Poster 539P

Final real-world safety and effectiveness results of REALITY-01 study: trastuzumab deruxtecan (T-DXd) in patients received ≥ 2 prior treatment lines for HER2+ metastatic or unresectable (m/u) breast cancer (BC)

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Background and objectives

- Despite global therapeutic advancements, a substantial unmet medical need persists to improve progression-free survival (PFS), Overall Survival (OS) and quality of life (QoL) in patients (pts) with HER2+ mBC. Attrition rate highlight that a significant proportion of pts might not receive or benefit from later-line treatment (tt) options[1].
- The phase II DESTINY-Breast01 trial demonstrated the efficacy of T-DXd in HER2+ mBC pts previously treated with trastuzumab emtansine (T-DM1), reporting an overall response rate (ORR) of 62%, a median PFS of 19.4 months (mo), and an OS of 29.1 mo[2].
- The phase III DESTINY-Breast02 subsequently confirmed these findings and reinforced the favourable benefit-risk profile of T-DXd, showing its ability to overcome resistance to prior ADCs[3] (i.e. T-DM1), while maintaining a relatively low incidence of T-DXd-related serious adverse drug reactions (ADRs) (11.4%). Confirmed ORR was 74.1% with T-DXd versus 27.2% with treatment of physician's choice, median PFS was 16.7 versus 5.5 mo (HR 0.30), and median OS was 35.7 versus 25.0 mo, corresponding to a 31% reduction in the risk of death (HR 0.69)[4].
- In France, the results of DESTINY-Breast01 and 02 supported early access of T-DXd for eligible pts before the Marketing Authorization (MA) through a Temporary Authorization for Use (Autorisation Temporaire d'Utilisation; ATU) program, as a monotherapy for the treatment of HER2+ m/u BC in pts previously treated with ≥ 2 lines of anti-HER2 tt.
- **This REALITY-01 study aims to fill gaps with real-world data for HER2+ m/u BC pts of both cohorts (during ATU and after MA) with T-DXd tt.**

Conclusions

- **REALITY-01 confirms the safety and effectiveness of T-DXd in real-world setting**.
- **A favourable benefit-risk profile in unselected populations:**
  - 96.1% of patients initiated T-DXd at the recommended dose (5.4 mg/kg), with only 16.3% requiring dose reductions due to any ADR, highlighting its manageable safety profile.
  - Only 11.1% of treatment discontinuations due to any ADR and 9.8% of serious adverse drug reactions, despite the inclusion of subgroups typically excluded from clinical trials.
  - No evidence of increasing toxicity in these vulnerable subgroups (ECOG 2–3, ≥ 70 yrs), confirming the manageability of T-DXd in routine clinical practice.
- **Sustained efficacy:**
  - Median progression-free survival of 17.6 months and objective response rate of 49.0%, consistent with pivotal trial results.
  - Reassuring data for elderly patients and those with impaired performance status (ECOG 2/3), where T-DXd demonstrates tolerability comparable to the general population.
- **These findings support T-DXd as astandard therapeutic option for heavily pre-treated HER2+ patients, including high-risk populations, and endorse its broader accessibility in clinical practice.**

This study was sponsored by Daiichi Sankyo and AstraZeneca. In March 2019, AstraZeneca entered into a global development and commercialization collaboration agreement with Daiichi Sankyo for trastuzumab deruxtecan (T-DXd; DS-8201).
Poster presented at ESMO congress 2025 by Jean-Yves Pierga. Corresponding author email address: jean-yves.pierga@curie.fr

Methods

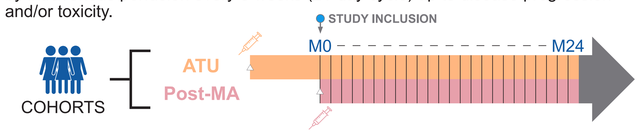
A non-interventional, ambispective, longitudinal, open-label, multicentre, phase IV study

Main eligibility criteria

- Adult patient (age ≥ 18 years (yrs)).
- HER2+ m/u BC, with at least 1 prior anti-HER2 treatment before T-DXd, previously treated by compassionate T-DXd or previously treated or planned to be treated by T-DXd, upon the investigator's decision.

Dosage and duration of treatment according to the SmPc

The recommended dosage for T-DXd was 5.4 mg/kg administered by intravenous perfusion every 3 weeks (21-day cycle) up to disease progression and/or toxicity.



Primary outcomes

- **Safety of T-DXd in real-life conditions as per the occurrence of:**
  - Gastro-intestinal disorders, Interstitial Lung Disease (ILD), left ventricular dysfunction, alopecia (any grade);
  - Other **grade ≥ 3** Adverse Drug Reactions (ADRs).

Secondary outcomes

- Risk factors for ADRs, description of T-DXd treatment over time, effectiveness of T-DXd in real-life conditions, HR-QoL.

Results

Patients' characteristics at T-DXd initiation

- At the data cut-off, i.e. July 2024, 50 centres recruited 306 pts with a **median follow-up duration of 23.3 mo**.

