ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESMO OPEN SCIENCE FOR OPTIMAL CANCER CARE

ORIGINAL ARTICLE

Global prevalence of FGFR2b protein overexpression in advanced gastric cancer and gastroesophageal junction cancers: pooled analysis of two bemarituzumab phase III studies

S. B. Maron[1*], R.-H. Xu[2], Z. A. Wainberg[3], S. Y. Rha[4], Y. Zhang[5], F. Pietrantonio[6], S. C. S. Oliveira[7], Y. Li[8], M.-H. Chen[9], K. Korphaisarn[10], E. Elimova[11], C. A. Calderon[12], F. V. Herpe[13,14], W. P. Yong[15], T. M. Dos Santos[16], M. Tan[17], K. Isse[16], R. E. Yanes[16] & K. Shitara[18]

[1]Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, USA; [2]Department of Medical Oncology, Sun Yat-sen University Cancer Center, Guangdong, China; [3]Division of Hematology and Oncology, David Geffen School of Medicine at UCLA, Los Angeles, USA; [4]Department of Internal Medicine, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea; [5]Department of Gastrointestinal Medical Oncology, Harbin Medical University Cancer Hospital, Harbin, Heilongjiang, China; [6]Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [7]Department of Medical Oncology, Liga Norte-Riograndense Contra O Cancer, Natal, Brazil; [8]Department of Medical Oncology, Guangxi Medical University Cancer Hospital, Nanning, China; [9]Department of Oncology, Taipei Veterans General Hospital, Taipei, Taiwan; [10]Division of Medical Oncology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand; [11]Department of Medicine, Princess Margaret Cancer Centre, Toronto, Canada; [12]Department of Oncology, Fundacion Cardiovascular de Colombia, Colombia; [13]Gastrointestinal Oncology Department, University Hospitals Gasthuisberg, Leuven; [14]University of Leuven, Leuven, Belgium; [15]Department of Haematology-Oncology, National University Hospital, Singapore; [16]Amgen Inc., Thousand Oaks; [17]Amgen Inc., South San Francisco, USA; [18]Department of Gastrointestinal Oncology, National Cancer Center Hospital East, Kashiwa, Japan

Available online 26 May 2026

Background: Fibroblast growth factor receptor 2 isoform IIIb (FGFR2b) protein overexpression is an emerging biomarker and a potential therapeutic target in gastric and gastroesophageal junction cancers (G/GEJC). Limited data exist on the global prevalence of FGFR2b overexpression in advanced G/GEJC using a validated assay. We assessed the prevalence of FGFR2b protein overexpression in a pooled analysis of tumor samples collected as part of the prescreening process for two global phase III studies of bemarituzumab as first-line treatment for locally advanced or metastatic G/GEJC.

Materials and methods: As of 20 February 2025, 7910 tumor samples from patients prescreened for enrollment in the FORTITUDE-101 (NCT05052801; $n = 3752$) and FORTITUDE-102 (NCT05111626; $n = 4158$) studies were centrally tested for FGFR2b protein overexpression by immunohistochemistry (IHC) and had evaluable results. FGFR2b overexpression was defined as both any percentage (>0%) of tumor cells (TCs) and ≥10% of TCs exhibiting moderate (2+) to strong (3+) membrane staining of FGFR2b. Prevalence was analyzed across defined patient and sample characteristics.

Results: The estimated prevalence of FGFR2b any 2+/3+ was 36.5% [95% confidence interval (CI) 35.4-37.6; 2887/7910] and that of FGFR2b ≥10% 2+/3+ was 16.6% (95% CI 15.7-17.4; 1310/7910). Prevalence estimates from this pooled analysis and a separate analysis for FORTITUDE-102 [any 2+/3+: 35.8% (95% CI 34.3-37.2); FGFR2b ≥10% 2+/3+: 17.3% (95% CI 16.1-18.4)] were consistent with results previously reported for FORTITUDE-101 (Rha SY, Zhang Y, Elme A, et al. Prevalence of FGFR2b protein overexpression in advanced gastric cancers during prescreening for the phase III FORTITUDE-101 trial. *JCO Precis Oncol*. 2025;9:e2400710). FGFR2b prevalence was consistent across patient and sample characteristics [age, sex, collection method (biopsy versus resection), collection site, location of primary tumor, and geographic region].

Conclusion: This study represents the largest prevalence assessment of FGFR2b overexpression in G/GEJC using a validated IHC assay. The observed estimates of 36.5% (any 2+/3+) and 16.6% (FGFR2b ≥10% 2+/3+) suggest that FGFR2b is prevalent in a meaningful proportion of patients with advanced G/GEJC.

Key words: biomarker, fibroblast growth factor receptor 2 isoform IIIb, gastric cancer, gastroesophageal junction cancer, immunohistochemistry

*Correspondence to: Steven Maron, MD, MSc, Memorial Sloan Kettering Cancer Center, 300 E 66th Street, Suite 1033, New York, NY 10065, USA. Tel: 646-888-6780

E-mail: marons@mskcc.org (S. B. Maron).

2059-7029/© 2026 The Authors. Published by Elsevier Ltd on behalf of European Society for Medical Oncology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

INTRODUCTION

Gastric cancer, including gastroesophageal junction cancer (G/GEJC), represents the fifth most prevalent malignancy and the fifth leading cause of cancer-related mortality with widely varying incidence globally.[1,2] The incidence rates of

Downloaded for Anonymous User (n/a) at Yonsei University College of Medicine from ClinicalKey.com by Elsevier on July 15, 2026. For personal use only. No other uses without permission. Copyright ©2026. Elsevier Inc. All rights reserved.

G/GEJC are markedly higher in Asia and certain regions of Europe than in Africa and North America, where the rates are relatively low.[2] Systemic chemotherapy comprising platinum- and fluoropyrimidine-based combinations is accepted worldwide as standard first-line treatment for metastatic G/GEJC; however, this treatment has yielded modest benefits with a median overall survival (OS) of <1 year.[3-6] Current progress in better understanding of the molecular profile of G/GEJC has led to the identification of several tumor biomarkers [human epidermal growth factor receptor 2 (HER2), microsatellite instability (MSI) status, programmed death-ligand 1 (PD-L1), and claudin-18 isoform 2 (CLDN18.2)] that are predictive of treatment efficacy and have proven to be effective therapeutic targets for G/GEJC.[7] Combining chemotherapy with biomarker-directed targeted therapies and/or antiprogrammed death 1 (PD-1)/anti—PD-L1 agents has shown meaningful benefit in G/GEJC.[8-13] Despite these advancements, major unmet needs persist, with limited effective treatments conferring a significant OS benefit.

