e-Poster #4005

Human epidermal growth factor receptor 2 expression across multiple solid tumor types: Insights from the ESPERANZA program

François Bocquet[1]; Heide Stirnadel-Farrant[2]; Georgie Weston[3]; Abdennour Ferhat[4]; David Chiu; Anuj Bhupendra Shah[5]; Lirong Zhang[6]; Adam Brown[7]; Kristen Sarlo[8]; Gregory Anagnostos[9]; Laura Girardat-Rotar[10]; Astrid Nardecchia[11]; Briana Coles[11]; Deolinda Sousa Pereira[12]; Nicolas Girard[13]; Remco Jan Geukes Foppen[14]; Nicolas Orsi[15], Albrecht Stenzinger[16]

[1]Institut de Cancérologie de l'Ouest, Angers, France; [2]AstraZeneca, Oncology Outcomes Research, UK; [3] AstraZeneca, Health Economics and Payer Evidence, United Kingdom; [4]AstraZeneca, Global Medical Affairs, UK; [5]AstraZeneca, Oncology Outcomes Research, US; [6]Daiichi Sankyo Global Oncology Marketing Access & Pricing (GOMAP) Germany; [7]Daiichi Sankyo Global Medical Affairs, Precision Medicine USA; [8]Daiichi Sankyo Global Medical Affairs, New Jersey, USA; [9]AstraZeneca Oncology Biometrics, South San Francisco, CA, USA; [10]IQVIA AG Switzerland; [11]IQVIA Ltd United Kingdom; [12]Portuguese Oncology Institute of Porto, Portugal; [13]Institut Curie, Paris, France; [14]Scientific Director Office, IRCCS Regina Elena National Cancer Institute, Rome, Italy; [15]Leeds Teaching Hospitals NHS Trust, UK; [16]Thoraxklinik am Universitätsklinikum Heidelberg, Germany

Objective

- To characterize the distribution of human epidermal growth factor receptor 2 (HER2) expression by immunohistochemistry (IHC) status across multiple advanced solid tumor types using archived tumor samples from the ESPERANZA (Epidemiological Study Assessing HER2 Status Across Solid Tumors) study (NCT06973161).

Conclusions

- HER2 expression differed across solid tumor types, with the highest distribution of HER2-positive (IHC 2+/3+) tumors identified in bladder cancer, non-small cell lung cancer (NSCLC), and endometrial cancer.
- HER2 expression of clinically relevant magnitude is observed across many solid tumors, supporting its role as an actionable biomarker in HER2-targeted therapies in the tumor-agnostic setting.
- These findings support broader consideration of HER2 testing in patients with advanced solid tumors to identify those who may be eligible for HER2-directed treatment strategies.

Acknowledgments

Under the guidance of the authors and in accordance with Good Publication Practice, medical writing and editorial support was provided by Smitha Sreedharan, PhD, of IQVIA and was funded by AstraZeneca and Daiichi Sankyo.

Other participating sites: Fondazione Policlinico Universitario Agostino Gemelli (Italy); Charité Comprehensive Cancer Center, Frankfurt University Hospital (Germany); Hospital 12 Octubre, Hospital Arnau de Vilanova, Clínica Universidad de Navarra, Hospital de la Santa Creu i Sant Pau (Spain); The Clatterbridge Cancer Centre, University College London Hospital (UK); Rigshospitalet (Denmark); BC Platforms (France); Guardian Research Network, Gundersen Medical Foundation (USA); London Health Sciences Centre Research Institute (Canada)

Disclosures

François Bocquet has no conflict of interests to declare.

Introduction

- HER2 overexpression occurs across multiple solid tumors beyond breast and gastric cancers.[1,2]
- Trastuzumab deruxtecan (T-DXd) is approved in multiple countries for unresectable/metastatic HER2+ (immunohistochemistry [IHC 3+]) solid tumors that have progressed after prior treatment and/or without alternative therapy options. [3-5]
- Real-world data describing the distribution of HER2 expression (IHC 0, IHC 1+, IHC 2+, and IHC 3+) across solid tumors remain limited.

