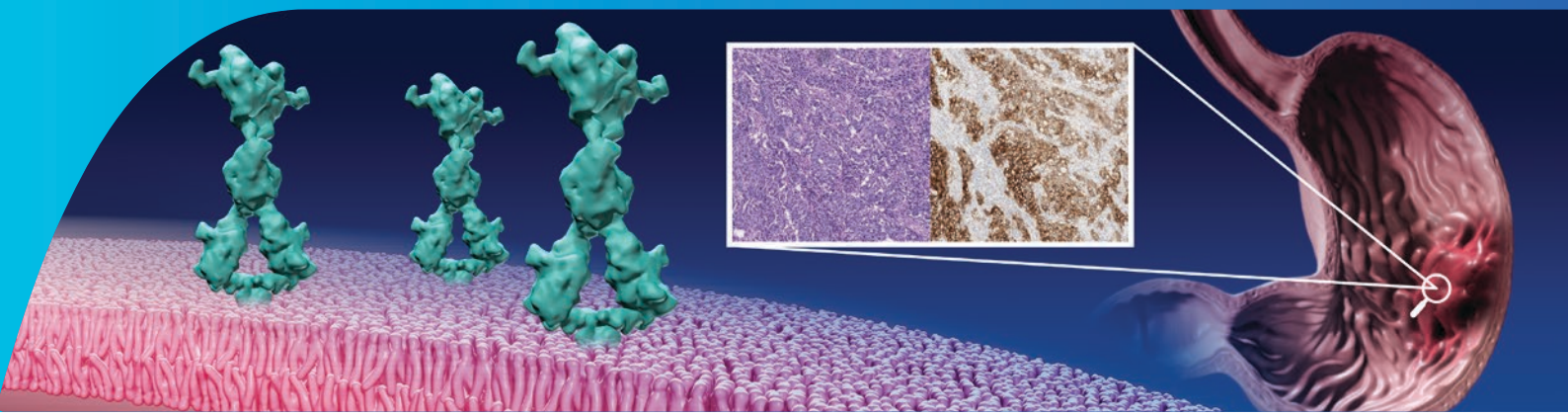
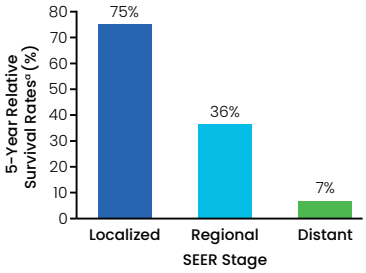
FGFR2b—An Emerging Biomarker and Investigational Target in Gastric Cancer



5-Year Relative US Survival Rates by Stage of Diagnosis from 2014-2020[1]



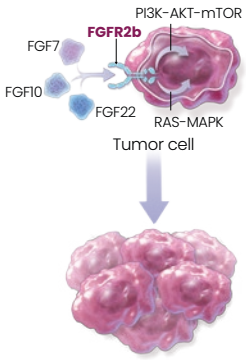
[a]Assessed between 2014 and 2020 in the US.[1]

GASTRIC CANCER IS THE FIFTH MOST COMMON CANCER AND THE FIFTH LEADING CAUSE OF CANCER-RELATED DEATH WORLDWIDE[2]

61% of patients with gastric cancer have advanced disease* at the time of diagnosis.[1]

The 5-year relative survival rate for patients with distantly metastatic gastric cancer at diagnosis is only 7% in the US.[1]

*This includes patients with regional disease, or those whose cancer have spread to regional lymph nodes, and metastatic disease at the time of diagnosis. There are 26,890 estimated new cases.[1]



OVEREXPRESSION OF FGFR2b PROTEIN DRIVES TUMORIGENESIS

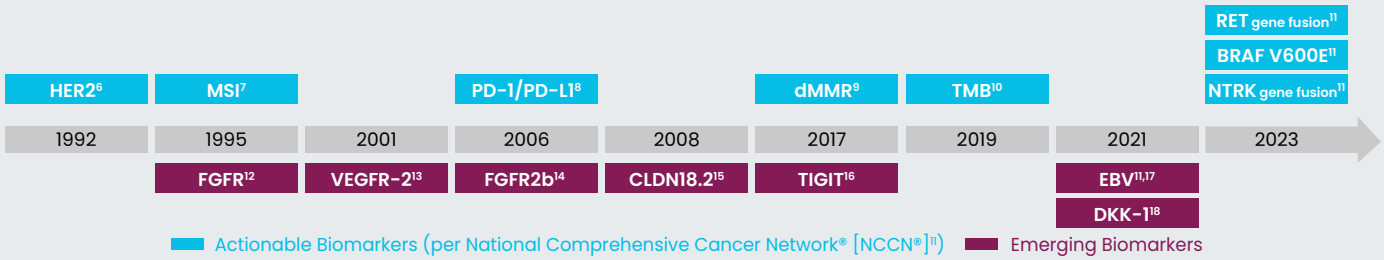
FGFR2b is a **receptor tyrosine kinase** primarily expressed on epithelial cells and involved in numerous cellular functions.[3]

