DESTINY-Breast06 post hoc analysis by physician's choice of chemotherapy: efficacy and safety of trastuzumab deruxtecan versus physician's choice of chemotherapy in hormone receptor–positive, HER2-low or -ultralow metastatic breast cancer

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Introduction

- DESTINY-Breast06 demonstrated a statistically significant and clinically meaningful progression-free survival (PFS) and time from randomization to second progression or death (PFS2) benefit with trastuzumab deruxtecan (T-DXd) versus physician's choice of chemotherapy (TPC) in hormone receptor–positive (HR+), human epidermal growth factor receptor 2 (HER2)-low or HER2-ultralow metastatic breast cancer (mBC) after receiving ≥1 endocrine therapy (ET),[1,2] leading to US Food and Drug Administration and European Medicines Agency approval of T-DXd in this setting[3,4]
- We report post hoc analysis of efficacy and safety of T-DXd versus TPC type (capecitabine or taxane) in DESTINY-Breast06

Conclusions

- T-DXd demonstrated a clinically meaningful efficacy benefit over both TPC subgroups, with improved PFS, objective response rate (ORR), duration of response (DOR), and PFS2, and safety outcomes for T-DXd were consistent with previous reports
- These findings further support T-DXd as an effective treatment option in HR+, HER2-low or HER2-ultralow mBC after ≥1 ET, with demonstrable benefits over treatment with capecitabine or a taxane (nab-paclitaxel or paclitaxel)

Methods

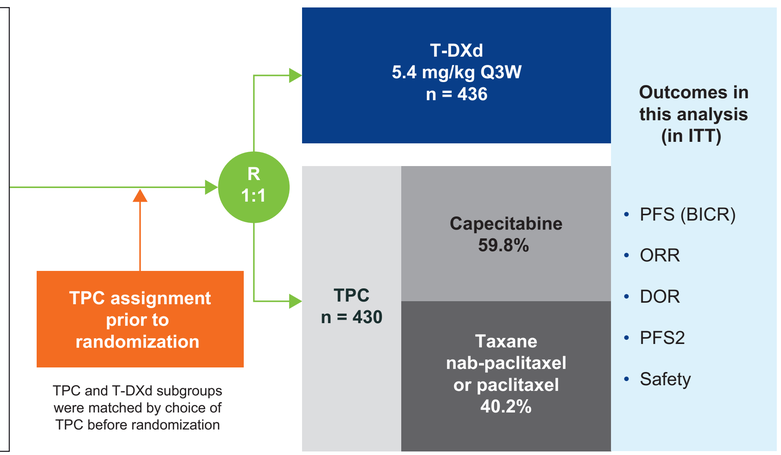
DESTINY-Breast06: a randomized, multicenter, open-label, phase 3 clinical trial (NCT04494425).[1,5]

Patient population

- HR+, HER2-low (IHC 1+ or IHC 2+/ISH−) or HER2-ultralow (IHC 0 with membrane staining) mBC
- Chemotherapy naïve in the mBC setting

Prior therapy

- ≥2 lines of ET ± targeted therapy for mBC **OR**
- 1 line for mBC **AND**
  - Progression ≤6 months of starting first-line ET + CDK4/6i **OR**
  - Recurrence ≤24 months of starting adjuvant ET

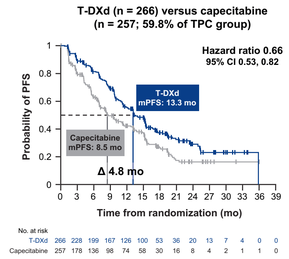


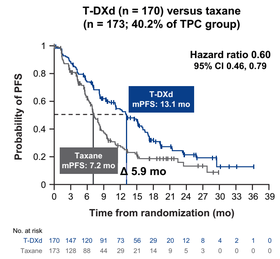
TPC and T-DXd subgroups were matched by choice of TPC before randomization

Median duration of follow up: 18.2 months (ITT)[1]

Results

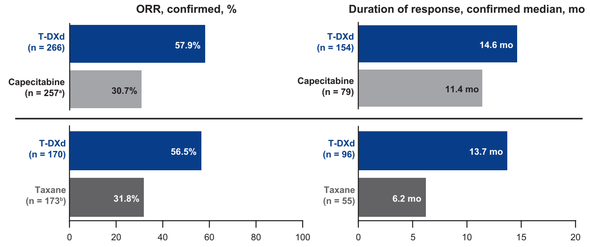
T-DXd demonstrated improvements in median PFS regardless of type of TPC.





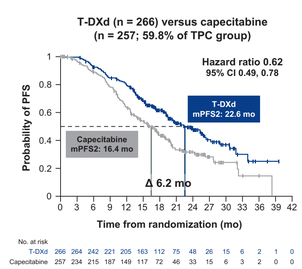
Progression was determined by BICR according to RECIST 1.1.

