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European real-world experience of patients with HER2+ advanced/metastatic breast cancer accessing trastuzumab deruxtecan (T-DXd) through a named patient program: first interim analysis of EUROPA T-DXd

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Objectives

- The primary objective of the real-world evidence EUROPA T-DXd study is to evaluate the real-world time to discontinuation (rwTTD) of trastuzumab deruxtecan (T-DXd) in patients with human epidermal growth factor receptor 2-positive (HER2+) advanced or metastatic breast cancer (a/mBC), who had received ≥2 prior anti-HER2 regimens, in a real-world clinical setting
- The key secondary study objectives are to describe: a) prior HER2-directed treatment patterns; b) reasons for T-DXd treatment discontinuation; c) adverse events (AEs); d) anti-emetic prophylaxis prior to T-DXd initiation; and e) real-world progression-free survival (rwPFS)

Conclusions

- Results from this first interim analysis confirm that the effectiveness of T-DXd in heavily pretreated patients with HER2+ mBC in a real-world clinical setting is comparable with the efficacy reported in the DESTINY-Breast01[1] and DESTINY-Breast02[2] clinical trials
- Median rwTTD: 20.8 months (95% confidence interval [CI] 17.0, not calculable [NC]); median rwPFS: not reached (95% CI 18.1, NC)
  - Real-world safety data were collected in line with local requirements for spontaneous AE reporting and not via the electronic case report form, which confounds the ability to compare with clinical trial data; however, no new safety concerns were identified
- Baseline characteristics and demographics are comparable with those observed in the DESTINY-Breast01[1] and DESTINY-Breast02[2] clinical trials

Plain language summary

Why did we perform this research?

Breast cancer cells can have different levels of a protein called human epidermal growth factor receptor 2 (HER2), which helps cancer cells to grow.[1] Trastuzumab deruxtecan (T-DXd) is used to treat breast cancers with a higher than normal level of the HER2 protein (HER2-positive/HER2+).[2,3] We want to find out how well T-DXd works in routine clinical practice and to understand its known side effects in patients with HER2+ breast cancer, which cannot be completely removed with surgery or when it has spread from the original site to other parts of the body (metastatic). Specifically, we are interested in patients who have previously received two or more other anticancer drugs that did not work or stopped working.

How did we perform this research?

EUROPA T-DXd is a study designed to collect data from routine clinical practice rather than from a clinical study (generating real-world data). Patient data are being obtained from medical centers across Europe that were already involved in a named patient program to help patients get treatment with T-DXd before it was otherwise available in their country.

What were the findings of this research?

Data from 170 patients were evaluated between October 24, 2022, and September 18, 2023. Of these patients, 47% were still receiving T-DXd and 53% had ended treatment at the time of this analysis. The main reason for ending treatment was disease progression. At the time of this analysis, half of the patients received T-DXd treatment for at least 21 months. Furthermore, cancer had progressed in less than half of the patients given T-DXd.

What are the implications of this research?

When used in routine clinical practice, T-DXd treatment is effective in patients with HER2+ advanced/metastatic breast cancer who have previously had other anticancer therapies.

Where can I access more information?

ClinicalTrials.gov. European real-world experience of previously treated advanced/metastatic HER2-positive breast cancer patients accessing trastuzumab deruxtecan. https://www.clinicaltrials.gov/study/NCT05458401.

References 1. Gutierrez C, Schiff R. *Arch Pathol Lab Med*. 2011;135:55–62; 2. Enhertu (fam-trastuzumab deruxtecan-nxki) highlights of prescribing information. 2022. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761139s021lbl.pdf (Accessed September 11, 2023); 3. Enhertu (trastuzumab deruxtecan) summary of product characteristics. 2023. Available from: https://www.ema.europa.eu/en/documents/product-information/enhertu-epar-product-information_en.pdf (Accessed September 7, 2023)

Poster

Supplementary material

Please scan this quick response (QR) code with your smartphone camera or app to obtain a copy of these materials. Alternatively, access at: https://bit.ly/495f3Ad

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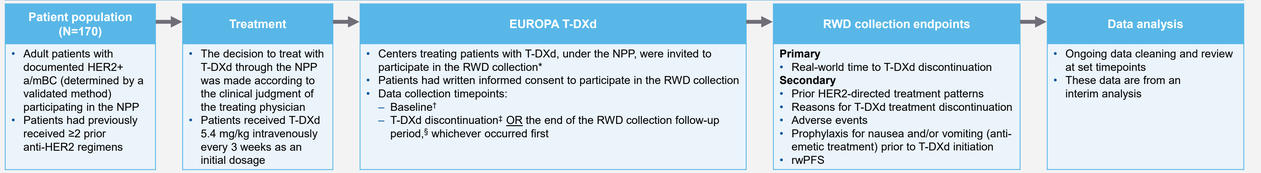
Introduction

