Poster P3-11-09

Incidence and Treatment Patterns of High-Risk HER2+ Early-Stage Breast Cancer (eBC) in the United States Community Oncology Setting

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Objective

- This real-world study aimed to describe the incidence of high-risk HER2+ early breast cancer (eBC) and further describe neoadjuvant, post-neoadjuvant and adjuvant treatment patterns and rates of metastases among patients with high-risk HER2+ eBC treated in the United States (U.S) community oncology setting.

Conclusions

- In this large sample of real-world patients with HER2+ eBC treated in the US community oncology setting, over one-third of patients met criteria of being at a high-risk of recurrence.
- Despite established guidelines for neoadjuvant systemic therapy for high-risk patients with HER2+ eBC, many patients did not initiate neoadjuvant treatment and had higher rates of metastatic recurrence.
- The findings reinforces the importance of neoadjuvant therapy for treating patients with high-risk HER2+ eBC and the need for more effective HER2 targeted therapy to improve health outcomes among this patient population.

Plain language summary

Why did we perform this research?
With the advent of novel HER2 targeted therapy for treatment of high-risk HER2+ eBC, it is important to understand the distribution of risk-status among patients and the current treatment landscape.

How did we perform this research?
This real-world retrospective observation cohort study was conducted among patients diagnosed with HER2+ eBC within The US Oncology Network. Data was sourced from the iKnowMed (iKM) electronic health record (EHR) system.

What were the findings of this research and what are the implications?
Among patients with HER2+ eBC, 38% were considered high-risk. Of these patients with high-risk HER2+ eBC, 37% of patients did not initiate neoadjuvant treatment despite established guidelines. Patients group with high-risk but not receiving neoadjuvant treatment had almost double the rate of metastatic recurrence than those who received neoadjuvant treatment. High-risk patients that were older, those in perimenopausal phase (vs. premenopausal) and those with positive (vs. negative) hormonal status were less likely to receive neoadjuvant treatment.

It is important to treat patients with high-risk HER2+ eBC with the most effective neoadjuvant treatment to improve outcomes of this patient population.

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Introduction

- Approximately 15-30% of breast cancer (BC) tumors display an increased expression of Human Epidermal growth factor receptor 2 (HER2), a tyrosine kinase receptor growth-promoting protein expressed on the surface of cancer cells.[1,2]
- Neoadjuvant treatment consisting of HER2-targeted therapy has become the standard of care for HER2+ eBC and is the preferred option for patients with tumors larger than 2 cm or with axillary lymph node involvement (categorized as high-risk HER2+ eBC).[3] Neoadjuvant treatments also provides an opportunity to assess response to therapy via pathologic complete response (pCR) at time of surgery and can guide choice of therapy post surgery.
- Trastuzumab deruxtecan, the novel antibody drug conjugate (ADC) is being investigated among patients with high-risk HER2+ eBC [DESTINY-Breast11] and among patients with HER2+ eBC and residual invasive disease as a post-neoadjuvant treatment [DESTINY-Breast05] [4,5]
- With the advent of new HER2 targeted therapies as potential options for treating HER2+ eBC, it is important to understand treatment patterns and clinical outcomes of patients with HER2+ eBC treated in the community oncology setting in the U.S.

Methods

- Data were sourced through structured fields in the iKnowMed (iKM) electronic health record (EHR) system, which includes 1.4 million patients treated annually.[6]
- Retrospective, observational cohort study of adult patients diagnosed with HER2+ eBC within The US Oncology Network between 01 January 2017 – 31 March 2023. Study eligible patients were followed until 30 September 2023, last patient record or date of death, whichever occurred first.
- Inclusion criteria: Patients with a diagnosis of HER2+ eBC (index date) and aged ≥21 at time of diagnosis, had at ≥2 visits within The US Oncology Network after index date, and either a) initiate neoadjuvant or adjuvant treatment during the study identification period or b) ≥1 visit within 60 days of index date and ≥1 visit 60 days after the first additional visit
- Exclusion criteria: Patients with prior diagnosis of breast cancer, patients receiving prior neoadjuvant or adjuvant treatment for breast cancer, enrolled in a clinical trial during the study observation period, receiving treatment for other documented primary cancer diagnoses following index date, and patients with inconsistent TNM staging or data discrepancies
- Incidence of high-risk HER2+ eBC was described.
  - Risk Definition: High Risk [T0-T4, N1-3,M0 or T3-T4,N0,M0], Moderate to High Risk [T2,N0,M0], Low Risk [T1a-T1c, N0,M0]
- For patients with high-risk HER2+ eBC, the baseline demographic characteristics, clinical characteristics (including risk status), treatment characteristics, and proportion of patients with distant metastases were analyzed descriptively. Multivariable logistic regression was used to assess factors associated with receipt of neoadjuvant treatment.

Results

Patient Identification

- The study included 5,487 patients with HER2+ eBC that met the study inclusion and exclusion criteria.
- There were 4,125 patients with documented TNM staging, of which 1,567 (38%) were high-risk (Figure 1).

Patient Characteristics

- High-risk patients with HER2+ eBC had a mean (SD) age of 56.6 (14.1) years, were majority White (n=967, 61.7%), with nodal involvement (n=1,413, 90.17%) and postmenopausal (n=909, 58%).

