Real-world treatment patterns and healthcare resource utilization among HER2+ metastatic breast cancer patients with and without brain metastases: a retrospective cohort study

Chiemeka Ike,[1] Naomi Schwartz,[1] Andy Surinach,[2] Yutong Liu,[2] Kendra DeBusk,[1] Thomas Walters[1]

[1]Health Economics & Outcomes Research, Seagen Inc., Bothell, WA; [2]Real World Evidence (RWE) Solutions, Genesis Research, Hoboken, NJ

Background

- The human epidermal growth factor receptor 2-positive (HER2+) subtype of breast cancer (BC) is an aggressive form of the disease associated with an increased likelihood of metastases, especially to the brain.[1-4]
- Although there are several HER2-directed therapies approved for patients with metastatic BC (MBC), outcomes remain poor among patients with brain metastases (BM).[5]
- Research into treatment patterns and healthcare resource utilization (HCRU) among HER2+ MBC patients with BM is lacking.

Objective

- To describe treatment patterns among women with HER2+ MBC with and without BM who received HER2-directed therapy, and to compare HCRU in the 6 months following MBC diagnosis in patients with and without BM.

Methods

- Retrospective cohort analysis of female patients with HER2+ MBC aged ≥18 years at MBC diagnosis, identified using the IBM Watson Health™ MarketScan commercial claims and Medicare Supplemental databases from July 2012 to December 2018.
- Patients with HER2+ MBC were identified based on ≥2 claims with ICD-9/10 codes for MBC and ≥1 claim for a HER2-directed agent (trastuzumab, lapatinib, pertuzumab, trastuzumab emtansine [T-DM1]).
- The MBC diagnosis date was defined as the index date.
- BM were identified at index and prior to the start of each LOT using ICD-9/10 codes.
- Additional eligibility requirements included continuous enrollment with medical and pharmacy benefits for ≥6 months before and ≥6 months after the index date.
- The first line (1L) of metastatic therapy was defined as the first HER2-directed therapy claim and any treatment within 30 days of the 1L start date.
- Subsequent lines of therapy (second line [2L], third line [3L]) correspond to a new HER2-directed therapy >28 days following the initiation of 1L therapy, or the initiation of any treatment following a treatment gap of ≥60 days.

Outcomes

- Treatment patterns: median duration of treatment stratified by the presence of BM prior to each LOT and proportion of individuals receiving different drug regimens for each LOT (1L, 2L, 3L).
- HCRU: inpatient admissions and associated total length of stay (LOS), emergency department (ED) visits, and claims for outpatient services (physician office visits, hospital outpatient encounters, laboratory services, infusions, injections, and radiation) in the 6 months post index, stratified by the presence of BM at index.

Analyses

- Descriptive statistics were used for demographics, clinical characteristics, and treatment patterns. Wilcoxon nonparametric tests were used to compare differences between patients with and without BM.

Results

- A total of 4,509 patients met the study criteria. Of these,103 (2.3%) patients had BM at index and a total of 590 (13.1%) patients had BM during the study period.
- The median follow-up time was similar for patients with BM (22.1 months) and without BM (23.2 months) at index.
- Baseline demographics and clinical characteristics are presented in **Table 1**.

Table 1. Patient demographics and clinical characteristics

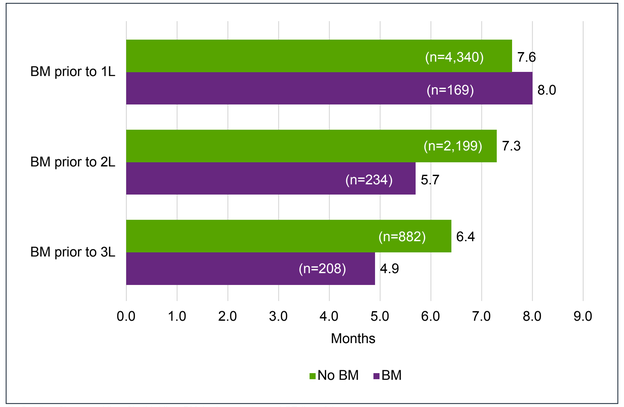
	BM at index (n=103)	No BM at index (n=4,406)
Demographics		
Age (years), mean (SD)	54.7 (10.5)	53.7 (11.1)
Baseline enrollment (months), median (IQR)	19.8 (9.5–36.0)	25.1 (13.9–42.0)
Follow-up enrollment (months), median (IQR)	22.1 (11.5–29.1)	23.2 (13.4–37.7)
Clinical characteristics		
Metastatic sites at index, n (%)		
Lymph nodes	26 (25.2)	3,325 (75.5)
Bone	36 (35.0)	791 (18.0)
Liver	24 (23.3)	484 (11.0)
Breast	6 (5.8)	239 (5.4)
Number of nonbreast metastatic sites, n (%)		
<3	64 (62.1)	4,102 (93.1)
≥3	39 (37.9)	304 (6.9)

BM, brain metastases; IQR, interquartile range.

