EE187

A cost-effectiveness analysis of trastuzumab deruxtecan versus trastuzumab emtansine in patients with human epidermal growth factor receptor 2-positive unresectable or metastatic breast cancer in Portugal

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Objectives

- To assess the cost effectiveness of trastuzumab deruxtecan (T-DXd) versus trastuzumab emtansine (T-DM1) in patients with human epidermal growth factor receptor 2 (HER2)-positive unresectable or metastatic breast cancer (uBC/mBC) who have received one prior anti-HER2-based regimen, considering the standard clinical practice in Portugal, and its costs.

Conclusions

- T-DXd is associated with increased costs, life-years (LYs), and additional quality-adjusted life-years (QALYs) compared with T-DM1 for patients with HER2-positive uBC/mBC who had received one prior anti-HER2-based regimen. This cost-effectiveness analysis presented resulting incremental cost-effectiveness ratios (ICERs) of 31,086€/LY and 25,260€/QALY and was considered valid to support the reimbursement decision by the local health authority.

Plain language summary

Why did we perform this research?

The Portuguese Health Technology Assessment System requires the submission of evidence of economic value, usually through an economic study, to support decision-making in the local reimbursement/funding process.

How did we perform this research?

An international model of cost-effectiveness was customized to local requirements for Portugal.

What were the findings of this research?

Treatment with T-DXd resulted in increased life expectancy and quality of life compared with T-DM1. The cost-effectiveness analysis was accepted and considered appropriate to support the reimbursement decision by the health authority.

What are the implications of this research?

T-DXd is recommended in adult patients with unresectable or metastatic HER2-positive breast cancer who have received one or more prior anti-HER2 regimens, in the Portuguese National Health Service.

Definitions **T-DXd**: T-DXd is an antibody-drug conjugate, which is a chemotherapy with a linker (deruxtecan) joined to an antibody (trastuzumab). Trastuzumab binds a protein found on cancer cells called HER2, where it releases the chemotherapy to kill these cells. [By binding to the cancer cell before releasing the chemotherapy, T-DXd reduces the level of chemotherapy exposed to the whole body so less side effects are seen]; **Unresectable:** a tumor that cannot be completely removed with surgery (unresectable); **Metastatic:** cancer that has spread from its original site (metastatic); **HER2-positive:** cells with a higher than normal level of a protein called HER2 (HER2-positive).

Background

- Breast cancer is the most common malignancy among women globally.[1] Approximately 20% of patients with breast cancer have HER2-positive breast cancer.[2-3]
- T-DXd is an antibody-drug conjugate composed of an anti-HER2 antibody, a tetrapeptide-based cleavable linker, and a topoisomerase I inhibitor payload.[4-5]
- In the phase 3 trial DESTINY-Breast03 (DB-03), T-DXd showed a significantly improved overall survival (OS) (HR 0.64, p=0.0037) and the longest reported median progression-free survival (PFS), 28.8 months versus 6.8 months (HR 0.33, p<0.0001), compared with T-DM1 in patients previously treated with a taxane and trastuzumab.[6]

Methods

Effectiveness model

- A 3-state partitioned survival model (PSM) was developed to evaluate the cost effectiveness of T-DXd in adult patients with unresectable or metastatic HER2-positive breast cancer who have received one or more prior anti-HER2 regimens, reflecting the natural history of the disease. Patients entered the model in the progression-free state and receive either T-DXd or T-DM1 and can remain progression-free, their disease can progress, or they can die. Patients in the post-progression state cannot return to the progression-free state, but they can remain alive in the post-progression state or die. Death is an absorbing state, meaning patients remain there permanently (Figures 1 and 2).
- The analysis was conducted from the Portuguese National Health Service perspective assuming a 4% discount rate for costs and consequences and a lifetime time horizon (37 years).

