Pilot Study to Assess the Prevalence of Advanced Gastrointestinal Stromal Tumor Identified Using German Claims Data

Abstract: EPH162

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INTRODUCTION

- Gastrointestinal stromal tumor (GIST) is the most common sarcoma of the GI tract.[1] Very limited data on GIST epidemiology is available for Germany, especially for advanced disease stages.
- GIST incidence is estimated to be 1.2-1.5 per 100,000 individuals per year in Europe.[2]
- GIST most commonly affects the stomach (50-60%) and small intestine (20-30%) and is less common in the colorectum (5-10%) and esophagus (<1%).[1]
- According to established treatment guidelines, the preferred initial treatment option for localized GIST is surgery.[1]
- Patients with advanced GIST (metastatic and non-resectable) are primarily treated with tyrosine kinase inhibitors (TKI) consisting of first-line imatinib, second-line sunitinib, third-line regorafenib, and fourth-line ripretinib (available in Germany as of 2022).
- The majority of patients with advanced GIST develop secondary mutations that may lead to treatment resistance. Especially in these challenging cases, there is a great medical need to cover the late stages of the disease with patient-individualized treatment.

OBJECTIVE

- This claims data analysis was conducted to gain insights into the prevalence, incidence, and treatment patterns of advanced GIST in Germany.

METHODS

- A retrospective claims data analysis was conducted using the Institute for Applied Health Research (InGef) research database.
- The InGef research database contains only approximately 4 million individuals (~1/20 of the German population) weighted to represent the German population in terms of age and gender, and region/federal state of residence (according to the Federal Statistical Office of Germany). Moreover, the InGef research database has proven to have good external validity to the German population in terms of morbidity, mortality, and drug use.[3]
- The claims data analysis included the period between January 1st, 2015 and December 31st, 2020 to include the six most recent available years in the database.
- The population consisted of three main cohorts:
  1. Prevalent patients with advanced GIST in 2020
  2. Incident patients with advanced GIST in 2020 based on a diagnosis- and TKI treatment-free pre-observation period of one year (January 1st, 2019 to December 31st, 2019)
  3. Patients with advanced GIST in 2020 who were eligible for fourth-line treatment with ripretinib after prior TKI treatment with imatinib and sunitinib and regorafenib based on a five-year pre-observation period.
- In absence of a specific International Statistical Classification of Diseases and Related Health Problems,10th revision, German Modification (ICD-10-GM) diagnosis code, GIST were identified by different ICD-10-GM codes for gastrointestinal malignancies based on suggestions from treatment guidelines[1, 4, 5] and German medical experts.
- Individuals with ≥1 primary or secondary inpatient or verified outpatient ICD-10-GM code indicating gastrointestinal tumors that include GIST in 2020 were included.
- Advanced GIST was defined by ≥1 prescription with imatinib or sunitinib or regorafenib identified by corresponding Anatomical Therapeutic Chemical Classification System (ATC), Key of Operations and Procedures (OPS), and Pharmacy Central Number (PZN) codes.
- Individuals who received ≥1 prescription for imatinib and sunitinib and regorafenib between January 1st, 2015 and December 31st, 2020 were classified as advanced GIST patients eligible for fourth-line treatment with ripretinib after prior TKI treatment.
- As imatinib, sunitinib, and regorafenib are approved for various malignancies, prevalent patients with records of the studied medications for approved indications other than advanced GIST were excluded.
- Identified patients were described in terms of demographic characteristics (age and gender).
- Patients with ≥1 ICD-10-GM code indicating gastrointestinal tumors that include GIST were stratified based on tumor localization.
- For advanced GIST patients in the three main cohorts, the number and percentage of patients with ICD-10-GM code C49.4 "Malignant neoplasms of connective tissue and other soft tissues of the abdomen" were determined separately to assess the frequency of the most specific available coding for GIST according to German medical experts.
- For ICD-10-GM, ATC, OPS, and PZN codes used for patient selection and stratification, please see Table 1.