Methods

Study Design

- This retrospective observational analysis used data from the ESPERANZA study (NCT06973161), which assessed archived tumor samples for HER2 expression across multiple tumor types.
- HER2 expression was assessed in all archived samples across multiple tumor types using HER2 IHC scores.
- Samples were archived between Jan 2017 and Dec 2022 from patients with advanced, unresectable, or metastatic disease who initiated second-line or later therapy.[6-8]
- Data source: Validated pathology services were available through participating sites/networks in Denmark [1], France [7], Germany [3], Italy [2], Portugal [1], Spain [4], United Kingdom (UK) [3], and US [2].
- Samples were analyzed by local testing in Europe and central testing in the US. HER2 IHC testing used validated assays, followed a harmonized global protocol, and was scored using the American Society of Clinical Oncology (ASCO)/College of American Pathologists (CAP) gastric scoring criteria.[9]

Statistical Analyses

- For patients with more than one test, the assessment closest to and before the index date was used to estimate tumor-specific IHC score distributions (0, 1+, 2+, 3+, or indeterminate) and corresponding 95% CIs.

Results

Table 1. HER2 expression profile by solid tumor type based on IHC score assessment

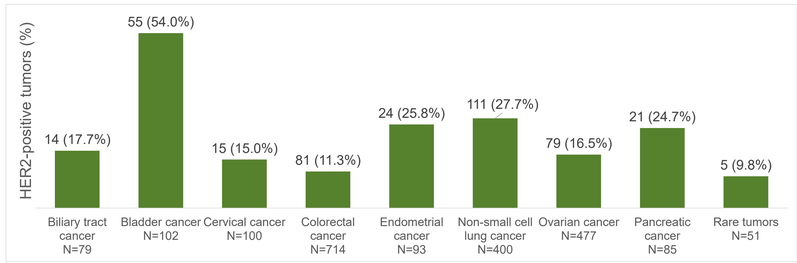
IHC Score	Biliary tract cancer N=79	Bladder cancer N=102	Cervical cancer N=100	Colorectal cancer N=714	Endometrial cancer N=93	Non-small cell lung cancer N=400	Ovarian cancer N=477	Pancreatic cancer N=85	Rare tumors N=51
IHC 0	49 (62.0%)	33 (32.4%)	78 (78.0%)	505 (70.7%)	47 (50.5%)	178 (44.5%)	271 (56.8%)	49 (57.6%)	32 (62.7%)
IHC 1+	10 (12.7%)	14 (13.7%)	7 (7.0%)	116 (16.2%)	20 (21.5%)	88 (22.0%)	124 (26.0%)	7 (8.2%)	9 (17.6%)
IHC 2+	11 (13.9%)	38 (37.3%)	11 (11.0%)	68 (9.5%)	21 (22.6%)	86 (21.5%)	67 (14.0%)	21 (24.7%)	3 (5.9%)
IHC 3+	3 (3.8%)	17 (16.7%)	4 (4.0%)	13 (1.8%)	3 (3.2%)	25 (6.2%)	12 (2.5%)	0 (0%)	2 (3.9%)
Indeterminate*	6 (7.6%)	0 (0%)	0 (0%)	12 (1.7%)	2 (2.2%)	23 (5.8%)	3 (0.6%)	8 (9.4%)	5 (9.8%)

*Indeterminate category included patients whose HER2 status could not be definitively classified as IHC 0, 1+, 2+, or 3+, potentially due to insufficient tissue for successful testing or inadequate sample quality for definitive biomarker testing.
All values in the table are presented as n (%).
HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry

Sample disposition

- A total of 2,101 samples were processed across nine tumor types.
- Valid HER2 IHC results were available for 97.2% (n=2,042) of samples, and 2.8% (n=59) of samples yielded indeterminate HER2 results. *In situ* hybridization (ISH) was not performed.
- Samples were predominantly obtained from Europe (79.9%), with 20.1% originating from North America.
- Most HER2 assessments were conducted on excisional biopsy (resection) (50.7%; n=1,066) or incisional biopsy (46.7%; n=981) samples, with minimal missing sample-type data (2.6%; n=54).
- HER2 testing was primarily conducted using the Roche Ventana 4B5 and HercepTest Dako assays, representing 61.6% (n=1,294) and 24.7% (n=518) of tests, respectively.

