FGFR2b – An Emerging Biomarker and Investigational Target in Gastric Cancer

There Remains an Unmet Need in Gastric Cancer

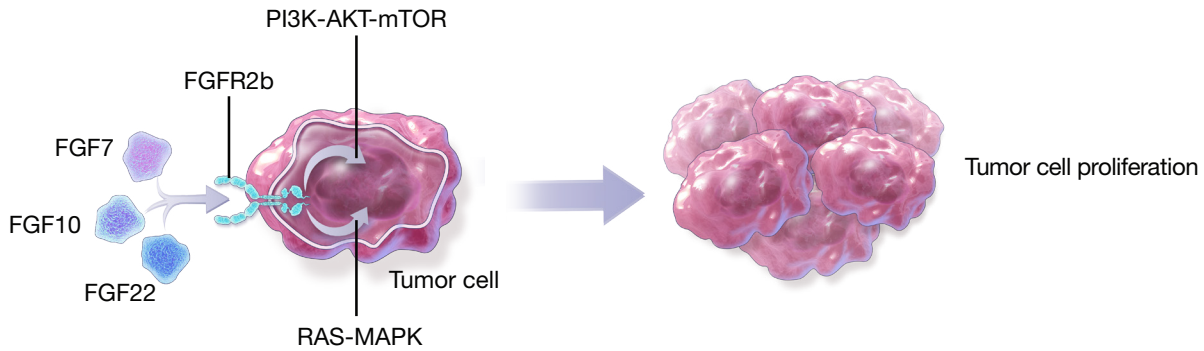
~30% patients with **metastatic G/GEJ** cancer overexpress the **FGFR2b** protein[1,*]

*Data from a randomized, double-blind, placebo-controlled, phase 2 study with a protocol allowing FGFR2b analyses on both fresh and archival samples (a majority of analyses were performed on fresh samples).[1]

> 50% of patients with gastric cancer present with **advanced-stage disease** at the time of diagnosis in the US[2,†]

†Advanced-stage defined as regionally advanced (Stage 3) and metastatic (Stage 4). Prescreening data from a retrospective study involving > 50,000 patients with gastric cancer.[2]

Overexpression of FGFR2b Protein Drives Tumorigenesis



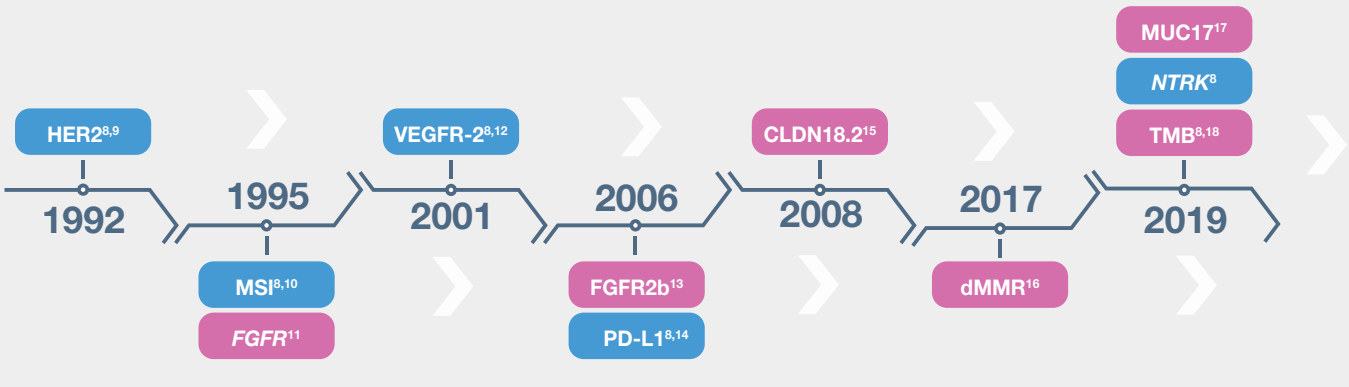
FGFR2b is a **receptor tyrosine kinase** primarily expressed on epithelial cells and involved in numerous cellular functions[3]

In addition to gastric cancer, **FGFR2b** protein is also expressed in **other cancerous tumors** (esophageal, lung, breast, pancreatic, colorectal, and gynecological cancers)[3-6]

Specifically targeting the FGFR2b protein may interrupt cancer cell proliferation while minimizing potential side effects seen with pan-FGFR inhibitors[7]

