Treatment Patterns, Clinical Outcomes, and Healthcare Resource Utilization (HRU) Among Patients With Hormone Receptor Positive (HR+) HER2-low or IHC 0 Metastatic Breast Cancer (mBC) – Data From an Integrated Delivery Network (IDN)

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Objective

- To assess treatment patterns, outcomes, and Health care Resource Use (HRU) for patients with HR+/HER2-low or HR+/IHC 0 mBC treated at an IDN in the US.

Conclusions

- Treatments for HR+/HER2-low mBC varied, with many patients receiving multiple LOT shortly after 1L and experiencing diminishing time on treatment. Treatment patterns were similar but clinical outcomes shorter in HR+/IHC 0 vs HER2-low disease.
- These results highlight a need for effective HER2 targeted therapies that extend duration of clinical benefit earlier in the disease management pathway.
- The role of HER2 targeted ADCs in IHC 0 (specifically HER2 null) needs to be further investigated.

Plain language summary

Why did we perform this research?
Most breast cancers are HER2-low or IHC 0,[1] and HER2-low patients appear to have slightly improved clinical outcomes compared with IHC 0 patients.[2] In the US, an estimated 40% to 70% of providers are affiliated with Integrated Delivery Networks (IDNs) and provider networks (PNs), and 30% to 70% of facilities are owned by them.[3] We conducted this study to understand how patients with HER2-low or IHC 0 mBC are treated in an IDN.

How did we perform this research?
This retrospective cohort study was conducted using the Mayo Clinic IDN deidentified database (Jan 2017–Jun 2022). We assessed real-world patient characteristics, treatment patterns, TTD, TTNT, and HRU for US patients with a diagnosis of HER2-low or IHC 0 mBC who completed ≥1 systemic treatment in the metastatic setting between Jan 2018 and Jun 2021.

What were the findings of this research and what are the implications?
To our knowledge, this is the first study to examine differences in treatments and outcomes among HR+/HER2-low and IHC 0 mBC patients from an IDN perspective. The results provide insights on variability in treatment approaches for patients treated at IDN–Mayo Clinic and highlight the need for better alternative treatment for improving patient outcomes.

Refere:ces: 1. Tarantino P, et al. Ann Oncol. 2023;34(8):645-659. 2. Molinelli C, et al. ESMO Open. 2023;8(4):101592. 3. Martin R. https://www.iqvia.com/-/media/iqvia/pdfs/us/us-location-site/market-access/integrated-delivery-networks.pdf

Abbreviations

1L, first line; 2L, second line; 3L, third line; ADC, antibody drug conjugate; BC, breast cancer; CDK4/6, cyclin-dependent kinase 4/6; ED, emergency department; EHR, electronic health record; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; HRU, healthcare resource utilization; HT, hormone therapy; IDN, integrated delivery network; IHC, immunohistochemistry; IO, immunotherapy; ISH, in situ hybridization; LOT, line of therapy; mBC, metastatic breast cancer; NCCN, National Comprehensive Cancer Network; OTT, other targeted treatment; rwTTD, real-world time to treatment discontinuation; rwTTNT, real-world time to next treatment; tx, treatment; US, United States.

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Introduction

- Historically, BC patients with an IHC score of 0, 1+, and 2+ without ISH amplification would be classified as having HER2-negative disease.[1, 4]
- However, about 50% of BC patients in the U.S constitute a distinct group of HER2-low patients, identified as having an IHC score of 1+ or a score of 2+ with a negative ISH test, and 65% to 85% of these HER2-low patients are HR+.[5-7]
- In addition, recent findings suggest that about 60% of IHC 0 patients could be re-classified as HER2 ultra-low (<0% but ≤10% staining).[8]
- With the advent of novel HER2-targeted ADCs such as trastuzumab deruxtecan for the treatment of HER2-low and ultra-low mBC,[9-10] it is important to understand current treatment patterns and outcomes in different healthcare settings.
- However, limited treatment and outcomes data exist for patients with HER2-low (IHC 1+ or IHC 2+ and ISH-) or IHC 0 mBC treated via an IDN.
  - An IDN provides a continuum of care as it consists of multiple providers affiliated to one parent company (e.g., acute care hospitals and associated outpatient facilities, medical groups, labs, other facilities).[3]

Methods

- We retrospectively analyzed deidentified structured and unstructured EHR data (01/2018–06/2022) from an IDN in the US.
  - The Mayo Clinic IDN covers >6 million patients across all US-based sites, including 3 main campuses in Minnesota, Arizona, and Florida, plus community clinics.
- Patients aged ≥18 years at diagnosis of HR+/HER2-low or HR+/IHC 0 mBC with ≥2 clinic visits and receipt of ≥1 LOT post mBC diagnosis were included.
- Patients receiving systemic therapy for another primary cancer, participating in a clinical trial during the observation period or with documented HER2+ status prior to initiation of 1L were excluded.
- Patient characteristics, treatment utilization, and HRU were analyzed descriptively.
- rwTTD and rwTTNT were estimated via Kaplan-Meier methods.

