in those with ECOG 2, indicating significantly shorter PFS in patients with impaired performance status ($p < 0.001$; Figure 3). Similarly, median OS was 30.3 months in patients with ECOG 0–1 and 10.5 months in those with ECOG 2 ($p < 0.001$; Figure 4). Brain metastasis status also influenced OS: median OS was 25.1 months in patients without brain metastases and 8.9 months in those with brain metastases, a difference that was clinically meaningful but of borderline statistical significance (Figure 5; $p = 0.068$). In contrast, PFS did not differ significantly between patients with and without brain metastases (median 5.6 vs 8.4 months; $p = 0.155$). Hormone receptor status (positive vs negative) and disease extent at diagnosis (de novo metastatic vs recurrent metastatic) were not associated with significant differences in PFS or OS (all $p > 0.05$).

Figure 1

Progression-free survival (PFS) in the study cohort

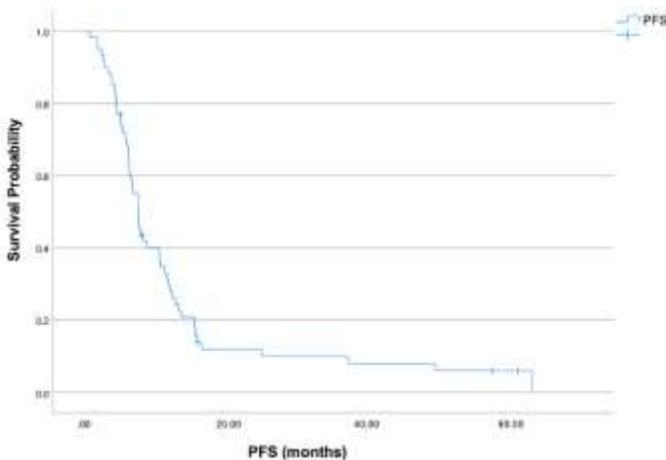


Figure 3

Progression-free survival (PFS) according to ECOG performance status

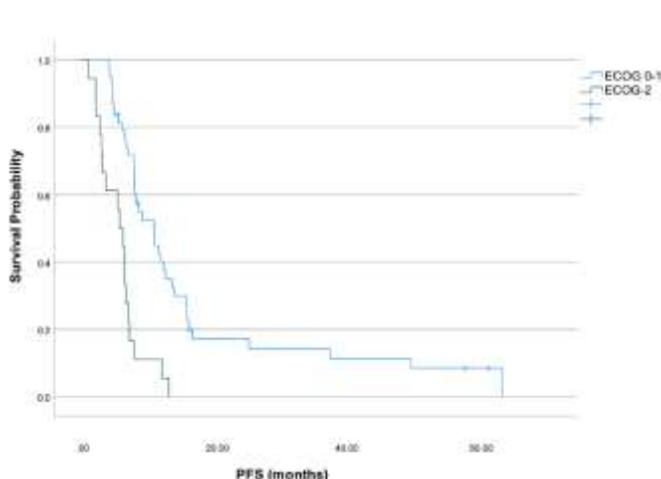


Figure 2

Overall survival (OS) in the study cohort.

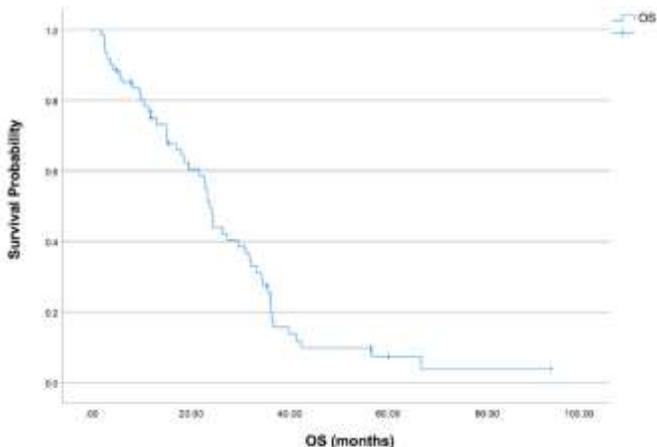


Figure 4

Overall survival (OS) according to ECOG performance status

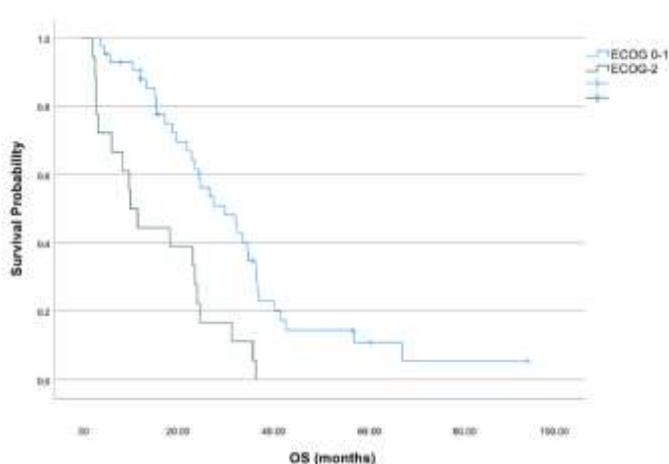
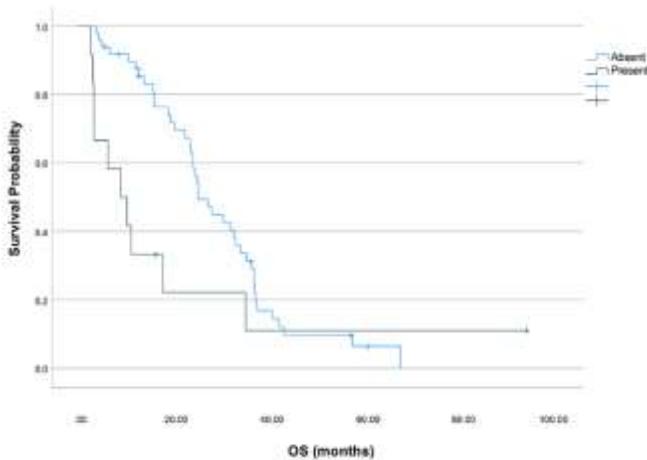