Bemarituzumab is a first-in-class, humanized monoclonal antibody specific to human fibroblast growth factor receptor 2b (FGFR2b; the IIIb splice isoform of FGFR2), which is an emerging biomarker frequently overexpressed in advanced G/GEJC.[14-16] Data from the global, randomized, phase II FIGHT study reported clinically meaningful improvements in efficacy with first-line bemarituzumab plus chemotherapy versus chemotherapy in patients with FGFR2b-overexpressing [moderate (2+) to strong (3+) membrane staining by immunohistochemistry (IHC) in any percent of tumor cells (TC)], non—HER2-positive, advanced G/GEJC, with enhanced benefits in FGFR2b ≥10% 2+/3+ patients.[14,17] These data informed the design of the phase III FORTITUDE-101 (NCT05052801) and FORTITUDE-102 (NCT05111626) studies of bemarituzumab, in which patients with FGFR2b-overexpressing, non—HER2-positive, advanced G/GEJC were enrolled.

The FIGHT study was the first to prospectively enroll FGFR2b-selected patients using tumor tissue IHC and reported a 29% prevalence of FGFR2b any 2+/3+ overexpression in advanced G/GEJC, which is substantially higher than that reported in previous retrospective studies (2.5%-4.9%) that employed different testing methods.[14,18-20] Given the paucity of robust data on the global prevalence of FGFR2b overexpression in G/GEJC, there is a critical need for understanding the prevalence of this biomarker in a global advanced G/GEJC population to optimize patient selection and treatment outcomes.

In a recent analysis, we utilized data from patients with advanced G/GEJC who were prescreened as part of determining eligibility for the FORTITUDE-101 study to assess the prevalence estimates of FGFR2b protein overexpression.[16] The estimated prevalence of FGFR2b any 2+/3+ was 37.8% [95% confidence interval (CI) 36.2-39.3] and that of FGFR2b ≥10% 2+/3+ was 16.2% (95% CI 15-17.4).[16] In this analysis, we pooled data from patients prescreened for FORTITUDE-101 and FORTITUDE-102 with the objective of assessing the prevalence of FGFR2b overexpression in the largest advanced G/GEJC dataset to date using a validated assay.

MATERIALS AND METHODS

Trials and patients

The population for this pooled analysis comprised patients prescreened for FGFR2b protein overexpression before screening for enrollment in the global phase III FORTITUDE-101 and FORTITUDE-102 studies (Supplementary Figure S1, available at https://doi.org/10.1016/j.esmoop.2026.107698). There was sufficient homogeneity of study methodologies and populations to enable pooling data from prescreened patients from the two studies. Both studies had a randomized, double-blind, placebo-controlled design and were conducted in the first-line setting for locally advanced or metastatic G/GEJC. FORTITUDE-101 was designed to assess the efficacy and safety of bemarituzumab plus chemotherapy [modified 5-fluorouracil, leucovorin, and oxaliplatin (mFOLFOX6)] versus placebo plus mFOLFOX6. FORTITUDE-102 assessed bemarituzumab plus chemotherapy plus nivolumab versus placebo plus chemotherapy plus nivolumab. The chemotherapy regimen for FORTITUDE-102 was either mFOLFOX6 or capecitabine and oxaliplatin, which was determined by the investigator before randomization. Eligible patients for both FORTITUDE-101 and FORTITUDE-102 were adults with unresectable, locally advanced, or metastatic gastric or gastroesophageal junction adenocarcinoma that exhibited FGFR2b overexpression and had no known positivity for HER2 and who had not received prior treatment for unresectable or metastatic disease. FGFR2b overexpression was defined as both any percentage (>0%) of TC (FGFR2b any 2+/3+) and ≥10% of TC (FGFR2b ≥10% 2+/3+) exhibiting moderate (2+) to strong (3+) membrane staining by IHC, whereas nonneoplastic gastric epithelium has no FGFR2b positivity. During study conduct, eligibility criteria for both studies were amended to include only patients with FGFR2b ≥10% 2+/3+ membrane-positive tumors.

FGFR2b status was confirmed centrally at prescreening using IHC on a tumor sample {either archival [within 6 months/180 days before signing prescreening informed consent at a central laboratory (Q2 Solutions)] or fresh biopsy}. Patients with FGFR2b overexpression in FORTITUDE-101 during prescreening were eligible to enter screening for FORTITUDE-102 and vice versa. Prescreening samples to assess FGFR2b status were taken from patients across 42 countries. Study designs are shown in Supplementary Figure S1 available at https://doi.org/10.1016/j.esmoop.2026.107698.

All patients in both studies provided written informed consent at prescreening and before enrollment. The study protocols and its amendments were approved by an independent ethics committee or institutional review board at each site. These trials were conducted in accordance

Downloaded for Anonymous User (n/a) at Yonsei University College of Medicine from ClinicalKey.com by Elsevier on July 15, 2026. For personal use only. No other uses without permission. Copyright ©2026. Elsevier Inc. All rights reserved.

with the Good Clinical Practice guidelines and Declaration of Helsinki.

FGFR2b IHC

Tissue specimens were fresh or archived formalin-fixed, paraffin-embedded tissue. FGFR2b protein expression was determined by an automated IHC test [VENTANA FGFR2b (FPR2-D) RxDx Assay (for investigational use only) (Roche Diagnostics, Tucson, AZ)] developed by Ventana Medical Systems, Inc (Tucson, AZ), using the anti-FGFR2b clone FPR2-D (which is specific for the "IIIb" isoform of the FGFR2 protein) on a BenchMark ULTRA IHC/ISH System.[21] Percentages of membranous TC staining at 1+ and 2+/3+ were visually estimated by board-certified pathologists using a microscope. FGFR2b protein overexpression was defined as any FGFR2b 2+ or 3+ staining of TC (FGFR2b any 2+/3+); the FGFR2b ≥10% subgroup included tumor samples that exhibited FGFR2b 2+ or 3+ staining in ≥10% of TC (FGFR2b ≥10% 2+/3+).

Statistical analysis

FGFR2b prevalence was summarized by the evaluable sample size (*N*), number of positive cases (*n*), and point estimate of prevalence (*n*/*N*). A two-sided 95% CI was calculated using the Wald method. All analyses were carried out using R version 4.2.3.