Results

Study Population

- Of the 1300 mBC patients who met selection criteria, 871 (67%) were HER2-low and 429 (33%) were IHC 0. Most had HR+ disease (HER2-low: n=790, 91%; IHC 0: n=352, 82%). **Table 1** provides characteristics for patients with HR+/HER2-low and HR+/IHC 0 mBC.

Table 1. Patient characteristics

	HR+/HER2-low (N=790)	HR+/IHC 0 (N=352)
Age at mBC diagnosis, mean (SD), y	61.17 (13.94)	60.48 (13.93)
Race, n (%)		
Asian	17 (2.2)	8 (2.2)
Black or African American	33 (4.2)	20 (5.7)
Native American/Pacific Islander	4 (0.5)	2 (0.6)
White	701 (88.7)	304 (86.4)
Other/Unknown	28 (3.5)	10 (2.8)
Chose not to disclose	7 (0.9)	8 (2.3)
Metastases sites, n (%)		
Adrenal gland	15 (1.9)	8 (2.3)
Bone	383 (48.5)	238 (67.6)
Digestive organs	224 (28.4)	152 (43.2)
Kidney	4 (0.5)	1 (0.3)
Nervous system	84 (10.6)	65 (18.5)
Ovary	11 (1.4)	6 (1.7)
Respiratory	163 (20.6)	106 (30.1)
Skin	45 (5.7)	22 (6.3)
Urinary organs	3 (0.4)	5 (1.4)
Other/unspecified	264 (33.4)	162 (46.0)

Treatment Utilization and Attrition by LOT

- Of the HR+/HER2-low mBC patients receiving 1L, 2L, and 3L therapy, 16%, 17%, and 13%, respectively, discontinued therapy or died (**Figure 1**). 373 patients (47%) progressed to 2L and 190 (24%) progressed to 3L therapy during the study follow-up period. Similar results were observed among HR+/IHC0 mBC patients (**Figure 1**).
- In 1L, most patients received an HT-based regimen (73% in each cohort), with chemotherapy (HR+/HER2-low: 16%, HR+/IHC0: 18%) as the next most common 1L treatment (**Figure 2**).
- Common 2L/3L therapies were HT alone (HR+/HER2-low: 33%-35%, HR+/IHC 0: 27%-28%), chemotherapy (HR+/HER2-low: 16%-19%, HR+/IHC 0: 27%-32%), CDK 4/6 inhibitor + HT (HR+/HER2-low: 16%-19%, HR+/IHC 0: 18%-23%), or OTT + HT (HR+/HER2-low: 9%-10%, HR+/IHC 0: 3%-12%) (**Figure 2**).
- The most followed treatment pathway was 3 sequences of HT-based regimen (**Figure 3**). A similar pathway was observed in the HR+/IHC 0 group.

[a]Includes some patients with HT in combination with chemotherapy. [b]Includes alpelisib, everolimus, olaparib, talazoparisb.