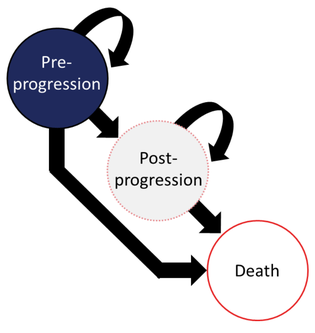


Figure 1. Three-state Model Structure

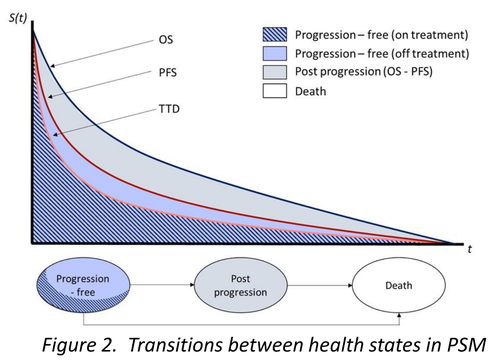


Figure 2. Transitions between health states in PSM

Clinical Data

- The time-to-event data from the DB03 study were used to inform efficacy in the T-DXd and T-DM1 arms of the model.
- Parametric models were fitted to time-to-event data for PFS, OS, and time-to-treatment discontinuation (TTD). The proportional hazards assumption was assessed to determine whether these models could be fitted to the entire dataset with the treatment group included as a covariate in the analysis.
- Following the recommendations of NICE technical support document 14, the base case parametric distributions applied for each survival curve were based on goodness-of-fit criteria (Akaike and Bayesian information criteria) and clinical plausibility. (Table 1).

Adverse Events (AEs)

- The model included AEs with a severity of Grade 3 or higher when 5% or more of patients in one of the treatment arms of DB-03 experienced the AE.

Utilities

- The quality-of-life data collected in DB-03 (EQ-5D-5L) was computed using the Portuguese value sets and used in the model.[7] The model base case scenario uses the utility values of 0.8214 and 0.8046 in the progression-free health state for T-DXd and T-DM1, respectively (from DB-03), and applies utility values calculated with the Lloyd algorithm for progressed disease - 0.5403 for T-DXd and T-DM1.

Costs

- The model included costs associated with drug acquisition, treatment administration, healthcare resources use, subsequent therapy, end-of-life and AEs obtained from Portuguese databases and literature.

Table 1. Distribution used for each health state

Curve	Distribution
PFS (T-DXd)	Log normal
PFS (T-DM1)	Log normal
OS (T-DXd)	Log-logistic
OS (T-DM1)	Log-logistic
TTD (T-DXd)	Log normal
TTD (T-DM1)	Log normal

Table 3. Healthcare resources cost per model cycle

Item	Cost per cycle
Medical visit	23.25 €
CT scan	24.65 €
Biochemistry	6.20 €
Hemogram	4.70 €

Table 2. Adverse events cost Healthcare resources cost per model cycle

Grade 3-4 adverse event	Cost
Neutrophil count decreased	1,030.96 €
Anaemia	1,208.19 €
White blood cell count decreased	988.31 €
Platelet count decreased	345.56 €
Nausea	798.79 €
Fatigue	1,270.88 €
Increased aspartate aminotransferase	2,438.32 €
Interstitial lung disease	3,238.53 €
Left ventricular ejection fraction decreased	3,127.59 €
Thrombocytopenia	345.56 €

Results

Base-case scenario

- The modelled curves for each treatment arm are presented in Figures 3 and 4, and cost-effectiveness results for the base-case scenario are presented in Table 4.

Figure 3. Modelled PFS curves on the base-case scenario.

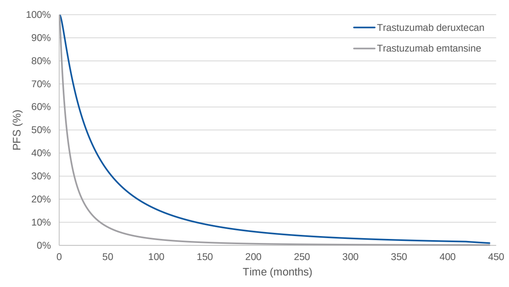


Figure 4. Modelled OS curves on the base-case scenario.