- In 2021, T-DXd monotherapy was conditionally approved in the European Union for adult patients with HER2+ a/mBC who received ≥2 prior anti-HER2 therapies,[3] based on data from the Phase 2 DESTINY-Breast01 trial[1]
- A Named Patient Program (NPP) (DS8201-0002-EAP-MA) was initiated in March 2021 to enable eligible patients with an unmet medical need to gain access to T-DXd when not yet available locally, either commercially or through an appropriate clinical trial
- Centers that treated or are treating patients under this NPP were invited to participate in the EUROPA T-DXd real-world data (RWD) collection
- EUROPA T-DXd (NCT05458401) is a multinational (Ireland, Italy, and Spain), multicenter, observational (retrospective and prospective) single-arm study of RWD investigating T-DXd in European adult patients with HER2+ a/mBC, who had received ≥2 prior anti-HER2 regimens; at the time of study initiation, T-DXd was not yet approved for use after ≥1 anti-HER2 regimen

Methods

Figure 1. Study design



*Pseudonymized data were captured as part of normal clinical practice or standard practice guidelines for the patient population in each country, via a customized electronic case report form (RWD collection was optional and independent of eligibility for the NPP); †the period directly prior to commencing T-DXd treatment; ‡when treatment discontinuation was for a reason other than death, progression, or withdrawn consent for data collection, follow-up occurred until disease progression or the closure of the RWD collection, whichever occurs first; §a minimum of 14 months after T-DXd initiation and before closure of the RWD documentation
+, positive; a/mBC, advanced/metastatic breast cancer; HER2, human epidermal growth factor receptor 2; NPP, Named Patient Program; RWD, real-world data; rwPFS, real-world progression-free survival; T-DXd, trastuzumab deruxtecan

Results and interpretation

- Between October 24, 2022, and September 18, 2023, 170 evaluable patients had received T-DXd treatment (**Tables 1** and **2**)
- In any setting, 40% of patients had received ≥5 lines of prior anti-HER2 therapies
- Median follow-up duration was 18.0 (range: 0.0–33.3) months*
- Primary cause of death was disease related in 14 patients

Table 1. Patient disposition

	All patients (N=170)
T-DXd assigned, n (%)	170 (100)
T-DXd ongoing, n (%)	80 (47.1)
T-DXd discontinued, n (%)	90 (52.9)
Disease progression	52 (57.8)
Death	12 (13.3)
Adverse events	9 (10.0)
Other	15 (16.6)
Missing	2 (2.2)
Median actual treatment duration (months)†	16.9

*Time from the start of T-DXd initiation to end of follow up; †includes all patients who participated in the study
T-DXd, trastuzumab deruxtecan

Table 2. Patient demographics and clinical characteristics

	All patients (N=170)*
Median age, years (range)	55.0 (32–91)
Female, n (%)	166 (97.6)
Median weight at T-DXd treatment initiation, kg	63.0
HER2 status,† n (%)	
IHC 1+	2 (1.2)
IHC 2+	48 (28.2)
IHC 3+	117 (68.8)
IHC Missing	3 (1.8)
ISH+	58 (34.1)
ISH−	5 (2.9)
ISH N/A	104 (61.2)
ISH Missing	3 (1.8)
HR status, n (%)	
Positive	108 (63.5)
Negative	58 (34.1)
Missing	4 (2.4)

Table 2 continued. Patient demographics and clinical characteristics

Site of metastatic disease, n (%)	
Lymph node	95 (55.9)
Bone	91 (53.5)
Liver	67 (39.4)
Lung	67 (39.4)
Brain	49 (28.8)
Other	44 (25.9)
Prior anti-HER2 therapy, n (%)	
Trastuzumab	160 (94.1)
T-DM1	149 (87.6)
Pertuzumab	124 (72.9)
Lapatinib	79 (46.5)
Tucatinib	17 (10.0)
Neratinib	16 (9.4)
Margetuximab	7 (4.1)
Intent of anti-HER2 therapy, n (%)	
Neo adjuvant	32 (18.8)
Adjuvant	52 (30.6)
Metastatic	158 (92.9)
Median lines of prior anti-HER2 therapies in any setting, n (range)	4 (0–12)
Median lines of prior anti-HER2 therapies in metastatic setting, n (range)	3 (0–6)
ECOG PS, n (%)	
0	54 (31.8)
1	60 (35.3)
2	10 (5.9)
3	1 (0.6)
Not done / Not documented / Unknown	35 (20.6)
Missing	10 (5.9)
Any anti-emetic prophylaxis treatment prior to T-DXd initiation	113 (66.5)