RESULTS

Patients

In total, 3752 patient tumor samples in FORTITUDE-101 and 4158 patient tumor samples in FORTITUDE-102 were assessed during prescreening for FGFR2b protein overexpression at any % moderate (2+) to strong (3+) membrane staining by IHC and ≥10% 2+/3+ TC positivity and had evaluable results (*N* = 7910 in the pooled analysis). The data cutoff for this pooled analysis was 20 February 2025. Baseline demographics and characteristics of prescreened patients with evaluable FGFR2b IHC results are shown in Table 1. Overall, 67.8% of patients were male. Around half of the population was from Asia-Pacific (APAC; 54.3%), followed by Europe, the Middle East, and Africa (EMEA; 31.0%), with the remainder being from Latin America (10.5%) or the United States (US)/Canada (4.2%). Differences in the proportion of samples per geographic

Table 1. Patient and sample characteristics for the pooled population

Characteristics, *n* (%)	Patients (*N* = 7910)
Sex	
Female	2548 (32.2)
Male	5362 (67.8)
Region	
APAC excluding Mainland China	1834 (23.2)
Mainland China	2461 (31.1)
EMEA	2449 (31.0)
Latin America	832 (10.5)
USA/Canada	334 (4.2)
Age, years	
<65	4235 (53.5)
≥65	3675 (46.5)
Tissue collection site	
Metastatic site	1259 (15.9)
Primary site	6651 (84.1)
Tissue collection method	
Biopsy	7159 (90.5)
Resection	722 (9.1)
Unknown	29 (0.4)
Location of primary tumor	
GC	5622 (71.1)
GEJC	1226 (15.5)
Unspecified[a]	1062 (13.4)

APAC, Asia-Pacific; EMEA, Europe, Middle East, and Africa; GC, gastric cancer; GEJC, gastroesophageal junction cancer; USA, United States of America.
[a]Unspecified includes both GC and GEJC.

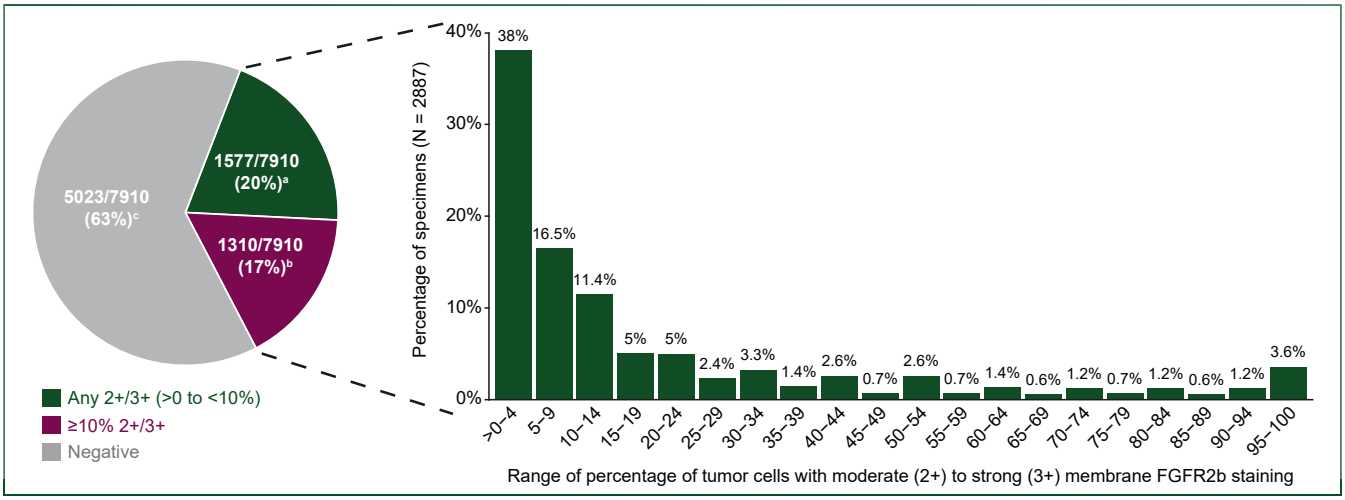

Figure 1. FGFR2b protein overexpression in advanced G/GEJC. The pie chart shows the prevalence of FGFR2b protein overexpression (2+/3+ membrane staining by IHC) in the pooled population. The bar graph shows the distribution of FGFR2b expression (moderate-to-strong membrane staining).
[a]19.9% (95% CI 19.1-20.8).
[b]16.6% (95% CI 15.7-17.4).
[c]63.5% (95% CI 62.4-64.6).
CI, confidence interval; FGFR2b, fibroblast growth factor 2 isoform IIIb; G/GEJC, gastric and gastroesophageal junction cancer; IHC, immunohistochemistry.

Downloaded for Anonymous User (n/a) at Yonsei University College of Medicine from ClinicalKey.com by Elsevier on July 15, 2026. For personal use only. No other uses without permission. Copyright ©2026. Elsevier Inc. All rights reserved.