Table 1. ICD-10-GM, ATC, OPS, and PZN codes used for patient selection and stratification

Code	Description	Code	Description
ICD-10-GM codes indicating gastrointestinal tumors that include GIST			
C15	Malignant neoplasm of the esophagus	C48.1	Malignant neoplasm of the retroperitoneum & peritoneum: more specifically designated parts of the peritoneum
C16	Malignant neoplasm of the stomach	C48.2	Malignant neoplasm of the retroperitoneum & peritoneum: peritoneum, unspecified
C17	Malignant neoplasm of the small intestine	C49.4	Malignant neoplasms of connective tissue & other soft tissues of the abdomen
C18	Malignant neoplasm of the colon	C49.9	Malignant neoplasm of other connective tissue & other soft tissues, unspecified
C20	Malignant neoplasm of the rectum	D48.1	Neoplasm of uncertain or unknown behavior in other & unspecified locations, connective tissue and other soft tissues
C26.9	Malignant neoplasm of other & unspecified digestive organs: inaccurately designated localizations		
ATC, OPS, and PZN codes for identification of TKI treatment			
ATC	L01XE01, L01EA01	Imatinib (first-line treatment)	
OPS	6-001.g		
ATC	L01XE04, L01EX01	Sunitinib (second-line treatment)	
OPS	6-003.a		
ATC	L01XE21, L01EX05	Regorafenib (third-line treatment)	
OPS	6-007.c		
PZN	09999117	Special PZN for the individual import of medicinal products in accordance with Section 73 (1) AMG*	
ICD-10-GM codes for other malignancies for which imatinib, sunitinib, and regorafenib are approved			
C44.9	Dermatofibrosarcoma protuberans (DFSP)	D47.4	Primary myelofibrosis
C91	Lymphoid leukemia	D47.5	Chronic eosinophil leukemia (CEL), hypereosinophilic syndrome (HES)
C92	Myeloid leukemia	C25	Malignant neoplasm of pancreas
C93	Monocytic leukemia	C64	Malignant neoplasm of kidney, except renal pelvis
C94	Other leukemias of specified cell type	C18+	Malignant neoplasm of colon
C95	Leukemia of unspecified cell type	C19	Malignant neoplasm of rectosigmoid, junction
D45	Polycythemia vera	C20+	Malignant neoplasm of rectum
D46	Myelodysplastic syndromes (MDS)	C21	Malignant neoplasm of anus and anal canal
D47.1	Chronic myeloproliferative disease	C22	Malignant neoplasm of liver and intrahepatic bile ducts
D47.3	Essential (hemorrhagic) thrombocythemia		

*Since regorafenib was withdrawn from the German market in 2016, the use of regorafenib is now only possible by way of individual import in accordance with Section 73 (1) Medicinal Products Act (AMG). The individual import is billed to the SHI using the special PZN 09999117.

+Regorafenib is commonly used in colon cancer. However, colon and rectum are not typical GIST localizations, so exclusion of patients with ICD-10-GM codes C18 and C20 was performed.

