For Pathologists

IN ADVANCED 1L GASTRIC/GASTROESOPHAGEAL JUNCTION (GASTRIC/GEJ) CANCERS,[1]

A NEW DIRECTION AWAITS

FGFR2b is an emerging protein biomarker overexpressed in **~38%*** of advanced gastric/GEJ cancer patients[2]

Discover more at FGFR2b.com

*FGFR2b protein overexpression is defined as any percentage of tumor cells with moderate (2+) to strong (3+) membranous staining, as detected by IHC.[2]

1L, first line; CLDN18.2, claudin-18 isoform 2; FGFR2b, fibroblast growth factor receptor 2, isoform IIIb; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; MSI-H, microsatellite instability-high; PD-L1, programmed cell death ligand 1.

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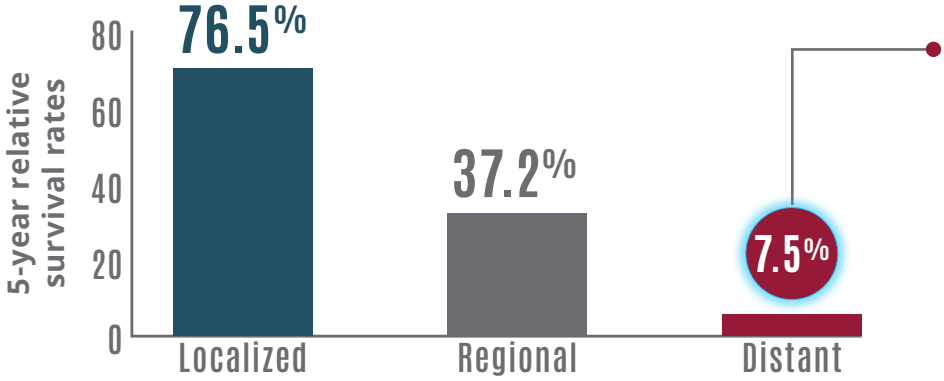
DESPITE TREATMENT ADVANCES, PROGNOSIS REMAINS POOR FOR MANY PATIENTS WITH ADVANCED GASTRIC/GEJ CANCERS[3]

5-year relative survival rates by stage at diagnosis from 2015 to 2021[4,*]



Distantly metastatic cancers have a survival rate **5x lower than regional gastric cancers**, and **10x lower than localized gastric cancers**[4,*]

THE LANDSCAPE OF GASTRIC/GEJ CANCERS IS EVOLVING[3]

As the biomarker landscape continues to evolve, it may inform advancements in precision medicine[3]

Gastric/GEJ cancers are complex and heterogeneous diseases characterized by the expression of a variety of biomarkers, including:[1,3,5-7]

HER2[5]	MSI-H[8]	PD-L1[9]	CLDN18.2[10]
22%	7%	50%–60%	38%

FGFR2b: AN EMERGING BIOMARKER IN GASTRIC/GEJ CANCERS

FGFR2b protein overexpression is prevalent in

~38%

of patients with advanced gastric/GEJ cancer[2,†]

FGFR2b protein overexpression may be prognostic and **associated with shorter survival** in gastric/GEJ cancers[11,12]

FGFR2b protein, the IIIb isoform of the *FGFR2* gene, is overexpressed on epithelial cell membranes in gastric/GEJ cancer **and is measured by immunohistochemistry (IHC)[12-14]**

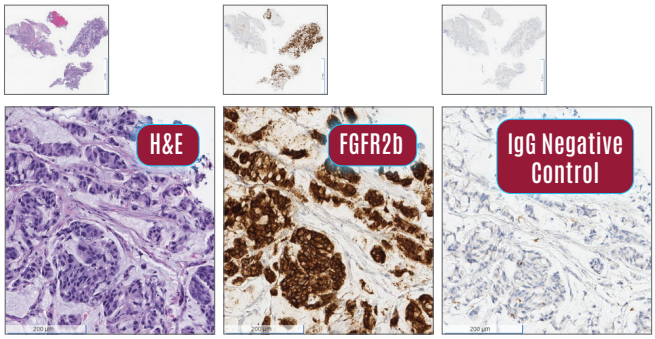
FGFR2b protein overexpression is distinct from *FGFR* genetic alterations (eg, amplifications). Therefore, NGS/PCR is insufficient[3,12,14]

*Assessed between 2015-2021 in the United States.[4]
†FGFR2b protein overexpression is defined as any percentage of tumor cells with moderate (2+) to strong (3+) membranous staining, as detected by IHC.[2]