Figure 1. HER2 positivity (IHC 2+ & 3+) across tumor types



HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry

HER2 expression across different tumor types

- HER2 expression was identified across all tumor types evaluated, with substantial variability in distribution.
- Bladder cancer showed the highest prevalence of HER2 IHC 3+ (16.7%) followed by NSCLC which also demonstrated relatively high rates of IHC 3+ (6.2%).
- Among HER2-positive tumors (IHC 2+ & IHC 3+), the highest percentages were observed in bladder cancer (54.0%), followed by NSCLC (27.7%), endometrial cancer (25.8%) and pancreatic cancer (24.7%) (Figure 1).

Discussion

- HER2 IHC3+ frequency was broadly consistent across most tumor types and aligned closely with estimates reported in a large real-world cohort by Bryant et al.,[10] the largest absolute differences were observed in NSCLC (+4.3% [6.2% in current study vs.1.9% in Bryant et al]) and bladder cancer (+2.8% [16.7% in current study vs.13.9% in Bryant et al]).
- The observed differences in NSCLC and bladder cancer may reflect variations in cohort characteristics and testing practices, including geographical representation, sample collection timing, single-site versus multicenter testing, HER2 scoring variability in non-breast/non-gastric tumors, tumor heterogeneity, and assay use.

References

1. Ecaterina E, et al. Targeting ERBB2 (HER2) amplification identified by next-generation sequencing in patients with advanced or metastatic solid tumors beyond conventional indications. JCO Precis Oncol. 2019;3:1–12.
2. Cheng X, et al. A comprehensive review of HER2 in cancer biology and therapeutics. Genes (Basel). 2024;15(7):903.
3. FDA, FDA grants accelerated approval to fam-trastuzumab deruxtecan-nxki for unresectable or metastatic HER2-positive solid tumors. May 2024. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-fam-trastuzumab-deruxtecan-nxki-unresectable-or-metastatic-her2
4. EMA, Enhertu (trastuzumab deruxtecan). June 2026. https://www.ema.europa.eu/en/documents/overview/enhertu-epar-medicine-overview_en.pdf
5. ENHERTU® Approved in Japan as First Tumor Agnostic HER2 Directed Medicine for Previously Treated Patients with HER2 Positive Metastatic Solid Tumors. March 2026. https://www.daiichisankyo.com/files/news/pressrelease/pdf/202603/20260323_E2.pdf
6. Meric-Bernstam F, et al. Efficacy and safety of trastuzumab deruxtecan in patients with HER2-expressing solid tumors (DESTINY-PanTumor02): a phase 2, multicentre, open-label study. Lancet Oncol. 2024;25(8):1103–1115.
7. Yoshino T, et al. Trastuzumab deruxtecan in patients with HER2-expressing metastatic colorectal cancer (DESTINY-CRC02): primary and updated analyses. Nat Med. 2023;29:299–307.
8. Li BT, et al. Trastuzumab deruxtecan in HER2-mutant non-small-cell lung cancer. N Engl J Med. 2022;386:241–251.
9. Bartley AN, et al. HER2 testing and clinical decision making in gastroesophageal adenocarcinoma: Guideline from the CAP, ASCP, and the ASCO. J Clin Oncol. 2017;35(4):446-464.
10. Bryant D, et al. A real-world experience in pan-tumor testing for HER2 IHC in more than 65,000 solid tumors. JAMA Oncol. 2025;11(8):919–921.

This study was sponsored by AstraZeneca and 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).
Presented as an ePoster at ESMO 2026. Corresponding author: Anuj Bhupendra Shah; anuj.shah@astrazeneca.com