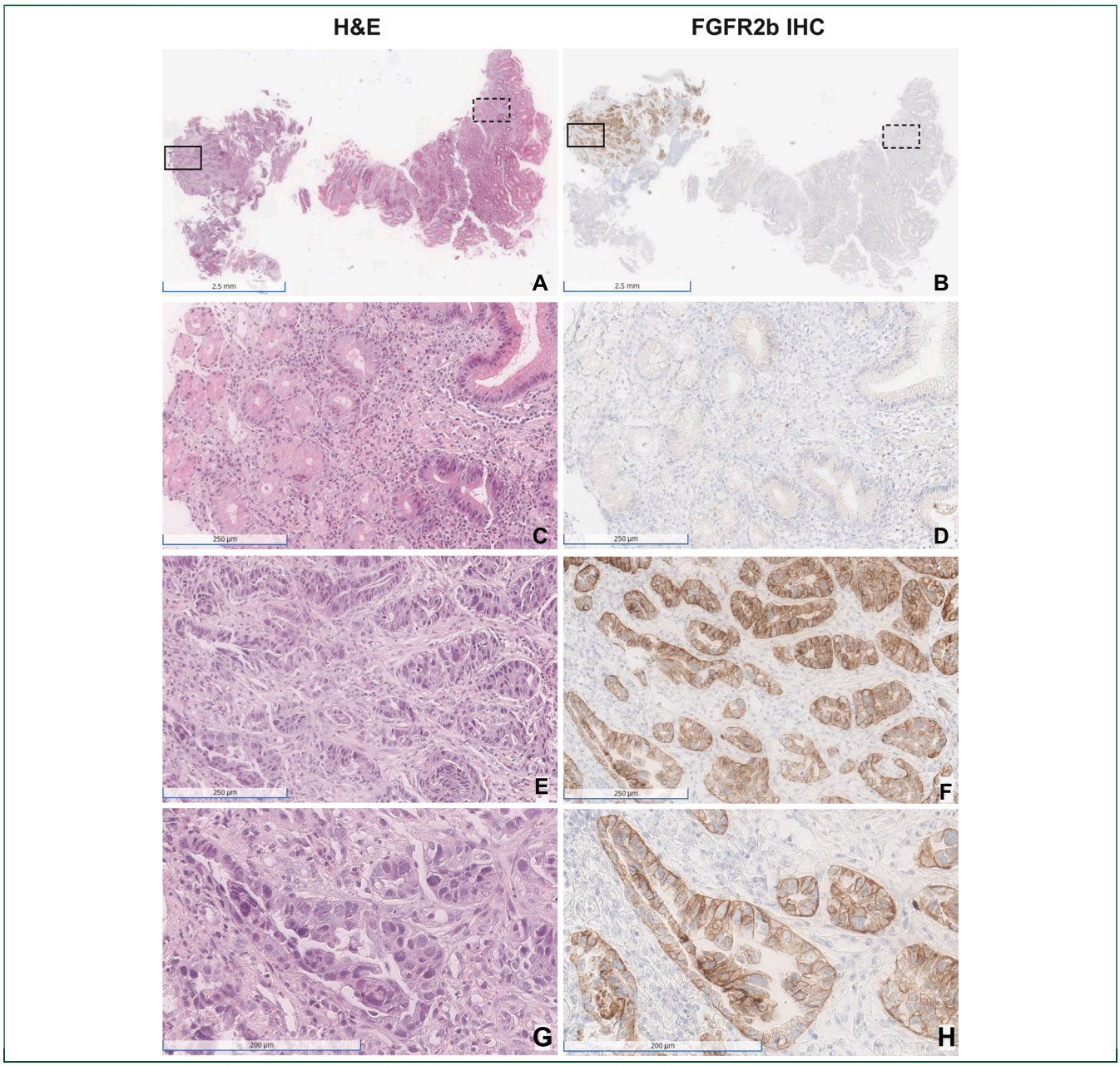

Figure 2. A biopsy sample from advanced G/GEJC. (A, C, E, G): H&E; (B, D, F, H): FGFR2b IHC staining. (A, B) 1x magnification. Right piece contains nonneoplastic tissue, and the left piece contains neoplastic tissue. Dashed box (nonneoplastic) is magnified in panels C and D. Solid box (neoplastic) is magnified in panels E and F. (C, D) 10x magnification. Nonneoplastic gastric epithelial cells are negative for FGFR2b IHC. (E, F) 10x magnification. Intestinal-type gastric adenocarcinoma shows a membranous FGFR2b-positive staining pattern. (G, H) 20x magnification. Membrane staining may be partial, such as basal-lateral and basal only patterns in the field of view. Intensity varies from weak, moderate, to strong.
FGFR2b, fibroblast growth factor 2 isoform IIIb; G/GEJC, gastric and gastroesophageal junction cancer; H&E, hematoxylin and eosin; IHC, immunohistochemistry.

region reflect the relative volume of prescreening that occurred in countries participating in the studies. The proportions of patients aged <65 and ≥65 years were 53.5% and 46.5%, respectively. Most tumor samples were collected from the primary tumor (84.1% versus 15.9% from a metastatic site) and were collected as biopsies (90.5% versus 9.1% as tumor resection). Among the prescreened patients with evaluable FGFR2b IHC results, 71.1% had GC, 15.5% had GEJC, and 13.4% had no tumor location specified.

Prevalence of FGFR2b protein overexpression

In the pooled analysis, 2887 of 7910 [36.5% (95% CI 35.4-37.6)] tumor samples tested positive for FGFR2b any 2+/3+ as shown in the pie chart in Figure 1. The subset of patients whose tumors displayed FGFR2b ≥10% 2+/3+ accounted for 1310 of the 7910 patients in the total evaluable population [16.6% (95% CI 15.7-17.4)], which represents 45.4% of the 2887 patients who tested positive for FGFR2b any 2+/3+ (Figure 1A). The bar graph in Figure 1 shows the distribution of FGFR2b overexpression.

Downloaded for Anonymous User (n/a) at Yonsei University College of Medicine from ClinicalKey.com by Elsevier on July 15, 2026. For personal use only. No other uses without permission. Copyright ©2026. Elsevier Inc. All rights reserved.

