Poster 12P

DESTINY-Breast Respond HER2-low Europe Non-interventional Study of Trastuzumab Deruxtecan (T-DXd) in HER2-low Metastatic Breast Cancer (mBC): Update on Baseline Characteristics and Anti-emetic Treatment

Jean-Yves Pierga[1], Francois P Duhoux[2], Daniel Egle[3], José Ángel García-Sáenz[4], Frédérique Penault-Llorca[5], Antonios Valachis[6], Hans Wildiers[7], Khalil Zaman[8], Petra Laeis[9], Markus Lucerna[9], Birgit Edlich[9], Valentina Guarneri[10,11]

[1]Department of Medical Oncology, Institut Curie, Université Paris Cité, Paris, France; [2]Department of Medical Oncology, King Albert II Cancer Institute, Cliniques universitaires Saint-Luc, Brussels, Belgium; [3]Department of Gynaecology and Obstetrics, Medical University of Innsbruck, Innsbruck, Austria; [4]Department of Medical Oncology, Hospital Clínico San Carlos, Instituto de Investigación Sanitaria Hospital Clínico San Carlos (IdISSC), Madrid, Spain; [5]Centre Jean Perrin, Université Clermont Auvergne, INSERM, U1240 Imagerie Moléculaire et Stratégies Théranostiques, Clermont-Ferrand, France; [6]Department of Oncology, Faculty of Medicine and Health, Örebro University, Örebro, Sweden; [7]Department of General Medical Oncology, University Hospitals Leuven, Leuven, Belgium; [8]Department of Oncology, Lausanne University Hospital CHUV, University of Lausanne, Lausanne, Switzerland; [9]Daiichi Sankyo Europe GmbH, Munich, Germany; [10]Medical Oncology 2, Veneto Institute of Oncology (IOV), IRCCS, Padova, Italy; [11]Department of Surgery, Oncology and Gastroenterology, University of Padova, Padova, Italy.

Objective

- To report a second snapshot of updated baseline characteristics and anti-emetic treatment from the ongoing, non-interventional DESTINY-Breast Respond HER2-low (DBRH2L) Europe study, up to October 17, 2025

Conclusions

- DBRH2L represents a more diverse range of patients with HER2-low mBC treated with T-DXd versus those from the pivotal DESTINY-Breast04 trial; proportion of older patients (median age: DBRH2L, 61 years; DB-04, 57 years) and overall performance status (DBRH2L: ECOG PS 1, 34.3%; 2, 6.3%; 3, 0.9%; DB-04: ECOG PS 1, 46.4%) differ
- Of the available data, less than half of the patients received combinations of ≥3 anti-emetic classes. Antiemetic prophylaxis may be further optimised in consideration of the emetogenic risk associated with T-DXd
- The ongoing DBRH2L Europe study will provide additional insights on real-world effectiveness, treatment management, treatment sequencing, safety and quality of life for patients in the European region with HER2-low mBC treated with T-DXd

Plain language summary

Why did we perform this research?

- Trastuzumab deruxtecan (T-DXd), a treatment for metastatic breast cancer (mBC) that targets the HER2 protein, has been assessed in several clinical trials. The DESTINY-Breast04 (DB-04) trial showed that T-DXd is effective for breast cancers that have low levels of HER2 expression
- Current information on the use of T-DXd in the HER2-low population is limited to clinical trials (e.g., DB-04 and -06). This study, DESTINY-Breast Respond HER2-low (DBRH2L) Europe, aims to look at the effectiveness and safety of T-DXd in real-world practice

How did we perform this research?

- The study includes patients receiving T-DXd for HER2-low mBC, as well as patients receiving traditional chemotherapy. Data will be collected on the treatment outcomes, patient-reported quality of life and side effects

What were the findings of this research?

- The data indicate that patients with HER2-low mBC treated with T-DXd in the real world are more diverse than those in the DB-04 trial
- Of the available data on anti-nausea medication use, less than half of the patients received a combination of ≥3 anti-nausea medications. These results suggest that the use of anti-nausea treatment could be further optimised in clinical practice

What are the implications of this research?

- This study will be the largest to date examining the real-world use of T-DXd in the European region, providing valuable insight into the effectiveness and safety of this treatment as well as how it is used and how it impacts the lives of patients

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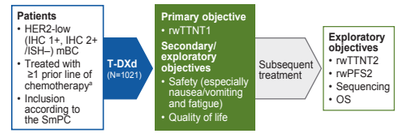
Introduction

- The DB-04 trial showed significantly longer PFS and OS in patients with HER2-low (IHC 1+ or IHC 2+/ISH–) mBC treated with T-DXd versus physician's choice of chemotherapy after one or two lines of chemotherapy[1]
- As such, HER2 expression is no longer seen as a binary classification but as a spectrum, including HER2-low as a targetable biomarker
- The ongoing, non-interventional DBRH2L Europe study will evaluate the real-world effectiveness and safety of T-DXd in patients with HER2-low mBC
- We report a second snapshot of updated baseline characteristics and anti-emetic treatment

