

Not All GISTs are Gastric: A Single-center Cohort of Non-gastric GIST

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Abstract

Objectives: Non-gastric gastrointestinal stromal tumors (GIST) are less common than gastric primaries, but are often considered higher risk. Real-world cohorts focusing on non-gastric GIST with long-term follow-up remain limited.

Methods: We conducted a single-center retrospective cohort study of consecutive adults with histologically confirmed GISTs (esophagus, small intestine, and colon/rectum) treated between January 2015 and June 2025. National Institutes of Health (NIH) risk categories documented in pathology reports were recorded, and Armed Forces Institute of Pathology (AFIP) (Miettinen-Lasota) risk groups were calculated when tumor size, mitotic activity (per 5 mm²), and primary site were available. Overall survival (OS) was estimated using the Kaplan-Meier method.

Results: Among 114 patients with GIST, 41 (36.0%) had non-gastric primaries (small intestine 73.2%, rectum 19.5%, esophagus 7.3%). Median age was 55 years (range, 30-83); median tumor size was 6.0 cm (range, 0.4-26.0); and median mitotic count was 6/5 mm² (range, 0-218). At diagnosis, 34 patients had localized disease and 7 had *de novo* metastatic disease; during follow-up, 10/34 (29.4%) patients developed recurrent metastasis, resulting in 17/41 (41.5%) patients with metastatic disease overall. NIH risk was available for 37/41 (90.2%) patients; of these, 22/37 (59.5%) were high risk. AFIP risk could be calculated in 26/41 (63.4%) patients; of these, 15/26 (57.7%) were classified as high risk. Metastatic sites most commonly involved the liver (47%) and the peritoneum (41%). After a median follow-up of 77 months, 4 of 41 (9.8%) patients had died; the 10-year OS was 86%.

Conclusion: In this real-world, non-gastric GIST cohort, high-risk disease was common, and metastases predominantly involved the liver and peritoneum. Favorable long-term survival appears achievable with high-quality surgery and guideline-consistent use of imatinib in routine practice.

Keywords: Gastrointestinal stromal tumors, survival analysis, non-gastric

Introduction

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal neoplasms of the gastrointestinal tract, with an annual incidence of approximately 1-1.5 per 100,000 in most series. The stomach accounts for 55-65% of primary sites and the small intestine for 20-30%, whereas colorectal and esophageal primaries are less frequent (1). Tumor size, mitotic activity, and anatomic location are the principal clinicopathologic determinants of malignant behavior, and non-gastric localization (e.g., small intestine, rectum) is widely recognized as an independent predictor of recurrence risk (1-3).

Risk stratification is commonly performed using the National Institutes of Health (NIH) consensus criteria, which integrates tumor size and mitotic count (4). After accounting for tumor size and mitotic activity, non-gastric GISTs, particularly jejuno-ileal and rectal primaries, have been associated with a higher risk of metastasis and cancer-related death than gastric GISTs (5,6). However, contemporary large databases and multicenter analyses suggest substantial outcome heterogeneity once molecular subtypes and access to effective targeted therapy are considered (7,8). Metastatic spread most frequently involves the liver and peritoneum, whereas lung and distant lymph node metastases are uncommon (9). Despite this, detailed cohorts focusing specifically on non-gastric primaries that jointly evaluate both localized and



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Received: 05.03.2026 **Accepted:** 20.07.2026 **Publication Date:** 07.08.2026

Cite this article as: Canaslan K, Yetginoğlu Ö, Yavuzşen T. Not all GISTs are gastric: a single-center cohort of non-gastric GIST. Int J Gastrointest Cancer Res. 2026;1:1-8



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metastatic presentations and include long-term follow-up remain limited.

Complete surgical resection is the standard approach for localized disease, and adjuvant imatinib for up to 3 years is recommended for high-risk and selected intermediate-risk patients to reduce recurrence (2). In metastatic or unresectable disease, imatinib followed by sunitinib and regorafenib constitutes the standard sequential tyrosine kinase inhibitor (TKI) therapy and is associated with meaningful improvements in survival. Neoadjuvant imatinib is increasingly used in rectal and duodenal/jejunal GIST to facilitate organ- or sphincter-preserving surgery (10,11).

We report real-world data on non-gastric GIST, focusing on clinicopathologic features, risk stratification [NIH-reported and Armed Forces Institute of Pathology (AFIP)-calculated], metastatic patterns, and treatment trajectories in localized and *de novo* metastatic presentations.

Material and Methods

Study Design and Setting

This single-center, retrospective cohort study screened consecutive adult patients who were evaluated and/or treated for GIST between January 2015 and June 2025.