Figure 5

Overall survival (OS) according to the presence of brain/CNS metastases



4. Discussion

In this single-center retrospective cohort study of 61 women with metastatic HER2-positive breast cancer treated with T-DM1, median PFS was 8.1 months and median OS was 24.5 months, with an objective response rate of 55.7%. These outcomes are similar to those reported for the T-DM1 arm in the EMILIA trial, which showed a median PFS of 9.6 months, a median OS of 30.9 months, and an objective response rate of 43.6% in previously treated patients⁵. The somewhat shorter OS in our cohort may be related, at least in part, to the inclusion of patients with ECOG 2 performance status, whereas EMILIA enrolled only patients with ECOG 0–1.

In our study, performance status was the most informative prognostic factor. Patients with ECOG 0–1 had almost double the median PFS and roughly three-fold longer median OS compared with those with ECOG 2, and both differences were highly significant. Taken together, these findings suggest that T-DM1 should ideally be introduced while performance status is still 0–1, rather than deferred to later lines when declining function and comorbidities may limit benefit and tolerability.

Brain metastasis was also associated with a clear reduction in OS in our cohort, although the p value was only borderline. Patients without brain/CNS metastases had a median OS of 25.1 months, compared with 8.9 months in those with brain/CNS involvement. The direction and size of this effect are in keeping with previous reports showing worse survival in patients with HER2-positive disease and CNS metastases, even in the era of modern HER2-directed therapy. In contrast, we did not observe a significant difference in PFS between patients with and without brain metastases, which may reflect the small number of patients with CNS disease, the impact of local brain-directed treatments, and the difficulty of capturing intracranial progression reliably in routine practice.

Our findings can also be viewed in the context of other real-world data. A large Turkish multicenter series of 414 patients reported a median PFS of 9.0 months and a median OS of 41.1 months with T-DM1, with better outcomes when it was used in earlier treatment lines⁹. Interestingly, while median PFS in our study was very similar to that cohort (8.1 vs 9.0 months), median OS was considerably shorter, which likely reflects differences in baseline prognosis and treatment sequence, including the presence in our cohort of patients with ECOG 2 performance status and a substantial proportion with brain/CNS metastases. In a retrospective analysis from The

Royal Marsden including 128 patients, median PFS and OS with T-DM1 were 8.7 and 20.4 months, respectively, with an overall response rate of 64.1% despite heavy pretreatment and a CNS metastasis rate of almost 40%¹⁰. The close agreement in PFS between these cohorts and ours supports the notion that T-DM1 maintains similar disease-control activity outside clinical trials, whereas differences in OS across studies are more likely driven by patient selection and access to post-T-DM1 therapies.

In the phase III TH3RESA trial, which included heavily pretreated patients with a median of four prior regimens after at least two HER2-directed therapies, trastuzumab emtansine improved overall survival compared with treatment of physician's choice (median OS 22.7 vs 15.8 months), despite almost half of the control arm subsequently receiving T-DM1. Median PFS was 6.2 months⁸. In our cohort, T-DM1 was used predominantly in the second-line setting and after widespread exposure to pertuzumab-containing regimens, yet we observed a similar range of outcomes (median OS 24.5 months and median PFS 8.1 months). Considered together with EMILIA and TH3RESA, these data suggest that the survival benefit of T-DM1 is preserved across different lines of therapy and in various practice settings, while absolute OS appears to be largely influenced by prior treatment burden, performance status and subsequent lines of systemic therapy.

Hormone receptor status and disease extent at diagnosis were not significantly associated with PFS or OS in our cohort. This may partly reflect the limited sample size, but it also suggests that once patients reach the stage of receiving T-DM1, factors such as performance status, metastatic burden and prior treatment exposure may be more relevant for prognosis than initial stage or hormone receptor co-expression.

This study has several limitations. It is retrospective, comes from a single center and includes a relatively small number of patients, so the findings should be interpreted in light of these constraints. We did not perform multivariable modeling because of the limited number of events, and overall survival was not adjusted for systemic therapies given after discontinuation of T-DM1. In addition, unmeasured factors such as comorbidities, the exact extent of metastatic disease and the intensity of follow-up may also have influenced outcomes.

On the other hand, the cohort reflects contemporary routine practice, with high rates of prior trastuzumab, pertuzumab and taxane use and predominant use of T-DM1 in the second-line setting. All patients were treated and followed at the same institution with consistent response assessment, allowing near-complete capture of progression and survival events. The study also provides real-world data on clinically relevant subgroups, including patients with ECOG 2 performance status and brain/CNS metastases, in whom prospective trial data remain limited.

Statement of ethics

The retrospective study protocol was reviewed and approved by the Ethics Committee of Adana City Training and Research Hospital, Adana, Turkey (Meeting No: 17, Date: 25 September 2025, Approval No: 736). The study was conducted in accordance with the Declaration of Helsinki and local regulatory requirements.

genAI

No artificial intelligence-based tools or generative AI technologies were used in this study. The entire content of the manuscript was originally prepared, reviewed, and approved by all authors.

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Conflict of interest statement

The authors declare that they have no conflict of interest.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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