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Interim results from the HER-TEMPO Study: Real-world study of treatment discontinuations and modifications for patients with HER2-low metastatic breast cancer on trastuzumab deruxtecan

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Objective

- The overarching aim of this study is to generate novel Canadian real-world evidence (RWE) on discontinuations and treatment modifications for human epidermal growth receptor 2 expression low (HER2-low) metastatic breast cancer (mBC) patients receiving trastuzumab deruxtecan (T-DXd) enrolled in AstraZeneca Canada's patient support program (PSP).

Conclusions

- Overall discontinuation rates indicate that patients are benefiting from treatment with T-DXd in a real-world Canadian setting.
- Time to treatment discontinuation (TTD) estimates are generally concordant with the pivotal DESTINY-Breast04 (DB-04) trial (NCT03734029).

Plain language summary

Why did we perform this research?

- To collect real-world data on T-DXd treatment discontinuation and modification to support implementation in clinical practice and contextualize treatment decisions.
- To evaluate the treatment tolerability and the ability of patients to continue to receive T-DXd.
- To assess the feasibility of using PSP to generate Canadian real-world data.

How did we perform this research?

- Data was collected from patients with HER2-low metastatic breast cancer receiving T-DXd enrolled in AstraZeneca Canada's PSP.

What were the findings of this research, and what are the implications?

- The time to treatment discontinuation estimated suggest that duration of treatment of T-DXd in a Canadian real-world setting is likely shorter than in the DB-04 trial.
- Overall, the results are generally consistent with the DB-04 trial despite nearly 60% of patients receiving 2 or more lines of chemotherapy in the metastatic setting.
- PSPs provide an effective means of generating real-world data, offering insights into discontinuation and treatment modification rates.

Additional materials

For additional Information on the HER-TEMPO study (NCT06386263), please click on the link below:
https://www.astrazenecaclinicaltrials.com/study/D9673R00032/

For the published protocol, please click on the link below:
https://pmc.ncbi.nlm.nih.gov/articles/PMC12458746/

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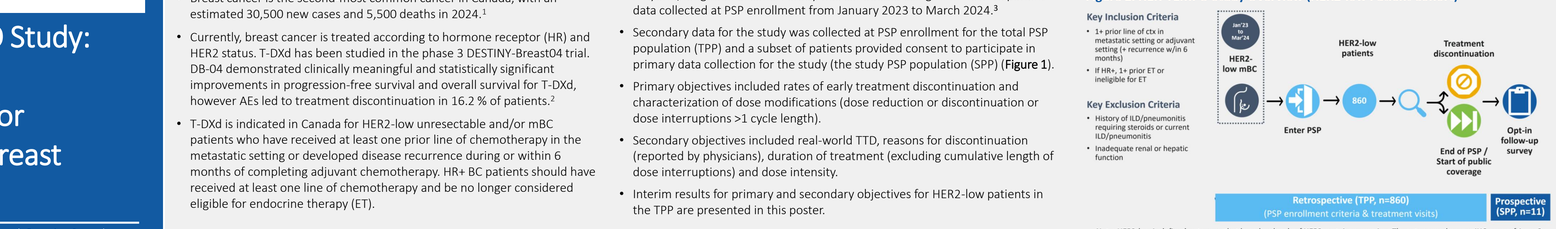
Introduction

- Breast cancer is the second-most common cancer in Canada, with an estimated 30,500 new cases and 5,500 deaths in 2024.[1]
- Currently, breast cancer is treated according to hormone receptor (HR) and HER2 status. T-DXd has been studied in the phase 3 DESTINY-Breast04 trial. DB-04 demonstrated clinically meaningful and statistically significant improvements in progression-free survival and overall survival for T-DXd, however AEs led to treatment discontinuation in 16.2 % of patients.[2]
- T-DXd is indicated in Canada for HER2-low unresectable and/or mBC patients who have received at least one prior line of chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy. HR+ BC patients should have received at least one line of chemotherapy and be no longer considered eligible for endocrine therapy (ET).

Study Design

- A hybrid, longitudinal cohort study was conducted using HER2-low BC patient data collected at PSP enrollment from January 2023 to March 2024.[3]
- Secondary data for the study was collected at PSP enrollment for the total PSP population (TPP) and a subset of patients provided consent to participate in primary data collection for the study (the study PSP population (SPP) (**Figure 1**).
- Primary objectives included rates of early treatment discontinuation and characterization of dose modifications (dose reduction or discontinuation or dose interruptions >1 cycle length).
- Secondary objectives included real-world TTD, reasons for discontinuation (reported by physicians), duration of treatment (excluding cumulative length of dose interruptions) and dose intensity.
- Interim results for primary and secondary objectives for HER2-low patients in the TPP are presented in this poster.

Figure 1. HER-TEMPO Study Overview (HER2-low Patient Cohort)



Note: HER2-low is defined as tumors that have low levels of HER2 protein expression. These tumours have an IHC score of 1+ or 2+, without HER2 gene amplification by ISH [i.e., have negative ISH]).