Study Population

The study population consisted of consecutive adult patients (≥ 18 years) with histologically confirmed GIST established on surgical or biopsy specimens and a primary non-gastric localization, including the esophagus, small intestine, colon, or rectum. Patients were required to have histologically confirmed non-gastric GIST and sufficient clinical information for baseline clinicopathologic characterization and survival follow-up. NIH risk was recorded when documented in pathology reports and was analyzed among evaluable patients. Patients were excluded if they were managed as having metastatic GIST with an unknown primary site (i.e., the primary tumor could not be identified despite diagnostic work-up) or were lost to follow-up, such that survival status could not be ascertained beyond the baseline assessment.

Data Sources and Data Collection

Clinical data were abstracted from institutional electronic medical records and pathology reports using a standardized case report form. Collected variables included sociodemographic characteristics (age at diagnosis and sex); clinical parameters (primary tumor site, date of diagnosis, treatment details, including surgery and systemic therapy, and follow-up dates); pathological features [tumor size in

centimeters, margin status (R0/R1/R2) when applicable, and mitotic activity]; and disease status variables (stage at diagnosis, sites of metastasis, and recurrence/progression when applicable).

Pathological Assessment and risk Stratification

Mitotic activity was recorded as the number of mitoses per 5 mm². NIH risk categories reported in routine pathology records were captured according to the NIH consensus criteria (4). In addition, we independently calculated AFIP (Miettinen-Lasota) risk groups using tumor size, mitotic activity (per 5 mm²), and primary tumor site (12). AFIP risk could be assigned only when the required parameters were available.

Outcomes

The primary outcome was overall survival (OS). OS was defined as the time from the date of diagnosis to death from any cause, or to last known follow-up (censored). The date of diagnosis was taken as the date of histopathologic confirmation. Remission/no evidence of disease (NED) was defined as the absence of radiologic and/or clinical evidence of active disease at the last evaluation, based on the treating physician's assessment and available imaging. Relapse was defined as radiologic recurrence after initial localized management or progression following a documented response or stable disease. Synchronous metastatic disease was defined as metastatic disease present at diagnosis. Metachronous metastatic disease was defined as metastatic recurrence developing during follow-up after an initially localized diagnosis.

Statistical Analysis

Continuous variables were summarized as mean $\pm$ standard deviation or median (min-max) depending on distribution; categorical variables were summarized as counts and percentages. OS was estimated using the Kaplan-Meier method, and survival curves were compared using the log-rank test where applicable. Two-sided p-values < 0.05 were considered statistically significant. Analyses were performed using IBM SPSS Statistics (version 29.0) and R (version 4.5).

Ethics

The study protocol was approved by the Dokuz Eylül University Institutional Ethics Committee of the study center (approval no: 2026/09-12, date: 02.03.2026). Given the retrospective nature of the study, the requirement for informed consent was waived in accordance with national regulations and institutional policy.

Results

Study Population and Primary Site Distribution

Among 114 patients with histologically confirmed GIST, 41 had non-gastric primary tumors, representing 36.0% of the overall cohort. The primary site distributions for the overall cohort and the non-gastric subgroup are shown in Figure 1.

Patient and Tumor Characteristics

The median age at diagnosis was 55 years (range 30-83), and 26 patients (63.4%) were male. The median tumor size was 6.0 cm (range, 0.4-26.0). The median mitotic count was 6 per 5 mm² (range 0-218), and Ki-67 ranged from 1% to 60%. NIH risk categories were available in 37/41 (90.2%) patients; among evaluable cases, 22/37 (59.5%) were classified as high risk. AFIP risk could be calculated in 26/41 patients (63.4%) using the available clinicopathologic parameters; among evaluable cases, 15/26 (57.7%) were classified as high risk. In localized disease, 11/22 (50.0%) evaluable patients were classified as high risk, whereas all evaluable *de novo* metastatic cases (4/4, 100%) were high risk. Baseline characteristics stratified by stage at diagnosis are presented in Table 1.

