Bridging HER2 Testing and Treatment: Real-World Evidence Across 22 Solid Tumors

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Key Findings:

- HER2 testing has grown exponentially in the past 10 years across all solid tumors
- Esophageal, gastric, bladder, and brain cancers have the highest prevalence of HER2 positivity while prostate, pancreatic, lung, and colorectal had the lowest
- Approx. 40% of HER2 positive solid tumors undergo HER2-directed therapies
- Breast, Liver, H&N, and Brain have the highest therapy adoption while lung and gastric indications have the lowest
- Older generations of HER2-directed therapies are favored over newer ones

Objectives

Successful utilization of HER2-targeted therapies remains a challenge, particularly outside of academic hospitals (i.e. community setting). Large language models (LLM's) are positioned to help rationalize prescribing behaviors and connect biomarker status with treatment decisions. We aim to investigate HER2 testing rates, prevalence, and prescribing habits across solid tumor types in a predominantly (>80%) community setting.

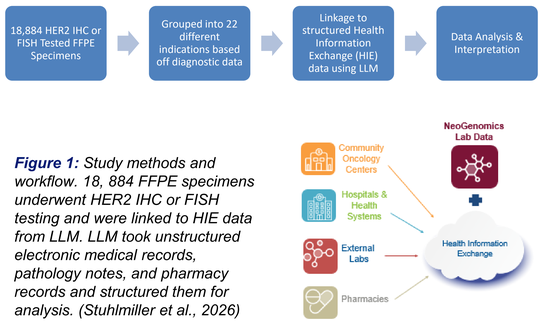

Figure 1: *Study methods and workflow. 18, 884 FFPE specimens underwent HER2 IHC or FISH testing and were linked to HIE data from LLM. LLM took unstructured electronic medical records, pathology notes, and pharmacy records and structured them for analysis. (Stuhlmiller et al., 2026)*

Methods

10-years of HER2 testing data and HER2 profiles of 18,844 Neogenomics patients from 12/2023 –12/2025 were analyzed/integrated with clinical data aggregated from national HIE and processed via the xCures platform (8/2025 – 12/2025). Structured data from electronic medical records were supplemented with LLM's and trained to perform natural language processing and extraction, which standardized information from pathology reports, progress notes, prescription, and imaging records. *(Stuhlmiller et al., 2026)*

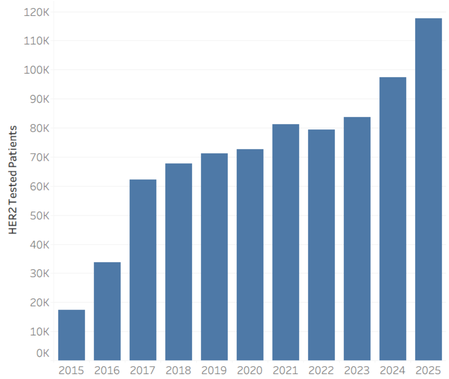

Figure 2: *Bar graph depicting HER2 FISH & IHC orders from 2015 – 2025 across all solid tumors. Since 2015, HER2 orders have increased over 5-fold, indicating a widespread adoption of HER2 testing across all solid tumors.*

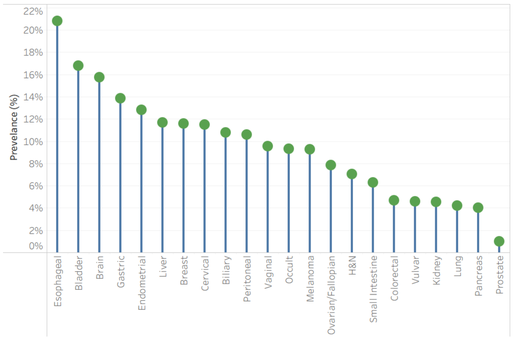

Figure 3: *Lollipop plot depicting prevalence of HER2-positivity (IHC & FISH) across 22 different solid tumor malignancies. Esophageal has the highest prevalence of HER2 (21%) while prostate has the lowest (1%).*