Treatment patterns

- **Figure 1** shows the median duration of treatment (in months) stratified by the presence of BM prior to each LOT.
- Median 1L duration was similar for patients with and without BM (8.0 vs 7.6 months), whereas 2L and 3L durations were shorter for patients with BM compared with those without BM (5.7 vs 7.3 months and 4.9 vs 6.4 months, respectively).

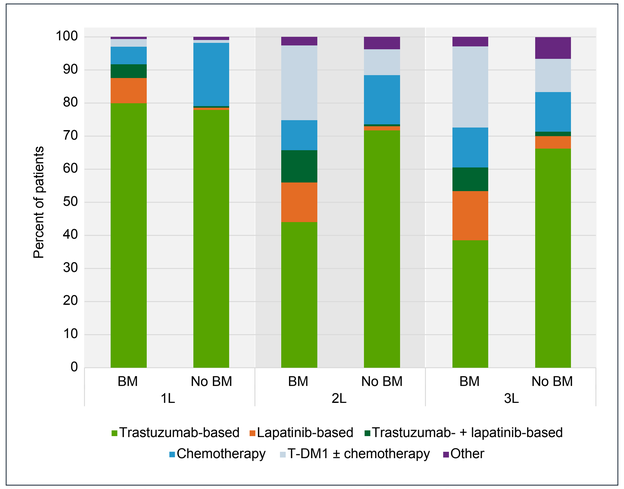
Figure 1. Median LOT treatment duration, by presence of BM prior to each LOT



1L, first line; 2L, second line; 3L, third line; BM, brain metastases; LOT, line of therapy.

- The most commonly used therapies were trastuzumab-based regimens across all LOTs: 1L (84.0% BM vs 78.3% no BM); 2L (53.8% BM vs 72.3% no BM); and 3L (45.7% BM vs 67.7% no BM) (**Figure 2**).
- T-DM1 use was lowest in 1L (2.4% BM vs 0.9% no BM).
- T-DM1 use was 2 times higher among patients with BM compared with patients without BM in both 2L (22.6% vs 7.9%) and 3L (24.5% vs 10.1%).
- Patients with BM had a higher frequency of lapatinib use compared with patients without BM (1L, 11.8% vs 1.2%; 2L, 21.8% vs 1.9%; 3L, 22.1% vs 5.1%).

Figure 2. Treatment patterns among patients with HER2+ MBC, by presence of BM at index



Other category includes treatments coded as "other" plus any regimens used by <1% of patients in each LOT.
1L, first line; 2L, second line; 3L, third line; BM, brain metastases; HER2+, human epidermal growth factor receptor 2-positive; LOT, line of therapy; MBC, metastatic breast cancer; T-DM1, trastuzumab emtansine.

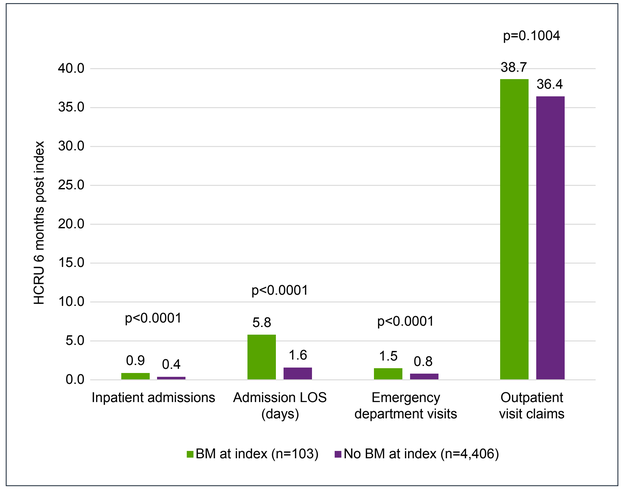
Healthcare resource utilization

- Compared with patients without BM at index, those with BM had significantly more inpatient admissions and significantly longer associated LOS (**Figure 3**).
- The number of ED visits was significantly higher among patients with BM at index compared with those without.

Limitations

- MarketScan only includes individuals with employer-based insurance and our study was limited to women who received HER2-directed therapy. Thus, these results may not be generalizable to all HER2+ MBC patients.
- The algorithm to define LOTs could not distinguish if discontinuation of a HER2-directed agent in a combination regimen constituted a new LOT or a modification within the current LOT.

Figure 3. Mean HCRU in the 6 months post index, by presence of BM at index



BM, brain metastases; HCRU, healthcare resource utilization; LOS, length of stay.

Discussion

- Among patients with HER2+ MBC who received HER2-directed therapy, use of trastuzumab-based regimens was substantially higher among patients without BM at index in 2L and 3L treatment.
- Lapatinib was used more frequently among patients with BM vs patients without BM at index in all LOTs.
- HCRU in the 6-month post-index period was significantly higher among patients with BM. This may result in increased costs to the healthcare system.
- These findings highlight the need for more effective systemic therapies that improve outcomes and reduce disease and healthcare system burden for HER2+ MBC patients with BM.

References

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Corresponding Author: Chiemeka Ike (cike@seagen.com).

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