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Clinical Outcomes of Trastuzumab Emtansine (T-DM1) Following Trastuzumab Deruxtecan (T-DXd) in Metastatic Breast Cancer: A Single-Center Experience

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Introduction

- HER2-positive metastatic breast cancer (MBC) remains an oncological challenge after disease progression to pertuzumab-trastuzumab, and fam-trastuzumab deruxtecan.
- Data on treatment outcomes with trastuzumab emtansine (T-DM1) following treatment on trastuzumab deruxtecan (T-Dxd) remain limited.
- This study evaluates the clinical outcomes of patients with HER2-positive MBC who received TDM-1 after prior therapy with T-Dxd.

Methods

- Demographics and clinical characteristics are summarized for the whole cohort. **(Table 1)**
- Continuous variables were summarized using medians and ranges, while categorical variables were summarized using frequencies and percentages.
- Overall survival (OS), defined as the time from the date of receiving T-DM1 to the date of death or last follow-up.
- Progression-free survival (PFS), defined as the time from the date of receiving first dose of T-DM1 to the date of first documented disease progression or death, whichever occurred first.
- Time to progression (TTP), defined as the time from the date of receiving first dose of T-DM1 to the date of disease progression. Deaths without documented progression are censored.
- Evaluated using the Kaplan-Meier method, and differences in survival curves were compared using the log-rank test.
- Cox proportional hazards regression models assessed associations between survival outcomes and clinical variables.
- The overall response rate was calculated based on the proportion of patients experiencing progressive or stable disease.
- A p-value <0.05 was considered significant. Analyses were performed using R version 4.2.2

Results

- All 22 patients were female with a median age of 55.5 years. (range: 20–82).
- Most patients were White (73%), with 59% HR+ and 18% HER2-low **(Table 1)**
- Sixty-four percent had received ≥3 lines of prior therapy.

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Results

Table 1. Summary of Patients and Clinical Characteristics

Measure	Level	All (N=22)
Age at metastatic disease, n (%)	18-40	6 (27)
	41-60	7 (32)
	61-70	8 (36)
	71-80	0 (0)
	>80	1 (5)
Gender, n (%)	Male	0 (0)
	Female	22 (100)
Race, n (%)	Asian	3 (14)
	Black or African American	2 (9)
	White	16 (73)
	Other	1 (5)
HR+ at Any time, n (%)	Negative	9 (41)
	Positive	13 (59)
HER2 low at Any time, n (%)	No	18 (82)
	Yes	4 (18)
Number of treatments prior to TDM-1, n (%)	2	8 (36)
	>=3	14 (64)
Death, n (%)	Dead	12 (55)
	Alive	10 (45)
Progressed, n (%)	Yes	20 (91)
	No	2 (9)
Follow-up (in months)	Median (Range)	9.10 (1.12 – 30.69)

- Median OS was 13.5 months (95% CI: 8.74–Not estimable (NE)). OS differed significantly by race (p = 0.014), although small subgroup sizes limit interpretation.) **(Figure 1, Table 2).**
- Median PFS was 2.1 months (95% CI: 1.35–2.69) **(Figure2, Table 2).**
- Median TTP was 2.2 months (95% CI: 1.38–2.69). HER2-low was associated with shorter TTP (1.47 months vs 2.27 months; HR: 5.30; p = 0.006) **(Figure 3, Table 2).**

Table 2. Summary of Overall Survival Univariate Analysis

Measure	Total#: #events	Yr1 survival probability	Median (95% CI) in months
OS-All	22:12	50	13.5 (8.74 – NE)
PFS-All	22:20	11	2.1 (1.35 – 2.69)
TTP-All	22:19	12	2.2 (1.38 – 2.69)

