

Frequency of documented IHC score in patients with HER2-negative breast cancer in the US: an observational study using Guardian Research Network data

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Objectives

To quantify, by breast cancer stage (early, locally-advanced, and metastatic), among patients from a network of community healthcare organizations across the US:

- 1) the proportion of patients with HER2-negative (defined as IHC 0, IHC1+, and IHC2+/ISH-) breast cancer (BC) who have documented HER2 IHC test results
- 2) the proportion of these patients who have low (IHC1+ or IHC2+/ISH-) or ultralow (IHC0 with membrane staining) levels of HER2 expression

Conclusions

- This study highlights significant variability in HER2 IHC testing and reporting practices in community settings.
- Despite clinical recommendations at the time of the study, one in six patients with HER2-negative breast cancer did not have a documented discrete IHC score, and very few had granular information on the observed percentage of HER2 expression.
- Identifying and documenting granularity in HER2 status can expand treatment options and potentially improve outcomes for a broader group of eligible patients

Plain language summary



Why did we perform this research?

This research was conducted to better understand how often HER2 expression levels are documented in patients' medical records for patients with HER2-negative breast cancer at community hospitals. Identifying patients with low or ultralow HER2 expression is relevant for determining patients' eligibility for HER2-directed therapies. Community hospitals have been under-represented in previous studies.



How did we perform this research?

We used electronic medical records (EMR) from the Guardian Research Network (GRN), which includes data from seven community healthcare organizations (HCOs) across the US. We applied a natural language processing (NLP) algorithm to identify HER2-negative patients and extract documented IHC scores from their pathology reports.



What were the findings of this research?

Of the 13,100 patients with HER2-negative breast cancer in this cohort, most (85%) had documented IHC scores. Among these 37% were scored IHC0, 41% IHC1+, 21% IHC2+, and 1% IHC3+. However, only one of the HCOs provided the information needed to identify patients who have HER2 ultralow expression.



What are the implications of this research?