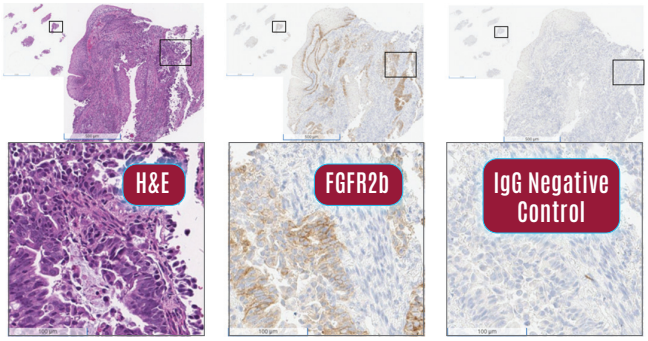
CLDN18.2, claudin-18 isoform 2; FGFR2b, fibroblast growth factor receptor 2, isoform IIIb; GEJ, gastroesophageal junction; HER2, human epidermal growth factor receptor 2; MSI-H, microsatellite instability-high; NGS, next-generation sequencing; PCR, polymerase chain reaction; PD-L1, programmed cell death ligand 1.

FGFR2b PROTEIN OVEREXPRESSION DETECTION BY IHC IN BOTH GASTRIC AND GEJ CANCERS[1,15,*]

FGFR2b staining example: stomach biopsy[15]

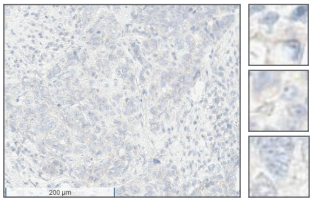


FGFR2b staining example: GEJ biopsy[15]

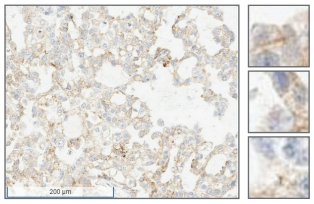


FGFR2b PROTEIN OVEREXPRESSION IS DEFINED AS TUMOR CELLS WITH MODERATE (2+) TO STRONG (3+) MEMBRANOUS STAINING, EG, ≥ 10% 2+/3+[1]

FGFR2b protein overexpression staining examples[15]



FGFR2b in gastric adenocarcinoma with **no (0) staining**



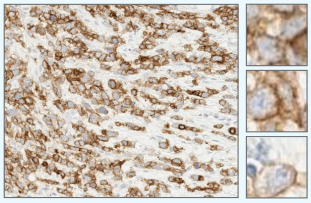
FGFR2b in gastric adenocarcinoma with predominantly **weak (1+) staining**

FGFR2b protein overexpression not detected in cell membrane[15]

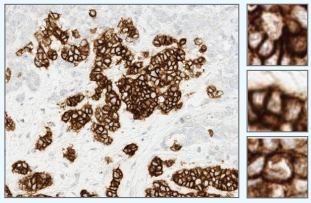
No tumor cells with moderate to strong membranous staining **OR** tumor cells only exhibiting:

- Negative to weak membranous staining and/or
- Cytoplasmic-only staining at any intensity

FGFR2b overexpression



FGFR2b in gastric adenocarcinoma with predominantly **moderate (2+) staining**



FGFR2b in gastric adenocarcinoma with predominantly **strong (3+) staining**

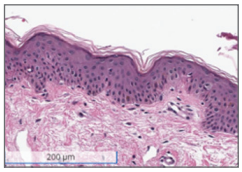
FGFR2b protein overexpression detected in cell membrane[15]

Any tumor cells with moderate to strong membranous staining, including any of the following:

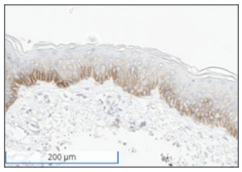
- Basal-lateral
- Partial or complete circumferential
- Basal only
- Apical only

A RECOMMENDED CONTROL FOR FGFR2b OVEREXPRESSION VIA IHC WAS NON-NEOPLASTIC SKIN TISSUE[16]

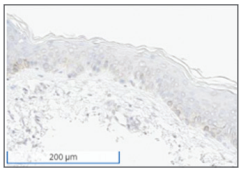
An appropriate control exhibits weak and moderate membrane staining in the epithelium of skin[15,16]



H&E of non-neoplastic skin



FGFR2b in non-neoplastic skin exhibiting weak (1+) to moderate (2+) membrane staining on basal epithelium



IgG negative control of non-neoplastic skin

*Roche Diagnostics has created the VENTANA® FGFR2b (FPR2-D) Mouse Monoclonal Antibody assay (Class 1) that recognizes the FGFR2b isoform via IHC.[15,16] FGFR2b, fibroblast growth factor receptor 2, isoform IIIb; GEJ, gastroesophageal junction; H&E, hematoxylin and eosin; IgG, immunoglobulin G; IHC, immunohistochemistry.

