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# Effects of trastuzumab deruxtecan on health-related quality of life and neurological function in patients with HER2+ advanced/metastatic breast cancer with or without brain metastases: DESTINY-Breast12 results

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## Objectives

- Health-related quality of life (HRQoL) and neurological function, assessed using the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Core 30 questionnaire (QLQ-C30), Neurologic Assessment in Neuro-Oncology (NANO) scale, and MD Anderson Symptom Inventory (MDASI) symptom items, were secondary endpoints of the DESTINY-Breast12 (NCT04739761) study
- This analysis explores HRQoL and neurological function in patients with HER2+ advanced/metastatic breast cancer (mBC), with or without stable or active brain metastases (BMs), treated with trastuzumab deruxtecan (T-DXd)

## Conclusions

- Estimated deterioration-free rates at 12 months were above 50% for cognitive, emotional, physical, and social functioning, and pain scores, regardless of the presence or absence of stable/active baseline BMs; further, the majority of patients had neurological stability at first score post baseline, which was maintained throughout treatment in 55.1% of patients in the baseline BMs cohort and 72.9% of patients without baseline BMs. In the baseline BMs cohort, mean severity in the last 24 hours scores for the majority of brain-tumor-specific MDASI symptom items were <3 at all timepoints with assessments for >10 patients, on a 0–10 scale where 0 was 'not present', and 10 was 'as bad as you can imagine'
- The findings for HRQoL and neurological function complement the overall clinical efficacy and safety profile of T-DXd in patients with HER2+ mBC, irrespective of the presence of stable or active BMs, and further support T-DXd as a valuable treatment option in this population

## Plain language summary

### Why did we perform this research?

The DESTINY-Breast12 study looked at trastuzumab deruxtecan (T-DXd) treatment in adults with breast cancer that had a high level of the human epidermal growth factor receptor 2 protein (HER2-positive [HER2+] breast cancer) and cancer cells that could not be completely removed with surgery or had spread from where they started despite several treatments (known as advanced/metastatic cancer). T-DXd has been shown to work well in participants with HER2+ advanced/metastatic breast cancer, including those with breast cancer that had spread to the brain.[1]

The aim of this analysis was to explore overall wellbeing (health-related quality of life; HRQoL) and how the body's nervous system was working (neurological function) in participants of DESTINY-Breast12 who were treated with T-DXd.

### How did we perform this research?

Participants and their doctors were asked to complete questionnaires that used numbered scales to report the participants' symptoms, feelings, and ability to perform daily tasks and activities during and after their treatment with T-DXd.

### What were the findings of this research?

While assessments were being collected, HRQoL and neurological function (including pain scores and cognitive, emotional, physical, and social function) were preserved in more than half of participants with HER2+ advanced/metastatic breast cancer who received T-DXd, even if the breast cancer had spread to the brain.

### What are the implications of this research?

Negative impacts on HRQoL and neurological function are common for people with breast cancer, especially for those whose breast cancer has spread to the brain.[2] Treatment with T-DXd may aid in preservation of mental and physical wellbeing, as well as helping to treat people's breast cancer.

### Where can I access more information?

ClinicalTrials.gov. A study of T-DXd in participants with or without brain metastasis who have previously treated advanced or metastatic HER2 positive breast cancer (DESTINY-B12). https://clinicaltrials.gov/study/NCT04739761.

1. Harbeck N, et al. *Nat Med*. 2024;doi 10.1038/s41591-024-03261-7: Sep 13 [Epub ahead of print]; 2. van Grinsven EE, et al. *Oncol Res Treat*. 2021;44:622–636

Poster

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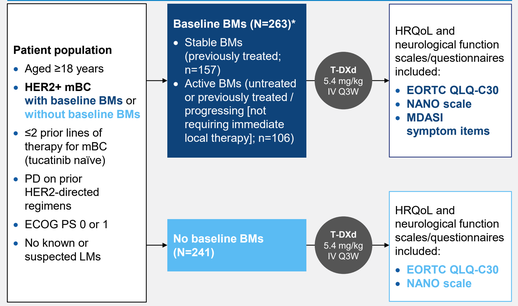
## Introduction

- T-DXd is a HER2-directed antibody-drug conjugate[1,2]
- In the prospective Phase 3b/4, single-arm, open-label DESTINY-Breast12 study of T-DXd (**Figure 1**), substantial and durable overall and intracranial clinical activity in HER2+ mBC were exhibited, including in a large cohort with stable and active BMs, with no new safety signals[3]
- In patients with BMs:[3]
  - 12-month progression-free survival (PFS) was 61.6% (95% confidence interval [CI] 54.9, 67.6), and 12-month central nervous system (CNS) PFS was 58.9% (95% CI 51.9, 65.3)
  - CNS objective response rate was 71.7% (95% CI 64.2, 79.3); this was similar in stable (79.2% [95% CI 70.2, 88.3]) and active BMs (62.3% [95% CI 50.1, 74.5])
- Efficacy in patients without BMs was consistent with previous reports[3]
- There is a lack of published data on neurological function in patients with HER2+ mBC in clinical trials, including those with BMs
- BMs and local therapies for BMs (eg radiotherapy) can impact patient HRQoL and neurological function;[4,5] DESTINY-Breast12 explored these outcomes in patients treated with T-DXd (**Table 1**)