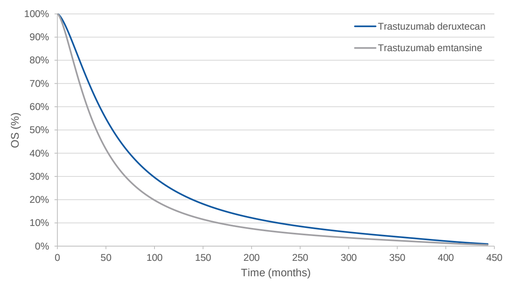


Table 4. Cost-effectiveness results for the base-case scenario.

Costs outcomes	T-DXd	T-DM1
Treatment	168,196.16 €	58,904.97 €
Treatment administration	912.61 €	435.33 €
Healthcare resources	5,910.10 €	4,643.20 €
Subsequent treatment	66,005.49 €	139,019.57 €
Adverse events	345.05 €	368.17 €
End-of-life	956.62 €	445.56 €
Total	**242,326.03 €**	**203,816.80 €**

Health outcomes	T-DXd	T-DM1
Health state – QALYs		
Progression-free health state	3.36	1.21
Post-progression health state	1.07	1.70
Total	**4.43**	**2.91**
Health state – LYs		
Progression-free health state	3.75	1.35
Post-progression health state	2.03	3.19
Total	**5.78**	**4.54**

- T-DXd was more effective than T-DM1, leading to a mean of 1.24 additional LYs (5.78 versus 4.54) and a mean of 1.52 additional QALYs (4.43 versus 2.91) per patient. The modelled median percentage of patients alive at 10 years was 24.1% for T-DXd and 15.7% for T-DM1. T-DXd versus T-DM1 was associated with ICERs of 31,086€/LY and 25,260€/QALY.

Sensitivity analysis

- Model robustness was demonstrated through scenario analyses. The probabilistic sensitivity analysis (PSA) also showed robust results, with probabilistic ICERs of 31,863€/LY and 25,937€/QALY. The cost-effectiveness acceptability curve shows that at a willingness-to-pay threshold of 30,000€ T-DXd has a probability of cost effectiveness of approximately 58.9% (Figures 5 and 6).

Figure 5. Cost-effectiveness plan

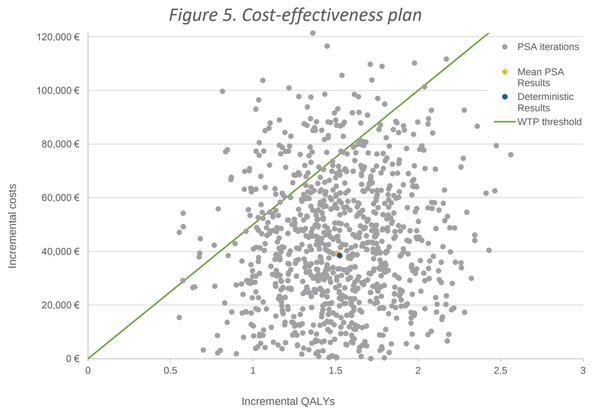
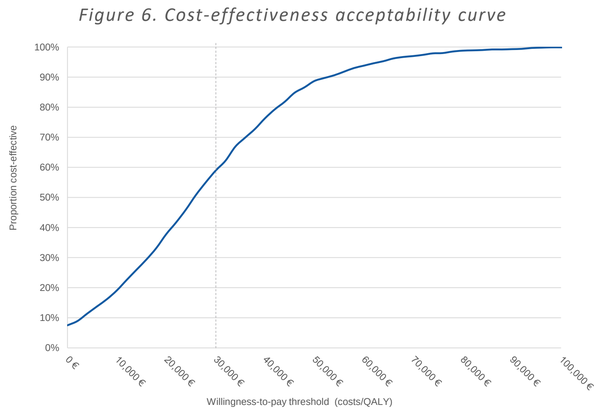


Figure 6. Cost-effectiveness acceptability curve



Acknowledgments

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Disclosures

All authors disclose employment by AstraZeneca / Daiichi Sankyo.

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