Poster 634eP

Long-Term Survival Outcomes in Patients with HER2+ Metastatic Breast Cancer Treated with Trastuzumab and Pertuzumab: A 2012–2024 US Real-World Analysis

Arielle Heeke[1], Danalyn Byng[2], Suyuan Zhang[3], Shannon Hunter[3], Kyle Dunton[4], Tara Harding[5], William Jacot[6]

[1]Department of Solid Tumor Oncology and Investigational Therapeutics, Atrium Health Levine Cancer Institute, Wake Forest University School of Medicine, Charlotte, NC, USA; [2]Daiichi Sankyo Europe GmbH, Munich, Germany; [3]Daiichi Sankyo, Inc, Basking Ridge, NJ, USA; [4]Daiichi Sankyo UK Ltd, Uxbridge, UK; [5]AstraZeneca, Cambridge, UK; [6]Institut du Cancer de Montpellier, INSERM U1194, Montpellier University, Montpellier, France

Objectives

- To describe demographic and clinical characteristics and treatment patterns of a real-world cohort of patients in the United States (US) who initiated a trastuzumab + pertuzumab (HP)-based regimen without prior chemotherapy or HER2-targeted therapy in the metastatic setting, either as 1L therapy or as 2L following one prior line of endocrine therapy (ET), for human epidermal growth factor receptor 2 (HER2)-positive (HER2+; immunohistochemistry 3+ or in situ hybridization-positive) metastatic breast cancer (mBC).
- To describe real-world time to treatment discontinuation or death (rwTTD/D), real-world time to next treatment or death (rwTTNT/D), and real-world overall survival (rwOS) from start of index line of therapy (LOT) in the overall cohort and stratified by hormone receptor (HR) status and de novo vs recurrent metastatic status.

Conclusions

- These results characterized real-world patient characteristics, treatment patterns, and long-term survival outcomes for patients receiving HP for HER2+ mBC in the US, providing data to help assess whether current treatment strategies remain sufficient.
- Median rwTTD/D and rwTTNT/D, surrogates for progression-free survival, were numerically shorter for the recurrent cohort (12.7 and 14.3 months, respectively) versus the de novo cohort (17.2 months and 18.9 months, respectively) and shorter than the progression-free survival observed in the THP arm of CLEOPATRA (18.5 months), perhaps reflecting the effect of previous HP treatment in this more modern real-world cohort.[1]
- This analysis had rwOS outcomes in line with those of CLEOPATRA (55.3 vs 57.1 months in CLEOPATRA) but included a larger proportion of patients with HR+ mBC than CLEOPATRA (65.4% vs 47.0% in CLEOPATRA), which reflects the evolving patient mix and care in the US since CLEOPATRA.[1,6]
- Median rwOS was numerically longer for patients with HR+ or de novo mBC, which is consistent with findings from previously published studies.[7,8]

Plain Language Summary

Why did we perform this research?

- In some patients with breast cancer that has spread (known as metastatic breast cancer, or mBC), the cancer expresses excess amounts of the human epidermal growth factor receptor 2 protein and is known as HER2+ mBC.
- For these patients, the first treatment is usually a combination of the drugs trastuzumab, pertuzumab, and taxane.
- Recent clinical studies suggest other types of treatments that target HER2 may be more effective for these patients. To determine the best treatment choices, it is important to know how patients are currently treated, their outcomes with current treatments, and factors contributing to treatment outcomes.

How did we perform this research?

- We analyzed an electronic database of health records for treatments and outcomes for patients in the United States with HER2+ mBC who received trastuzumab and pertuzumab from January 2012 to September 2024.

What were the findings and implications of this research?

- These results characterized current treatment patterns for patients with HER2+ mBC after receiving trastuzumab and pertuzumab, providing insight into how treatments are sequenced for patients in real-world settings.
- These results showed that survival outcomes for this population in a real-world setting were similar to outcomes seen previously in clinical trials, helping to inform how new treatment options can best be incorporated into their care.

Where can I access more information?

- Please reach out to Dr. Arielle Heeke at Arielle.heeke@advocatehealth.org.