## Methods

**Figure 1. Two-cohort study design**




*Concomitant use of ≤3 mg of dexamethasone daily or equivalent allowed for symptom control of BMs. No hypothesis testing or comparison of cohorts
BM, brain metastasis; ECOG PS, Eastern Cooperative Oncology Group performance status; EORTC, European Organisation for Research and Treatment of Cancer; HER2, human epidermal growth factor receptor 2; HER2+, human epidermal growth factor receptor 2–positive; HRQoL, health-related quality of life; IV, intravenous; LM, leptomeningeal metastasis; mBC, metastatic breast cancer; MDASI, MD Anderson Symptom Inventory; NANO, Neurologic Assessment in Neuro-Oncology; PD, disease progression; Q3W, every 3 weeks; QLQ-C30, Quality of Life Core 30 questionnaire; T-DXd, trastuzumab deruxtecan

**Table 1. HRQoL and neurological function scales/questionnaires**

| Scale/questionnaire | Reported by | Measures of interest | Endpoint(s) and definitions |
|---|---|---|---|
| ***HRQoL*** | | | |
| **EORTC QLQ-C30*** | Patient | • GHS/QoL<br>• Functional scales:<br>– Cognitive, emotional, physical, role, and social functioning<br>• Multi-item symptom scales:†<br>– Pain, fatigue, nausea/vomiting | **Clinically meaningful deterioration at any time during assessment collection**<br>• Change from baseline‡ in: cognitive functioning: ≤−4 points, emotional and physical functioning, pain: ≤−10 points, fatigue and GHS: ≤−8 points, nausea/vomiting: ≤−11 points, role functioning: ≤−6 points, social functioning: ≤−7 points[6,7]<br>**Time to deterioration**<br>• Time from first dose of study intervention until the date of first clinically meaningful deterioration confirmed at subsequent assessment |
| ***Neurological function*** | | | |
| **NANO scale** | Clinician | Nine domains: gait, strength, ataxia, sensation, visual fields, facial strength, language, level of consciousness, behavior | **Change from first post-baseline‡ score to worst on-treatment score at any point during treatment**<br>• Worst score: derived from assessments between start of study treatment and 47 days following date of last dose of study treatment, and prior to starting any subsequent anticancer therapy<br>• Outcomes:§ neurological response, neurological progression, neurological stability, not assessed |
| **MDASI symptom items (BMs cohort only)** | Patient | Nine symptoms specific to brain tumors: weakness on one side of body, difficulty understanding, difficulty speaking, seizures, difficulty concentrating, problems with vision, change in appearance, change in bowel pattern, irritability | **Mean severity in the last 24 hours scores for brain-tumor-specific outcomes, at all timepoints with assessments for >10 patients**<br>• On a 0–10 numeric rating scale, with 0 being 'not present' and 10 being 'as bad as you can imagine'[8] |

**Assessment schedule:** every 3 weeks from Cycle 1 Day 1 and end-of-treatment visit (all endpoints), and for up to 24 weeks post end of treatment or second progression (EORTC QLQ-C30, MDASI symptom items)

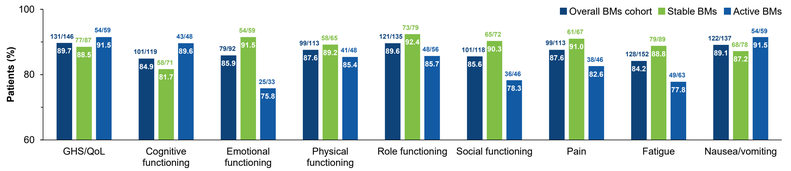
*Patients with no clinically meaningful deterioration or ≥2 missed assessments were censored at the time of their last evaluable PRO assessment; those with no evaluable visits were censored at Day 1 (date of first study intervention administration); †plus additional single items assessing appetite loss, constipation, diarrhea, dyspnea, financial difficulties, and insomnia; ‡baseline defined as the last result obtained prior to the start of study treatment; §neurological response: ≥2 level improvement in ≥1 domain without worsening in other domains from baseline / best level of function; neurological progression: ≥2 level worsening from baseline / best level of function within ≥1 domain or worsening to the highest score within ≥1 domain; neurological stability: score does not meet criteria for neurological response, neurological progression, or not assessed; not assessed: all nine domains were not evaluated by investigator. BM, brain metastasis; EORTC, European Organisation for Research and Treatment of Cancer; GHS, Global Health Status; HRQoL, health-related quality of life; MDASI, MD Anderson Symptom Inventory; NANO, Neurologic Assessment in Neuro-Oncology; PRO, patient-reported outcome; QLQ-C30, Quality of Life Core 30 questionnaire; QoL, quality of life