Figure 1. Flow chart of analysis sets and pts disposition

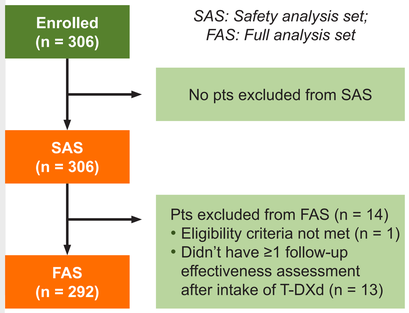


Table 1. Characteristics of pts at T-DXd initiation

Number of patients	**306**
Age	
Median age, n (Min-Max)	59 (27–90)
≥ 70 yrs, n (%)	58 (19.0)
ECOG performance status, n (%)	
0–1	207 (67.6)
2–3	52 (17.0)
Missing	47 (15.4)
CNS metastasis, n (%)	
Yes	89 (29.1)
Parenchymal	*68 (22.2)*
Leptomeningeal	*29 (9.5)*
Missing	*3 (1)*
No	212 (69.3)
Missing	5 (1.6)
Hepatic failure, n (%)	
Yes	20 (6.5)
No	283 (92.5)
Missing	3 (1)
Renal failure, n (%)	
Yes	4 (1.3)
No	298 (97.4)
Missing	4 (1.3)
History of lung disease history, n (%)	
Yes	38 (12.4)
No	268 (87.6)
Previous lines of anti-cancer systemic treatment for metastatic or locally advanced disease, n (%)	
≤ 3	146 (47.7)
≥ 4	159 (52.0)
Missing	1 (0.3)

Safety and tolerability (SAS; n = 306)

- ADRs of interest were reported in 85.3% (n = 261) of pts, of whom 11.1% (n = 34) (95% CI: [7.8–15.2]) discontinued T-DXd tt.
- Out of a total of 979 T-DXd-related ADRs, 3.9% (n = 38) were serious. At least one interstitial lung disease/pneumonitis (ILD) was reported in 14.7% of all patients (n = 45) and a total of 48 ILD events occurred: 5.6% of all patients (n = 17) had grade 1, 4.9% (n = 15) grade 2, 2.3% (n = 7) grade 3, 1.0% (n = 3) grade 5 and 1.0% (n = 3) had ungraded ILD's.* Among these patients, the median time to onset of ILD was 123 days (range, 31–760).
- A total of 37.6% of pts (n = 115) experienced grade ≥ 3 ADRs: the only one observed in more than 10% of pts was haematotoxicity, reported in 18.0% of cases (n = 55).

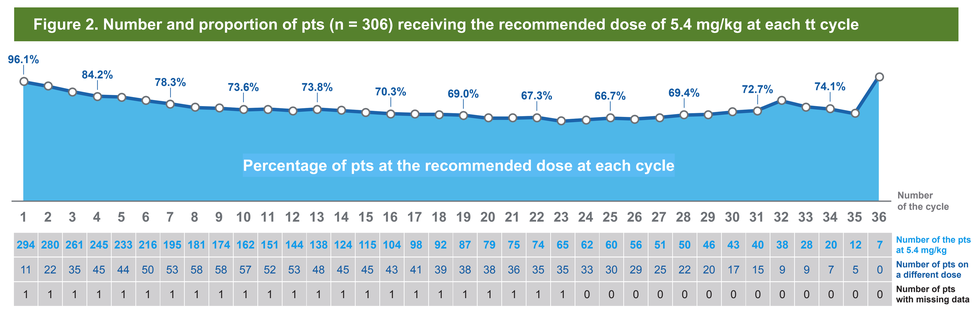
Table 2. Occurrence of T-DXd-related ADRs in all patients, stratified by age group and baseline ECOG performance status

