Development and Validation of a Claims-based Approach to Identify Patients with Metastatic Triple Negative Breast Cancer (mTNBC)

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INTRODUCTION

- Upon first or recurrent diagnosis of breast cancer (BC), all patients receive testing for hormone receptor (HR) and human epidermal growth factor receptor 2 (HER2) status to determine the best course of treatment.[1,2]
- HER2 expression is clinically recognized as negative (-) or positive (+), and HR positivity is determined by presence of estrogen receptors (ER) and/or progesterone receptors (PR). Triple-negative breast cancer (TNBC) is an aggressive BC subtype, with higher recurrence and lower 5-year survival rates than other subtypes.[3]
- Due to the lack of biomarker data and specific diagnosis codes for breast cancer subtypes, claims-based studies among patients with TNBC 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 metastatic TNBC (mTNBC) 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, 2017 to September 30, 2023) was the index date (**Figure 1**).
- All patients had 6-month baseline and ≥3-month follow-up periods.
- Patients met a treatment-based proxy for TNBC, defined as no claims for treatments indicated for HR+ HER2- breast cancer (CDK4/6 inhibitor, mTOR inhibitor, PIK3CA inhibitor, AKT inhibitor), HR+ breast cancer (endocrine therapy), or HER2+ breast cancer (trastuzumab, pertuzumab, margetuximab, ado-trastuzumab emtansine, fam-trastuzumab deruxtecan3, lapatinib, neratinib, tucatinib) in the study period from September 1, 2016 to December 31, 2023) in PharMetrics Plus.

METHODS

- All patients were required to have ≥1 line of therapy during follow-up. Potential treatments included chemotherapy and targeted therapy (PD-1/PD-L1, PARP, VEGF, NTRK, RET inhibitors; and ADCs). Patients with fam-trastuzumab deruxtecan on/after August 6, 2022 were allowed to remain in the cohort, due to the expanded approval to HER2- low metastatic BC (mBC).

RESULTS

Patient selection

- Out of 32,396 mBC patients identified in claims, 3,651 (11.3%) patients had ≥1 line of therapy and were defined as having TNBC using the treatment-based proxy.
- Of these, 117 (3.2%) patients were linkable to OncEMR (**Figure 1**).

Biomarker data availability in OncEMR

- Half of the patients in the linked cohort (N=54) had non-missing data on ER, PR, and HER2 status in OncEMR (**Figure 2**).

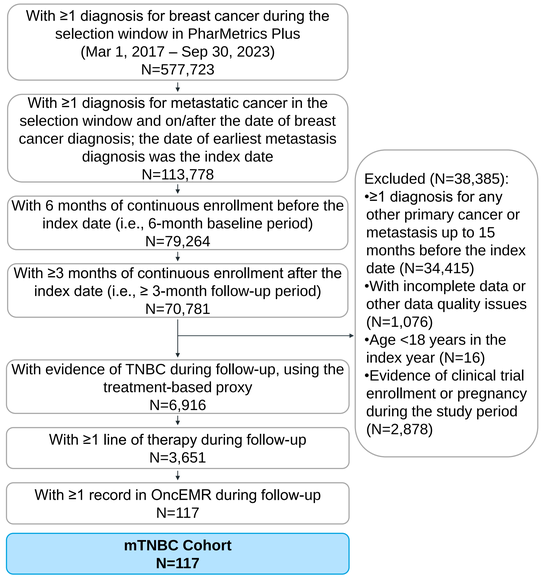
Performance of claims-based definition of TNBC

- The positive predictive value of the treatment-based proxy was 98.1% for HER2- status (**Figure 3**) and 68.5% for HR- status (**Figure 4**), using biomarker status during the follow-up period.
- In total, 37 (68.5%) patients identified via treatment-based proxy in claims were classified as having TNBC in OncEMR.

