Development and Validation of a Claims-based Approach to Identify Patients with Metastatic HR+/HER2- Breast Cancer

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INTRODUCTION

- Patients with first or recurrent diagnosis of breast cancer (BC) undergo a series of tests for hormone receptor (HR) and human epidermal growth factor receptor 2 (HER2) status to identify the BC subtype and determine the best course of treatment.[1,2]
- HR positivity is determined by presence of estrogen receptors (ER) and/or progesterone receptors (PR), while HER2 negativity is indicated by a low score from an immunohistochemistry (IHC) assay. HR+/HER2- is the most common BC subtype, accounting for 70% of all BC, and is associated with high risk of relapse, with more than 50% of recurrences occurring after 5 years.[3,4]
- Due to the lack of biomarker data and specific diagnosis codes for BC subtypes, claims-based studies among patients with HR+/HER2- BC often use treatment-based proxies. However, the performance of these proxies is not well-characterized.

OBJECTIVE

- This retrospective cohort study used claims data to develop a treatment-based proxy to identify patients with HR+/HER2- metastatic BC (mBC) in the United States (US) and evaluated the performance of the proxy using electronic medical records (EMR).

METHODS

Study design: Retrospective cohort study.

Data source: IQVIA PharMetrics® Plus database, comprised of fully adjudicated, de-identified medical and pharmacy claims, and IQVIA Oncology EMR (OncEMR), which includes data from medium and large community-based medical oncology and comprehensive cancer centers in the US.

Study population:

- Adults (≥18 years) with ≥1 ICD-10 diagnosis code for BC and metastasis were identified in PharMetrics Plus and linked to OncEMR; the date of the earliest diagnosis code for metastasis in the selection window (March 1, 2019 to November 30, 2022) was the index date (**Figure 1**).
- All patients had 6-month baseline and ≥3-month follow-up period.
- Patients met a treatment-based proxy for HR+/HER2- defined as:
  - ≥1 claim for treatment indicated for HR+/HER2- breast cancer (CDK4/6 inhibitor, mTOR inhibitor, PIK3CA inhibitor) or HR+ breast cancer (endocrine therapy) during the follow-up period, AND
  - no claims for treatments indicated for TNBC (sacituzumab govitecan, atezolizumab, pembrolizumab) or HER2+ breast cancer (trastuzumab, pertuzumab, margetuximab, ado-trastuzumab emtansine, fam-trastuzumab deruxtecan, lapatinib, neratinib, tucatinib) during the follow-up period in PharMetrics Plus.

METHODS

- All patients were required to have ≥1 line of therapy during follow-up. Potential treatments included endocrine therapy, chemotherapy and targeted therapy (CDK4/6, mTOR, PIK3CA and PARP inhibitors, immunotherapy, and antibody drug conjugate [ADC]).

RESULTS

Patient selection

- Out of 19,117 mBC patients identified in claims, 11,419 (11.3%) patients had ≥1 line of therapy and were defined as having HR+/HER2- status using the treatment-based proxy.
- Of these, 392 (3.4%) patients were linkable to OncEMR (**Figure 1**).

Biomarker data availability in OncEMR

- 45.9%, 44.4% and 46.9% patients had non-missing data ER, PR and HER2, respectively.
- Nearly 40% of the patients in the linked cohort (N=154) had non-missing data on all three of ER, PR and HER2 status in OncEMR (**Figure 2**).

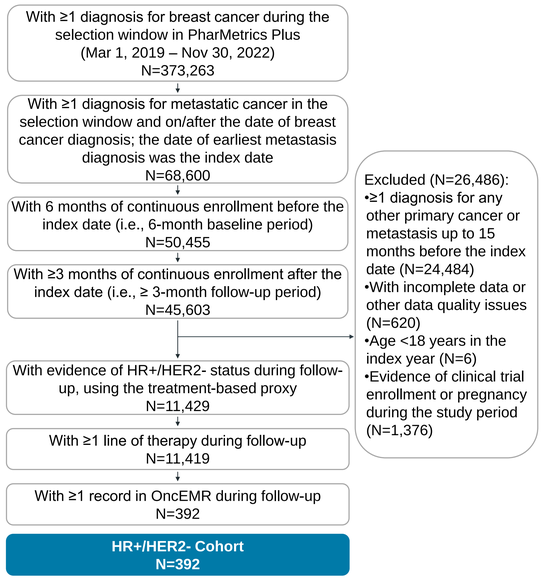
Performance of claims-based definition of HR+/HER2-

- The positive predictive value of the treatment-based proxy was 100% for HR+ status (**Figure 3**) and 95.5% for HER2- status (**Figure 4**), using biomarker status during the follow-up period.
- In total, 147 (95.5%) patients identified via the treatment-based proxy in claims were classified as having HR+/HER2- status in OncEMR.