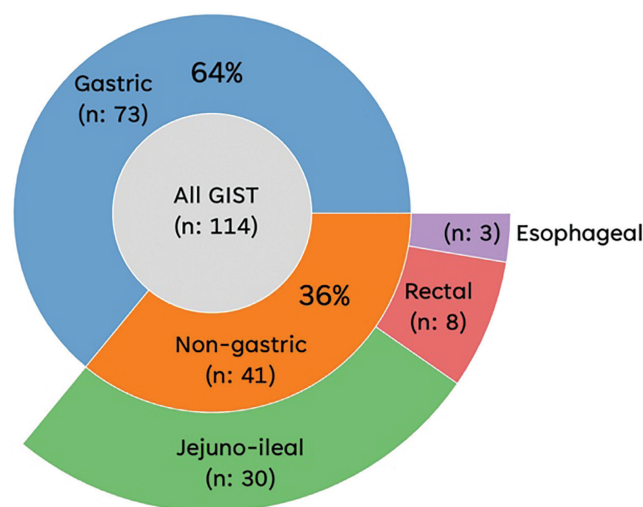


Figure 1. Distribution of primary tumor sites in the overall GIST cohort (n=114) and the non-gastric subgroup (n=41). The chart depicts the proportions of gastric GIST (n=73, 64.0%) and non-gastric GIST (n=41, 36.0%) within the total cohort. Non-gastric primary sites are further stratified into jejunum-ileal (n=30), rectal (n=8), and esophageal (n=3)

GIST: Gastrointestinal stromal tumor

Table 1. Baseline characteristics and clinical course of non-gastric GIST patients (n=41), stratified by stage at diagnosis

Characteristic	Overall (n=41)	Localized at diagnosis (n=34)	<i>De novo</i> metastatic at diagnosis (n=7)
Age, years	55 (30-83)	51.5 (30-83)	60.0 (42-68)
Sex, n (%)			
Male	26 (63.4)	20 (58.8)	6 (85.7)
Female	15 (36.6)	14 (41.2)	1 (14.3)
Primary tumor site, n (%)			
Small intestine	30 (73.2)	24 (70.6)	6 (85.7)
Rectum	8 (19.5)	7 (20.6)	1 (14.3)
Esophagus	3 (7.3)	3 (8.8)	0 (0.0)
Tumor size, cm (n=33)	6.0 (0.4-26.0)	6.0 (0.4-26.0)	7.5 (4.0-15.4)
Mitotic count, per 5 mm ² (n=34)	6 (0-218)	5 (0-218)	18.5 (0-71)
Ki-67, % (n=33)	5 (0-60)	5 (0-60)	10 (4-45)
NIH risk group (n=37)			
Very low/no risk	4/37	4/32	-
Low	6/37	6/32	-
Intermediate	5/37	5/32	-
High	22/37	17/32	5/5 (100)
AFIP risk group (n=26)			
Very low/no risk	2/26	2/22	-
Low	5/26	5/22	-
Intermediate	4/26	4/22	-
High	15/26	11/22	4/4 (100)
Recurrent metastasis after localized diagnosis, n (% of localized)		10 (29.4)	

GIST: Gastrointestinal stromal tumor, NIH: National Institutes of Health, AFIP: Armed Forces Institute of Pathology

Disease Status and Risk Stratification

At diagnosis, 7 patients had *de novo* metastatic disease and 34 had localized disease. During follow-up, 10 of the initially localized patients developed recurrent metastatic disease, resulting in a total of 17 of 41 (41.5%) patients experiencing metastatic disease overall (*de novo* + recurrent).

Treatment Patterns

Among localized cases (n=34), 17 received adjuvant imatinib, and 1 patient received neoadjuvant imatinib followed by adjuvant imatinib.

All metastatic patients received first-line imatinib. In the second-line setting, 3 patients received high-dose imatinib and 6 received sunitinib.

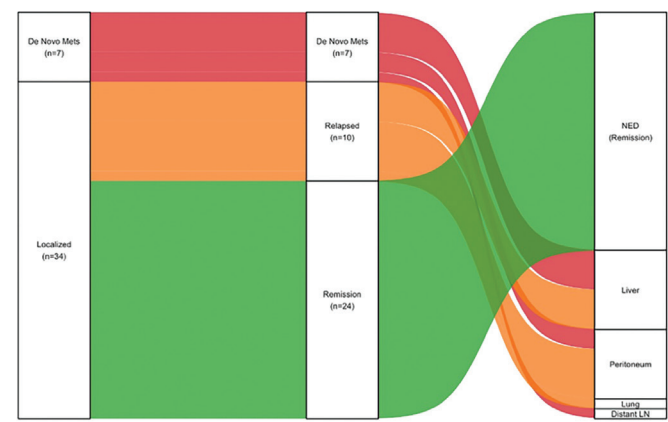


Figure 2. Clinical course and metastasis patterns in non-gastric GIST (n=41). Sankey diagram illustrating transitions from initial disease status (localized vs. *de novo* metastatic) to subsequent clinical states (remission vs. relapse) and metastatic destinations. Metastatic sites include the liver, peritoneum, lungs, and distant lymph nodes

GIST: Gastrointestinal stromal tumor, NED: No evidence of disease, LN: Lymph node

Metastatic Sites and Clinical Course

Among the 17 patients who developed metastatic disease at any time, 7 had synchronous metastatic disease at diagnosis and 10 developed metachronous metastatic recurrence after initially localized disease. The most common metastatic sites were the liver (8/17, 47.1%) and the peritoneum (7/17, 41.2%). Metastatic patterns, stratified by synchronous versus metachronous presentation, are summarized in Table 2. The overall clinical trajectories are summarized in Figure 2.