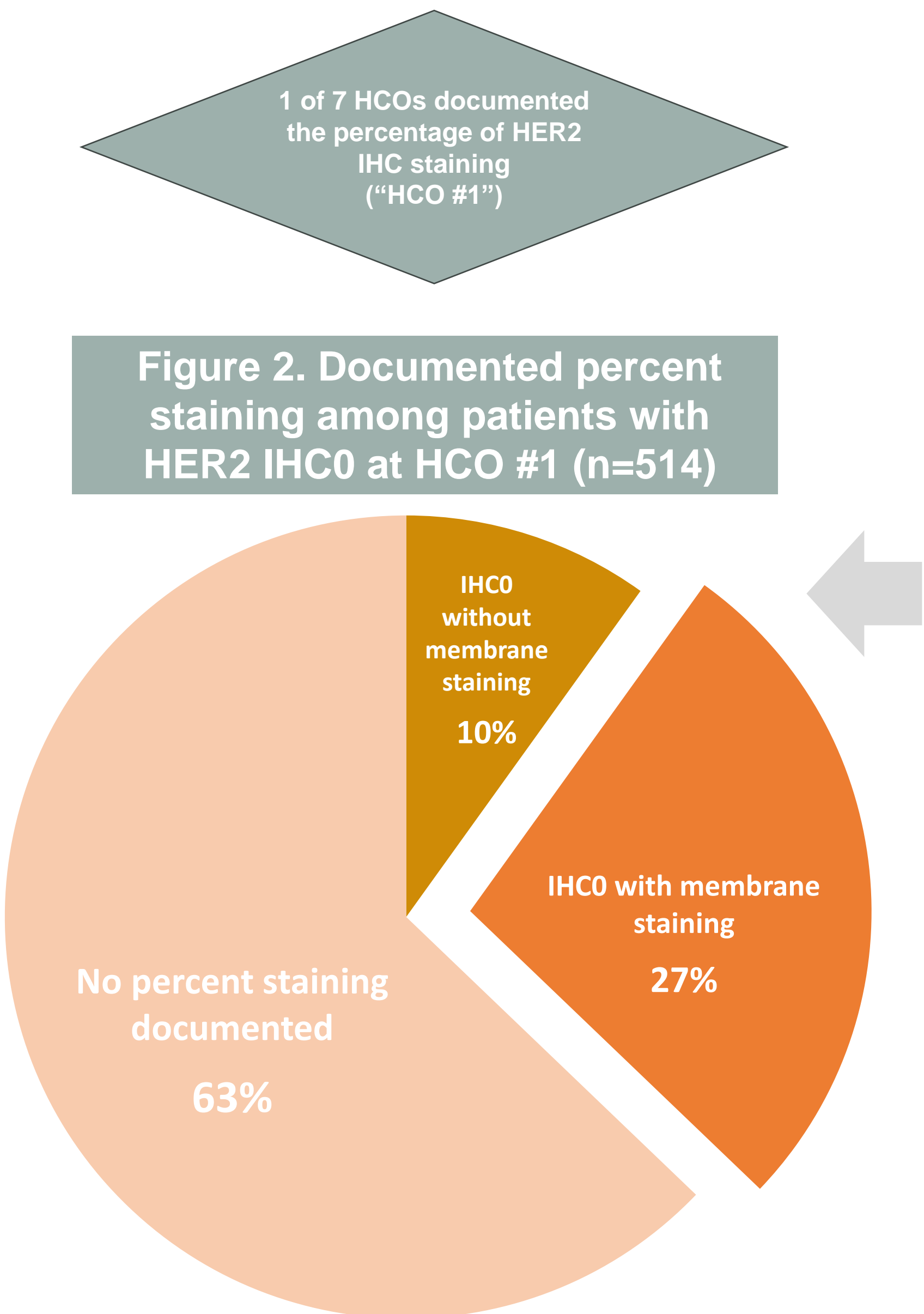
This study highlights that many patients with HER2-negative breast cancer lack detailed HER2 expression documentation, which could impact their eligibility for HER2-directed therapies. Improving documentation practices may improve patient care and selection of the most appropriate and effective treatments.

Introduction

- HER2 status**, traditionally reported as positive or negative, is now recognized in varying levels of expression, (HER2-positive includes IHC2+/ISH+ and IHC3+; HER2-negative includes IHC0, IHC1+, and IHC2+/ISH-) necessitating precise identification for appropriate treatment.¹
- Patients with HER2 IHC0** include those with membrane staining (percent staining >0%≤10%) 'HER2-ultralow' and those without membrane staining (percent staining 0%).
- Data from the DESTINY-Breast04 and DESTINY-Breast06** trials indicate clinical relevance in identifying patients with low (IHC1+ and IHC2+/ISH-) and ultralow (IHC0 with membrane staining) HER2 expression.
- Updated 2023 ASCO-CAP HER2 testing** in breast cancer guidelines recommend including semi-quantitative IHC scores in pathology reports to identify patients who may be eligible for HER2-low directed therapies.²

Results and interpretation

- The analytic cohort comprised 13,100 patients whose breast cancer was classified as HER2-negative; 10,746 (82.0%) had early-stage breast cancer, 355 (2.7%) locally advanced, and 1,999 (15.3%) metastatic.
- Most patients (n=11,174, 85.3%) had documented IHC scores, of which 37.0% were IHC0, 41.3% IHC1+, 20.5% IHC2+, and 1.3% IHC3+.



- Of 191 HER2-negative patients at this one center who had IHC0 and documented percent staining, 51 (26.7%) had 0% staining and 73.3% had membrane staining (>0%≤10%).
- 27% (n=140) of patients at HCO #1 were classified as ultralow; this population represents a subset of HER2-negative breast cancer patients who may benefit from HER2-directed therapies.
- In centers that do not report this level of granularity, these patients may simply be classified as HER2-negative and may not be identified as eligible for HER2-directed therapies

References

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- Wolff AC, Somerfield MR, Dowsett M, et al. J Clin Oncol. doi:10.1200/JCO.22.02864

Disclosures

- Employee of AstraZeneca Pharmaceuticals Ltd.
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- Employee of AstraZeneca Pharmaceuticals LP.