Methods

- DBRH2L Europe (NCT05945732) is a multicenter, observational, prospective, non-interventional study, including patients from 206 sites across 9 European countries
  - Patients may also be included retrospectively in France, as some patients already received T-DXd via an early access program
- The study design (**Figure 1**) has been previously published.[2] Briefly, the study is enrolling patients with HER2-low mBC who received ≥1 prior line of chemotherapy in the metastatic setting and are being treated with either T-DXd (N=1021) or standard chemotherapy (N=96), based on the SmPC[3]
- The primary objective is the effectiveness of T-DXd based on rwTTNT
- Secondary objectives include:
  - Assessment of treatment patterns and sequencing, baseline demographics and clinical characteristics
  - Assessment of the safety and tolerability of T-DXd via safety events of interest and patient-reported outcomes
  - Assessment of real-world time to treatment discontinuation
  - Detailed assessment of geriatric status, nausea/vomiting, and quality of life via questionnaires
- The data cutoff for this second snapshot analysis was October 17, 2025

Figure 1. DBRH2L Europe study design



The study included a disease registry of patients treated with conventional chemotherapy (N=96). [a]Patients who have received prior chemotherapy in the metastatic setting, or patients who have developed disease recurrence during or within 6 months of completing adjuvant chemotherapy are eligible for T-DXd treatment according to the SmPC.[3] Patients with HR+ disease must have received ≥1 endocrine therapy in the metastatic setting.

Results

Enrolled patients in the snapshot analysis, up to October 17, 2025

- A total of 680 patients have been enrolled from nine European countries (**Figure 2**)

Baseline, biopsy and disease characteristics

- The enrolled population to date includes older patients, patients with higher ECOG performance status and a relevant number of patients with brain metastases compared with DB-04 (**Table 1**)
- Most patients presented with HR+ tumours (**Table 2**)

Prior treatment received

- Patients with any prior systemic anti-cancer treatment received a median of 3 prior lines of therapy (range: 1–6 lines) in the metastatic setting before initiation of the study (**Figure 3**)
- Patients receiving T-DXd were most commonly treated with CDK4/6i-based regimens in 1L (59.5%), whereas chemotherapy-based regimens were the most common treatments in 2L and beyond
  - The most common chemotherapy used was capecitabine (61.1%)

Figure 2. Number (and percentage) of patients in each country included in the snapshot analysis

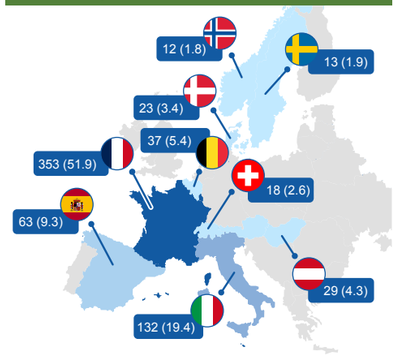
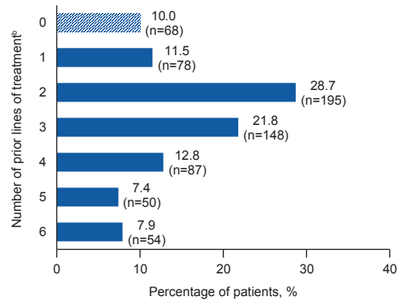


Figure 3. Number of prior lines of treatment in the metastatic setting[a]



[a]0 lines includes patients with missing data on prior treatment line. The population may include some patients that were fast progressors in the early setting and thus eligible for T-DXd treatment without prior chemotherapy in the metastatic setting according to the SmPC.[3] [b]The number of prior treatments refers to the metastatic setting.

- The most common class of anti-emetic treatments used was 5-HT3 RAs, by 76.8% (n=119) of patients. This was followed by NK1 RAs (69.0%, n=107), glucocorticoids (47.7%, n=74), D2 antagonists (40.6%, n=63) and atypical antipsychotics (14.2%, n=22)
- Single-agent, and combinations of 2, 3 and ≥4 anti-emetic classes were administered in 21.3% (n=33), 34.2% (n=53), 20.0% (n=31) and 24.5% (n=38) of patients, respectively (**Table 3**)
- Less than half of the patients received combinations of ≥3 anti-emetic classes

Table 1. Baseline characteristics

Baseline characteristics	Total (n=680)
Age, years, median (range)[a]	61.0 (30–90)
<65 years, n (%)	406 (59.7)
65–74 years, n (%)	158 (23.2)
≥75 years, n (%)	106 (15.6)
ECOG PS, n (%)[b]	
0	243 (35.7)
1	233 (34.3)
2	43 (6.3)
3	6 (0.9)
Visceral disease at diagnosis of metastatic disease, n (%)[c]	
Yes	265 (39.0)
No	373 (54.9)
Baseline brain metastases, n (%)[d]	70 (10.3)
Stable	33 (4.9)
Active	29 (4.3)
Lung-related comorbidities, n (%)	
No	661 (97.2)
Yes	19 (2.8)

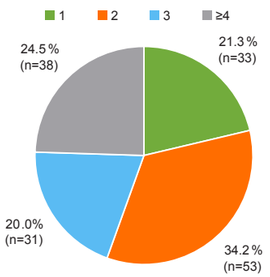
[a]Age for 10 patients was missing. [b]ECOG PS for 155 patients was missing. [c]Status for 42 patients was unknown or missing. [d]Status for 8 patients was unknown or not recorded.