*Ireland (n=12), Italy (n=111), Spain (n=47); †HER2 status was determined per local laboratory assessment by a validated method
ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; IHC, immunohistochemistry; ISH, in situ hybridization; N/A, not available; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan

Safety

- Safety data, as collected via a pharmacovigilance system,* revealed:
  - Treatment-emergent adverse events (TEAEs) (any grade) were reported in 67/166 (40.4%) patients [vs >99% in clinical trials[2]]
  - TEAEs leading to discontinuation of T-DXd were reported in 34/166 (20.5%) patients† [vs 14% in clinical trials[2]]
  - TEAEs leading to dose interruption delays of T-DXd were reported in 9/166 (5.4%) patients [vs 33% in clinical trials[2]]
  - A dual or triplet anti-emetic regimen with prophylactic intent was reported in 46.6% and 8.2% of patients respectively

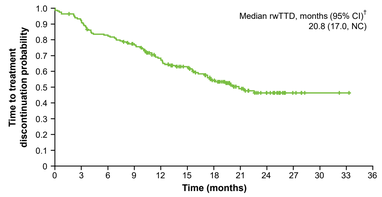
*To comply with pharmacovigilance legislation, physicians treating under the NPP report serious and non-serious AEs and/or safety information using an AE report form and targeted questionnaires; †includes disease progression, n=25 (15.1%)

rwTTD and rwPFS

- Among all patients, median rwTTD was 20.8 months (95% confidence interval [CI] 17.0, not calculable [NC]) (**Figure 2**) and median rwPFS was not reached (95% CI 18.1, NC) (**Figure 3**)
- In patients with (n=49)* or without (n=121) brain metastases at T-DXd initiation:
  - Median rwTTD was 17.7 months (95% CI 12.2, NC) and 21.4 months (95% CI 16.2, NC), respectively
  - Median rwPFS was not reached (95% CI 12.5, NC) and 22.6 months (95% CI 18.1, NC), respectively†
- In patients with (n=67)* or without (n=103) liver metastases at T-DXd initiation:
  - Median rwTTD was 12.9 months (95% CI 10.3, 20.8) and not reached (95% CI 19.4, NC), respectively
  - Median rwPFS was 17.8 months (95% CI 11.4, NC) and not reached (95% CI 22.6, NC), respectively
- Median levels of rwTTD and rwPFS are expected to be reached with further maturation of the data

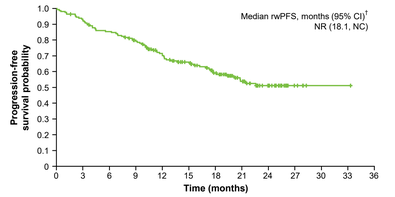
*Metastatic site was recorded as soon as it was identified; patients could have had more than one metastatic site. †rwPFS was longer for patients with brain metastases versus patients without brain metastases, as was observed in a similar patient population in clinical trials[4]

Figure 2. rwTTD*



*rwTTD is defined as time from T-DXd initiation date to time of T-DXd discontinuation for any reason; †CI for median was computed using the Brookmeyer-Crowley method; check marks indicate censored data to the time of T-DXd discontinuation for any reason
CI, confidence interval; NC, not calculable; rwTTD, real-world time to discontinuation; T-DXd, trastuzumab deruxtecan

Figure 3. rwPFS*



*rwPFS is defined as time from T-DXd initiation to the earliest of death or progression; †CI for median is computed using the Brookmeyer-Crowley method; check marks indicate censored data to the time of an event
CI, confidence interval; NC, not calculable; NR, not reached; rwPFS, real-world progression-free survival; T-DXd, trastuzumab deruxtecan

Study limitations

- Limitations of the EUROPA T-DXd study could include:
  - Potential for selection bias in favor of larger, high-enrolling (NPP) centers
  - Reliance on accurate retrospective electronic case report form entry for most data, due to inclusion of patients who had already completed therapy or were receiving ongoing therapy
  - Potential for bias toward patients more willing to participate or provide consent, owing to superior health status
  - Potential for underreporting of safety events
  - Data collection was restricted to T-DXd treatment under the NPP; data could not be collected from those patients who switched to commercially available T-DXd treatment

References

1. Modi S, et al. *N Engl J Med*. 2020;382:610–621; 2. André F, et al. *Lancet*. 2023;401:1773–1785; 3. Enhertu (trastuzumab deruxtecan) summary of product characteristics. 2023. Available from: https://www.ema.europa.eu/en/documents/product-information/enhertu-epar-product-information_en.pdf (Accessed September 7, 2023); 4. Jerusalem G, et al. *Cancer Discov*. 2022;12:2754–2762

Disclosures

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