Please scan this quick response (QR) code with your smartphone camera or app to obtain a copy of these materials. Alternatively, please click on the link below.

https://bit.ly/DSESMO2025

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Corresponding author email address: Arielle.heeke@advocatehealth.org
Presenting author email address: William.Jacot@icm.unicancer.fr

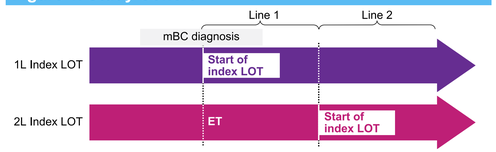
Introduction

- Since the Phase 3 CLEOPATRA trial (NCT00567190) and subsequent FDA approval in 2012 of taxane + HP (THP), this regimen has been the standard of care 1L treatment for HER2+ mBC.[1–3]
  - However, taxanes are not suitable for all patients for a variety of reasons including toxicity, prior taxane exposure, and patient preference.
- A 2025 interim analysis of the Phase 3 DESTINY-Breast09 trial demonstrated that the HER2-directed antibody drug conjugate trastuzumab-deruxtecan in combination with pertuzumab was associated with significantly improved progression-free survival compared with THP.[4]
- Real-world evidence can refine the role of 1L HP in HER2+ mBC by:
  - Providing data on current treatment patterns and outcomes in this population in the US; and
  - Contextualizing the DESTINY-Breast09 trial results to provide insights into survival and treatment sequencing to guide alternative 1L strategies for this population.

Methods

- This retrospective, observational study used the US-based, electronic health record (EHR)-derived deidentified Flatiron Health Research Database.[5]
- Patients with HER2+ mBC were treated at a contributing site from 1 January 2012 to 30 September 2024.
- Eligible patients initiated an HP-based regimen (index LOT), without prior chemotherapy or HER2-targeted therapy in the metastatic setting, either as 1L therapy or as 2L following one prior line of endocrine therapy (ET) and met additional inclusion and exclusion criteria (**Figure 1**).
- Real-world overall survival (rwOS): time from start of index LOT to death. Patients without death were censored at date of last confirmed activity in the database.
- Real-world time to treatment discontinuation or death (rwTTD/D): time from start of index LOT to treatment discontinuation date or death, whichever occurred first. A patient with no subsequent LOT was recorded as having a discontinuation event or was censored at treatment discontinuation date if confirmed structured activity was or was not observed, respectively, ≥120 days after treatment end date.
- Real-world time to next treatment or death (rwTTNT/D): time from start of index LOT to initiation of next LOT or death, whichever occurred first. Patients without subsequent LOT or death were censored at date of last confirmed activity in the database.
- All analyses were descriptive in nature. Time-to-event analyses were performed for rwOS, rwTTD/D, and rwTTNT/D using Kaplan-Meier estimation for the overall cohort and stratified by HR status (HR+ vs HR-) and metastases type (de novo vs recurrent mBC).

Figure 1. Study Cohort



Additional inclusion criteria:
- HER2+ record at any time prior to or on the start of index LOT or up to 30 days after
- Start of index LOT ≥90 days prior to 30 September 2024 (date of data cutoff)

Exclusion criteria:
- T-DXd received at any time prior to or in the index LOT

Index LOT was the first occurring LOT containing trastuzumab and pertuzumab. 1L=first-line; 2L=second-line; ET=endocrine therapy; HER2=human epidermal growth factor receptor 2; LOT=line of therapy; mBC=metastatic breast cancer; T-DXd= trastuzumab-deruxtecan.