Investigation of patients misclassified by the claims-based definition

- The remaining 7 (4.5%) patients had evidence of HER2+ BC subtype based on biomarker data in OncEMR and were misclassified by the treatment-based proxy.
- All 7 patients had evidence of HR+/HER2+ disease. Two of them had claims for chemotherapy and all of them had claims for endocrine therapy
- Treatment patterns were also evaluated in the sample identified in PharMetrics Plus before OncEMR linkage (N=11,419); 99.5% of patients had endocrine therapy, 32.0% had chemotherapy and 23.6% of patients had targeted therapy during the ≥3-month follow-up period.

Figure 1. Patient selection



Only the last selection criterion used OncEMR data. All other steps were applied in PharMetrics Plus.

Figure 2. Proportion of patients in the linked cohort with available biomarker data in OncEMR during ≥3-month follow-up

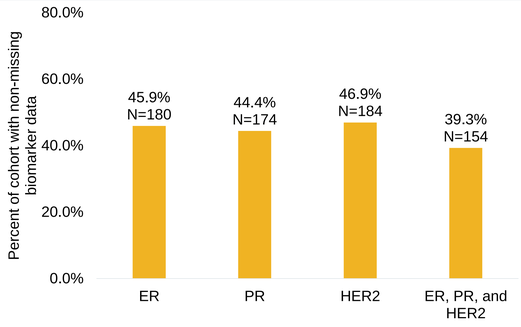
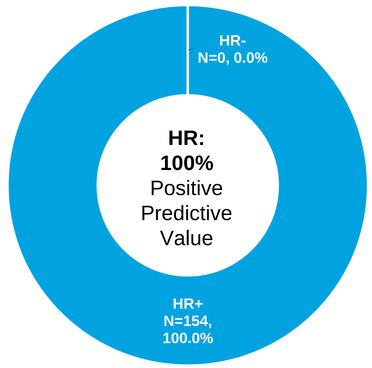
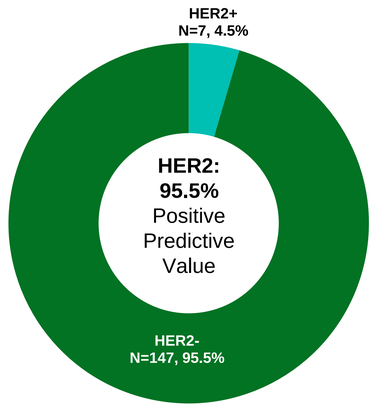


Figure 3. Distribution of HR results from OncEMR in the HR+/HER2- mBC cohort identified via treatment-based proxy



HR+ includes patients with ER+ or PR+ status and HR- includes patients with ER- and PR- status.

Figure 4. Distribution of HER2 results from OncEMR in the HR+/HER2- mBC cohort identified via treatment-based proxy



LIMITATIONS

- Despite excellent performance of the current treatment-based proxy, the overall sample size was small. If the performance in the linked sample can be generalized to the sample identified in claims before linkage (N=11,419), about 514 patients with HR+/HER2+ disease would have been misclassified as HR+/HER2-. Although improvements to the proxy might be possible to avoid misclassifying HER2 status in larger samples, the advent of HER2-directed therapies for patients across the spectrum of HER2 status, including HER2 ‘low’ and ‘ultralow’ subgroups within ‘HER2-negative’, presents a challenge

CONCLUSIONS

- The treatment-based proxy can be used to reliably identify patients with HR+/HER2- mBC and subsequently evaluate clinical and economic outcomes available in claims databases.
- The treatment-based proxy demonstrated an excellent positive predictive value for both HR+ and HER2- status. All patients were correctly classified to HR+ status and over 95% of patients were correctly classified to HER2- status.
- The small minority of misclassified HER2+ patients were included due to the presence of endocrine therapy during follow-up. Therefore, to further improve the proxy, additional requirements can be added to such patients where evidence of chemotherapy or targeted therapy would also be required for inclusion.

Abbreviations

ADC, Antibody drug conjugate; BC, Breast cancer; CDK4/6, Cyclin-dependent kinase 4 and 6; ER, Estrogen receptor; HER2, Human epidermal growth factor receptor 2; HR, Hormone receptor; mTOR, mammalian target of rapamycin; NTRK, Neurotrophic tyrosine receptor kinase; PARP, Poly(ADP-ribose) polymerase; PD-1, Programmed death protein 1; PD-L1, Programmed death ligand 1; PIK3CA, Phosphatidylinositol 3-kinase, catalytic, alpha polypeptide gene; PR, Progesterone receptor; RET, Rearranged during transfection; US, United States; VEGF, Vascular endothelial growth factor.

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Disclosures

Nazneen Fatima Shaikh, Jenny Tse, Dajun Tian, and Aimee Near are employed by IQVIA. Simon Collin is employed by AstraZeneca Pharmaceuticals Ltd.

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