RESULTS FROM THE GERMAN REGISTRY PLATFORM SAPHIR

PREVALENCE OF FGFR2B EXPRESSION, CHARACTERISTICS, TREATMENT AND OUTCOMES IN PATIENTS WITH METASTATIC GASTRIC AND GASTROESOPHAGEAL JUNCTION ADENOCARCINOMA IN GERMANY

Lukas Haug[1],
Kai Ringwald[2],
Adrian Binninger[2],
Lia Tzala[3],
Kumiko Isse[3],
Ria Winkelmann[1],
Philipp Stenzel[1],
Eyck von der Heyde[4],
Christian Müller[5],
Dieter Semsek[6],
Anja Servatius[7],
Istvan Majer[8],
Hayden Honeycutt[3],
Florian Lordick[9],
Peter Wild[1],
Martina Jänicke[2],
Karin Potthoff[2].

1 Goethe University Frankfurt, Dr. Senckenberg Institutes of Pathology and Human Genetics, University Hospital Frankfurt, Frankfurt, Germany
2 iOMEDICO AG, Freiburg, Germany
3 Amgen Ltd., London, United Kingdom
4 Onkologische Schwerpunktpraxis, Hannover
5 Evangelische Kliniken Essen-Mitte, Essen, Germany
6 Praxis für interdisziplinäre Onkologie & Hämatologie, Freiburg i.Br., Germany
7 Amgen GmbH, Munich, Germany
8 Amgen (Europe) GmbH, Rotkreuz, Switzerland
9 Universitätsklinikum Leipzig, Leipzig, Germany

BACKGROUND

Fibroblast growth factor receptor 2 isoform IIIb (FGFR2b) is a potential predictive and therapeutic target biomarker in gastric and gastroesophageal junction adenocarcinoma (GC/GEJ). Real-World data on the prevalence of FGFR2b expression in metastatic GC/GEJ and on characteristics, treatments and outcomes in patients overexpressing FGFR2b are still rare.

METHODS

SAPHIR is an open, non-interventional, prospective, multicenter clinical research platform in Germany (NCT04290806), providing clinical real-world data from patients with metastatic esophageal cancer and GC/GEJ since December 2019. Details on methods have been published previously (Potthoff *et al.* 2023 and Potthoff *et al.* 2025).

Patients included in this specific analysis initiated first-line treatment for metastatic GC/GEJ between September 2021 and March 2024 and consented to donate tumor samples from routine treatment, that had been collected less than 4 years prior to central testing. They were followed until June 30, 2025 (data cut).

FGFR2b protein overexpression was centrally tested besides four other biomarkers (HER2, PD-L1, CLDN18.2 and MSI/MMR), for available tumor samples and determined as a percentage of tumor cells (TC) exhibiting membranous staining at intensities of 0/1+/2+/3+ using VENTANA FGFR2b (FPR2-D) RxDx Assay (for Investigational Use Only) (Roche Diagnostics). For analysis, two cut-offs for FGFR2b positivity were defined: any % of TC and ≥10 % of TC exhibiting moderate-to-strong (2+/3+) membranous FGFR2b staining.

Medical data from SAPHIR were combined with results from centralized testing, and analyzed to describe patient and tumor characteristics, treatment patterns, clinical and patient reported outcomes. Here, we present data on patients tested centrally for HER2 and FGFR2b, using descriptive statistics and overall survival (OS), measured as time from start of first-line treatment until death, with patients alive at data cut being censored at last contact.

RESULTS

FGFR2b protein overexpression results from central testing were available for 225 of 976 enrolled patients with metastatic GC/GEJ at time of database cut **(Figure 1)**. Median age of these patients was 68.3 years, 63 % were male, 67 % had GC tumors, and 26.8 %/44.6 % had an ECOG performance status of 0/1 at start of first-line treatment **(Table 1)**.

Overall, FGFR2b protein overexpression was observed in 33.8 % (n=76, CI: 27.6, 40.4) of patients at any % and 25.3 % (n=57, CI: 19.8, 31.5) at ≥10 % (2+/3+ TC positivity) **(Figure 2)**. Among 200 patients with HER2-negative metastatic GC/GEJ, results on FGFR2b overexpression were comparable with 35.0 % (n=70, CI: 28.4, 42.0, any %) of tumors and 27.5 % (n=55, CI: 21.4, 34.2, ≥10 %), respectively.

Most frequent first-line treatments were FOLFOX (29 %), FLOT (19 %) and FOLFOX+nivolumab (12 %). It is important to notice that FGFR2b status collected within the biobank module of SAPHIR was not known to treating physicians prior to start of first-line treatment, and thus is not expected to have any influence on the choice of treatment.

Among all patients, median OS was 8.4 months (95 %-CI 6.2-10.1, 80.7 % events) for tumors with ≥10 %, and 8.2 months (95 %-CI 7.0-9.7, 88.7 % events) for tumors with <10 % FGFR2b protein overexpression respectively, independent of treatment strategy, or other characteristics **(Figures 3 and 4)**.