RESULTS

Prevalence and incidence of advanced GIST in 2020

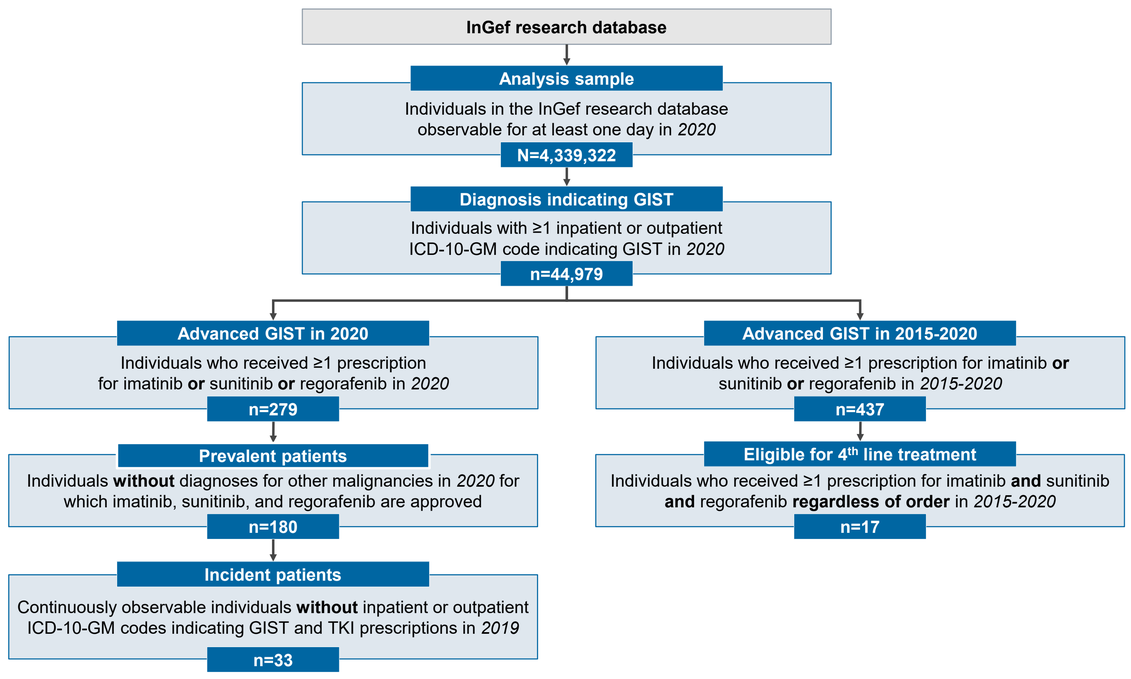
- In the InGef research database, n=44,979 patients received ≥1 inpatient or outpatient ICD-10-GM code indicating gastrointestinal tumors that include GIST (see Figure 1). Thereof, n=279 patients received ≥1 TKI prescription in 2020.
- After removing patients with diagnoses for other malignancies in 2020, n=180 patients were identified as prevalent patients with advanced GIST in 2020. This corresponds to a prevalence rate of 4.1 per 100,000 individuals.
- Among prevalent patients, n=33 patients did not have an ICD-10-GM code indicating gastrointestinal tumors that include GIST and did not receive treatment with a TKI in 2019. This corresponds to an incidence rate of advanced GIST of 0.8 per 100,000 individuals.
- Prevalent patients were on average 66.5 years old (SD=13.8) (see Figure 2) and 50.6% were male.
  - Approximately 40% of patients were between 18-64 years, while approximately 28% were between 64-74 years and up to 33% were ≥75 years old.
  - The mean age was numerically higher for men than for women (67.1 years vs 65.8 years).

RESULTS (CONTINUED)

Prevalence and incidence of advanced GIST in 2020

- In comparison, incident patients were slightly older with a mean age of 67.6 years (SD=14.8) (see Figure 2) and less patients were male (48.5%).
  - The age distribution showed an even distribution across the age groups.
  - The mean age was numerically lower for men than for women (65.8 years vs 69.3 years).

Figure 1. Results of the patient selection in the InGef research database

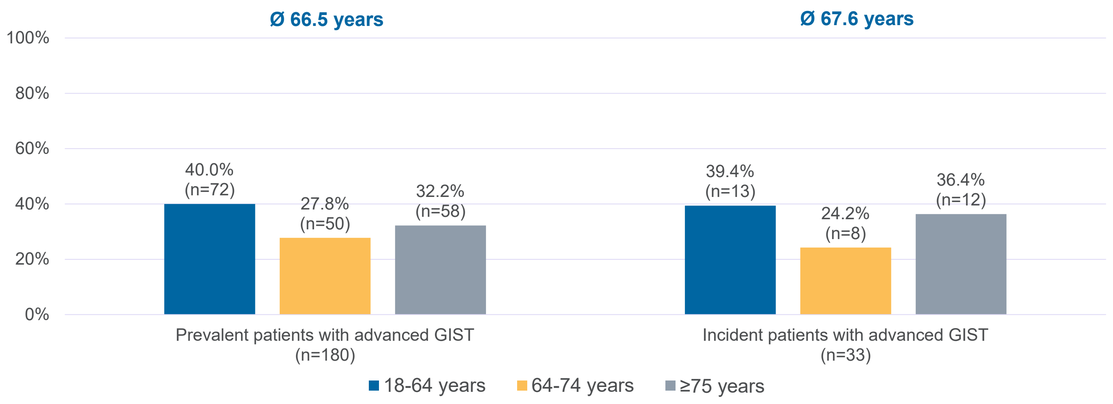


*As there is no specific ICD-10-GM code for GIST in Germany, other tumor entities of the gastrointestinal tract may have been included in the 2nd selection step.