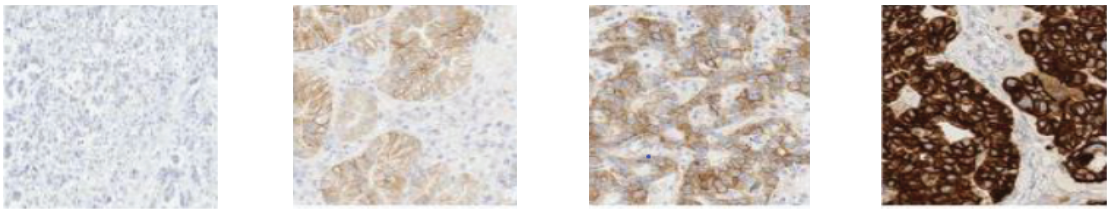
The biomarker landscape has evolved in recent years, **opening the** path for precision medicine.

Appearance of Gastric Cancer Biomarkers in Peer-Reviewed Literature



FGFR2b Protein Overexpression can be Detected by IHC in G/GEJ Cancer

The protein overexpression is defined as **2+/3+** staining[1]



No Staining (0) | **Low-Moderate (1+)** | **Moderate-Strong (2+)** | **Strong (3+)**

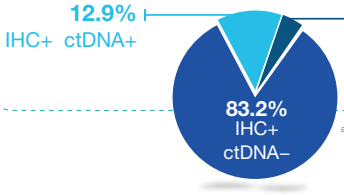
Patients with FGFR2b-overexpressed gastric cancer and an H-score† ≥ 150 showed shorter overall survival (P = 0.001)[19]

†H-score is the sum of the percentage of stained tumor cells multiplied by an ordinal value corresponding to the intensity (0 = none, 1 = 1+, 2 = 2+, and 3 = 3+) and ranges from 0 to 300.[19]

FGFR2b protein overexpression and ***FGFR2*** **gene amplification** are **distinct**[4]

FGFR2b protein overexpression **(assessed by IHC)** may occur in the absence of *FGFR2* gene amplification **(assessed using ctDNA);** thus, it is important to test for FGFR2b protein overexpression using IHC[4]

***FGFR2*/FGFR2b Status of Patients With G/GEJ Cancer**[4,a]



IHC = FGFR2b protein expression;
ctDNA = *FGFR2* gene amplification

[a]Data from a randomized, double-blind, placebo-controlled, phase 2 study of patients with metastatic gastric cancer.[1]

Prevalence of FGFR2b overexpression in advanced gastric cancer (~ 30%)* and FGFR2b's potential association with lower overall survival makes it a compelling target for ongoing investigations[1,3,19]

*Eligible prescreened patients in the Phase 2 FIGHT trial

Biomarker Testing Considerations in Patients With Gastric Cancer

IHC is an established testing methodology with **high sensitivity** (up to 100%)* and **specificity** (~ 97%)† and is also cost-efficient with a fast turnaround time[20-23]

Existing workflows for biomarker testing may allow for seamless integration of FGFR2b testing[20,24]

Implementation of **reflex testing protocols** for gastric cancer biomarkers can reduce time to biomarker identification[25]

Retaining **FGFR2b** and other biomarker test **results** in a patient's **EHR** allows for easier access to providers as the landscape advances[26]

Multidisciplinary tumor boards and other formal venues can help educate on effective biomarker testing strategies, the evolving guidelines as well as targeted therapy approvals[26-28]

*Sensitivity of IHC assays depends on pretreatment conditions, antibody clones, and signal detection systems.[29] †Concordance between 22C3 and 28-8 pharmDx assays was 97% in 3,050 matched samples with PD-L1 expression data for both assays.[21]

ABBREVIATIONS: AKT, protein kinase B; CLDN18.2, claudin-18 isoform 2; ctDNA, circulating tumor DNA; dMMR, deficient mismatch repair; EHR, electronic health record; FGF, fibroblast growth factor; FGFR, FGF receptor; FGFR2, FGF receptor 2; FGFR2b, FGFR 2, isoform IIIb; G/GEJ, gastric/gastroesophageal junction; HER2, human epidermal growth factor receptor 2; IHC, Immunohistochemistry; MAPK, mitogen-activated protein kinase; MSI, microsatellite instability; mTOR, mammalian target of rapamycin; MUC17, mucin 17; NTRK, neurotrophic tyrosine receptor kinase; PD-L1, programmed cell death ligand 1; PI3K, phosphoinositide 3-kinase; RAS, rat sarcoma; VEGFR-2, vascular endothelial growth factor receptor 2; TMB, tumor mutational burden; US, United States.

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