	Total	ECOG 0–1	ECOG 2–3	< 70 yrs	≥ 70 yrs	ECOG 0–1		ECOG 2–3	
						< 70 yrs	≥ 70 yrs	< 70 yrs	≥ 70 yrs
Number of patients	**306**	207	52	248	58	172	35	43	9
Any ADR, n (%)	**261 (85.3)**	**181 (87.4)**	**43 (82.7)**	**212 (85.5)**	**49 (84.5)**	**151 (87.8)**	**30 (85.7)**	**36 (83.7)**	**7 (77.8)**
Associated with dose reduction	50 (16.3)	37 (17.9)	10 (19.2)	40 (16.1)	10 (17.2)	28 (16.3)	9 (25.7)	9 (20.9)	1 (11.1)
Associated with study drug interruption	72 (23.5)	53 (25.6)	14 (26.9)	53 (21.4)	19 (32.8)	39 (22.7)	14 (40.0)	11 (25.6)	3 (33.3)
Associated with study drug discontinuation	34 (11.1)	22 (10.6)	8 (15.4)	26 (10.5)	8 (13.8)	19 (11.0)	3 (8.6)	6 (14.0)	1 (22.3)
Associated with an outcome of death	4 (1.3)	2 (1.0)	2 (3.8)	3 (1.2)	1 (1.7)	1 (0.9)	1 (2.9)	2 (4.7)	0 (0.0)
Any grade ≥ 3 ADR, n (%)	**115 (37.6)**	**81 (39.1)**	**23 (44.2)**	**94 (37.9)**	**21 (36.2)**	**65 (37.8)**	**16 (45.7)**	**20 (46.5)**	**3 (33.3)**
Associated with dose reduction	29 (9.5)	19 (9.2)	7 (13.5)	25 (10.1)	4 (6.9)	15 (8.7)	4 (11.4)	7 (16.3)	0 (0.0)
Associated with study drug interruption	49 (16.0)	37 (17.9)	9 (17.5)	39 (15.7)	10 (17.2)	29 (16.9)	8 (22.9)	8 (18.6)	1 (11.1)
Associated with study drug discontinuation	23 (7.5)	15 (7.2)	6 (11.5)	19 (7.7)	4 (6.9)	13 (7.6)	2 (5.7)	5 (11.6)	1 (11.1)
Associated with an outcome of death	4 (1.3)	2 (1.0)	2 (3.8)	3 (1.2)	1 (1.7)	1 (0.6)	1 (2.9)	2 (4.7)	0 (0.0)
Any Serious ADR, n (%)	**30 (9.8)**	**16 (7.7)**	**11 (21.2)**	**24 (9.7)**	**6 (10.3)**	**14 (8.1)**	**2 (5.7)**	**9 (20.9)**	**2 (22.2)**

T-DXd treatment exposure (SAS; n = 306)

- **Median duration of T-DXd treatment was 11.9 mo** (range, 0.7–26.7).
- 21.6% of pts (n = 66) completed the study according to the protocol (after 2 years of follow-up).
- Median number of cycles of T-DXd received per patient was 15.0 (range, 1–36).

Figure 2. Number and proportion of pts (n = 306) receiving the recommended dose of 5.4 mg/kg at each tt cycle



Effectiveness (FAS; n = 292)

- **Median PFS was 17.6 mo.** Median OS was not reached. The 2-year OS rate was 63.4% (95% CI: [57.5–68.8]).
- Among the 292 pts of the FAS, **66.4% (n = 194) had at least one on-treatment assessment and ORR was 49.0%** (95% CI: [41.7–56.2]), including 25.8% (n = 50) of CR.
- Among the 120 pts who achieved a complete or partial response (CR/PR), the median duration of response** was 13.4 mo (95% CI: [9.0–17.4]).

Figure 3. Progression Free Survival

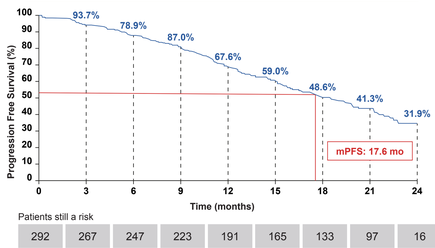


Figure 4. Overall Survival

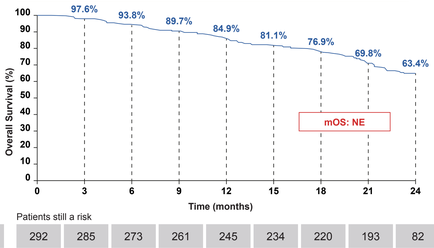
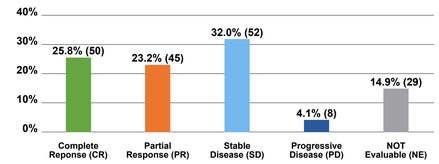


Figure 5. Best Overall Response Rate in patients with at least one on-treatment assessment (n = 194), % (n)



Focus on mCNS

- At T-DXd initiation, 89 pts (29.1%) had mCNS, of which 29.2% (n = 26) were symptomatic.
- Among the mCNS pts who underwent at least one on-treatment CNS assessment (n = 54), 46.3% pts (n = 25) achieved a complete or partial response.
- The median PFS for patients with CNSm at T-DXd initiation was 14.8 months (95% CI: [13.0–19.1]), with a 12-month PFS rate of 64.8% (95% CI: [53.8–73.7]).

* If a subject has more than one event, he is counted once at each level of summation.
**Censoring rules: if pts lost to follow-up, censor date will be last contact date available; if pts who have non-CNS progression or not known to have died at the end of study or at the date of cut-off, censor date will be the last disease evaluation date (i.e. date of last imaging).

Abbreviations

T-DXd: trastuzumab deruxtecan; m/u: metastatic or unresectable; BC: breast cancer; PFS: progression-free survival; OS: overall survival; QoL: quality of life; pts: patients; T-DM1: trastuzumab emtansine; ORR: overall response rate; mo: month; HR: Hazard ratio; MA: Marketing Authorization; ATU: Autorisation Temporaire d'Utilisation (Temporary Authorization for Use); ADR: adverse drug reaction; ECOG: Eastern Cooperative Oncology Group

Disclosures

First Author: Participation on boards, as a speaker at meetings (Daiichi Sankyo); Principal Investigator of the REALITY-01 study (Daiichi Sankyo)

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