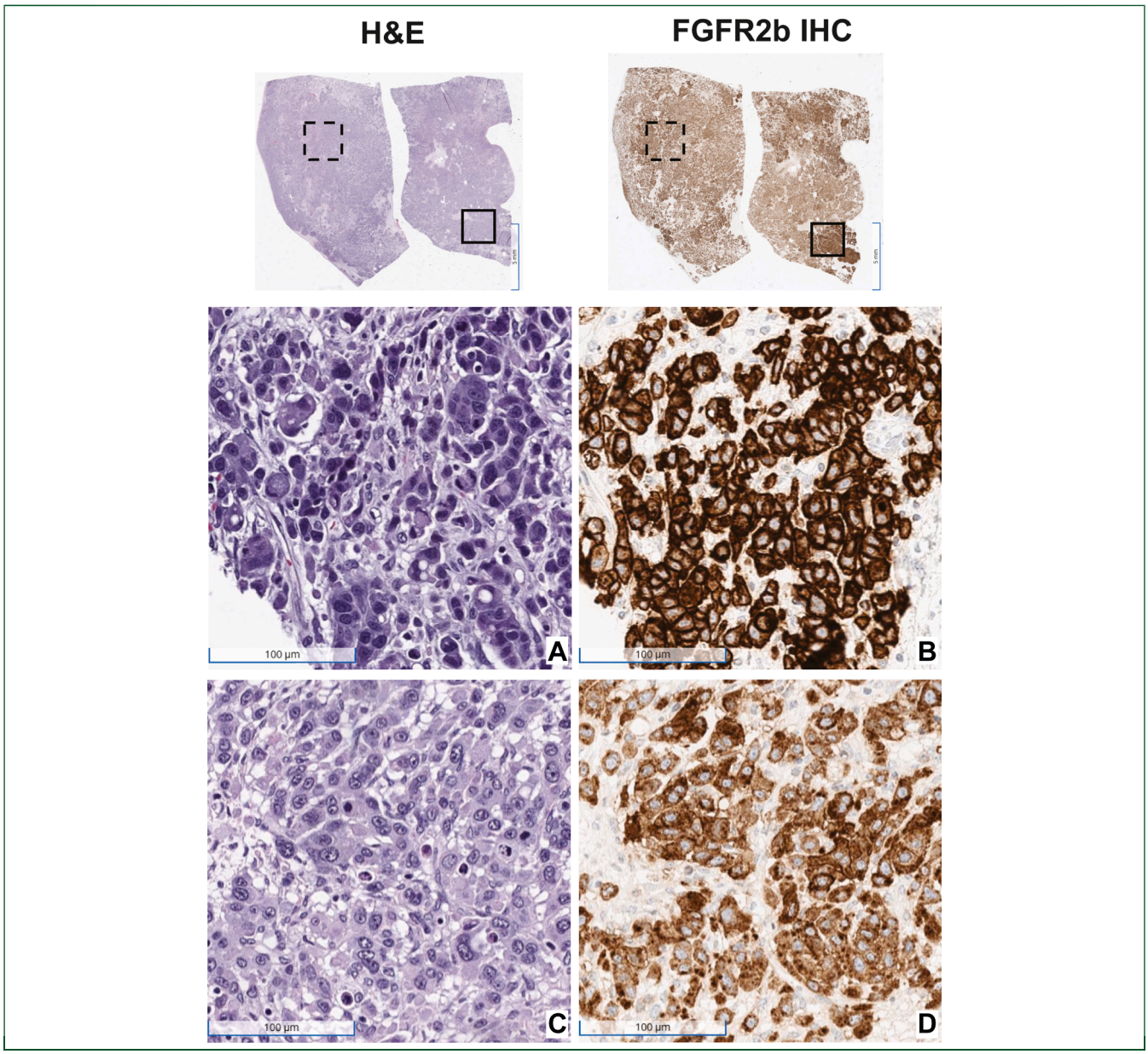

Figure 3. A surgical resection sample from advanced G/GEJC. Top images are low magnification, illustrating the locations of magnified images of panels A-D. (A, C) H&E, (B, D) FGFR2b IHC; (A, B) solid boxes: diffusely invading carcinoma cells with strong membrane staining. (C, D) dotted boxes: same morphological tumor cells with a cytoplasmic staining pattern that lacks definitive membrane staining.
FGFR2b, fibroblast growth factor 2 isoform IIIb; G/GEJC, gastric and gastroesophageal junction cancer; H&E, hematoxylin and eosin; IHC, immunohistochemistry.

Supplementary Figure S2, available at https://doi.org/10.1016/j.esmoop.2026.107698 (stacked bar graph), demonstrates the FGFR2b membrane staining across intensity levels in individual specimens, wherein a large proportion of TC was stained at 0 or 1+ staining intensity (negative and weak staining; 0 = gray, 1+ = light blue). Representative images of membrane staining in biopsy and surgical specimens are shown in Figures 2 and 3. The prevalence of FGFR2b any 2+/3+ and FGFR2b ≥10% 2+/3+ was consistent across patient and sample characteristic subgroups [age, sex, collection site, collection method (biopsy versus resection), location of primary tumor, and region; Figure 4].

FGFR2b prevalence estimates among patients prescreened for FORTITUDE-102 alone are comparable to those reported previously for FORTITUDE-101.[16] In FORTITUDE-102, 1488 of 4158 samples [35.8% (95% CI 34.3-37.2)] from patients tested positive for FGFR2b any 2+/3+ (Supplementary Figure S3, available at https://doi.org/10.1016/j.esmoop.2026.107698). The subset of patients whose tumors displayed FGFR2b ≥10% 2+/3+ accounted for 718 of the 4158 patients in the total evaluable population [17.3% (95% CI 16.1-18.4)], which represents approximately half of the 1488 patients that tested positive for FGFR2b any 2+/3+ (Supplementary Figure S3) available at https://doi.org/10.1016/j.esmoop.2026.107698.

Downloaded for Anonymous User (n/a) at Yonsei University College of Medicine from ClinicalKey.com by Elsevier on July 15, 2026. For personal use only. No other uses without permission. Copyright ©2026. Elsevier Inc. All rights reserved.

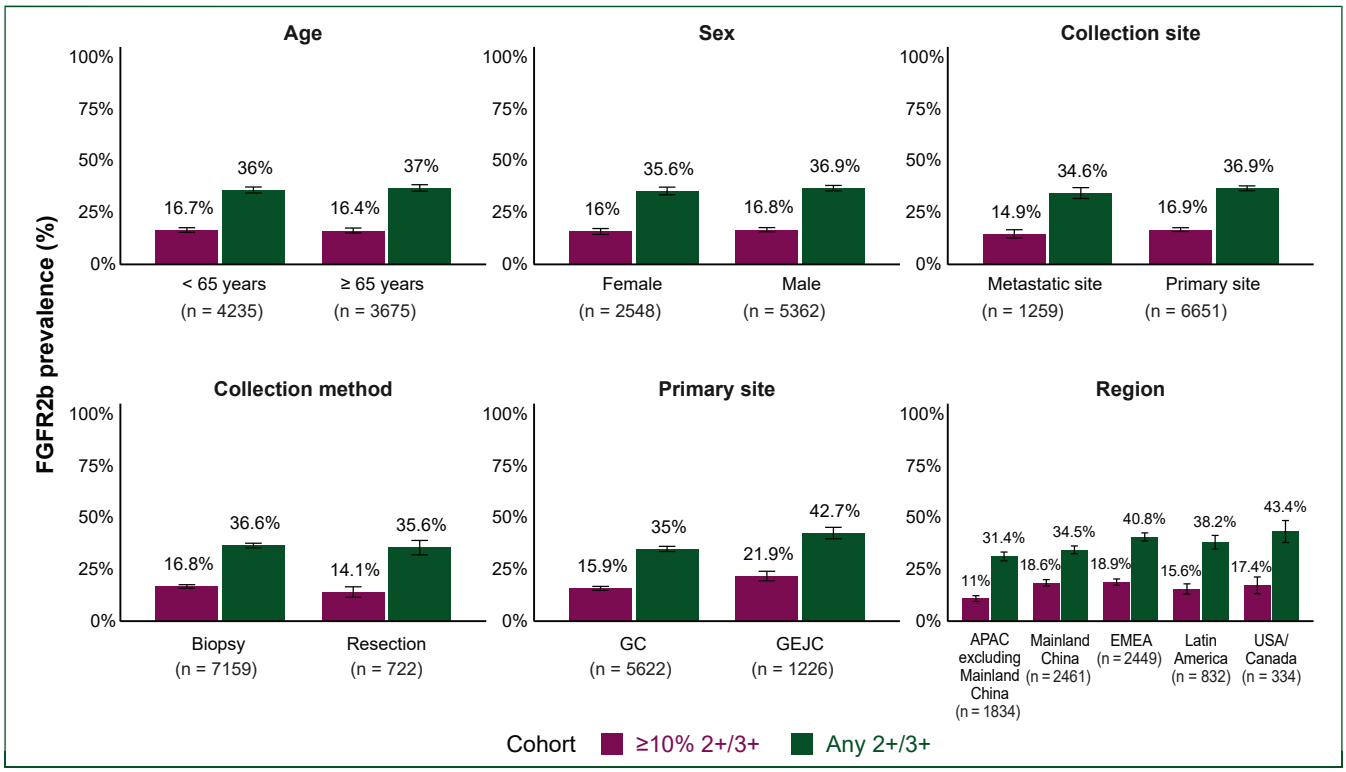

Figure 4. FGFR2b prevalence by patient and sample characteristic subgroups. FGFR2b prevalence at any 2+/3+ and at ≥10% 2+/3+ by patient and sample characteristic subgroups. Error bars represent 95% confidence intervals. Patients with unknown sample collection methods or unspecified indications were not included in the individual subgroup analysis.