Table 2. Biopsy and disease characteristics

Biopsy or disease characteristics, n (%)	Total (n=680)
Sample used for most recent HER2 status testing[a]	
Archival tissue	286 (42.1)
Newly obtained tissue	376 (55.3)
Biopsy tissue type[b]	
Primary tumour	229 (33.7)
Metastasis	426 (62.6)
HR status[c]	
HR+	532 (78.2)
HR–	107 (15.7)
HER2 IHC score[d,e]	
0	34 (5.0)
1+	390 (57.4)
2+	230 (33.8)
3+	5 (0.7)

[a]Type of sample used for HER2 status testing was missing for 18 patients. [b]Biopsy tissue type was unknown or missing for 25 patients. [c]HR status for 41 patients was unknown or missing. [d]All patients had a history of HER2-low disease as determined by IHC for inclusion in the study; however, these data reflect HER2 IHC scores from the most recent biopsy. [e]Status for 21 patients was unknown, not recorded, or missing.

Figure 4. Number of anti-emetic substance class combinations (N=155)



Anti-emetic treatment

- Under ESMO and MASCC guidelines, T-DXd is classed at the high end of the moderately emetogenic drugs category. The guidelines recommended the use of a ≥3 drug combination of anti-emetic regimens with T-DXd[4]
- Data on concomitant anti-emetic treatment was available in 155 (22.8%) patients (**Figure 4**)

Table 3. Anti-emetic treatment regimens according to number of class combinations

Concomitant anti-emetic treatment[a]	Total, n (%)
1 drug regimen (N=33)	
D2 antagonist	15 (45.5)
5-HT3 RA	6 (18.2)
NK1 RA	6 (18.2)
Glucocorticoid	5 (15.2)
Atypical antipsychotic	1 (3.0)
2 drug regimen (N=53)	
5-HT3 RA + NK1 RA	31 (58.5)
5-HT3 RA + glucocorticoid	7 (13.2)
5-HT3 RA + D2 antagonist	6 (11.3)
Other combinations[b]	9 (17.0)
3 drug regimen (N=31)	
5-HT3 RA + glucocorticoid + NK1 RA	16 (51.6)
5-HT3 RA + D2 antagonist + NK1 RA	9 (29.0)
Other combinations[c]	6 (6.5)
≥4 drug regimen (N=38)	
5-HT3 RA + D2 antagonist + glucocorticoid + NK1 RA	22 (57.9)
5-HT3 RA + atypical antipsychotic + glucocorticoid + NK1 RA	14 (36.8)
Other combinations[d]	2 (5.3)

Drug combinations with less than five patients are represented in other combinations. [a]Concomitant treatment is any treatment taken during the treatment period that includes treatment with 1) the start date on or after the index date and before study treatment stop date (included) or 2) the start date before the index date and the stop date after or on the index date but prior to the study treatment stop date (included). If a patient had more than one medication per preferred term, the patient is counted once at each level of summation. [b]D2 antagonist + NK1 RA, n=4; D2 antagonist + glucocorticoid, n=3; glucocorticoid + NK1 RA, n=2. [c]5-HT3 RA + glucocorticoid + atypical antipsychotic, n=3; 5-HT3 RA + atypical antipsychotic + D2 antagonist, n=1; 5-HT3 RA + D2 antagonist + glucocorticoid, n=1; 5-HT3 RA + atypical antipsychotic + NK1 RA, n=1. [d]5-HT3 RA + atypical antipsychotic + D2 antagonist + NK1 RA, n=1; 5-HT3 RA + atypical antipsychotic + D2 antagonist + glucocorticoid + NK1 RA, n=1.

Abbreviations

1/2L, first/second line; 5-HT3 RA, 5-hydroxytryptamine receptor antagonist; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; D2, dopamine 2; DB-04, DESTINY-Breast04; DBRH2L, DESTINY-Breast Respond HER2-low; ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; IHC, immunohistochemistry; ISH, in situ hybridization; MASCC, Multinational Association for Supportive Care in Cancer; mBC, metastatic breast cancer; NK1 RA, neurokinin 1 receptor antagonist; OS, overall survival; (rw)PFS, (real-world) progression-free survival; rwTTNT, real-world time to next treatment; SmPC, summary of product characteristics; T-DXd, trastuzumab deruxtecan.

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Disclosures

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