# Medication Use in Indolent Systemic Mastocytosis (ISM) in Germany Prior to Avapritinib EMA Approval

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## Background

- Systemic mastocytosis (SM) is a clonal mast cell disease driven by the KIT D816V mutation and caused by mast cell accumulation and activation.[1]
- SM is characterized by debilitating heterogenous manifestations, including anaphylaxis.[2]
- Indolent systemic mastocytosis (ISM), a subtype of SM, represents about 85% of all cases of SM.[3]

## Objective

- This study aimed to assess the medications used in ISM prior to the European Medicines Agency (EMA) approval of the first targeted therapy (avapritinib) in December 2023.[4]

## Methods

- A retrospective analysis based on German statutory health insurance (SHI) claims data from the Institute for Applied Health Research Berlin (InGef) research database was conducted.
- The analyzed sample of the InGef database (~5% of the German population[5]) is adjusted by age and sex to represent the German population and shows good overall concordance with the German population in terms of morbidity, mortality and drug use[6].
- ISM is a rare disease for which there is no specific International Statistical Classification of Diseases, German Modification, 10th edition (ICD-10-GM) code. The diagnosis code D47.0 *"Histiocyte and mast cell tumor of uncertain or unknown behavior"* (which includes ISM among others) was used to identify relevant patients in the SHI claims data. We assume that the proportion of diagnoses other than ISM among ICD-10-GM code D47.0 is small and can therefore be neglected.
- For the analysis of ISM medication use for 2021, adult (≥18 years) patients with at least two ICD-10-GM diagnosis codes for ISM (D47.0) in two different quarters in the inpatient (primary or secondary diagnosis) and/or outpatient sector (diagnosis certainty: verified) were selected.
- To omit overlap due to progression of ISM to advanced SM (AdvSM) (approximately 5-10%[2]), patients with ISM and AdvSM diagnosis codes (ICD-10-GM: C94.3 *"Mast cell leukemia"* or C96.2 *"Malignant mast cell tumor"*) within the same year were excluded.
- Assessed medications (based on the Anatomical Therapeutic Chemical (ATC) and German procedure (OPS) classification codes, if applicable) were predefined and included the treatment options for SM according to the German SM Onkopedia guidelines.[2]
- Furthermore, the specialty of the physician who recorded the ISM diagnosis in the outpatient setting was determined.

## Results

### Patient selection

- A total of 164 ISM patients were identified in 2021.
- After exclusion of 13 patients with AdvSM, 151 adult ISM patients (female: 64%, median age: 57 years) remained (see **Figure 1**).

### Figure 1. Flow-chart of patient selection

All individuals in the InGef sample database continuously observable in 2021 (including patients deceased in 2021)

**n=3,876,822**

↓

Patients with at least two recorded ICD-10-GM diagnosis codes D47.0 *"Histiocyte and mast cell tumor of uncertain or unknown behavior"* (which includes ISM among others) in different quarters in the inpatient or outpatient sector in 2021

**n=164**

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All patients without any ICD-10-GM diagnosis code for AdvSM (C94.3 *"Mast cell leukemia"* or C96.2 *"Malignant mast cell tumor"*) in the inpatient or outpatient sector in 2021