Figure 1: Overall Survival-All Patients

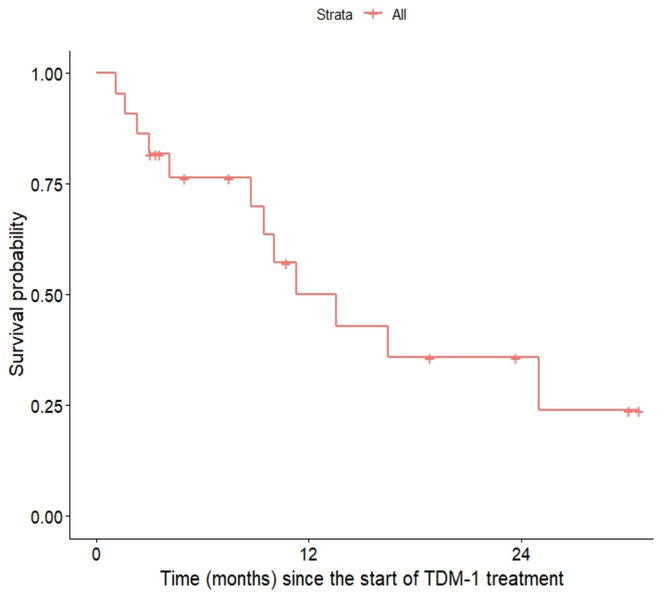


Figure 2: Progression-free Survival- All Patients

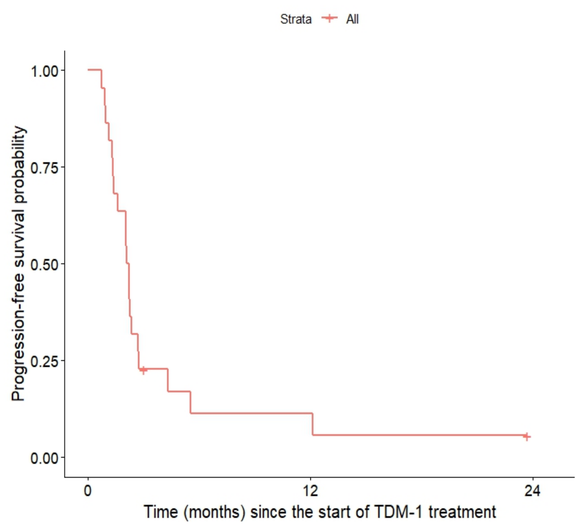
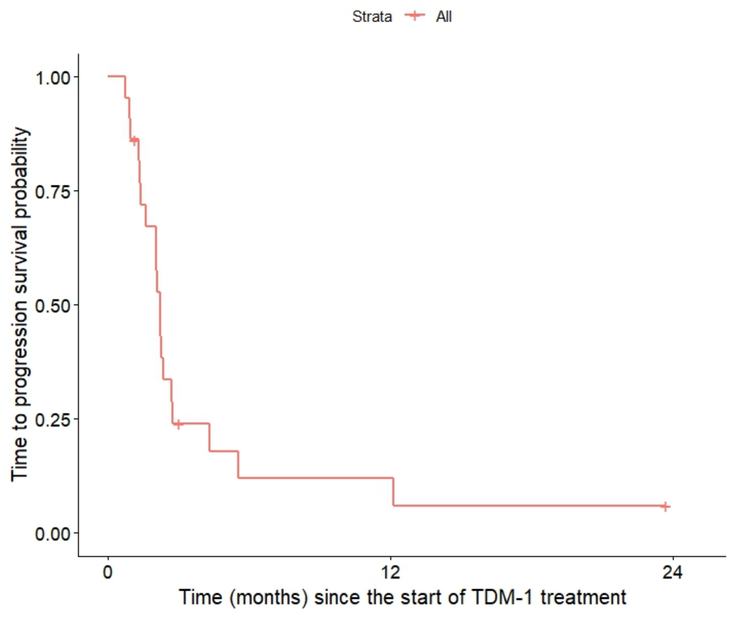


Figure 3: Time to Progression- All Patients



Conclusions

- This study provides real-world evidence of the limited clinical efficacy of TDM-1 following resistant to T-Dxd in HER2-positive MBC.
- Further research is warranted to develop novel therapeutic agents in this subgroup of patients and also to develop strategies to avoid resistant to T-Dxd.

Acknowledgment

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