Results and Interpretation

Table 1. Clinical Characteristics at Start of Index LOT

Characteristic	Participants, n (%) (N=2,667)
Age, median (Q1, Q3)	**59 (50, 68)**
Female	**2,644 (99.1)**
Hormone receptor status*	
HR+	**1,745 (65.4)**
HR-	**879 (33.0)**
Unknown	**43 (1.6)**
De novo stage IV**	
Yes	**1,489 (55.8)**
No	**1,046 (39.2)**
Unknown	**132 (4.9)**
ECOG performance-status score	
0	**1,055 (39.6)**
1	**745 (27.9)**
≥2	**307 (11.5)**
Unknown	**560 (21.0)**
Index LOT number†	
1	**2,387 (89.5)**
2	**280 (10.5)**
Calendar year of index LOT	
2012–2014	**339 (12.7)**
2015–2016	**498 (18.7)**
2017–2018	**520 (19.5)**
2019–2020	**482 (18.1)**
2021–2022	**524 (19.6)**
2023–2024	**304 (11.4)**

*HR+ if the closest endocrine receptor or progesterone receptor test that occurred prior to or on the the start of index LOT was positive. HR- only if both tests were negative. **Assessed at mBC diagnosis. †Index LOT is the first occurring LOT containing trastuzumab and pertuzumab. ECOG=Eastern Cooperative Oncology Group; LOT=line of therapy; Q=quartile.

Patient Characteristics and Treatment Patterns:

- This study included 2,667 patients; patient characteristics and are presented in **Table 1**.
- The proportion of patients with de novo mBC initiating index LOT increased from 47.2% in 2012–2014 to 69.1% in 2023–2024 and was 55.8% over the entire study period.
- HP-based index LOT was THP for 2,156 (80.8%) patients and a combination of HP, ET, and chemotherapy (taxane, non-taxane, or both) for 905 (33.9%) patients.
- Duration of index LOT was ≥24 months for 719 (27.0%) patients and treatment sequencing after index LOT is described in **Figure 2**.

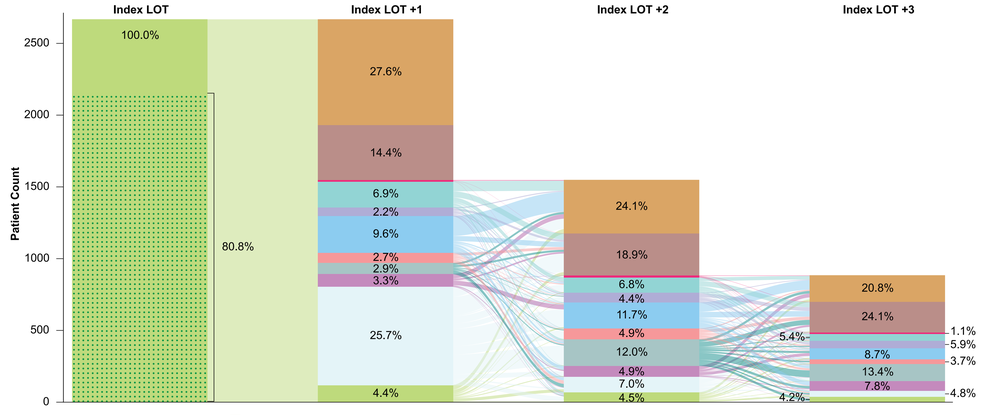
Clinical Outcomes:

- Median follow-up time by reverse Kaplan-Meier method for the overall cohort was 54.5 months (95% confidence interval [CI]: 51.7–57.3).
- For the overall, de novo mBC, and recurrent mBC cohorts, the 2-year event-free survival probabilities (95% CI) for rwTTD/D were 36.3 (34.4–38.3), 39.6 (36.9–42.3), and 31.6 (28.7–34.6), respectively, and for rwTTNT/D were 39.3 (37.4–41.3), 43.0 (40.3–45.7), and 34.3 (31.3–37.3), respectively.
- Clinical outcomes by cohort and overall are presented in **Table 2** and **Figure 3**.

Strengths and Limitations:

- This study provides a needed analysis of real-world treatment patterns and outcomes for a large cohort of US patients with HER2+ mBC who received 1L standard of care using data spanning 12 years from a robust EHR database.
- Custom LOT rules were developed based on oncologist feedback to better capture treatment patterns in HER2+ mBC. However, the algorithm is based solely on treatment regimens; while it may be reasonable to assume that progression of disease will result in a change in therapy, the algorithm does not consider progression information for the assignment of line numbers.
- The use of EHR and the retrospective nature of this study mean that results should be interpreted with caution as there is the potential for misclassification and selection bias
- As early breast cancer treatment patterns for the 39.2% of patients in this cohort with recurrent mBC were not captured, their impact on subsequent treatment patterns and outcomes could not be evaluated.