**n=151**

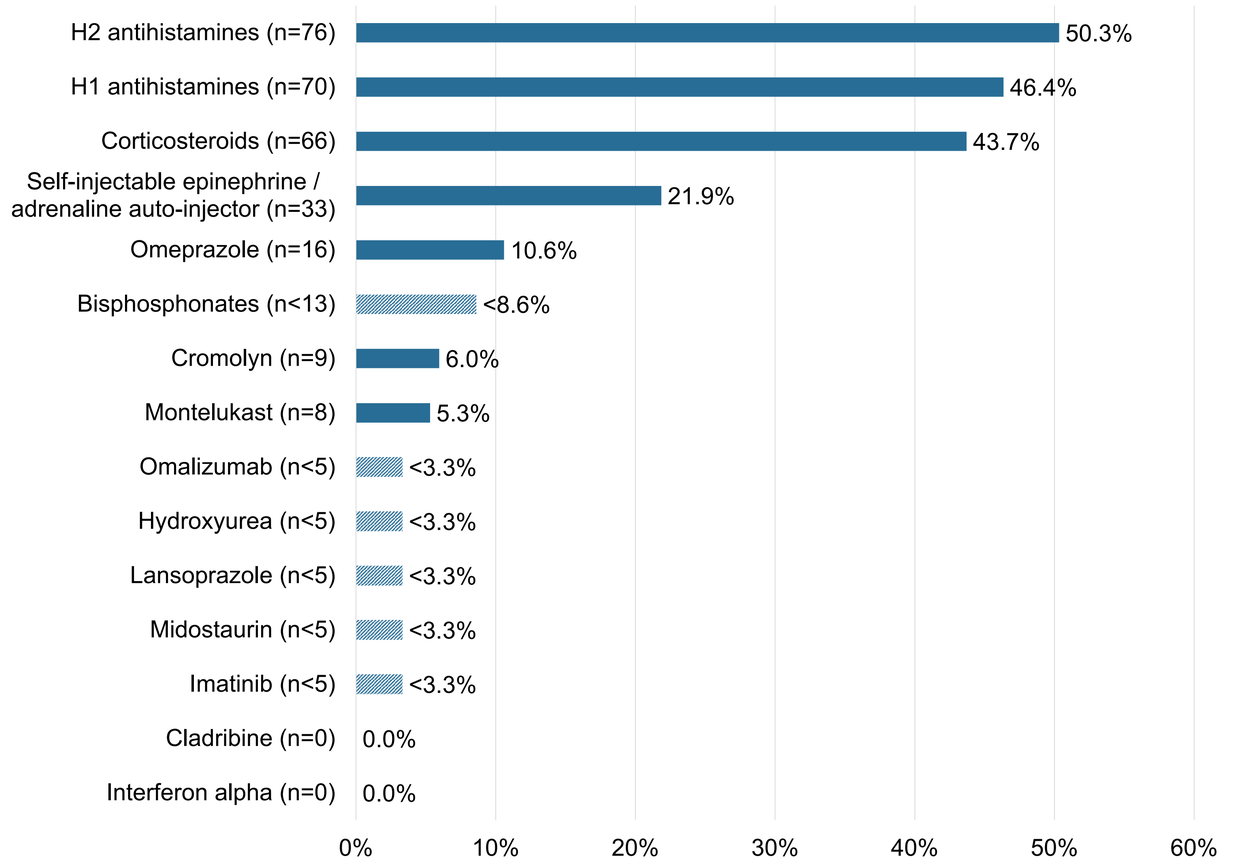
*Abbreviations: AdvSM, Advanced systemic mastocytosis; ICD-10-GM: International Statistical Classification of Diseases and Related Health Problems, 10th Revision, German Modification; InGef, Institute for Applied Health Research Berlin; ISM, Indolent systemic mastocytosis.*

## Results (Continued)

### ISM medication use

- In 2021, 77% of the ISM population received at least one treatment option.
- Most common treatments were best supportive care (BSC) like H2 antihistamines (50%), H1 antihistamines (46%), corticosteroids (44%), adrenaline auto-injectors (22%), and proton pump inhibitors (omeprazole 11%, lansoprazole less than 3.3%) (see **Figure 2**).
- Omalizumab was rarely used (less than 3.3% in all cases).
- Other treatments used for AdvSM (but not approved for use in ISM) were rarely used, e.g., midostaurin (less than 3.3%), cladribine (0%) and interferon (0%).