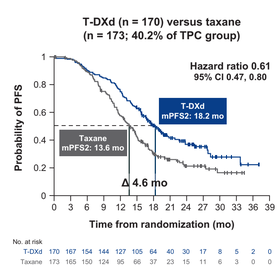
T-DXd improved confirmed ORR and DOR versus both TPC subgroups.



Responses required confirmation after 4 weeks. Median DOR was calculated using the Kaplan–Meier technique. ORR and DOR were determined by BICR according to RECIST 1.1.
[a]59.8% of TPC group.
[b]40.2% of TPC group.

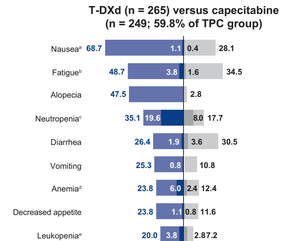
T-DXd was associated with improved PFS2 versus both TPC subgroups.

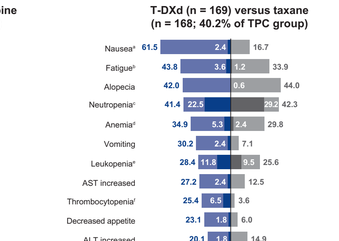




Second progression was determined by the investigator according to local standard clinical practice.

The most common grade ≥3 treatment-related AEs were neutropenia for T-DXd and taxane, and palmar-plantar erythrodysesthesia for capecitabine.





T-DXd, any grade | T-DXd, grade ≥3 | Capecitabine, any grade | Capecitabine, grade ≥3 | Taxane, any grade | Taxane, grade ≥3

[a]Use of antiemetic agents was recommended, but not mandated, prior to each dose of T-DXd for prevention of chemotherapy-induced nausea and vomiting.
[b]Includes the preferred terms fatigue, asthenia, malaise, and lethargy.
[c]Includes the preferred terms neutropenia and neutrophil count decreased.
[d]Includes the preferred terms anemia, hemoglobin decreased, hematocrit decreased, and red blood cell count decreased.
[e]Includes the preferred terms leukopenia and white blood cell count decreased.
[f]Includes the preferred terms platelet count decreased and thrombocytopenia.

Adjusted for treatment duration, the overall safety profile of T-DXd was generally similar to or better than that of capecitabine or taxane.

	T-DXd n = 265	Capecitabine n = 249	T-DXd n = 169	Taxane n = 168
Total exposure, patient-years	271.79	171.59	166.67	91.94
TEAEs grade ≥3, n (%) EAIR per patient-year	138 (52.1) 0.51	107 (43.0) 0.62	91 (53.8) 0.55	78 (46.4) 0.85
TEAEs associated with drug interruptions, n (%) EAIR per patient-year	138 (52.1) 0.51	92 (36.9) 0.54	72 (42.6) 0.43	68 (40.5) 0.74
TEAEs associated with dose reduction, n (%) EAIR per patient-year	59 (22.3) 0.22	113 (45.4) 0.66	48 (28.4) 0.29	48 (28.6) 0.52
TEAEs associated with treatment discontinuation, n (%) EAIR per patient-year	39 (14.7) 0.14	15 (6.0) 0.09	23 (13.6) 0.14	24 (14.3) 0.26
TEAEs leading to death, n (%) EAIR per patient-year	5 (1.9) 0.02	6 (2.4) 0.03	6 (3.6) 0.04	0 0

Includes AEs with the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first). Patients with multiple events in the same category were counted only once in that category. Patients with events in more than one category were counted once in each of those categories. EAIR was defined as the number of patients with at least one event divided by the sum of the patient years of exposure among all the patients in the treatment group.

Poster | Supplementary material | Plain language summary

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Abbreviations

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BICR, blinded independent central review; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; CI, confidence interval; DOR, duration of response; EAIR, exposure-adjusted incidence rate; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; HR+, hormone receptor–positive; IHC, immunohistochemistry; ISH, in situ hybridization; ITT, intent-to-treat; mBC, metastatic breast cancer; mo, months; mPFS, median progression-free survival; mPFS2, median time from randomization to second progression or death; ORR, objective response rate; PFS, progression-free survival; PFS2, time from randomization to second progression or death; PPE, palmar-plantar erythrodysesthesia; Q3W, every 3 weeks; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumours; TEAE, treatment-emergent adverse event; T-DXd, trastuzumab deruxtecan; TPC, physician's choice of chemotherapy.

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Disclosures

The presenting author, Alyssa Morgan, PharmD, BCOP, is an employee of AstraZeneca.

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