APAC, Asia-Pacific; EMEA, Europe, Middle East, and Africa; FGFR2b, fibroblast growth factor 2 isoform IIIb; GC, gastric cancer; GEJC, gastroesophageal junction cancer; USA, United States of America.

DISCUSSION

In this pooled analysis of data from >7500 patients with advanced G/GEJC who were prescreened for the global phase III FORTITUDE-101 and FORTITUDE-102 studies, the estimated prevalence of FGFR2b any 2+/3+ was 36.5% (95% CI 35.4-37.6) and that of FGFR2b ≥10% 2+/3+ was 16.6% (95% CI 15.7-17.4) of the total evaluable population. These data represent robust estimates of the prevalence of FGFR2b protein overexpression among patients with advanced G/GEJC using a validated assay. Collectively, these data support that FGFR2b overexpression is a highly prevalent biomarker, according to this method, which may have important clinical implications for patients with HER2-negative advanced G/GEJC who face a poor prognosis and limited treatment options.

This analysis represents the largest global sample to date of patients with advanced G/GEJC to be prospectively assessed for FGFR2b status using a validated IHC assay through centralized testing. FGFR2b protein overexpression is an emerging biomarker and a potential therapeutic target in G/GEJC.[7,16] Outside of this effort, FGFR2b membrane overexpression has not been routinely assessed in G/GEJC clinical trials or in real-world practice, and there is a limited amount of published data describing its prevalence and potential prognostic impact. The prevalence of FGFR2b any 2+/3+ was 37.3% (95% CI 35.7-38.8; 1399/3752) in FORTITUDE-101, 35.8% (95% CI 34.3-37.2; 1488/4158) in FORTITUDE-102, and 36.5% (95% CI 35.4-37.6; 2887/7910) in the pooled analysis, demonstrating consistency across studies and robustness of the FGFR2b-detection methodology. Currently, there is no standardized assay for FGFR2b approved by health authorities for diagnostic purposes.

In the current studies, FGFR2b examination by IHC was focused on membrane expression. Observations at higher magnification were important to confirm true membrane staining. A pathologist evaluated each case to determine percentages of positive FGFR2b expression in whole tumor sections in an accurate and consistent manner. In addition, FGFR2b expression among prescreened patients showed variability in both staining intensity and distribution. Some specimens demonstrated low percentages of TC with moderate (2+) or strong (3+) membrane staining, whereas others exhibited uniformly strong staining intensity, highlighting the heterogeneity in expression of FGFR2b across assessed TC. A majority of the tumor FGFR2b-positive prescreened patients exhibited low levels of membrane staining, with 38% of specimens showing only >0%-4% of TC stained with moderate (2+) to strong (3+) intensity. Around 3.6% of specimens exhibited very high FGFR2b expression (2+/3+ staining in 95%-100% of TC), suggesting a heterogeneous expression pattern across TC.

Downloaded for Anonymous User (n/a) at Yonsei University College of Medicine from ClinicalKey.com by Elsevier on July 15, 2026. For personal use only. No other uses without permission. Copyright ©2026. Elsevier Inc. All rights reserved.

Although regional variation in FGFR2b overexpression was observed in both the ≥10% 2+/3+ cohort (11%-18.9%) and the any 2+/3+ cohort (31.4%-43.4%), data from FORTITUDE-101 and FORTITUDE-102 indicate consistent prevalence across countries with robust prescreening cohorts (>100 prescreened patients). Although differences in preanalytical variables (e.g. tissue preparation, collection method) may in part contribute to regional variability, comparable regional heterogeneity has been reported with other actionable biomarkers, including HER2 (10% to 56%), suggesting that geographic differences in tumor biology likely play an important role.[22-25] Further studies are warranted to better define regional prevalence patterns of FGFR2b overexpression.

The current actionable biomarkers in G/GEJC exhibit varying prevalence in global studies; examining biomarker overlap is an area of active interest to support future testing and combination treatment strategies.[9,26-36] Although this study was not designed to assess the extent of overlap of FGFR2b protein overexpression with other established GC biomarkers, a real-world study in a Japanese cohort has suggested limited overlap.[37] In that study by Sato et al,[37] FGFR2b prevalence estimates by IHC (FGFR2b any 2+/3+, 29%; FGFR2b ≥10% 2+/3+, 11%) using samples from 130 Japanese patients with advanced G/GEJC were generally similar to the estimates reported in the current study; the authors further reported limited overlap of FGFR2b overexpression with HER2, PD-L1, mismatch repair status, and Claudin 18 (clone 43-14A) expression. Future work examining biomarker overlap with FGFR2b in global studies is needed.

ACKNOWLEDGEMENTS

This study was funded by Amgen. Medical writing support was funded by Amgen Inc and was provided by Shubha Dastidar, PhD, CMPP (Cactus Life Sciences, part of Cactus Communications), Erica Sommermann, PhD (Amgen Inc), and Qais Al-Hadid, PhD (Amgen Inc). This research was funded in part through the NIH/NCI Cancer Center Support Grant P30CA008748 to MSK.

INFORMED CONSENT

All patients in both studies provided written informed consent at prescreening and before enrollment.

ETHICAL APPROVAL

The study protocols and its amendments were approved by an independent ethics committee or institutional review board at each site. These trials were conducted in accordance with the Good Clinical Practice guidelines and Declaration of Helsinki.

DATA SHARING STATEMENT

Because this study reports prescreening data rather than clinical trial data, there is no plan to share data.

FUNDING

This study was funded by Amgen Inc.