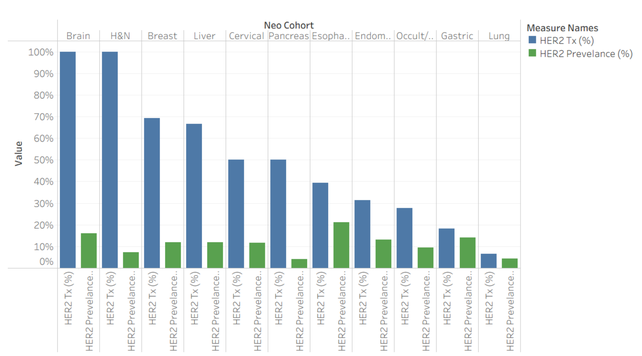

Figure 4: *Clustered bar graph depicting prevalence of HER2 along with proportion of patients receiving HER2-directed therapies in indications with available treatment data. Treatment data was extracted from unstructured electronic medical records, including prescriptions, which were put into a structured format using an LLM and the analyzed. HER2-directed therapies are defined as FDA-approved therapies (monoclonal antibodies, antibody-drug conjugates, small molecules, etc.) which target or bind to HER2.*

Results

HER2 testing data showed a 4.5-fold increase in testing, with 2023-2025 growing >17% year-over-year. The most frequently tested malignancies were breast, lung, colorectal, gastric, and endometrial carcinomas (89% of HER2 testing). Esophageal (21.3%), bladder (17.1%), brain (16.1%), gastric (14.1%), endometrial (13.1%), liver (12%), and breast (12%) had the highest prevalence of HER2 positivity (IHC 3+ or FISH+) while prostate (1%), pancreas (4.1%), lung (4.3%), kidney (4.7%), vulva (4.7%), and colorectal (4.8%) had the lowest. In patients with available treatment information 90 days within testing date, 38.3% (56% excluding patients only on steroid therapy) of HER2 positive patients received HER2-targeted therapy. The most administered therapy was pertuzumab+trastuzumab (52%) followed by trastuzumab (25%), trastuzumab deruxtecan (6.3%); pertuzumab (5.4%), trastuzumab emtansine (3.1%), pertuzumab+trastuzumab+trastuzumab emtansine (1.8%), other combination therapies (1.8%) and ERBB2 TKI's (1.3%).

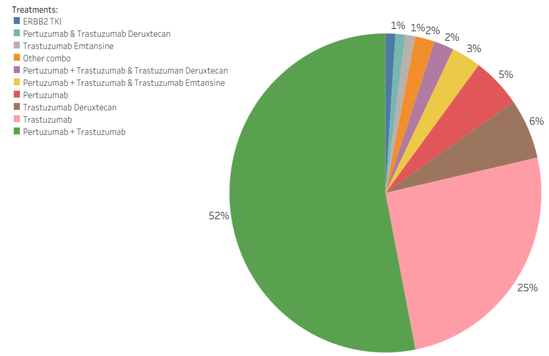

Figure 5: *Pie chart depicting utilization of all FDA-approved HER2 directed therapies across all patients. These data suggest an underutilization of newer generation HER2-targeted therapies and a preference for older generation ones (i.e trastuzumab and pertuzumab). Likely indicating complex treatment decision making based off other genomic/biomarker results, clinical features, and previous treatment history.*

Conclusions

Although HER2 is expressed in multiple solid tumors and testing has increased dramatically, HER2-targeted therapies are only prescribed in 38% of patients and newer generation HER2-targeted therapies are not frequently utilized. The most administered therapy was pertuzumab+trastuzumab (52%) followed by trastuzumab (25%), and trastuzumab deruxtecan (6.3%) Future research will focus on how HER2 scoring (breast vs. gastric), HER2 testing methodologies (i.e. – IHC vs. ISH), and biomarkers (i.e. CGP) may influence treatment decisions.

References:

Stuhlmiller, T. J., Rabe, A., Rapp, J., Awawda, A., Kouser, H., Lui, K., Salamon, H., Chuyka, D., Mahoney, W., Furgason, J. M., Paul, M., Scarpa, F. J., Kesari, S., Newton, M., Wong, K. K., Kramer, G. A., & Shapiro, M. A. (2025). A scalable method for validated data extraction from electronic health records with large language models. medRxiv. https://doi.org/10.1101/2025.02.25.25322898

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