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Long-term outcomes of first-line (1L), guideline-recommended treatment versus alternative regimens in HER2+ metastatic breast cancer (mBC): a retrospective observational study of US electronic health records

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Objective

- To assess the real-world long-term outcomes of US guideline-recommended treatment or alternative treatments in the 1L setting for patients with human epidermal growth factor receptor 2–positive (HER2+) mBC

Conclusions

- Patients with HER2+ mBC who received US guideline-recommended 1L standard of care (SOC) had more durable treatment outcomes than those who received other 1L regimens
- Differences in disease characteristics at 1L treatment initiation (eg hormone receptor [HR] status, recurrent versus de-novo mBC, and site of metastasis) may have influenced treatment regimen choice and impacted long-term treatment outcomes

Plain language summary

Why did we perform this research?

Around one in five breast cancers (BC) have increased levels of a protein called human epidermal growth factor receptor 2 (HER2), which causes the cancer cells to grow and eventually spread from the breast (HER2-positive [HER2+] metastatic BC [mBC]).[1,2]

A variety of treatments are available to patients with HER2+ mBC. The first treatment a patient is given is known as the first-line treatment (1L), and US guidelines recommend a combination of taxane, trastuzumab, and pertuzumab (THP) followed by maintenance therapy as the 1L treatment for patients with HER2+ mBC.[3] We performed this study to compare the long-term treatment benefits experienced by patients with HER2+ mBC who received US guideline-recommended 1L treatment or alternative 1L treatments.

How did we perform this research?

We used a database of electronic medical records to gather information about patients with HER2+ mBC, the 1L treatments they received, how long they received their 1L and subsequent treatments for, and how long it took until their cancer progressed (grew, got worse, or spread), or they died. We focused on patients diagnosed with HER2+ mBC who received their 1L treatment between 2015 and 2024.

What were the findings of this research?

We saw that the patient group who received the US guideline-recommended 1L treatment remained on 1L treatment and subsequent treatments for longer before their disease progressed, or they died. We also saw that these patients had cancers with different characteristics compared with patients who received other treatments.

What are the implications of this research?

This study found that patients with HER2+ mBC who received the US guideline-recommended 1L treatment did better than those who received other 1L treatments. Some differences in tumor characteristics may have affected which treatments were chosen and/or how well they worked. Overall, these results highlight the importance of doctors using the guideline-recommended treatment as early as possible to maximize long-term benefit.

Where can I access more information?

Information about the National Comprehensive Cancer Network (NCCN) Guidelines can be found here: https://www.nccn.org

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Poster

Supplementary material

Please scan this quick response (QR) code with your smartphone camera or app to obtain a copy of the virtual poster or the supplementary material. Alternatively, please visit: https://bit.ly/3JJfm6y

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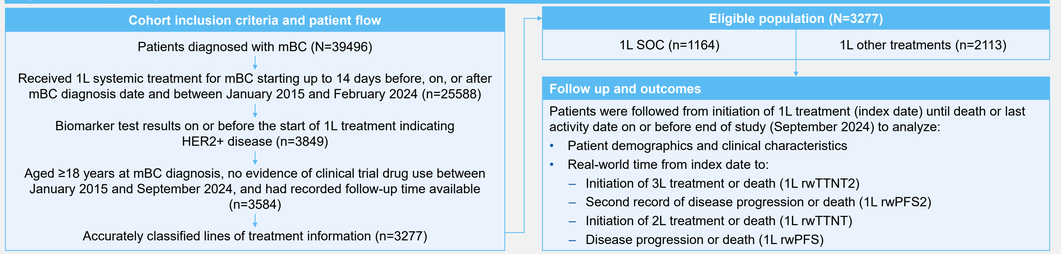
Introduction