Methods

- STUDY DESIGN & SETTING:** This retrospective cohort study utilized electronic medical record data from the Guardian Research Network, which includes data from 7 community healthcare organizations (HCOs) across the US, comprising 40+ cancer centers and 90+ hospitals.
- STUDY COHORT:** Patients were eligible for inclusion if they were ≥18 years old, diagnosed with BC (ICD10 code C50), had ≥1 clinical evaluation related to their cancer from Jan 1, 2018 to Nov 15, 2023, and had HER2-negative breast cancer status as determined by a natural language processing (NLP) algorithm applied to structured and unstructured EMR data during the study period.
- ANALYTIC COHORT:** Patients were classified into subgroups based on the highest IHC score documented during the study period and their breast cancer stage at the time of this score. IHC scores were abstracted from unstructured pathology reports using an NLP algorithm. Patients whose highest score during the study period was IHC0 were further classified into groups based on their documented percentage of membrane staining.

Figure 1. HER2-Negative Breast Cancer Patient Selection Flowchart as Identified from EMR within GRN

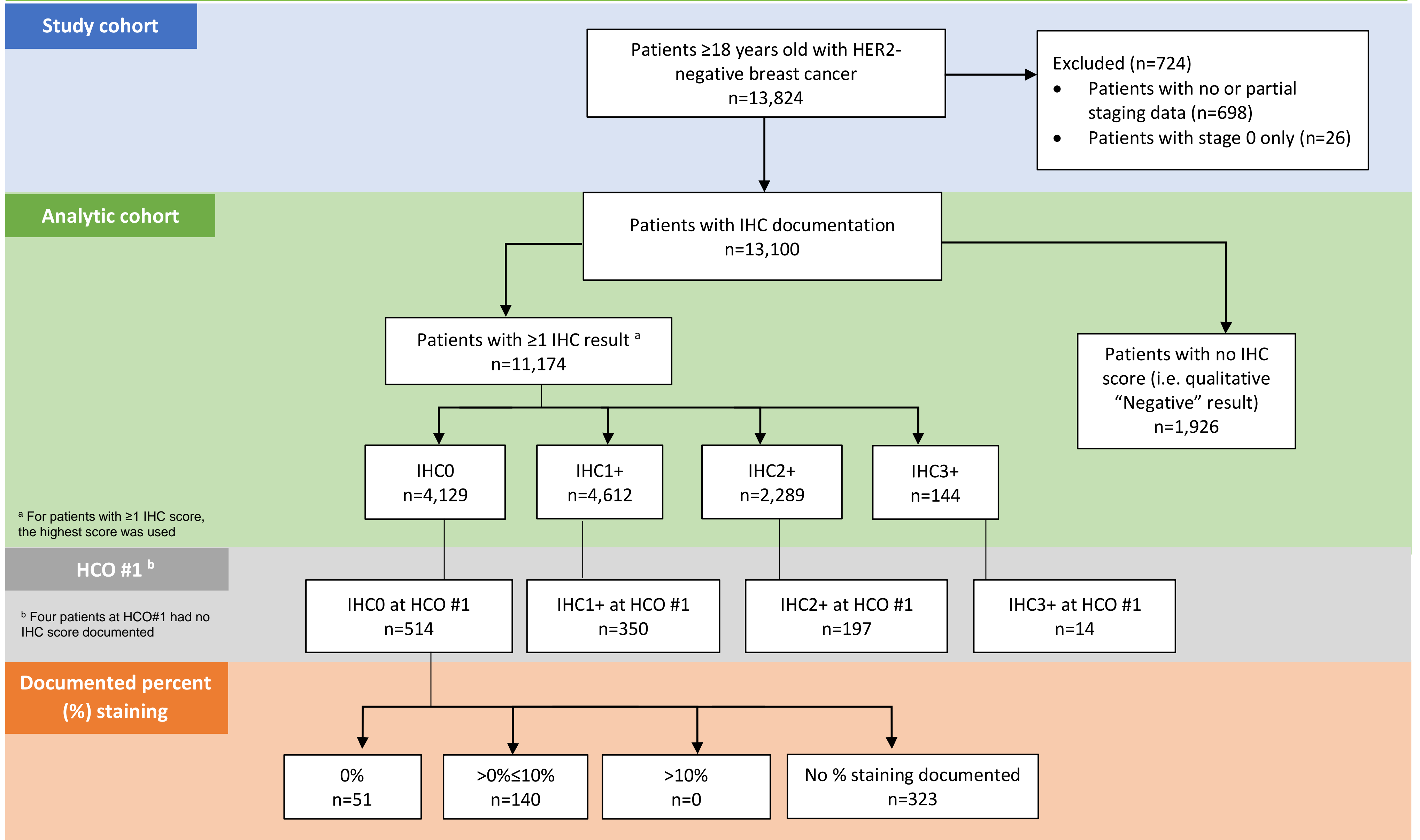


Table 1: IHC score by breast cancer stage* in HER2-negative cohort based on highest IHC score

Analytic cohort				
	All HER2-negative patients n=13,100	Early-stage HER2-negative n=10,746	Locally-advanced HER2-negative n=355	Metastatic HER2-negative n=1,999
IHC0	4,129 (31.5%)	3,369 (31.4%)	118 (33.2%)	642 (32.1%)
IHC1+	4,612 (35.2%)	3,845 (35.8%)	98 (27.6%)	669 (33.5%)