Figure 1. Patient Attrition by LOT

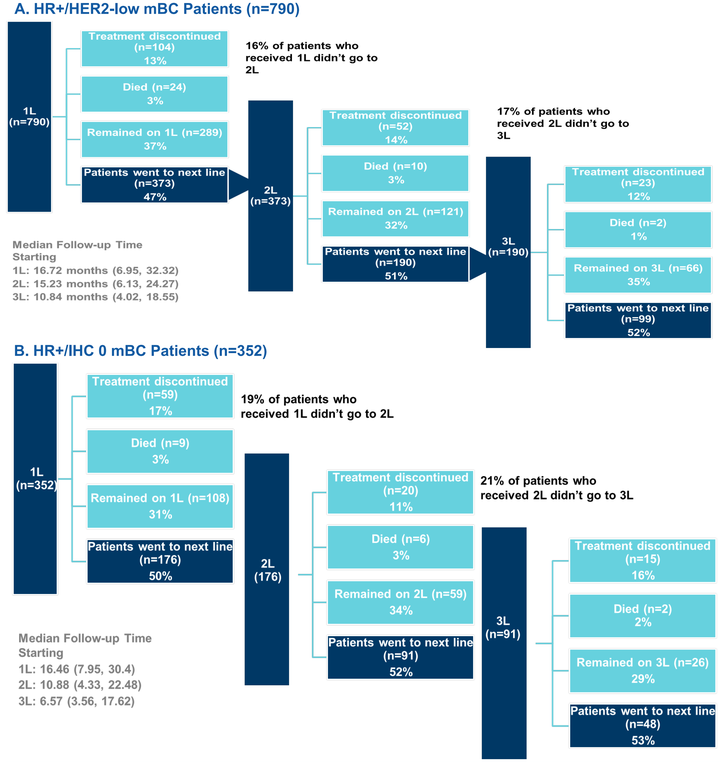


Figure 2. Treatment Utilization by LOT

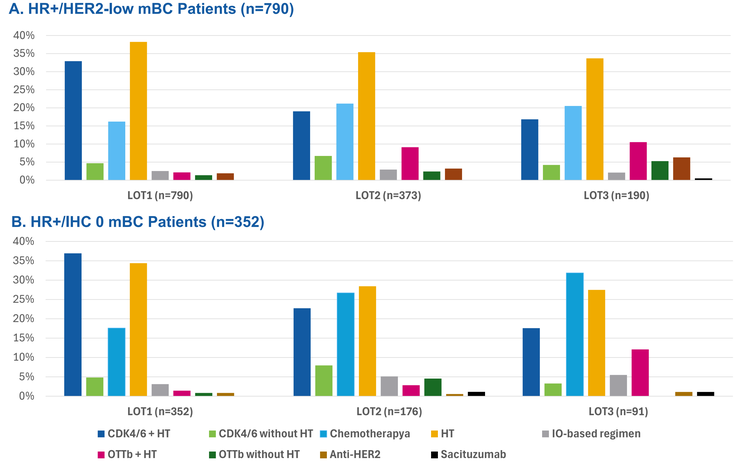
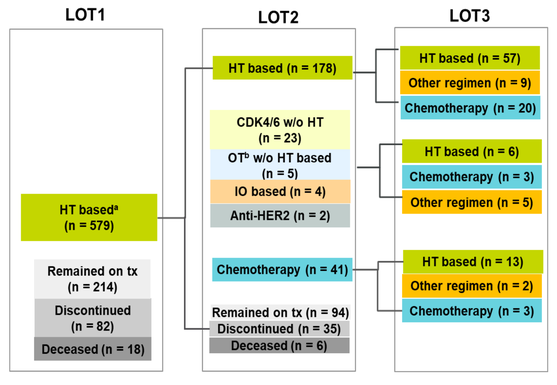


Figure 3. Treatment Pathways: HR+/HER2-low mBC with 1L HT-based Regimen



[a] HT-based regimen includes HT, CDK4/6 + HT, OTT + HT. [b] OTT includes alpelisib, everolimus, olaparib, talazoparib.

Table 2. Treatment outcomes

	HR+/HER2-low		
	LOT1 (n=790)	**LOT2 (n=373)**	**LOT3 (n=190)**
rwTTD, median (95% CI), mo	11.0 (9.23-12.63)	9.13 (6.77-11.17)	6.9 (5.5-8.47)
rwTTNT, median (95% CI), mo	15.37 (13.13-18.20)	12.33 (10.17-13.33)	8.43 (6.77-10.00)
Hospitalization, n (%)	130 (16.56)	43 (11.53)	18 (9.47)
ED visits, n (%)	129 (16.43)	67 (17.96)	24 (12.63)
	HR+/IHC 0		
	LOT1 (n=352)	**LOT2 (n=176)**	**LOT3 (n=91)**
rwTTD, median (95% CI), mo	8.67 (7.70-10.33)	7.53 (5.37-9.80)	4.07 (3.10-5.60)
rwTTNT, median (95% CI), mo	12.17 (10.00-15.23)	9.80 (7.40-14.83)	5.60 (4.03-9.30)
Hospitalization, n (%)	53 (15.27)	22 (12.50)	9 (9.89)
ED visits, n (%)	48 (13.83)	22 (12.50)	15 (16.48)

Treatment Outcomes

- Among HR+/HER2-low and HR+/IHC 0 patients, median rwTTD and rwTTNT decreased in later LOT (Table 2)
- The hospitalization rates ranged from 9-16% for HR+/HER2-low and 9-15% for HR+/IHC 0 patients (**Table 2**). The observed decreasing rates of hospitalization are likely due to loss of follow-up for many patients in later lines. Further time to event analysis for the resource use endpoints in warranted.

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