DISCLOSURES

SBM reports research support from AstraZeneca and Guardant Health; consulting fees from Amgen, Elevation Oncology, and Purple Oncology; SAB for Purple Oncology and OneCellDx; and equity options in OneCellDx. R-HX has served in a consulting or advisory role for Amgen, Merck-Serono, Roche, Astellas, AstraZeneca, Junshi, Hengrui, BeiGene, and CSPC. ZAW reports research grants from Bristol Myers Squibb (BMS) and Arcus and consulting fees from Amgen, Arcus, Astellas, AstraZeneca, BeOne, Daiichi, Bayer, BMS, Jazz, Merck, Ipsen, Gilead, Novartis, Alligator, Regeneron, Janssen, and Roche/Genentech. SYR reports consulting or advisory role at Amgen, Arcus Biosciences, Astellas Pharma, AstraZeneca, Daiichi Sankyo, Eisai, Indivumed, LG Chem, MSD Oncology, Ono Pharmaceutical, and Toray Industries; speaker's bureau fees from Amgen, Arcus Biosciences, Astellas Pharma, AstraZeneca, BMS/Ono, Daiichi Sankyo/UCB Japan, Eisai, and MSD Oncology; and research funding from Amgen (Inst), ASLAN Pharmaceuticals, Astellas Pharma, AstraZeneca, Bayer, BeiGene, BMS, Daiichi Sankyo, Eisai, Indivumed, Lilly, MSD Oncology, Roche/Genentech, Sillajen, and Zymeworks. FP reports receiving research funding (to Institution) from Lilly, BMS, Incyte, AstraZeneca, Amgen, Agenus, Rottapharm, Johnson&Johnson, GSK, Tempus, and BeOne; personal honoraria as an invited speaker from BeOne, Daiichi Sankyo, Seagen, Astellas, Ipsen, AstraZeneca, Servier, Bayer, Takeda, Johnson&Johnson, BMS, MSD, Amgen, Merck-Serono, Pierre-Fabre, Incyte, and AstraZeneca; advisory/consultancy from BMS, MSD, Amgen, Pierre-Fabre, Johnson&Johnson, Servier, Bayer, Takeda, Astellas, GSK, Daiichi Sankyo, Pfizer, BeOne, Jazz Pharmaceuticals, Incyte, Rottapharm, Merck-Serono, Italfarmaco, Gilead, AstraZeneca, Agenus, Revolution Medicine; and travel expenses from Amgen, Merck-Serono, Pierre-Fabre, Servier, Astellas, Incyte, and Johnson&Johnson.

KK reports research grants from Amgen, AstraZeneca, MSD, and Roche and speakers bureau fees from Amgen, AstraZeneca, BMS, Eisai, MSD, Roche, Taiho, and Servier.

EE reports research grants from Amgen, Arcus Biosciences, AstraZeneca Canada, Bold Therapeutics, BMS, Jazz Pharmaceuticals, and Zymeworks; consulting fees or other remuneration (payment) from AbbVie, Astellas Pharma, AstraZeneca, BeiGene, Signatera, and Viracta Therapeutics, Adaptimmune, BMS, Jazz Pharmaceuticals, Daiichi Sankyo, Roche, Amgen, and Zymeworks; has a family member employed by Merck Vaccines Steering Committee — Jazz and AstraZeneca. FVH reports research grants from Amgen, Astellas, and Roche Diagnostics and consulting fees or other remuneration (payment) from MSD, Merck, and Amgen. WPY reports consulting fees or other remuneration (payment) from Amgen, Astellas, AstraZeneca, BMS, Ipsen, and MSD; speakers bureau fees from Eisai, Merck, and Taiho. TMDS reports employee and stockholder at Amgen Inc. MT reports employee and stockholder at Amgen Inc. KI reports employee and stockholder at

Downloaded for Anonymous User (n/a) at Yonsei University College of Medicine from ClinicalKey.com by Elsevier on July 15, 2026. For personal use only. No other uses without permission. Copyright ©2026. Elsevier Inc. All rights reserved.

Amgen Inc. REY reports employee and stockholder at Amgen Inc. KS reports research grants at Astellas, Ono Pharmaceutical, Daiichi Sankyo, Taiho Pharmaceutical, Chugai, Merck Pharmaceutical, Amgen, Eisai, PRA Health Sciences, Syneos Health, AstraZeneca, PPD-SNBL K.K., and Toray; consulting fees or other remuneration (payment) at BMS, Takeda, Ono Pharmaceutical, Novartis, Daiichi Sankyo, Amgen, Boehringer Ingelheim, Merck Pharmaceutical, Astellas, Guardant Health Japan, Janssen, AstraZeneca, Zymeworks Biopharmaceuticals, ALX Oncology Inc., Bayer, GlaxoSmithKline K.K., HEALIOS K.K., Moderna. Inc, and Arcus Biosciences Inc.; and speakers bureau fees from BMS, Ono Pharmaceutical, Janssen, Eli Lilly, Astellas, and AstraZeneca. All other authors have declared no conflicts of interest.