Methods

- Baseline demographic and clinical characteristics were collected for the overall HER2-low mBC population and stratified by HR status.
- Dose changes were described descriptively as the number and proportion of patients who experience a dose modification or dose interruption.
- TTD for any reason was measured in months from the date of initiation of T-DXd to the date of treatment discontinuation, death, or closure of the PSP, whichever occurs first.
- Reasons for discontinuation were documented by the treating physician using pre-specified reasons.
- Treatment duration was measured in months from the date of initiation of T-DXd to the date of treatment discontinuation, excluding the cumulative length of any dose interruptions.
- Time-to-event outcomes were analyzed using the Kaplan-Meier method; other outcomes were summarized descriptively.

Results

Demographic and clinical characteristics

- The study population had a mean age of 61.8 years, with the majority being female (96.5%) (**Table 1**).
- Most patients had ECOG of 0 or 1, IHC score of 2+.
- Most patients did not develop disease recurrence within 6 months (57.3%).

Table 1. Demographic and clinical characteristics

Characteristic		HER2-low Patients (N=860)	HR-positive Patients (n=793)	HR-negative Patients (n=63)
Age	Median (Range)	62.0 (29.0-94.0)	62 (29-94)	63 (34-79)
Sex	Female, n (%)	830 (96.5%)	763 (96.2%)	63 (100.0%)
ECOG	0, n (%)	295 (34.3%)	272 (34.3%)	22 (34.9%)
	1, n (%)	532 (61.9%)	490 (61.8%)	39 (61.9%)
	2, n (%)	32 (3.7%)	30 (3.8%)	Sup.*
IHC/ISH	IHC 0 / ISH-missing, n (%)	Sup.*	Sup.*	0 (0.0%)
	IHC 1+ / ISH-negative or ISH-missing, n (%)	372 (43.3%)	341 (43.0%)	29 (46.0%)
	IHC 2+ / ISH-negative, n (%)	486 (56.5%)	450 (56.7%)	34 (54.0%)
	IHC 2+ / ISH-missing, n (%)	Sup.*	Sup.*	0 (0.0%)
HR status	HR positive, n (%)	793 (92.6%)	793 (100%)	-
	HR negative, n (%)	63 (7.4%)	-	63 (100%)
	Missing, n (%)	4 (0.5%)	-	-
Patient weight, kg (n=847)**	Median (Range)	65.0 (30.5 – 143.0)	65.3 (33-143)	64 (30.5-110.1)
Prior lines of chemotherapy in metastatic setting	0, n (%)	Sup.*	Sup.*	0 (0.0%)
	1, n (%)	345 (40.2%)	318 (40.1%)	25 (39.7%)
	2, n (%)	233 (27.1%)	218 (27.5%)	15 (23.8%)
	3+, n (%)	270 (31.4%)	245 (30.9%)	23 (36.5%)
	Missing, n (%)	Sup.*	Sup.*	0 (0.0%)
If HR+, number of prior lines of endocrine therapy (metastatic setting) (n=793)	1, n (%)	-	294 (37.1%)	-
	2, n (%)	-	337 (42.5%)	-
	3+, n (%)	-	144 (18.2%)	-
	0 or Missing, n (%)	-	18 (2.3%)	-
Developed disease recurrence within 6 months of completing neoadjuvant or adjuvant therapy	Yes, n (%)	50 (5.8%)	41 (5.2%)	8 (12.7%)
	No, n (%)	493 (57.3%)	462 (58.3%)	31 (49.2%)
	Missing, n (%)	317 (36.9%)	290 (36.6%)	24 (38.1%)

*Aggregated counts due to small cell size < 10.
**Number of patients with available weight data. There were missing HR status in 4 patients.
Abbreviations: ECOG = Eastern Cooperative Oncology Group Performance Status; HER2 = human epidermal growth factor receptor 2; HR = Hormone Receptor; IHC = immunohistochemistry; IQR = Interquartile Range; ISH = in situ hybridization; kg = kilogram; N = number; SD = Standard Deviation.

Dosing

- Patients had an initial dose of 5.4 mg/kg (670 [77.9%]), 4.4 mg/kg (84 [9.8%], >4.4 mg/kg and <5.4 mg/kg (40 [4.7%]), >5.4 mg/kg (30 [3.5%]), 3.2 mg/kg (12 [1.4%]). Number of patients with an initial dose of >3.2 mg/kg and <4.4 mg/kg, ≤3.2 mg/kg or missing was suppressed due to counts <10.
- Dose intensity (**Table 2**), measured as the total amount of drug delivered over the course of treatment divided by the standard amount expected over the same period of treatment.

Table 2. Dose intensity

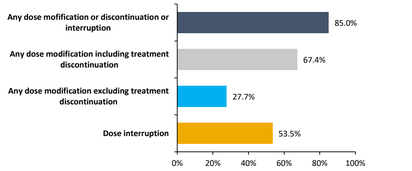
Dose intensity [a,b]	Estimate
Mean (SD)	0.83 (0.20)
Median (IQR, range)	0.88 (0.29, 0.71 – 1.00)

[a] One patient excluded due to dose outliers.
[b] 28 patients excluded due to missing dose outliers.
Abbreviations: IQR = Interquartile Range; RMST = restricted mean survival time; SD = Standard Deviation; SE = Standard Error.

