Poster P1-11-19

A real-world evidence study of treatment patterns in patients with HER2-positive metastatic breast cancer who have received at least 2-lines of therapy

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Objectives

- The study objectives were to:
  - Describe the demographic and clinical characteristics of patients with HER2+ mBC who received ≥2 lines of therapy (LoTs) in the metastatic setting.
  - Describe their treatment patterns and 2L-associated outcomes.

Conclusions

- The study shows the treatment trajectory of HER2+ mBC patients in real-world US clinical practice is variable
- Clinical outcomes on current SoC highlight the need for effective treatment being used earlier where a greater proportion of the eligible population can benefit.
  - The vast majority of HER2+ mBC patients discontinued 2L (88%, median TTD 7.2 months), with disease progression the most common reason for discontinuation.
  - Of the patients who discontinued 2L therapy 20% died during or just after 2L therapy highlighting patient attrition seen in the metastatic setting.
  - Approximately two-thirds of the 2L patients received a subsequent therapy.

Plain language summary

Why did we perform this research?
- In some people with breast cancer, the first treatment they are given does not work or stops working and they need a different treatment (a second-line treatment). We did this study to understand how these people are treated and how well the treatments work. Specifically, we looked at people with cancer that had higher than normal levels of a protein (biomarker) called HER2 and that had spread to other parts of the body (HER2-positive metastatic breast cancer).

How did we perform this research?
- We used an existing database to get information about the treatments and outcomes of people in the US with HER2-positive metastatic breast cancer. We focused on people who started a second-line treatment between January 2014 and February 2021.

What were the findings of this research?
- We saw that a variety of treatments were used. People discontinued their second-line treatment for a variety of reasons, progression (the cancer continued to grow or spread) being the most common. Most people then had to receive a third-line treatment.

What are the implications?
- This study highlights the need for better second-line treatment options for people with HER2-positive metastatic breast cancer.

Where can I access more information?
- Please reach out to Della Varghese at della.varghese@astrazeneca.com.

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Introduction

- Until recently, standard-of-care (SoC) treatment for HER2-positive metastatic breast cancer (HER2+ mBC) patients consisted of trastuzumab+/-pertuzumab plus chemotherapy in first line (1L) and ado-trastuzumab emtansine (T-DM1) in second line (2L).[1]
- In 2022, trastuzumab deruxtecan (T-DXd) was approved for patients with at least 1 prior therapy following DESTINY-Breast03 trial results.[2]
- Contemporary real-world data on treatment patterns and outcomes of HER2+ mBC patients following 1L therapy is limited; such data will help understand if eligible patients receive optimal and timely targeted therapies.

Methods

Study design: Retrospective cohort study of patients receiving cancer care in US community health systems.

Data source: Syapse Learning Health Network (LHN) is a longitudinal database of US patients with cancer that integrates data from clinical systems, reference labs, and external sources. The LHN consists of 460+ hospitals, 1,350+ oncologists and 216,000+ newly diagnosed patients.

Sample selection: Adult patients with documented HER2+ mBC who received ≥2 LoTs in the metastatic setting; who initiated 2L (index date) between January 2014-February 2021, inclusive; with ≥2 clinical contacts noted in the electronic health record (EHR); with ≥1 clinical contact after index date.

Clinical outcomes
- Time to treatment discontinuation (TTD): Time from index to 2L discontinuation/death; patients without the endpoint were censored at first of last contact or data cut-off.
- Time to next treatment (TTNT): Time from index to 3L initiation/death; patients without the endpoint were censored at first of last contact or data cut-off.
- Real-world progression-free survival (rwPFS): Time from index to clinician-confirmed progression/ death; patients without the endpoint were censored at first of 3L initiation, last contact or data cut-off.

Analyses
- Descriptive statistics described patient characteristics and treatment patterns.
- Distribution of time-to-event outcomes (in months) were estimated using the Kaplan-Meier estimator; patients were followed from index until the first of: date of last contact in the EHR, death or data cut-off (February 2022), allowing for a potential follow-up of 12 or more months.
- Additionally, clinical outcomes were also evaluated among a subgroup of patients who received a trastuzumab-based (T-based) 2L, a common treatment choice in 2L beyond T-DM1.

Results

Population characteristics
- Among ~ 15,000 breast cancer patients with abstracted data, 312 HER2+ mBC patients received ≥2 LoTs.
- Median follow-up was 22 months from index (IQR, 13-37).
- The demographic and clinical characteristics have been described in **Table 1**.
  - The African American population was typically diagnosed at a younger age (median age 50 [IQR, 44-61] vs. 54 [IQR, 46-62] years), with more advanced disease (stage IV disease at initial diagnosis; 69% vs 62%) vs. Whites.

Table 1. Demographic & clinical characteristics of included patients

	All (n=312)	T-based 2L (n=116)
Median age (yrs) at index, (IQR)	59 (50, 66)	60 (50, 67)
Female, n (%)	308 (99)	116 (100)
Race, n (%)		
White	216 (69)	83 (72)
Black or African American	64 (21)	24 (21)
Other	8 (3)	2 (2)
Unknown	24 (8)	7 (6)
Non-Hispanic/Non-Latino,[1] n (%)	268 (86)	102 (88)
Region of residence, n (%)		
Midwest	277 (89)	108 (93)
South/East	35 (11)	8 (7)
Metastatic diagnosis,[1] n (%)		
De novo	193 (62)	72 (62)
Recurrent	114 (37)	42 (36)
Site(s) of distant metastasis at index,[2] n (%)		
Bone	180 (58)	62 (53)
Distant lymph node	131 (42)	46 (40)
Lung	120 (38)	41 (35)
Liver	120 (38)	39 (34)
Brain	83 (27)	30 (26)
Other	57 (18)	17 (15)
Hormone receptor positive at index,[1] n (%)	169 (54)	65 (56)
Charlson Comorbidity Index,[3] n (%)		
0	53 (17)	23 (20)
1	7 (2)	2 (2)
2+	156 (50)	51 (44)
Unknown	96 (31)	40 (34)

[1] The denominator includes "Unknown" category. [2] Site(s) of distant metastasis assessed from mBC diagnosis up to 30 days after index. Multiple metastases at the same organ site are counted once. "Site(s) of distant metastasis" includes all that apply. The "Other" category may capture more than one site. [3] Calculated based on conditions present in the year prior to mBC diagnosis.