## Results

### Baseline BMs

- Median total treatment duration in the BMs cohort (N=263) was 11.5 months
- At data cutoff (February 8, 2024), 118 patients were continuing to receive T-DXd treatment
- Estimated deterioration-free rates at 12 months were >50% for cognitive, emotional, physical, and social functioning, and pain scores (**Figure 2**)

**Figure 2. Patients with clinically meaningful deterioration of EORTC QLQ-C30 at any time while assessments were being collected (evaluable patients)**




| | GHS/QoL | Cognitive functioning | Emotional functioning | Physical functioning | Role functioning | Social functioning | Pain | Fatigue | Nausea/vomiting |
|---|---|---|---|---|---|---|---|---|---|
| **Time to deterioration, months** | | | | | | | | | |
| 25th percentile | 0.8 | 2.1 | 3.4 | 2.7 | 1.4 | 1.4 | 2.0 | 1.0 | 1.0 |
| **Deterioration-free estimate, % (confidence interval)*** | | | | | | | | | |
| At 6 months | 44.9 (38.2, 51.4) | 59.7 (52.8, 65.8) | 70.9 (64.5, 76.4) | 61.1 (54.4, 67.1) | 54.2 (47.4, 60.5) | 59.2 (52.5, 65.4) | 61.4 (54.7, 67.5) | 46.5 (39.6, 53.0) | 49.3 (42.6, 55.7) |
| | 45.2 (36.5, 53.5) | 60.1 (51.1, 68.0) | 69.2 (60.9, 76.2) | 63.4 (54.7, 70.8) | 53.4 (44.6, 61.4) | 57.2 (48.4, 65.1) | 60.3 (51.5, 68.0) | 45.1 (36.4, 53.5) | 53.0 (44.2, 61.0) |
| | 44.4 (33.8, 54.4) | 58.9 (47.9, 68.3) | 73.7 (63.0, 81.7) | 57.5 (46.5, 67.1) | 55.7 (44.8, 65.3) | 62.3 (51.2, 71.6) | 63.3 (52.2, 72.6) | 48.6 (37.4, 58.8) | 43.9 (33.5, 53.9) |
| At 12 months | 40.3 (33.6, 46.9) | 53.5 (46.3, 60.1) | 63.3 (56.2, 69.6) | 56.8 (49.9, 63.2) | 44.5 (37.4, 51.4) | 54.3 (47.2, 60.8) | 53.4 (46.2, 60.1) | 40.2 (33.3, 47.0) | 46.2 (39.4, 52.8) |
| | 41.0 (32.3, 49.6) | 55.3 (46.0, 63.6) | 59.3 (50.0, 67.5) | 58.4 (49.3, 66.4) | 44.3 (35.0, 53.1) | 52.0 (42.8, 60.3) | 52.8 (43.5, 61.3) | 40.3 (31.7, 48.9) | 49.5 (40.4, 58.0) |
| | 39.2 (28.9, 49.4) | 50.9 (39.4, 61.3) | 70.1 (58.6, 78.9) | 54.6 (43.4, 64.5) | 45.0 (33.8, 55.5) | 57.8 (46.4, 67.6) | 54.2 (42.6, 64.5) | 39.7 (28.4, 50.7) | 41.3 (30.9, 51.3) |

Evaluable patients had baseline data, evaluable visits, and a baseline score allowing for a 10-point deterioration. *Derived by Kaplan-Meier estimator
BM, brain metastasis; EORTC, European Organisation for Research and Treatment of Cancer; GHS, Global Health Status; QLQ-C30, Quality of Life Core 30 questionnaire; QoL, quality of life

- The majority (86.6%) of patients had neurological stability at first score post baseline; neurological stability was maintained throughout treatment for 55.1% of patients (**Table 2**)

**Table 2. First post-baseline NANO score to worst NANO score (n=254)**

| | Worst NANO score at any timepoint during treatment, n (%) | | | | |
|---|---|---|---|---|---|
| **First post-baseline NANO score, n (%)** | Neurological response | Neurological stability | Neurological progression | Not assessed | Total |
| Neurological response | 0 | 1 (0.4) | 3 (1.2) | 0 | 4 (1.6) |
| Neurological stability | 0 | **140 (55.1)** | 80 (31.5) | 0 | **220 (86.6)** |
| Neurological progression | 0 | 7 (2.8) | 18 (7.1) | 0 | 25 (9.8) |
| Not assessed | 0 | 3 (1.2) | 2 (0.8) | 0 | 5 (2.0) |
| Total | 0 | 151 (59.4) | 103 (40.6) | 0 | 254 (100.0) |