Table 1. Demographic and Clinical Characteristics

Characteristics	High-risk patients N=1,567
Age	
Mean (SD)	56.6 (14.1)
Race, n (%)	
White	967 (61.7)
African American	157 (10.0)
Asian	88 (5.6)
Other	111 (7.1)
Not documented	244 (15.6)
Menopausal status, n (%)	
Perimenopausal	23 (1.5)
Premenopausal	513 (32.7)
Postmenopausal	909 (58.0)
Not documented	122 (7.8)
ECOG (30 days prior to adjuvant treatment), n (%)	
0	140 (31.2)
1	115 (25.6)
2-5	13 (2.9)
Not documented	181 (40.3)
HR status, n (%)	
Negative	508(32.4)
Positive	1055 (67.3)
Not Documented	4 (0.3)
Duration of follow-up period [months]	
Median (IQR)	31.9 (20, 47.5)

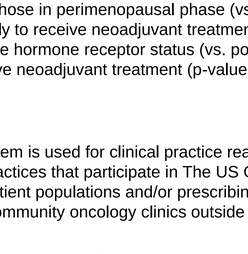
Treatment Patterns

- Among high-risk eBC patients, 62.6% (n=981) initiated neoadjuvant and post-neoadjuvant treatment, 28.7% (n=449) initiated adjuvant treatment only (See treatment distribution in Figure 2), and 8.7% (n=137) of patients didn't receive any treatment.

Metastatic recurrence during the follow-up period

- During the follow-up period (median 31.9 months), the proportion of patients reaching metastatic recurrence was almost double among high-risk patients without neoadjuvant treatment compared to those with neoadjuvant treatment (10.9% vs. 4.6%; p-value <0.001) (Table 2).

Figure 1. Risk status among patients with HER2+ eBC (n=4,125)*

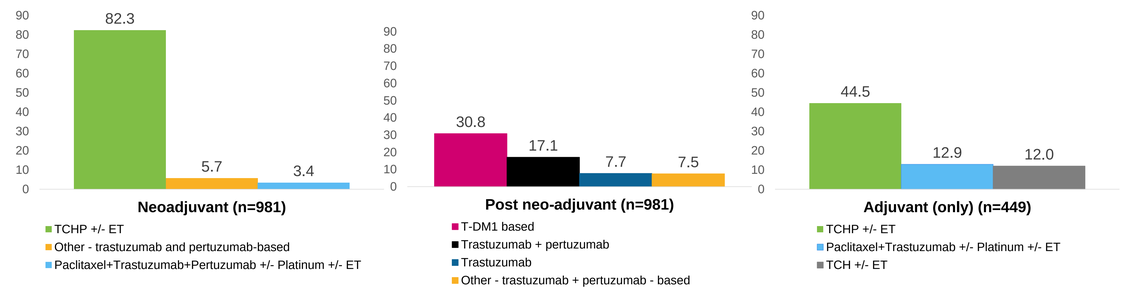


*High Risk: [T0-T4,N1-3,M0 or T3-T4,N0,M0]; Moderate to High Risk: [T2,N0,M0]; Low Risk: [T1a-T1c, N0,M0]

Table 2. Metastatic recurrence among high-risk patients with and without neoadjuvant treatment

	High-risk patients (overall) N=1,567	High-risk patients initiating neoadjuvant treatment N=981	High-risk patients without neoadjuvant treatment N=586	P-value
Diagnosis of metastatic breast cancer during the study observation period, n (%)	109 (7.0%)	45 (4.6%)	64 (10.9%)	<0.0001
Time to metastatic diagnosis from eBC diagnosis date, (months)				
Mean (SD)	17.3 (15.6)	24.1 (12.5)	12.5 (15.9)	<0.0001
Median (IQR)	15.4 (1.8,27.1)	24.4 (14.1,32.7)	2.8 (1.1,22.9)	

Figure 2. Treatment distribution among patients with high-risk HER2+ eBC§



§ *TCHP: docetaxel + platinum + trastuzumab + pertuzumab; T-DM1: trastuzumab emantansine; TCH: docetaxal + platinum + trastuzumab; ET: Endocrine Therapy*

Factors associated with neoadjuvant treatment initiation

- Multivariable logistic regression model demonstrated that older patients and those in perimenopausal phase (vs. premenopausal) were less likely to receive neoadjuvant treatment; whereas patients with a negative hormone receptor status (vs. positive) were more likely to receive neoadjuvant treatment (p-value <0.05).[Table 3]

Limitations

- The iKM system is used for clinical practice reasons, not solely research. Practices that participate in The US Oncology Network may have patient populations and/or prescribing practices that differ from other community oncology clinics outside of The US Oncology Network.
- The follow-up period is limited to assess long-term outcomes.

Table 3. Factors associated with neoadjuvant treatment initiation among patients with high-risk HER2+ eBC

Covariate	Without neoadjuvant	Neoadjuvant (modeled as event)	Odds Ratio (95% CI)^
Age	412	797	0.96 (0.95-0.97)
Menopausal status			
Premenopausal (reference)	101	320	-
Perimenopausal	10	11	0.37 (0.15-0.92)
Postmenopausal	301	466	1.2 (0.80-1.80)
Hormone Receptor status			
Positive (reference)	302	509	
Negative	110	288	1.6 (1.25-2.15)

^p-value <0.05; Race and practice location were also included in the model but there were no differences by category.