Investigation of patients misclassified by the claims-based definition

- The remaining 17 (31.5%) patients had evidence of other breast cancer subtypes based on biomarker data in OncEMR and were misclassified by the treatment-based proxy.
- Most of these patients (N=16) had evidence of HR+/HER2- disease.
  - › Two of these patients had HR- results at some point during the study period.
  - › All 16 patients had claims for chemotherapy and no evidence of targeted therapy during the study period.
- Treatment patterns were also evaluated in the sample identified in PharMetrics Plus before OncEMR linkage (N=3,651); 97.2% of patients had chemotherapy and 29.2% 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

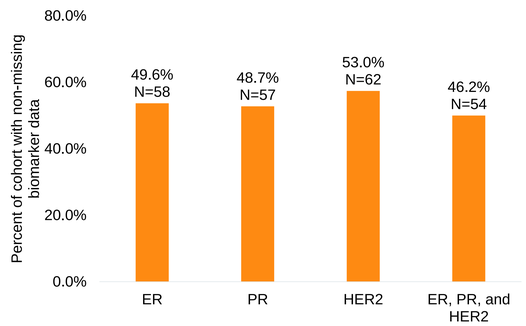


Figure 3. Distribution of HER2 results from OncEMR in the mTNBC cohort identified via treatment-based proxy

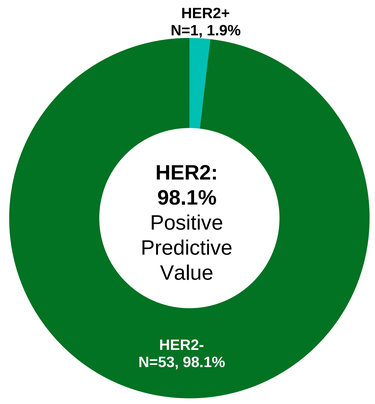
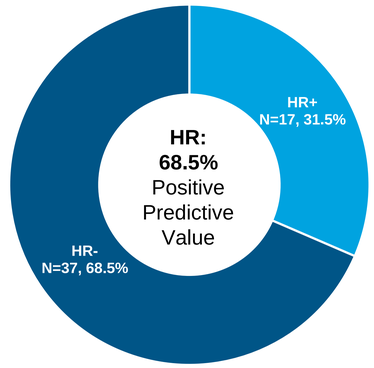


Figure 4. Distribution of HR results from OncEMR in the mTNBC cohort identified via treatment-based proxy



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

LIMITATIONS

- The treatment-based proxy did not include a requirement for targeted therapies indicated for TNBC (e.g., sacituzumab govitecan, atezolizumab, pembrolizumab, olaparib, talazoparib). While requiring such treatments may have improved the performance of the claims-based definition of TNBC, chemotherapy is the standard of care for patients with mTNBC not eligible for PD-1/PD-L1 immunotherapy.[4] Therefore, a treatment requirement would have limited the sample size for this study and limited the generalizability of these findings to patients eligible for targeted therapy.

CONCLUSIONS

- The treatment-based proxy for TNBC defined based on the absence of treatments indicated for HR+ or HER2+ mBC demonstrated an excellent positive predictive value for HER2- disease. However, nearly one-third of patients had an HR+ result in OncEMR.
- Although patients with mTNBC can be identified using this proxy, additional criteria are needed to better classify patients treated with chemotherapy only. In such patients, evidence of targeted treatment indicated for TNBC can be required to help reduce ER- misclassification and further improve the proxy.
- The treatment-based proxy should be re-evaluated as more treatment options become available for TNBC.

Abbreviations

ADC, Antibody drug conjugate; BC, Breast cancer; ER, Estrogen receptor; HER2, Human epidermal growth factor receptor 2; HR, Hormone receptor; NTRK, Neurotrophic tyrosine receptor kinase; PARP, Poly (ADP-ribose) polymerase; PD-1, Programmed death protein 1; PD-L1, Programmed death ligand 1; PR, Progesterone receptor; RET, Rearranged during transfection; US, United States; VEGF, Vascular endothelial growth factor.

References

1. Allison KH, et al. Estrogen and Progesterone Receptor Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologists Guideline Update. Arch Pathol Lab Med. 2020 May;144(5):545-563. doi: 10.5858/arpa.2019-0904-SA.
2. Wolff AC, et al. Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer. Arch Pathol Lab Med. 2023 Sep 1;147(9):993-1000. doi: 10.5858/arpa.2023-0950-SA.
3. Dent R, et al. Triple-negative breast cancer: clinical features and patterns of recurrence. Clin Cancer Res. 2007 Aug 1;13(15 Pt 1):4429-34. doi: 10.1158/1078-0432.CCR-06-3045.
4. Al Sukhun S, et al. Systemic Treatment of Patients With Metastatic Breast Cancer: ASCO Resource-Stratified Guideline. JCO Glob Oncol. 2024 Jan;10:e2300285. doi: 10.1200/GO.23.00285.

Disclosures

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

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