Real-world experience with trastuzumab deruxtecan for metastatic breast cancer at a major Australian cancer centre

Michelle Li[1,2], Courtney van Geelen[2], Luis E. Lara Gonzalez[2], Kylie Clarke[2], Senthil Lingaratnam[2,3], Prudence A. Francis[1,2], Sherene Loi[1,2]

[1]Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia [2]Sir Peter MacCallum Department of Oncology, University of Melbourne, Melbourne, VIC, Australia [3]Department of Pharmacy, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia

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Background

- Trastuzumab deruxtecan (T-DXd) is approved for use in both HER2-low and HER2-positive metastatic breast cancer (MBC), with demonstrated significant clinical benefit compared to traditional chemotherapy.[1-2]
- However, real-world treatment toxicities such as nausea, vomiting and cachexia can substantially impair patients' quality of life and lead to early discontinuation of T-DXd.
- Other published real-world data sets estimate discontinuation rates due to treatment toxicity to be between 3-13.9%.[3-6]
- Here, we evaluated the real-world efficacy and tolerability of T-DXd in an Australian context.

Methods

- We conducted a retrospective cohort study of patients aged ≥18 years with MBC treated with T-DXd between May 2019 – December 2024 at a single tertiary Australian cancer centre.
- Demographic, clinicopathologic, treatment and toxicity data were extracted from medical records.
- Real-world PFS (rwPFS) was defined as the time from start of treatment to evidence of disease progression or death, as determined by clinical documentation with no centralized review of imaging.
- Kaplan-Meier analysis was utilized for progression-free survival (PFS), with censoring of patients still on treatment.

Results

- Data from 75 patients was analyzed with a median follow-up of 15.5 months (95% CI 16.3–3.23, range: 0.8–68.7).
- Median age was 46 years (22.7% ≥65 years).
- All patients were female.
- Most patients had ductal histology (77.3%).
- 64% had recurrent metastatic disease. 36% had de novo metastatic disease.
- 36 patients (48%) were HER2-low. 39 patients (52%) were HER2-positive.
- Hormone receptor (HR) positivity was observed in 60%, with 36% being HER2-low and 24% being HER2-positive.
- Median number of lines of prior treatment received for metastatic disease in HER2-low was 2 (range: 0–14) and in HER2-positive was 2 (range: 0–6).
- At time of data cut-off, 27 patients (36%) were still receiving T-DXd.

Treatment-related toxicities

- Common toxicities were nausea, vomiting and weight loss [see Table 1].
- **Nausea** of any grade occurred in 94.7% and was ≥G3 in 9.3%.
- **Vomiting** of any grade occurred in 65% and was ≥G3 in 6.7%.
- **Weight loss** of any grade, as measured over the entire duration of treatment, occurred in 38.7% and was ≥G3 (≥20%; parenteral feeding) in 4%.

Toxicity	All patients (n=75)			HER2-low (n=36)			HER2-positive (n=39)		
	Any grade	G2	≥G3	Any grade	G2	≥G3	Any grade	G2	≥G3
Nausea	71 (94.7%)	25 (33.3%)	7 (9.3%)	36 (100%)	14 (38.9%)	4 (11.1%)	35 (89.7%)	11 (28.2%)	3 (7.7%)
Vomiting	45 (65%)	3 (4%)	5 (6.7%)	19 (52.8%)	3 (8.3%)	2 (5.6%)	26 (66.7%)	0 (0%)	3 (7.7%)
Weight loss	29 (38.7%)	13 (17.3%)	3 (4%)	14 (38.9%)	7 (19.4%)	1 (2.8%)	15 (38.5%)	6 (15.4%)	2 (5.1%)

Table 1. Common treatment toxicities with T-DXd.

Dose reductions (DRs)

- T-DXd DRs occurred in 33 patients (44%).
- 6 (8%) received an upfront DR for performance status.
- 27 (36%) had at least two DRs, often due to nausea/vomiting (21.3%).
- DRs typically occurred after a median of 6 cycles (range: 1–40).