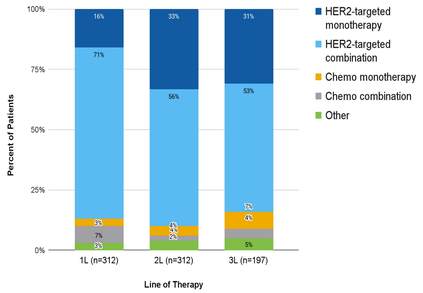
Treatment characteristics
- More than half of the 312 patients (54%) had initiated their 2L metastatic therapy from 2018 and onwards; 37% received only 2 LoTs, 28% received 3 LoTs and 35% received ≥4 LoTs.
- Majority of the 312 patients had received T-based regimen in 1L (78%).
- In 2L, 89% of the 312 patients received a HER2-targeted treatment, monotherapy or combination (**Figure 1**).
  - Most frequent 2L regimens included T-DM1 (29%), trastuzumab/pertuzumab/taxane (10%) and T-DM1/trastuzumab (8%).
- Subsequently, 63% of the 312 patients received 3L therapy (**Figure 1**).
  - Among these 197 patients, the most frequent 3L regimens included T-DM1 (19%), T-DXd (10%) and capecitabine/lapatinib (8%).

2L Discontinuation
- Around 88% of patients discontinued 2L (**Table 2**)
- The most common reason for discontinuation among those who discontinued 2L (n=274) was progression/worsening of cancer (**Table 2**).

Clinical outcomes
- Clinical outcomes for all 312 patients from the start of 2L have been presented in **Figure 2**.
- Among the 116 patients who received a T-based 2L, median TTD, TTNT and rwPFS were: 10.6 months (95% CI, 7.4-14.0), 14.9 months (95% CI, 9.9-22.0), and 13.6 months (95% CI, 8.3-20.2), respectively.

Limitations/strengths
- The study has a relatively small sample size, and the sample is mostly from the Midwest and may not be representative of all patients cared for in the US community health setting.
- There is some latency in mortality data reporting; however, mortality data are updated every two weeks.
- Off-label combinations (e.g., T-DM1/trastuzumab) are observed, therefore the results should be interpreted with caution.
- The study investigated contemporary treatment patterns and outcomes in routine clinical care using comprehensive, high-quality data curated by trained certified tumor registrars.

Figure 1. Treatment distribution across LoTs*



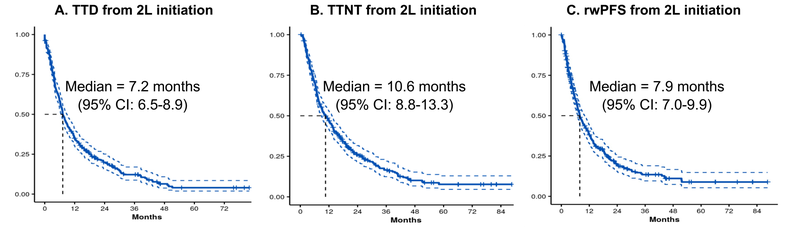
[1]HER2-targeted: Regimens containing trastuzumab, T-DM1, T-DXd, lapatinib, margetuximab, neratinib, pertuzumab, tucatinib, or pyrotinib; Chemotherapy: Regimens containing chemotherapeutic agents that do not include HER2-targeted therapies; Other: Regimens that do not include a HER2-targeted therapy or chemotherapy. Regimens were classified as monotherapy or combination, independent of inclusion of endocrine therapies. Endocrine therapy introduction or discontinuation alone did not determine the beginning or end of a LoT.

Table 2. 2L Treatment attrition

	All (n=312)	T-based 2L (n=116)
Ongoing 2L at end of follow-up, n (%)	38 (12)	21 (18)
Discontinued 2L, n (%)	274 (88)	95 (82)
Initiated 3L*	197 (72)	75 (79)
Ongoing 2L at the time of death*	7 (2)	1 (1)
Died after 2L, prior to 3L start*	49 (18)	11 (12)
No further treatment during follow-up*	21 (8)	8 (8)
Most common reasons for discontinuation, n (%)		
Progression/worsening of cancer*	128 (47)	39 (34)
Intolerance/toxicity in absence of progression*	47 (17)	22 (19)
End of planned therapy*	25 (9)	19 (16)

*Distribution is based on patients who discontinued 2L.

Figure 2. 2L Outcomes among patients with HER2+ mBC with ≥2 LoTs



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1. NCCN Clinical Practice Guidelines in Oncology. *Breast Cancer*. V4.2022.
2. Cortés J, et al. Trastuzumab deruxtecan versus trastuzumab emtansine for breast cancer. *N Engl J Med*. 2022;386(12):1143-1154.

Disclosure
Della Varghese is an employee of AstraZeneca, and has ownership interest in stocks/stock options.

Abbreviations
1L, first line; 2L, second line; HER2+ mBC, HER2-positive metastatic breast cancer; LoTs, lines of therapy; SoC, standard of care; T-based, trastuzumab-based; T-DM1, ado-trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TTD, time to treatment discontinuation; TTNT, time to next treatment; rwPFS, real-world progression-free survival

Poster

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