Figure 2. Treatment Patterns Before and After Index LOT in the Overall Cohort



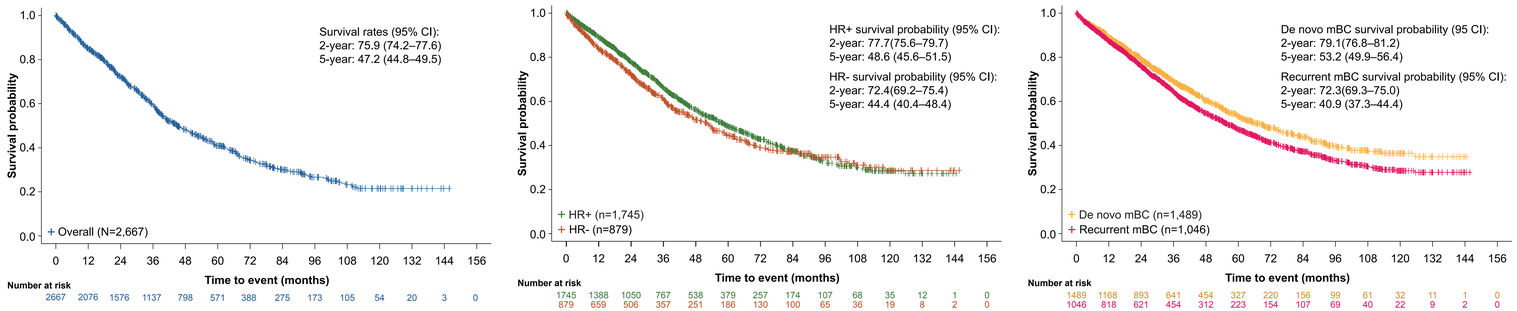
Sankey diagram where percentage represents the proportion of patients who received that treatment. The denominator for each regimen includes the number of people who received the previous line, including death and censored events. Percentage shown only for treatments received by ≥1% of patients. 280 patients (10.5%) had a pre-index endocrine therapy line (not shown) as permitted by the study protocol. ADC=antibody drug conjugate; chemo=chemotherapy; ET=endocrine therapy; HER2=human epidermal growth factor receptor 2; LOT=line of therapy; mAB=monoclonal antibody; T-DM1=ado-trastuzumab emtansine; TKI=targeted tyrosine kinase inhibitor.

Table 2. Clinical Outcomes

Cohort	Median TTE, months (95% CI)		
	rwOS	rwTTD/D	rwTTNT/D
Overall (N=2,667)	**55.3 (52.1–59.3)**	**15.4 (14.5–16.3)**	**17.1 (15.9–18.2)**
By HR status			
HR+ (n=1,745)	**58.0 (52.9–63.5)**	**16.5 (15.2–17.9)**	**17.5 (16.2–18.8)**
HR- (n=879)	**52.3 (45.1–58.1)**	**13.8 (12.5–15.2)**	**15.9 (14.5–18.2)**
By metastatic status			
De novo (n=1,489)	**66.5 (59.7–75.6)**	**17.2 (15.9–18.7)**	**18.9 (17.8–21.2)**
Recurrent (n=1,046)	**45.0 (40.4–50.2)**	**12.7 (11.8–14.1)**	**14.3 (12.9–16.0)**

CI=confidence interval; HR=hormone receptor; rwOS=real-world overall survival; rwTTD/D=real-world time to discontinuation or death; rwTTNT/D=real-world time to next treatment or death; TTE=time to event.

Figure 3. Real-World Overall Survival



Kaplan-Meier curves showing rwOS outcomes for the (A) overall cohort, (B) cohorts stratified by HR status, and (C) cohorts stratified by metastatic status. CI=confidence interval; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; rwOS=real-world overall survival; rwTTD/D=real-world time to treatment discontinuation or death.

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