Addressing Barriers to Identifying HER2-Low Metastatic Breast Cancer Patients in a Large Community Oncology Practice

Lauren Carpenter,[1] Kelli Corona,[1] Bob Phelan,[1] Shenitha Edwards[1]

[1] Cancer Specialists of North Florida, 7015 AC Skinner Pkwy, Ste. 2, Jacksonville, FL, United States

BACKGROUND

- HER2, an important BC biomarker,[1] is routinely determined by IHC and/or ISH[2,3]
- Approximately 50% of US patients with mBC exhibit HER2-low expression, defined as IHC 1+ or IHC 2+ without gene amplification (ISH-)[4-6]
- T-DXd, a HER2-directed antibody and topoisomerase inhibitor conjugate, was the first FDA-approved treatment for unresectable or metastatic HER2-low BC[7]
- The ASCO-CAP Guidelines for HER2 testing in BC recommend that all newly diagnosed BC patients have HER2 testing performed and all patients who subsequently develop mBC have an additional HER2 test performed[3,8]
- The 2023 ASCO-CAP Guideline Update affirmed previous testing guidelines that categorize HER2-low BC as HER2-negative disease.[3,8] However, the 2023 CAP BC biomarker testing reporting template noted that a HER2 IHC 1+ score or an IHC 2+ score and ISH- result may be reported as HER2-low disease[9]
- Lack of integration between laboratory information systems and EHRs may create barriers to identifying patients with HER2-low disease
- Given the evolving treatment landscape for HER2-low BC, we used retrospective data from a large community oncology practice to detect challenges in identifying patients with HER2-low mBC as a quality improvement initiative

METHODS

- We conducted a retrospective chart review to identify patients with mBC treated from January 1, 2023—August 11, 2023, across 10 outpatient hematology/oncology clinics in Northeast Florida
- EHRs were queried within the OncoEMR® (Flatiron Health, New York, NY) system using keywords (metastatic, metastasis, stage IV, HER2, IHC, FISH, pathology)
- To obtain patients' HER2 status, pathology reports were searched within their OncoEMR profile, which required up to a 6-step, multi-selection process
- Results were compared between the EHR summary report, EHR discrete data fields, and the embedded laboratory reports
- HER2 test results were identified regardless of stage when tested and categorized as positive, low, negative, or indeterminate (**Table 1**)
- If patients were noted as being "HER2-negative" on the EHR summary report, IHC score and ISH results were queried to discern if they could be HER2 low
- The following factors were evaluated:
  - Number of patients with HER2-low or indeterminate mBC
  - Time required to determine HER2 status via the OncoEMR profile
  - Concordance between pathology report and documentation in OncoEMR (summary page, physician's notes)
  - Number of laboratories providing IHC and ISH results

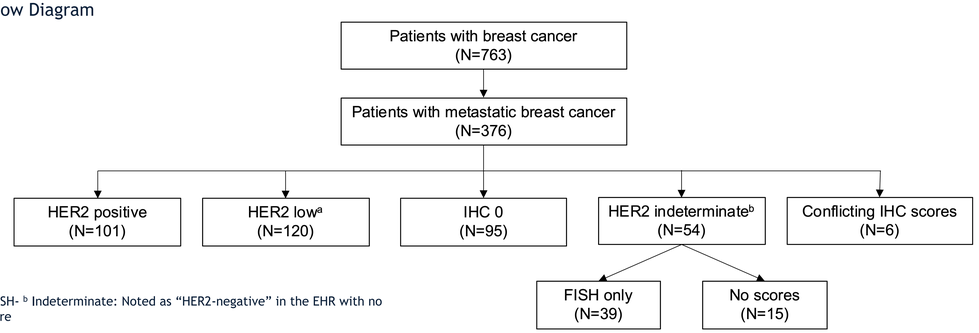
RESULTS

- Across 10 clinics and 28 ordering providers, 376 patients with mBC were identified; approximately one-third had HER2-low disease based on IHC scores and FISH results (**Figure 1**)
- Disagreement in HER2 status among the summary report (**Figure 2**), clinical notes, and pathology reports was not uncommon. Average time required to confirm HER2-low status from opening the patient profile to finding HER2 IHC results in pathology reports ranged from 3 to 5 minutes; however, up to 15 minutes was needed if individual pathology reports were not embedded

Table 1. HER2 Status Categories

HER2 Status			
Positive	**Low**	**Negative**	**Indeterminate**
IHC 3+ or IHC 2+/FISH+	IHC 1+ or IHC 2+/ISH-	IHC 0	Noted as "HER2-negative" in clinical notes but did not have HER2 IHC score documented in EHR or embedded pathology report

Figure 1. Patient Flow Diagram



[a] HER2 low: IHC 1+ or 2+/ISH- [b] Indeterminate: Noted as "HER2-negative" in the EHR with no documented HER2 IHC score

Figure 2. OncoEMR Clinical Summary Page

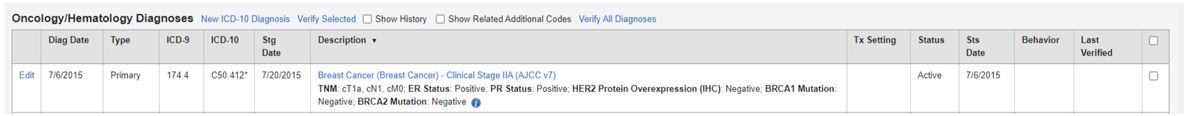
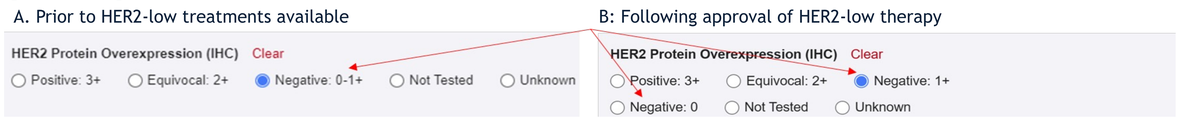


Figure 3. Change in OncoEMR HER2-Low Data Field



[a]Prior to the approval of T-DXd for certain mBC patients with HER2-low disease, OncoEMR included a field that combined results for IHC 0-1+. Although this field was updated post-T-DXd HER2-low approval, data entered prior to the update cannot be edited, and a new HER2 IHC test may need to be entered to update these results.