- After the results of the CLEOPATRA study, taxane, trastuzumab, and pertuzumab (THP) followed by maintenance based on HER2-targeted therapy became the SOC for 1L treatment for patients with HER2+ mBC according to US guideline recommendations[1,2]
- However, in a real-world observational cohort study, less than half of patients with HER2+ mBC received US guideline-recommended 1L treatment[3]
- There is limited real-world evidence of long-term treatment outcomes for patients receiving US guideline-recommended 1L SOC or other regimens for HER2+ mBC

Methods

- This was a retrospective observational study in patients with HER2+ mBC who received 1L treatment post mBC diagnosis **(Figure 1)**
- De-identified data were obtained from the US nationwide Flatiron Health electronic health record-derived database, comprising longitudinal patient-level data originating from more than 280 US cancer clinics (~800 sites of care; primarily community oncology settings), and curated via technology-enabled abstraction[4,5]
- US guideline-recommended 1L SOC was defined as THP followed by trastuzumab/pertuzumab maintenance after response, with concurrent endocrine therapy (ET) in HR-positive (HR+) disease

Figure 1. Study design



1L, first-line; 2L, second-line; 3L, third-line; HER2+, human epidermal growth factor receptor 2–positive; mBC, metastatic breast cancer; SOC, standard of care

Results

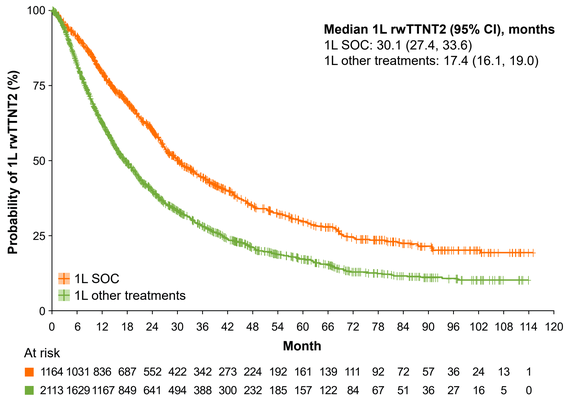
- A total of 3277 patients with HER2+ mBC were eligible for the study. Patient demographics and clinical characteristics can be found in **Table 1**
- Non-guideline-recommended 1L regimens received were HER2-targeted combination therapy (37.0%), ET alone (32.5%), HER2-targeted monotherapy (17.1%), chemotherapy alone (6.5%), and other (7.0%). Further details can be found in **Supplementary Table 1**

Table 1. Patient demographics and clinical characteristics

	1L SOC (n=1164)	1L other treatments (n=2113)
Mean age at index date, years (SD)	58.7 (12.4)	61.4 (14.1)
Practice type, n (%)		
Academic	249 (21.4)	507 (24.0)
Community	884 (75.9)	1572 (74.4)
Academic/community	31 (2.7)	34 (1.6)
Stage at initial BC diagnosis, n (%)		
I–III (recurrent at index date)	401 (34.5)	1209 (57.2)
IV (*de novo*)	714 (61.3)	677 (32.0)
Unknown	49 (4.2)	227 (10.7)
ECOG performance status,* n (%)		
0–1	688 (59.1)	968 (45.8)
2	109 (9.4)	172 (8.1)
3–4	18 (1.5)	63 (3.0)
Unknown	349 (30.0)	910 (43.1)
HR status, n (%)		
HR+	711 (61.1)	1582 (74.9)
HR−	433 (37.2)	512 (24.2)
Unknown	20 (1.7)	19 (0.9)
Number of metastatic sites, n (%)		
1	460 (39.5)	727 (34.4)
2–3	484 (41.6)	651 (30.8)
≥4	153 (13.1)	158 (7.5)
Missing	67 (5.8)	577 (27.3)
Sites of metastasis, n (%)		
Bone	664 (57.0)	868 (41.1)
Brain	88 (7.6)	235 (11.1)
Liver	472 (40.5)	468 (22.1)
Lung	386 (33.2)	524 (24.8)
Median follow-up time, months (95% CI)	54.3 (50.0, 58.9)	52.0 (48.5, 54.7)
Follow-up outcomes, n (%)		
Received 3L treatment	383 (32.9)	784 (37.1)
Died	308 (26.5)	703 (33.3)
Censored	473 (40.6)	626 (29.6)