IHC2+*	2,289 (17.5%)	1,786 (16.6%)	73 (20.6%)	430 (21.5%)
IHC3+***	144 (1.1%)	105 (1.0%)	4 (1.1%)	35 (1.8%)
No IHC score documented****	1,926 (14.7%)	1,641 (15.3%)	62 (17.5%)	223 (11.2%)
HCO #1				
	All HER2-negative patients n=1,079	Early-stage HER2-negative n=951	Locally-advanced HER2-negative n=48	Metastatic HER2-negative n=80
IHC0	514 (47.6%)	452 (47.5%)	27 (56.2%)	35 (43.8%)
IHC1+	350 (32.4%)	313 (32.9%)	11 (22.9%)	26 (32.5%)
IHC2+*	197 (18.3%)	174 (18.3%)	9 (18.8%)	14 (17.5%)
IHC3+***	14 (1.3%)	10 (1.1%)	0 (0.0%)	4 (5.0%)
No IHC score documented****	4 (0.4%)	2 (0.2%)	1 (2.1%)	1 (1.2%)

* Breast cancer stage within +/- 90 days of IHC test result. Early-stage BC: AJCC stages 1A, 1B, 2A, 2B, or 3A or corresponding TNM staging; locally-advanced BC: stages 3B, 3C or corresponding TNM staging; metastatic BC: ICD-10 codes C77, C78, C79; AJCC stage IV, TNM M1, or NLP derived "Stage IV" or "M1" disease
** All patients with IHC2+ and ISH+ as highest score were confirmed to have documentation of HER2-negative status during study period
*** All patients with IHC3+ documented as highest score were confirmed to have documentation of HER2-negative status during study period
**** All patients without a documented IHC score had qualitative documentation of HER2-negative status in medical record, e.g., HER2 status="Negative"

Abbreviations

BC = breast cancer; HER2 = Human epidermal growth factor 2; IHC = immunohistochemistry; EMR = electronic medical record; HCO = healthcare organization

Acknowledgements

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Plain language summary

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