REFERENCES: 1. Feng Y, et al. *Genes Dis*. 2018;5(2):77-106. **2.** Marchiò C, et al. *Semin Cancer Biol*. 2021;72:123-135. **3.** Wolff AC, et al. *J Clin Oncol*. 2018;36(20):2105-2122. **4.** Mehta S, et al. Prevalence of low HER2 expression among HER2 negative metastatic breast cancer patients in US: multi-site, retrospective chart review study. Poster presented at NCCN Annual Conference, March 18-20, 2021; Virtual. **5.** Scott M, et al. *J Clin Oncol*. 2021;39(15_suppl):1021-1021. **6.** Watanabe A, Pavilack-Kirker M, Lam C. Patient characteristics, treatment patterns, and clinical outcomes of patients with locally advanced or metastatic HER2-low breast cancer. Poster presented at NCCN Annual Conference, March 31-April 2, 2022; Virtual. **7.** ENHERTU [package insert] (2022). Daiichi Sankyo: Basking Ridge, NJ. **8.** Wolff AC, et al. *Arch Pathol Lab Med*. 2023;147(9):993-1000. **9.** CAP. Template for reporting results of biomarker testing of specimens from patients with carcinoma of the breast. (2023) Version 1.5.0.1. https://documents.cap.org/documents/Breast.Bmk_1.5.0.1.REL_CAPCP.pdf.

ACKNOWLEDGMENTS: Medical writing support was provided by Catherine Mirvis, BA, from OPEN Health, and was funded by Daiichi Sankyo, Inc.
DISCLOSURES: This study is sponsored by Daiichi Sankyo. In March 2019, AstraZeneca entered into a global development and commercialization collaboration agreement with Daiichi Sankyo for trastuzumab deruxtecan (T-DXd; DS-8201).
ABBREVIATIONS: ASCO, American Society of Clinical Oncology; BC, breast cancer; CAP, College of American Pathologists; EHR, electronic health record; FDA, Food and Drug Administration; FISH, fluorescent in situ hybridization; HER2, Human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; mBC, metastatic BC; T-DXd, fam-trastuzumab deruxtecan-nxki.

RESULTS (cont'd)

- **54 patients had indeterminate HER2 status; 72% had FISH testing only and 28% did not have a pathology report in their EHR**
  - Of those with FISH results only, >90% were tested prior to approval of T-DXd for HER2-low mBC in August 2022, which underscores the need to reassess HER2 status at progression using IHC
  - Approximately 20% of patients did not have HER2 testing performed at metastatic diagnosis, although 5% had a documented rationale (eg, bone-only disease, tissue quantity insufficient for testing).
- **Six patients had conflicting IHC scores**; among these, 3 had an increase in IHC score over time (eg, from IHC 0 to 2+ [n=1], IHC 1+ to 2+ [n=2]).
  - Reasons for conflicting scores included samples obtained at different times, tested at different laboratories, and/or obtained from various tumor sites
- Barriers identified in determining HER2-low status included:
  - **Discrepancies in reporting HER2 status:** There was a lack of concordance across the OncoEMR summary page, clinical notes, and pathology reports
  - **Multiple laboratories were used for HER2 IHC (n=21) and FISH (n=6) testing**
    - About 90% of pathology reports called "HER2-low" disease "HER2-negative"
    - Pathology report layout varied, with some laboratories including HER2 results on a front summary page and others placing them deep within the report
    - In ~42% of cases, IHC scores were not reported on the first page
  - **Prior classification and lack of identification of HER2-low disease in OncoEMR (Figure 3)**
  - **Difficulty identifying and accessing pathology results:** Reports were not consistently categorized under the "pathology" tab within OncoEMR. Although the report may be flagged as being from pathology, it could be appended under "External MD notes," "Misc," or "Lab Reports"

CONCLUSIONS

- Challenges exist for community oncology practitioners when determining a patient's HER2 status
- Community practices typically receive pathology reports from numerous different laboratories, which have different report formats and may not prominently display the HER2 IHC score
- Pathology reports may not be easily located or queried within the EHR
- Although OncoEMR has a clinical summary page that contains information on the patient's IHC score, the previous classification scheme identified patients with an IHC score of 1 as HER2 negative. Clinicians may not cross-reference the original pathology report while reviewing clinical notes or patient referrals
- About 90% of patients with HER2-low disease were classified as HER2 negative in either the pathology report, summary page, or clinical notes
- Overall, 10% of patients with mBC received HER2 testing by FISH only. While this was more common prior to the approval of T-DXd for HER2-low disease, patients who were previously tested for HER2 by FISH alone should undergo IHC testing
- Potential actions to improve identification of HER2-low patients in community oncology practices include reducing the number of laboratories used to allow for consistency in laboratory result reporting and/or choosing preferred testing partners that integrate reporting within the EHR

Encore Presentation from Miami Breast Cancer Conference, March 7-10, 2024, Miami Beach, FL