Dose Modification and Interruptions

- The proportion of patients with a dose modification/interruptions is presented in Figure 2.
- Dose modifications were defined for patients starting at a dose of 5.4mg/kg as a change to a dose of 4.4 mg/kg or treatment discontinuation. For patients starting at a lower dose, a dose modification was a change to a lower dose ≤3.2 mg/kg, the next recommended higher dose, or treatment discontinuation.
- A dose interruption was defined as a as a gap in treatment lasting at least one cycle length (3 weeks or 21 days) followed by a resumption of treatment at any dose.

Figure 2. The proportion of dose modification and interruptions



Note: Dose modification and interruptions were limited to patients with an initial dose of 5.4mg/kg or a lower recommended dose of 4.4 mg/kg or 3.2 mg/kg. A tolerance of ±5% was applied to the recommended dose to allow for imprecision in measuring weight and dosage (e.g. doses between 95% x 5.4 mg/kg and 105% x 5.4 mg/kg were considered a dose of 5.4 mg/kg). A tolerance of 3 days (i.e. 24 days) was applied to the length of interruption interval to account for scheduling changes.

Treatment Discontinuations

- The probability of remaining on treatment or discontinuing treatments is presented in **Table 3**.
- There were 860 patients who started treatment in the PSP and at data cut-off 279 patients who remained on treatment .

Table 3. Probability of remaining on treatment and discontinuation

Time	On treatment, % (95% CI)	Discontinuation, % (95% CI)
3 months (90 days)	78.3% (75.5% - 81.2%)	21.7% (18.8% - 24.5%)
6 months (180 days)	55.9% (52.4% - 59.7%)	44.1% (40.3% - 47.6%)
9 months (270 days)	40.0% (36.2% - 44.2%)	60.0% (55.8% - 63.8%)

Time to Treatment Discontinuations

- TTD is presented in **Figure 3**. Median TTD was greater in patients HR positive disease compared to those with HR negative disease (**Figure 4**).

Figure 3. Time to treatment discontinuation for TPP

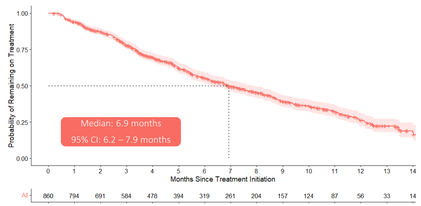
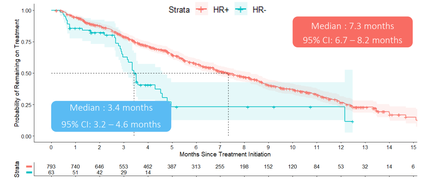


Figure 4. Time to treatment discontinuation by HR status



Reasons for Discontinuation

- There were 465 (54.1%) discontinuations in the study, with most patients experiencing drug discontinuation due to progression (243 [52.3%]) (**Table 4**).

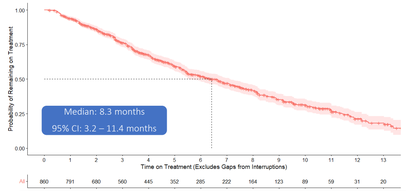
Table 4. Reasons for Discontinuation

Reason	Overall (n = 243)
Progression, n (%)	243 (52.3%)
Prescriber decision, n (%)	73 (15.7%)
Patient death, n (%)	68 (14.6%)
Patient decision other than progression, n (%)	29 (6.2%)
Adverse event, n (%)	17 (3.7%)
Therapy switching other than progression/Other, n (%)	12 (2.6%)
Not available/Unknown, n (%)	23 (4.9%)

Treatment Duration

- Treatment duration, as defined as the date of treatment initiation to the date of treatment discontinuation (excluding the cumulative length of any dose interruptions), had a median of 6.4 months (95% CI: 8.3, 3.2 - 11.4 months) and restricted mean survival time (RMST) of 7.5 months (**Figure 5**).

Figure 5. Duration of Treatment for TPP



Implications

As the early clinical trials for T-DXd included limited data on Canadian patients, this study was designed to generate novel Canadian RWE on discontinuations and treatment modifications for HER2-low mBC patients by utilizing data generated from AstraZeneca Canada's PSP for T-DXd.

Overall, discontinuation rates indicate that patients are benefitting from treatment with T-DXd in a real-world setting and are generally consistent with the DB-04 trial.

Time to treatment discontinuation estimates suggest that duration of treatment is likely shorter than in DB-04 (8.2 months vs 6.9 months, respectively) which is expected in a real-world setting which includes patients with higher degree of disease severity, reflected by more lines of prior chemotherapy in the metastatic setting compared to DB-04. Furthermore, shorter durations are anticipated in HER2-low cohort due to the fixed duration of the PSP and limited follow-up data for patients who go on to receive T-DXd via public coverage

Additionally, a subgroup analysis shows that HR positive patients have a longer time to treatment discontinuation.

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Disclosures

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