REFERENCES

1. Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2024;74(3):229-263.
2. International Agency for Research on Cancer. GLOBOCAN 2022: stomach cancer fact sheet. Available at https://gco.iarc.who.int/media/globocan/factsheets/cancers/7-stomach-fact-sheet.pdf. Accessed April 4, 2026.
3. Lordick F, Carneiro F, Cascinu S, et al. Gastric cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. *Ann Oncol*. 2022;33(10):1005-1020.
4. Moehler M, Shitara K, Garrido M, et al. LBA6_PR Nivolumab (nivo) plus chemotherapy (chemo) versus chemo as first-line (1L) treatment for advanced gastric cancer/gastroesophageal junction cancer (GC/GEJC)/esophageal adenocarcinoma (EAC): first results of the CheckMate 649 study. *Ann Oncol*. 2020;31:S1191.
5. Smyth EC, Nilsson M, Grabsch HI, van Grieken NC, Lordick F. Gastric cancer. *Lancet*. 2020;396(10251):635-648.
6. Wagner AD, Syn NL, Moehler M, et al. Chemotherapy for advanced gastric cancer. *Cochrane Database Syst Rev*. 2017;8(8):Cd004064.
7. Sato Y, Okamoto K, Kawano Y, et al. Novel biomarkers of gastric cancer: current research and future perspectives. *J Clin Med*. 2023;12(14):4646.
8. Janjigian YY, Kawazoe A, Bai Y, et al. Pembrolizumab plus trastuzumab and chemotherapy for HER2-positive gastric or gastro-oesophageal junction adenocarcinoma: interim analyses from the phase 3 KEYNOTE-811 randomised placebo-controlled trial. *Lancet*. 2023;402(10418):2197-2208.
9. Janjigian YY, Shitara K, Moehler M, et al. First-line nivolumab plus chemotherapy versus chemotherapy alone for advanced gastric, gastro-oesophageal junction, and oesophageal adenocarcinoma (CheckMate 649): a randomised, open-label, phase 3 trial. *Lancet*. 2021;398(10294):27-40.
10. Rha SY, Oh DY, Yañez P, et al. Pembrolizumab plus chemotherapy versus placebo plus chemotherapy for HER2-negative advanced gastric cancer (KEYNOTE-859): a multicentre, randomised, double-blind, phase 3 trial. *Lancet Oncol*. 2023;24(11):1181-1195.
11. Shah MA, Shitara K, Ajani JA, et al. Zolbetuximab plus CAPOX in CLDN18.2-positive gastric or gastroesophageal junction adenocarcinoma: the randomized, phase 3 GLOW trial. *Nat Med*. 2023;29(8):2133-2141.
12. Shitara K, Lordick F, Bang YJ, et al. Zolbetuximab plus mFOLFOX6 in patients with CLDN18.2-positive, HER2-negative, untreated, locally advanced unresectable or metastatic gastric or gastro-oesophageal junction adenocarcinoma (SPOTLIGHT): a multicentre, randomised, double-blind, phase 3 trial. *Lancet*. 2023;401(10389):1655-1668.
13. Qiu MZ, Oh DY, Kato K, et al. Tislelizumab plus chemotherapy versus placebo plus chemotherapy as first line treatment for advanced gastric or gastro-oesophageal junction adenocarcinoma: RATIONALE-305 randomised, double blind, phase 3 trial. *BMJ*. 2024;385:e078876.
14. Wainberg ZA, Enzinger PC, Kang YK, et al. Bemarituzumab in patients with FGFR2b-selected gastric or gastro-oesophageal junction adenocarcinoma (FIGHT): a randomised, double-blind, placebo-controlled, phase 2 study. *Lancet Oncol*. 2022;23(11):1430-1440.
15. Xiang H, Chan AG, Ahene A, et al. Preclinical characterization of bemarituzumab, an anti-FGFR2b antibody for the treatment of cancer. *MAbs*. 2021;13(1):1981202.
16. Rha SY, Zhang Y, Elme A, et al. Prevalence of FGFR2b protein overexpression in advanced gastric cancers during prescreening for the phase III FORTITUDE-101 trial. *JCO Precis Oncol*. 2025;9:e2400710.
17. Wainberg ZA, Kang YK, Lee KW, et al. Bemarituzumab as first-line treatment for locally advanced or metastatic gastric/gastroesophageal junction adenocarcinoma: final analysis of the randomized phase 2 FIGHT trial. *Gastric Cancer*. 2024;27(3):558-570.
18. Ahn S, Lee J, Hong M, et al. FGFR2 in gastric cancer: protein overexpression predicts gene amplification and high H-index predicts poor survival. *Mod Pathol*. 2016;29(9):1095-1103.
19. Han N, Kim MA, Lee HS, Kim WH. Evaluation of fibroblast growth factor receptor 2 expression, heterogeneity and clinical significance in gastric cancer. *Pathobiology*. 2015;82(6):269-279.
20. Yashiro M, Kuroda K, Masuda G, et al. Clinical difference between fibroblast growth factor receptor 2 subclass, type IIIb and type IIIc, in gastric cancer. *Sci Rep*. 2021;11(1):4698.
21. Gemo AT, Deshpande AA, Palencia S, et al. Abstract 5446: FPA144: a therapeutic antibody for treating patients with gastric cancers bearing FGFR2 gene amplification. *Cancer Res*. 2014;74(Suppl 19). 5446-5446.
22. Janjigian YY, Cecchini M, Shitara K, et al. Genomic landscape of late-stage gastric cancer: analysis from KEYNOTE-059, KEYNOTE-061, and KEYNOTE-062 studies. *JCO Precis Oncol*. 2025;9:e2400456.
23. Lei YY, Huang JY, Zhao QR, et al. The clinicopathological parameters and prognostic significance of HER2 expression in gastric cancer patients: a meta-analysis of literature. *World J Surg Oncol*. 2017;15(1):68.
24. Martínez-Ciarpaglini C, Barros R, Caballero C, et al. Comprehensive histopathological analysis of gastric cancer in European and Latin American populations reveals differences in PDL1, HER2, p53 and MUC6 expression. *Gastric Cancer*. 2025;28(2):160-173.
25. Nakauchi M, Court C, Walch HS, et al. Genomic and clinical parallels between US and Japanese gastric cancers: a propensity score-matched cohort study. *Br J Surg*. 2025;112(12):znaf280.
26. Shitara K, Ajani JA, Moehler M, et al. Nivolumab plus chemotherapy or ipilimumab in gastro-oesophageal cancer. *Nature*. 2022;603(7903):942-948.
27. Kim KC, Koh YW, Chang HM, et al. Evaluation of HER2 protein expression in gastric carcinomas: comparative analysis of 1414 cases of whole-tissue sections and 595 cases of tissue microarrays. *Ann Surg Oncol*. 2011;18(10):2833-2840.
28. Cho EY, Park K, Do I, et al. Heterogeneity of ERBB2 in gastric carcinomas: a study of tissue microarray and matched primary and metastatic carcinomas. *Mod Pathol*. 2013;26(5):677-684.
29. Park DI, Yun JW, Park JH, et al. HER-2/neu amplification is an independent prognostic factor in gastric cancer. *Dig Dis Sci*. 2006;51(8):1371-1379.
30. Shan L, Ying J, Lu N. HER2 expression and relevant clinicopathological features in gastric and gastroesophageal junction adenocarcinoma in a Chinese population. *Diagn Pathol*. 2013;8:76.
31. Yano T, Doi T, Ohtsu A, et al. Comparison of HER2 gene amplification assessed by fluorescence in situ hybridization and HER2 protein expression assessed by immunohistochemistry in gastric cancer. *Oncol Rep*. 2006;15(1):65-71.
32. Yoon HH, Shi Q, Sukov WR, et al. Association of HER2/ErbB2 expression and gene amplification with pathologic features and prognosis in esophageal adenocarcinomas. *Clin Cancer Res*. 2012;18(2):546-554.
33. Schoemig-Markiefka B, Eschbach J, Scheel AH, et al. Optimized PD-L1 scoring of gastric cancer. *Gastric Cancer*. 2021;24(5):1115-1122.
34. Chao J, Fuchs CS, Shitara K, et al. Assessment of pembrolizumab therapy for the treatment of microsatellite instability-high gastric or

Downloaded for Anonymous User (n/a) at Yonsei University College of Medicine from ClinicalKey.com by Elsevier on July 15, 2026. For personal use only. No other uses without permission. Copyright ©2026. Elsevier Inc. All rights reserved.

gastroesophageal junction cancer among patients in the KEYNOTE-059, KEYNOTE-061, and KEYNOTE-062 clinical trials. *JAMA Oncol*. 2021;7(6):895-902.

35. Shitara K, Xu RH, Ajani JA, et al. Global prevalence of claudin 18 isoform 2 in tumors of patients with locally advanced unresectable or metastatic gastric or gastroesophageal junction adenocarcinoma. *Gastric Cancer*. 2024;27(5):1058-1068.
36. Klempner SJ, Janjigian YY, Wainberg ZA. Claudin18.who? Examining biomarker overlap and outcomes in claudin18.2-positive gastroesophageal adenocarcinomas. *ESMO Open*. 2023;8(2):100778.
37. Sato S, Rhodes SL, Aoki Y, et al. 1420P Fibroblast growth factor receptor 2 isoform IIIb (FGFR2b) protein overexpression and biomarker overlap in patients with advanced gastric or gastroesophageal junction cancer (GC/GEJC). *Ann Oncol*. 2024;35:S885-S886.

Downloaded for Anonymous User (n/a) at Yonsei University College of Medicine from ClinicalKey.com by Elsevier on July 15, 2026. For personal use only. No other uses without permission. Copyright ©2026. Elsevier Inc. All rights reserved.