Preliminary Real-World Comparative Analysis of Trastuzumab Deruxtecan *versus* Trastuzumab Emtansine in Second Line HER2-Positive Metastatic Breast Cancer

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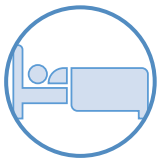
Introduction:

- Trastuzumab deruxtecan (T-DXd) recently received financial approval by the portuguese medicine's authority – *INFARMED* - to be used in second line HER2-positive metastatic breast cancer (2L HER2+ mBC).
- Before this, trastuzumab emtasine (T-DM1) was the standard of care.

Objectives:

- Compare our hospital's T-DM1 historical clinical data with the most recent T-DXd data.

Methods:



Clinical and pharmacy records analysis

All patients in 2L HER2+ mBC treated with T-Dxd or T-DM1 until 31st May 2025 selected

Median time to treatment discontinuation from all cause´s estimated through Kaplan-Meier survival analysis

Log-rank test used for comparison

Extrapolation of immature T-DXd data with different parametric survival distributions

AIC criteria used for best fit

Area under the curve (AUC) comparison of fitted curves

Calculation of mean survival time gained up to 48 months with 95% confidence intervals (95%CI)

Statistical analyses were performed using R software, version 4.5.1.

Results:

Table 1 - Age, treatment duration, outcomes and discontinuation details by treatment group.

	T-DM1 (N=79)	T-DXd (N=11)	p value
Age, years			0.264
• Median (range)	54.1 (31.2, 90.1)	45.9 (27.4, 71.2)	
Treatment duration, months			0.514
• Median (range)	5.0 (0.7, 48.9)	6.5 (1.4, 10.8)	
Response rate			
• Tumor response (TR)	2 (2.5%)	3 (27.3%)	
• Stable disease (SD)	10 (12.7%)	6 (54.5%)	
• Disease progression (DP)	62 (78.5%)	1 (9.1%)	
• Missing data	5 (6.3%)	1 (9.1%)	
Treatment discontinuation			
• Yes	75 (94.9%)	2 (18.2%)	
• No	4 (5.1%)	9 (81.8%)	
Reason for discontinuation			
• N-Miss	4	9	
• DP	59 (78.7%)	1 (50.0%)	
• Toxicity/Severe infection	12 (16.0%)	0 (0.0%)	
• Death	4 (5.3%)	0 (0.0%)	
• Lost for follow-up	0 (0.0%)	1 (50.0%)	

All patients were women. One-way ANOVA test.

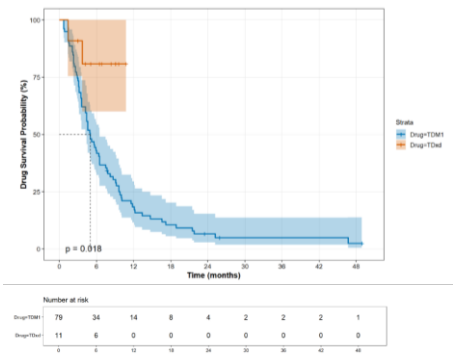


Figure 1 - Kaplan-Meier drug survival curves of observed real world data for both drugs. Median time until treatment discontinuation of all causes was 5.0 months (95%CI, 4.2-6.5) for T-DM1 group, and not reached for T-DXd group. Log-rank test (chi-square = 5.633, p = 0.0176).

Table 2 - Survival summary data.

	records	n.max	n.start	events	rmean	se(rmean)	median	0.95LCL	0.95UCL
Drug=T-DM1	79	79	79	75	8.644377	1.189054	5	4.2	6.5
Drug=T-DXd	11	11	11	2	40.016162	5.664408	NA	NA	NA

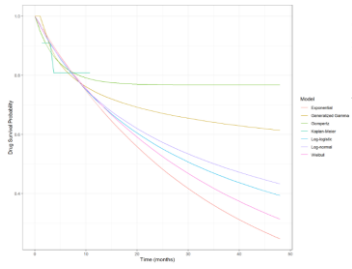


Figure 2 – Fit of different parametric survival models to the T-DXd curve. Exponential model showed the best fit (AIC = 20.15).

Table 3 - Comparative model AIC values.

	df	AIC
exp_model	1	20.14641
weibull_model	2	22.12142
gompertz_model	2	21.64964
loglogistic_model	2	22.01800
lognormal_model	2	21.72770
gengamma_model	3	21.42218

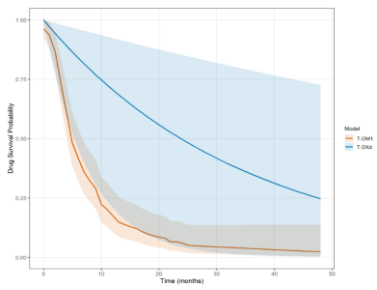


Figure 3 – Fitted curves for both observed T-DM1 data and extrapolated T-DXd data with respective 95% confidence intervals. The estimated probability of a patient to be on treatment at 48 months was 24.7% (95% CI, 0.58-70.5) for T-DXd compared to 2.46% (95% CI, 0.44-13.8) for T-DM1.

Table 4 - Difference in the restricted mean survival time (RMST) up to 48 months for T-DXd vs T-DM1 with 95% confidence interval (bootstrap analysis).

Group	RMST_48m	Lower_95CI	Upper_95CI
T-DXd	25.86	NA	NA
T-DM1	8.17	NA	NA
Difference	17.69	16.8	17.8

Conclusion:

- On average, patients treated with T-DXd stay in treatment 17.7 months longer than with T-DM1, in a period up to 48 months (95% CI, 16.8–17.8).
- Although T-DXd data was immature, model extrapolation and comparative analysis with historical T-DM1 data showed results in line with published clinical trials and real-world studies (median PFS, 17–28 months, T-DXd, 6–9 months, T-DM1).
- In hospital settings, early validation of clinical outcomes is crucial for addressing real-world cost-effectiveness analysis and reinforce medication utilization policies.

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