CONCLUSION

We show that the combination of prospectively collected registry with centrally tested biobank data provides important context for FGFR2b protein overexpression in a German population and highlights the potentially eligible patient population for emerging FGFR2b-targeted therapies. Depending on the cut-off, between 28 % and 35 % of HER2 negative patients with metastatic GC/GEJ would qualify for a treatment with a FGFR2b-targeted treatment. Data on patient characteristics, historic treatment and outcome can serve as a valuable reference to study the impact of future treatments on this patient population.

Table 1: Patient characteristics at start of first-line treatment

	≥ 10 % 2+/3+	< 10 % 2+/3+	Total
Patients (N)	57	168	225
Age (years)			
Median	67.2	68.5	68.3
25 %/75 % quantiles	60.7/73.2	59.1/75.4	59.8/75.1
≥ 65 years	34 (59.6 %)	103 (61.3 %)	137 (60.9 %)
Sex			
Male	39 (68.4 %)	102 (60.7 %)	141 (62.7 %)
ECOG performance status			
0	12 (21.1 %)	37 (22.0 %)	49 (21.8 %)
1	20 (35.1 %)	70 (41.7 %)	90 (40.0 %)
≥ 2	16 (28.1 %)	34 (20.2 %)	50 (22.2 %)
Unknown to site	8 (14.0 %)	27 (16.1 %)	35 (15.6 %)
Missing	1 (1.8 %)	0 (0.0 %)	1 (0.4 %)
Any comorbidity			
Yes	44 (77.2 %)	132 (78.6 %)	176 (78.2 %)
Charlson comorbidity index			
≥ 1	17 (29.8 %)	47 (28.0 %)	64 (28.4 %)
Most frequent sites of metastasis			
Peritoneum	27 (47.4 %)	77 (45.8 %)	104 (46.2 %)
Liver	19 (33.3 %)	65 (38.7 %)	84 (37.3 %)
Lymph node	20 (35.1 %)	61 (36.3 %)	81 (36.0 %)
Lung	6 (10.5 %)	21 (12.5 %)	27 (12.0 %)
Bone	8 (14.0 %)	14 (8.3 %)	22 (9.8 %)

Figure 1: Patient flow chart

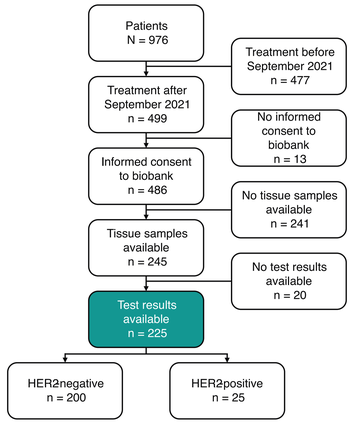


Figure 2: FGFR2b prevalence from central testing

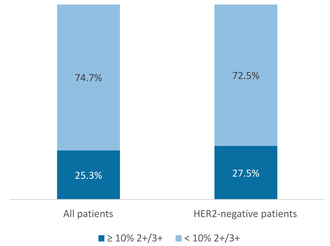


Figure 3: Overall survival – patients with FGFR2b overexpression (≥10 % 2+/3+).

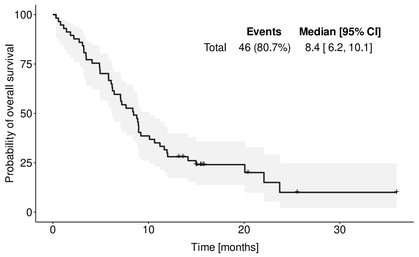
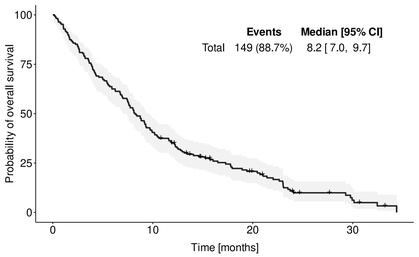


Figure 4: Overall survival – patients without FGFR2b overexpression (<10 % 2+/3+)



Abbreviations:
GC/GEJ: gastric and gastroesophageal junction adenocarcinoma | FGFR2b: Fibroblast growth factor receptor 2 isoform IIIb | HER2: Human epidermal growth factor receptor 2 | TC: tumor cells | OS: Overall survival | ECOG PS: Eastern Cooperative Oncology Group

References:
[1] Potthoff, K. et al., 2023. SAPHIR: Real-world clinical research platform for molecular testing, treatment, and clinical and patient-reported outcomes in patients with gastroesophageal cancer in Germany. *ESMO Real World Data and Digital Oncology*, 2, 100007. doi:10.1016/j.esmorw.2023.100007.

[2] Potthoff, K. et al., 2025. Local and central testing for HER2, PD-L1, MSI/MMR, EBV, and CLDN18.2 in advanced gastric cancer: Results from the SAPHIR registry. *ESMO Real World Data and Digital Oncology*, 8. doi:10.1016/j.esmorw.2025.100164.

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LH: Consulting honoraria: AstraZeneca, MSD | **KR:** None | **AB:** None | **LT:** Employment Amgen | **KI:** Employment Amgen | **HW:** None | **PS:** None | **EvdH:** None | **CM:** None | **DS:** None | **AS:** Employment Amgen | **IM:** Employment Amgen | **HH:** Employment Amgen | **FL:** None | **PW:** None | **MJ:** None | **KP:** None

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