Toxicity	Patients who experienced dose reduction (n=33)
Nausea/vomiting	16 (48.4%)
Performance status decline	5 (15.2%)
Fatigue	2 (6.1%)
Diarrhoea	2 (6.1%)
Hepatotoxicity	2 (6.1%)
Neutropaenia	2 (6.1%)
Thrombocytopaenia	1 (3%)
Interstitial lung disease	1 (3%)
Duodenitis	1 (3%)
Patient preference	1 (3%)

Table 2. Primary reason for first dose reduction of T-DXd.

Treatment discontinuation

- Treatment discontinuation due to toxicity occurred in 7 patients (9.3%), most often due to **interstitial lung disease (ILD; 5 patients, 6.7%).**
- ILD occurred at a median of 2.76 months (range: 1.77–8.15).
- 1 patient (1.3%) discontinued due to hepatotoxicity + thrombocytopaenia.
- 1 patient (1.3%) discontinued due to fatigue.

Real-world progression-free survival on T-DXd (PFS1)

- **rwPFS1 in HER2-low: 6.5 months** (95% CI 5.8-10.3, range: 0.2-31)
- **rwPFS1 in HER2-positive: 19.3 months** (95% CI 15.6-23.6, range: 1.1-52.4)
- Median rwPFS1 was higher in HR+ HER2-low (7.23 months, 95% CI 6-11.7, range: 1.3-31) compared to HR- HER2-low (5.5 months, 95% CI 2.5-8.6, range: 0.2-12.9).

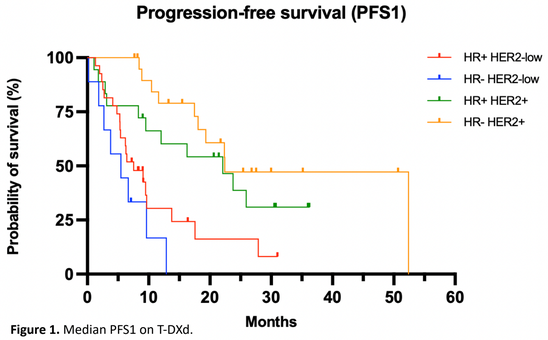


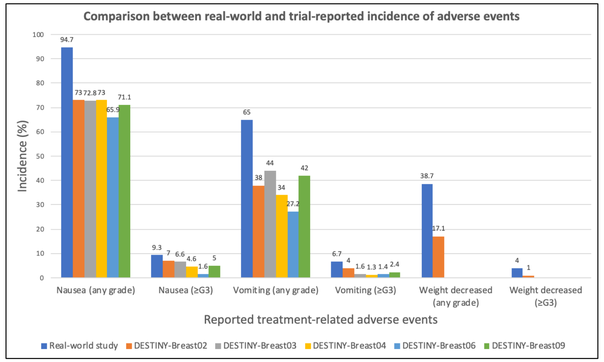
Figure 1. Median PFS1 on T-DXd.

Therapies received post T-DXd

- 48 patients (64%) had progressed on T-DXd.
- 32 (42.7%) received next line therapy, most commonly capecitabine in HER2-low (7 patients, 9.3%) and T-DM1 in HER2-positive (4 patients, 5.3%).
- **Median rwPFS2 was 3.4 months** (95% CI 2.8-7, range: 0.7-20.5).

Discussion

- Common treatment-related toxicities, particularly nausea and vomiting (any grade and ≥G3) occurred in the real-world setting at rates higher than reported in clinical trial data.
- Decrease in weight was not commonly reported in major phase III trials, however our preliminary data also suggests this occurred more frequently in the real-world setting.



Conclusions

- In this real-world cohort, T-DXd demonstrated substantial activity in HER2-low and HER2-positive MBC, consistent with trial data.
- Treatment-related toxicities – especially nausea, vomiting, weight loss and ILD – led to dose modifications and discontinuation in ~10% of patients.
- Interventions targeting emesis and cachexia may help improve tolerability and duration of treatment.

Corresponding author:
Dr Michelle Li, Peter MacCallum Cancer Centre | MichelleM.Li@petermac.org

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