Advanced GIST patients eligible for fourth-line treatment

- Between 2015-2020, n=437 patients with advanced GIST received ≥1 TKI prescription (see Figure 1).
- From these, n=17 patients received prior treatment with imatinib and sunitinib and regorafenib, corresponding to 0.4 per 100,000 individuals and thus classified as eligible for fourth-line treatment.

Figure 2. Age distribution

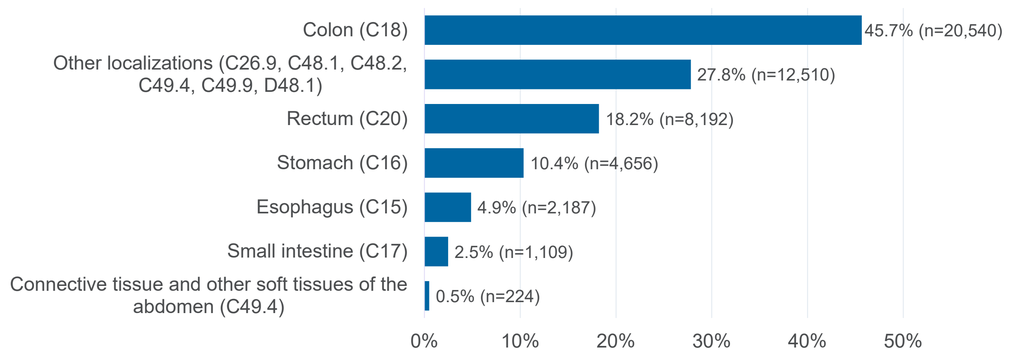


* Due to data protection regulation, patient counts <5 and corresponding percentages could not be reported.

Tumor localizations

- Among the n=44,979 patients of the second selection step with a diagnosis indicating gastrointestinal tumors that include GIST, the most common tumor localizations were colon, other localizations, rectum, and stomach (see Figure 3). Gastrointestinal tumors of the esophagus, small intestine, and tissue of the abdomen were rare.
- Analysis of the frequency of ICD-10-GM code C49.4 "Malignant neoplasms of connective tissue and other soft tissues of the abdomen" showed that the more specific coding used in GIST centers of excellence was used only in 10.0% of prevalent patients and not at all in incident patients and patients eligible for fourth-line treatment with ripretinib.

Figure 3. Tumor localization of prevalent patients with a diagnosis indicating GIST* in 2020



*As there is no specific ICD-10-GM code for GIST in Germany, other tumor entities of the gastrointestinal tract may have been included in the assessment. Tumor location could be coded to more than one location.

LIMITATIONS

- GIST is a rare oncologic disease, making it difficult to achieve an adequately large sample for representative studies and claims data analysis.
- Nevertheless, the results of this claims data analysis can be generalized to the German population, since the InGef research database contains an age-, gender-, and region/federal state of residence-adjusted sample of approximately 4 million individuals according to the Federal Statistical Office of Germany.
- As there is no specific ICD-10-GM code for GIST in Germany in contrast to the ICD-10-CM version, GIST was identified by the inclusion of different diagnosis codes according to tumor localization and in combination with TKI prescriptions.
- However, it is possible that other tumor entities of the gastrointestinal tract were included due to the broad approach.
- Finally, GIST patients might have been enrolled in trials and received treatments not recorded in this database, which could lead to an underestimation of the reported epidemiology of GIST in Germany.

CONCLUSIONS

- Although the identification of GIST patients is challenging due to a lack of a specific ICD-10-GM code, this claims data analysis allowed a first estimate on the prevalence and incidence of advanced GIST in Germany.
- The applied algorithm showed a feasible approach for planning and set-up of real-world evidence studies in the future.
- The generated results are reliable and comparable to previous European estimates and could be used to extrapolate to the entire German population.
- As true for other rare cancer types, sarcoma-specific ICD-10-GM codes would greatly facilitate epidemiological and healthcare research in GIST.
- Based on the coding schemes available to date, a combination of ICD-10 coding of localization and International Classification of Diseases for Oncology (ICD-O) coding of morphology may represent a viable approach for clinical practice and research in GIST.

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