FGFR2b protein overexpression is prevalent in 20%–30% of patients with advanced G/GEJ cancer.[4,†]

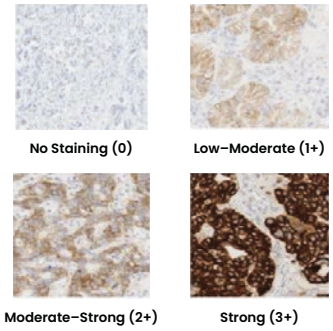
In addition to gastric cancer, FGFR2b is overexpressed in other cancers including esophageal, lung, breast, pancreatic, colorectal, and gynecological cancers.[3,5]

†Approximate range based on the 910 pre-screened patients for a phase 2 trial in locally advanced or metastatic G/GEJ cancer, of which 274 patients (30%) were pre-screened positive for FGFR2b any 2+/3+ tumor cell staining by IHC, and on the 155 enrolled patients, of which 96 patients (62%) exhibited FGFR2b ≥ 10% 2+/3+ tumor cell staining by IHC.[4]

THE BIOMARKER LANDSCAPE CONTINUES TO EVOLVE, HELPING TO INFORM ADVANCEMENTS IN PRECISION MEDICINE‡



‡Timeline reflects the first appearance of G/GEJ biomarkers in peer-reviewed literature.



FGFR2b PROTEIN OVEREXPRESSION CAN BE DETECTED BY IHC IN G/GEJ CANCER*

Protein overexpression is defined as the presence of moderate (2+) to strong (3+) membranous staining of tumor cells.[4,19]

FGFR2b protein overexpression may be associated with poor prognosis.[20,21]

*Currently, FGFR2b testing is in the context of investigational clinical trials with no approved test in the market.[22]

FGFR2b PROTEIN OVEREXPRESSION AND *FGFR2* GENE AMPLIFICATION ARE DISTINCT AND MAY DEFINE DIFFERENT POPULATIONS

The phase 2 randomized, double-blind, placebo-controlled study of patients with metastatic G/GEJ cancer, demonstrates that FGFR2b protein overexpression can be detected at a higher rate with IHC than with ctDNA; thus, FGFR2b protein overexpression evaluation by IHC is not interchangeable with *FGFR2* gene amplification assessment.[4]

BIOMARKER TESTING CONSIDERATIONS IN PATIENTS WITH GASTRIC CANCER[11,23-27]

Biopsy

Multiple tissue biopsies (6–8) should be performed to provide adequate material for histologic and molecular interpretation.[11,23]

Turnaround Time

Typically 2–4 days.[24]

Testing

Implementation of reflex testing protocols for gastric cancer biomarkers may lead to faster informed clinical decisions for patients.[25]

Results

Retaining biomarker test results in a patient's EHR may allow for easier access.[26]

Patient Management

Multidisciplinary tumor boards and other formal venues can help educate on biomarker testing strategies and evolving guidelines.[27]

ABBREVIATIONS: AKT, protein kinase B; CLDN18.2, claudin-18 isoform 2; ctDNA, circulating tumor DNA; DKK-1, Dickkopf-1; dMMR, deficient mismatch repair; EBV, Epstein–Barr virus; EHR, electronic health record; FGF, fibroblast growth factor; FGFR, FGF receptor; FGFR2, FGF receptor 2; FGFR2b, FGFR2 isoform IIIb; G/GEJ, gastric/gastroesophageal junction; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ITIM, immunoreceptor tyrosine-based inhibitory motif; MAPK, mitogen-activated protein kinase; MSI, microsatellite instability; mTOR, mammalian target of rapamycin; NTRK, neurotrophic tyrosine receptor kinase; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; PI3K, phosphoinositide 3-kinase; RAS, rat sarcoma; TIGIT, T-cell immunoglobulin and ITIM domain; TMB, tumor mutational burden; US, United States; VEGFR-2, vascular endothelial growth factor receptor 2.

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