Evaluable patients had a first score value and at least another on-treatment value
NANO, Neurologic Assessment in Neuro-Oncology

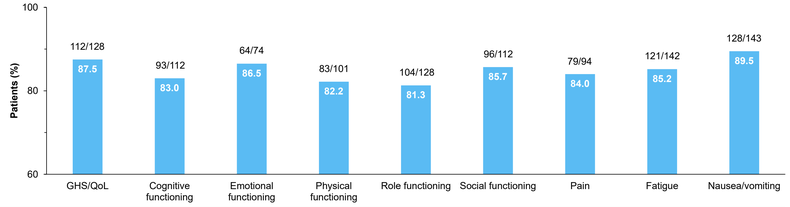
### Brain-tumor-specific MDASI symptom items

- On a 0–10 numeric rating scale, with 0 being 'not present' and 10 being 'as bad as you can imagine', mean severity in the last 24 hours scores for brain-tumor-specific MDASI symptom items at all timepoints with assessments for >10 patients were ≤2 for difficulty concentrating, difficulty speaking, difficulty understanding, and seizures; <3 for change in appearance, irritability, and weakness on one side of the body; and <4 for change in bowel patterns and vision
  - For each visit, only patients with non-missing results at both baseline and that visit were included in the analysis; the number of patients with data decreased continually over time

### No baseline BMs

- Median total treatment duration in the no baseline BMs cohort (N=241) was 12.0 months
- At data cutoff, 95 patients were continuing to receive T-DXd treatment
- Four of the 241 patients with no BMs at baseline developed new symptomatic CNS metastases (incidence rate 0.017 [95% CI 0.00452, 0.04250]) during the study
- Estimated deterioration-free rates at 12 months were >50% in patients with HER2+ mBC and no baseline BMs for cognitive, emotional, physical, and social functioning, and pain scores (**Figure 3**)

**Figure 3. Patients with clinically meaningful deterioration of EORTC QLQ-C30 at any time while assessments were being collected (evaluable patients)**




| | GHS/QoL | Cognitive functioning | Emotional functioning | Physical functioning | Role functioning | Social functioning | Pain | Fatigue | Nausea/vomiting |
|---|---|---|---|---|---|---|---|---|---|
| **Time to deterioration, months** | | | | | | | | | |
| 25th percentile | 1.2 | 2.7 | 6.2 | 2.8 | 1.4 | 1.8 | 2.8 | 0.7 | 0.8 |
| **Deterioration-free estimate, % (confidence interval)*** | | | | | | | | | |
| At 6 months | 54.7 (47.5, 61.2) | 61.1 (54.0, 67.5) | 75.6 (69.1, 81.0) | 67.7 (60.7, 73.6) | 52.3 (45.0, 59.1) | 57.7 (50.5, 64.2) | 65.2 (58.1, 71.3) | 42.2 (35.2, 49.0) | 43.2 (36.3, 49.9) |
| At 12 months | 44.3 (37.0, 51.4) | 54.9 (47.5, 61.6) | 69.1 (62.0, 75.1) | 61.3 (53.9, 67.8) | 45.3 (37.9, 52.5) | 51.1 (43.7, 58.1) | 61.2 (53.8, 67.8) | 38.3 (31.2, 45.3) | 38.6 (31.7, 45.4) |

Evaluable patients had baseline data, evaluable visits, and a baseline score allowing for a 10-point deterioration. *Derived by Kaplan-Meier estimator
EORTC, European Organisation for Research and Treatment of Cancer; GHS, Global Health Status; QLQ-C30, Quality of Life Core 30 questionnaire; QoL, quality of life

- The majority (91.9%) of patients had neurological stability at first score post baseline; neurological stability was maintained throughout treatment for 72.9% of patients (**Table 3**)

**Table 3. First post-baseline NANO score to worst NANO score (n=236)**

| | Worst NANO score at any timepoint during treatment, n (%) | | | | |
|---|---|---|---|---|---|
| **First post-baseline NANO score, n (%)** | Neurological response | Neurological stability | Neurological progression | Not assessed | Total |
| Neurological response | 0 | 1 (0.4) | 2 (0.8) | 0 | 3 (1.3) |
| Neurological stability | 0 | 172 (72.9) | 45 (19.1) | 0 | 217 (91.9) |
| Neurological progression | 0 | 6 (2.5) | 10 (4.2) | 0 | 16 (6.8) |
| Not assessed | 0 | 0 | 0 | 0 | 0 |
| Total | 0 | 179 (75.8) | 57 (24.2) | 0 | 236 (100.0) |

Evaluable patients had a first score value and at least another on-treatment value
NANO, Neurologic Assessment in Neuro-Oncology

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DESTINY Breast12