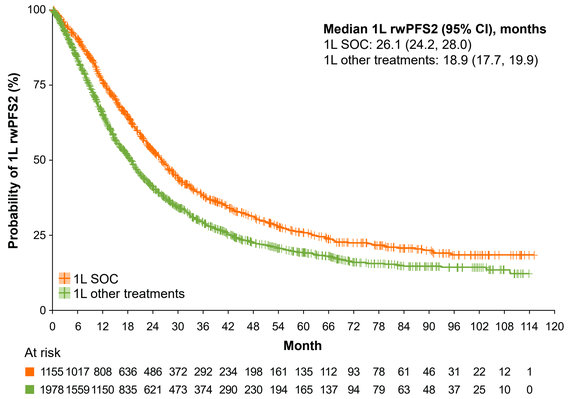
*≤60 days before index date
1L, first-line; 3L, third-line; BC, breast cancer; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; HR, hormone receptor; SD, standard deviation; SOC, standard of care

Figure 2. Median 1L rwTTNT2 was longer for patients treated with 1L SOC compared with those who received 1L other treatments



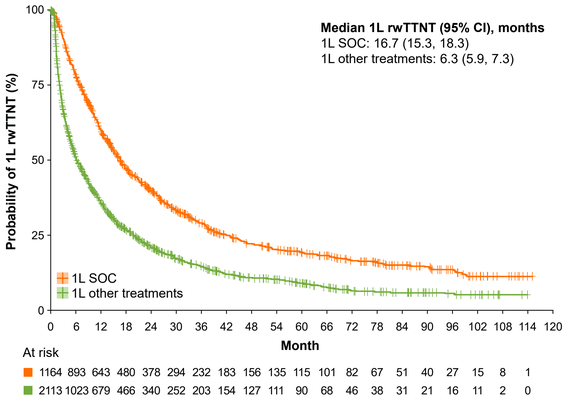
1L, first-line; CI, confidence interval; rwTTNT2, real-world time to next treatment 2; SOC, standard of care

Figure 3. Median 1L rwPFS2 was also prolonged in patients treated with 1L SOC compared with patients who received 1L other treatments



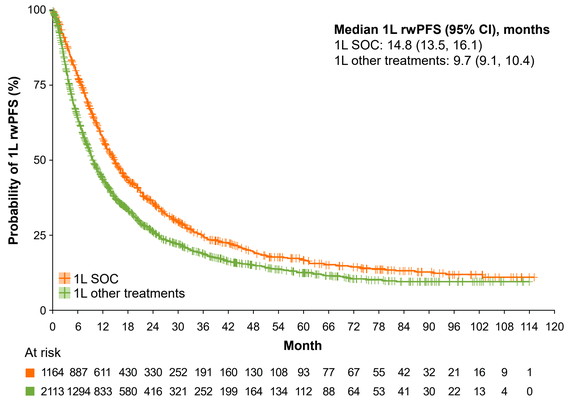
1L, first-line; CI, confidence interval; rwPFS2, real-world progression-free survival 2; SOC, standard of care

Figure 4. Median 1L rwTTNT was more than 10 months longer for patients treated with 1L SOC compared with patients who received 1L other treatments



1L, first-line; CI, confidence interval; rwTTNT, real-world time to next treatment; SOC, standard of care

Figure 5. Median 1L rwPFS was prolonged in patients treated with 1L SOC compared with patients who received 1L other treatments



1L, first-line; CI, confidence interval; rwPFS, real-world progression-free survival; SOC, standard of care

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Disclosures

Maki Inoue-Choi is an employee of AstraZeneca.

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1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer V.4.2025. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed August 19, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org
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