### Figure 2. ISM medication use in 2021

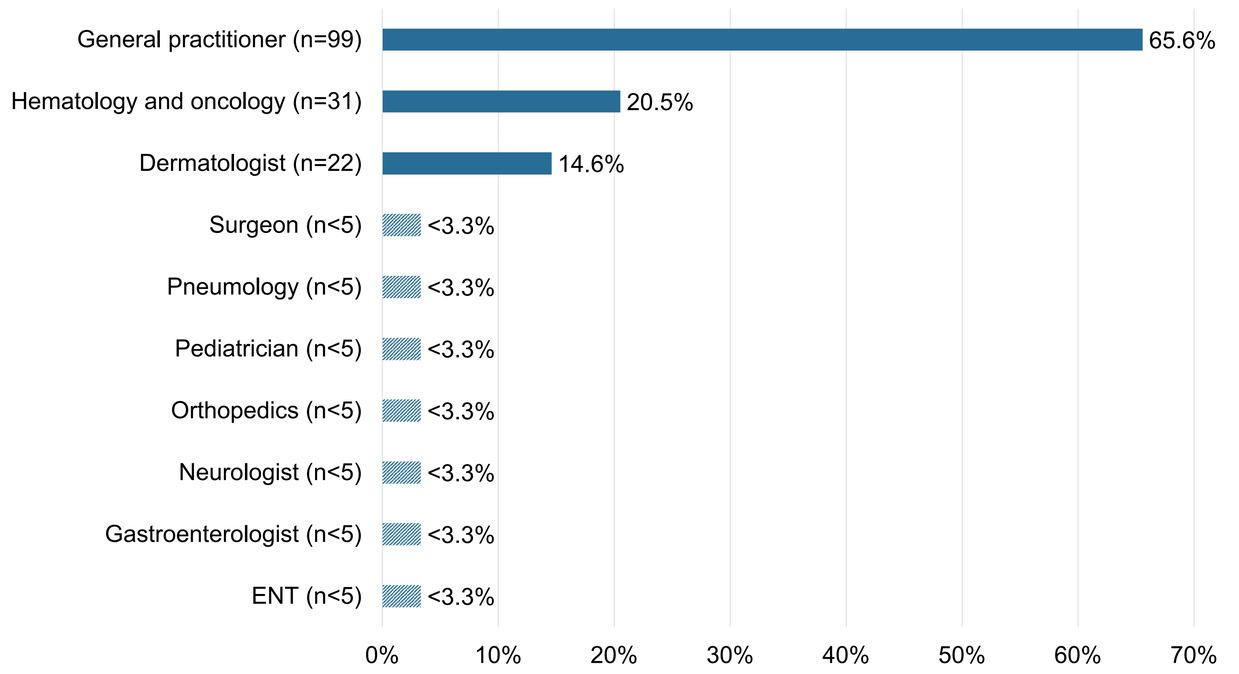



*Due to data protection regulations, results for n<5 cannot be presented (striped bars). No matches were found for the following medications: azacitidine, brentuximab vedotin, cannabidiol, cyclosporine, cytarabine, dasatinib, nilotinib, peginterferon alfa-2a, tacrolimus, and zafirlukast.*

### Specialty of physician

- Most ISM diagnoses were recorded by general practitioners (66%), followed by hematology and oncology specialists (21%), and dermatologists (15%) (see **Figure 3**).

### Figure 3. Specialty of physician who recorded ISM diagnosis




*Abbreviations: ENT, Ear, nose and throat. Due to data protection regulations, results for n<5 cannot be presented (striped bars). As two diagnoses were requested, double counting may occur.*

## Conclusion

- Prior to EMA approval of avapritinib, most ISM patients in Germany were treated with BSC consisting of H1 and H2 antihistamines, corticosteroids, and proton pump inhibitors amongst others.
- Cytoreductive off-label therapies such as cladribine and interferon were not utilized in ISM patients.
- Midostaurin was administered in a few individual cases (less than 3.3%), but it was not considered a standard treatment option.

### References

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