TECHNICAL DETAILS TO CONSIDER FROM DIAGNOSIS TO REPORTING

SAMPLE INTEGRITY & SIZE

- National Comprehensive Cancer Network® (NCCN®) recommends obtaining 6-8 biopsies to conduct histological interpretation and biomarker testing[6,7]
- Obtaining sufficient and quality tumor tissue during biopsy is critical for biomarker testing and avoiding re-biopsy[6,7,17]

INTEGRATED TEST REQUISITIONS

- Support inclusion of all actionable IHC biomarkers to simplify the ordering process[18-20]

MITIGATING TURNAROUND TIME

- Reflex testing can accelerate biomarker result turnaround times, enhancing clinical decision-making efficiency[21,22]

FGFR2b SCORING

- FGFR2b overexpression is defined as moderate to strong membranous 2+ to 3+ staining in tumor cells and examined via percentage of tumor cells, eg, ≥10% of tumor cells with 2+ to 3+ staining[1,3,10]

DIAGNOSIS/ BIOPSY → PROCESSING → ORDERING → TESTING/ CONTROLS → INTERPRETING → REPORTING

PRE-ANALYTICS

- Routinely processed, formalin-fixed paraffin-embedded (FFPE) tissues are suitable for FGFR2b detection where 10% neutral buffered formalin is the recommended fixative for IHC staining[16,23]

EPITOPE STABILITY

- Sectioned tissue should be stained immediately, as antigenicity may diminish over time (epitope unstable >45 days)[16]

VALIDATION

- To ensure accuracy and reproducibility, consider College of American Pathologists (CAP) guidelines when adopting a new IHC assay in laboratory practices[24]

QUALITY CONTROL

- FGFR2b is expressed in normal skin tissue and can serve as a positive control[16]

ACCURATE REPORTING

- CAP-recommended inclusion of qualitative and semi-quantitative IHC results, eg, stain intensity and percentage of stained tumor cells in pathology reports can aid in comprehensive, clear documentation[24,25]

Roche Diagnostics has created the VENTANA® FGFR2b (FPR2-D) Mouse Monoclonal Antibody assay (Class 1) that recognizes the FGFR2b isoform via IHC[16,26]

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommend testing for certain actionable biomarkers with IHC at diagnosis of metastatic gastric/GEJ* cancers, including HER2, PD-L1, MMR, and CLDN18.2[6,7]

*Testing recommendations for GEJ cancers, HER2, and CLDN18.2 are in adenocarcinoma.

CLDN18.2, claudin-18 isoform 2; FGFR2b, fibroblast growth factor receptor 2, isoform IIIb; GEJ, gastroesophageal junction; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; NCCN, National Comprehensive Cancer Network; MMR, mismatch repair; PD-L1, programmed cell death ligand 1.

References: 1. Wainberg ZA, et al. *Gastric Cancer*. 2024;27:558-570. **2.** Rha SY, et al. *JCO Precis Oncol*. 2025;9:32400710. **3.** Sato Y, et al. *J Clin Med*. 2023;12:4646. **4.** National Cancer Institute. https://seer.cancer.gov/statfacts/html/stomach.html. Accessed May 1, 2025. **5.** Van Cutsem E, et al. *Gastric Cancer*. 2015;18:476-484. **6.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Esophageal and Esophagogastric Junction Cancers V.3.2025. ©National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed April 22, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **7.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Gastric Cancer V.2.2025. ©National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed April 4, 2025. To view the most recent and complete version of the guideline, go online to NCCN. org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **8.** Amonkar M, et al. *J Clin Oncol*. 2019;37:e15074-e15074. **9.** Mastracci L, et al. *Pathologica*. 2022;114:352-364. **10.** Shitara K, et al. *Lancet*. 2023;401:1655-1668. **11.** Ahn S, et al. *Mod Pathol*. 2016;29:1095-1103. **12.** Han N, et al. *Pathobiology*. 2015;82:269-279. **13.** Angerilli V, et al. *Pathologica*. 2023;115:71-82. **14.** Zhang J, et al. *Cells*. 2019;8:637. **15.** Data on file, Amgen; 2021. **16.** Roche Diagnostics. https://elabdoc-prod.roche.com/eLD/api/downloads/65a1283e-a4f6-ee11-2591-005056a71a5d?countryIsoCode=XG. Accessed May 10, 2025. **17.** Roberts MC, et al. *JCO Precis Oncol*. 2021;5:701-709. **18.** Catenacci DV, et al. *Future Oncol*. 2019;15:2073-2082. **19.** Ye DM, et al. *Oncol Lett*. 2020;19:17-29. **20.** Lordick F, et al. *Ann Oncol*. 2022;33:1005-1020. **21.** Anand K, et al. *Clin Lung Cancer*. 2020;21:437-442. **22.** Cheema PK, et al. *J Oncol Pract*. 2017;13:e130-e138. **23.** Magaki S, et al. *Methods Mol Biol*. 2019;1897:289-298. **24.** Goldsmith JD, et al. *Arch Pathol Lab Med*. 2024;148:e111-e153. **25.** Kim S-W, et al. *J Pathol Transl Med*. 2016;50:411-418. **26.** FDA.gov. www.accessdata.fda.gov. Accessed May 1, 2025.

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