Follow-up and Survival

After a median follow-up of 77 months, 4 of 41 patients (9.8%) had died. The Kaplan-Meier-estimated 10-year OS rate was 86%, and the survival curve is presented in Figure 3.

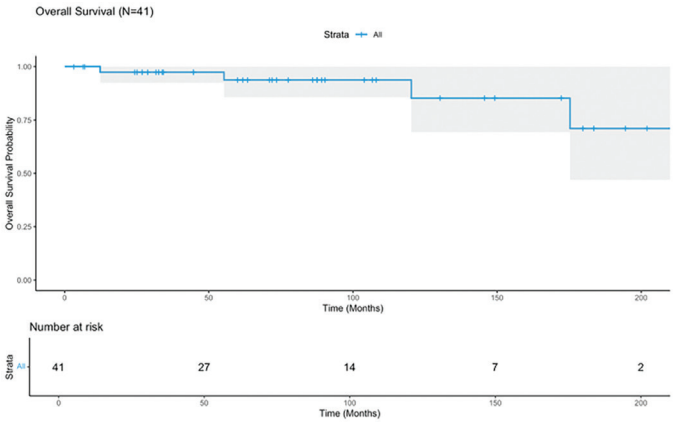


Figure 3. Overall survival in the non-gastric GIST cohort (n=41). Kaplan-Meier estimate of overall survival from date of diagnosis to death from any cause or last follow-up. Tick marks indicate censored observations. Shaded bands represent 95% confidence intervals. Numbers at risk are displayed beneath the plot

GIST: Gastrointestinal stromal tumor

Table 2. Metastatic patterns among patients with non-gastric GIST who developed metastatic disease			
Metastatic characteristic	Synchronous metastatic disease (n=7)	Metachronous metastatic disease (n=10)	Overall metastatic cohort (n=17)
Liver metastasis	4 (57.1)	4 (40.0)	8 (47.1)
Peritoneal metastasis	2 (28.6)	5 (50.0)	7 (41.2)
Lung metastasis	0 (0.0)	1 (10.0)	1 (5.9)
Distant lymph node metastasis	1 (14.3)	0 (0.0)	1 (5.9)
Data are presented as n (%). Patients could have more than one metastatic site			
GIST: Gastrointestinal stromal tumor			

Discussion

In this real-world cohort of GIST, non-gastric tumors accounted for 36% of all GIST cases, and 17% of patients had *de novo* metastatic disease at diagnosis. Among those presenting with localized disease, NIH stratification was skewed toward high-risk categories, consistent with prior evidence that a non-gastric location confers a less favorable prognosis even after accounting for tumor size and mitotic activity.

In prior large cohorts, non-gastric primaries have comprised approximately half of all GIST cases (52-55%) (13-16) providing important national context for our observed proportion of 36%. This discrepancy may reflect differences in referral patterns, diagnostic pathways, and institutional case mix. Across published series, the most frequent non-gastric primary sites are consistently the small intestine, colon, and rectum, which align with the distribution in our cohort.

Given that risk categories were routinely documented in pathology reports using the NIH consensus criteria (4), we captured NIH risk as reported and additionally calculated AFIP (Miettinen-Lasota) groups when the required parameters were available to incorporate anatomic site into risk assessment (2,12). Because the anatomic site is a key determinant of relapse risk in GIST, incorporating site through AFIP may improve interpretability when comparing non-gastric cohorts across studies. A key observation in our cohort is the predominance of high-risk disease among evaluable cases, regardless of the risk framework applied. This risk enrichment is clinically plausible for a non-gastric-focused series, as multiple large pathological series have shown that extra-gastric primaries have a higher risk of relapse/metastasis than gastric tumors even when tumor size and mitotic activity are comparable (17,18).

Treatment patterns in this cohort largely reflect contemporary standards. Adjuvant imatinib use in localized disease tracked the high-risk burden and is supported by randomized evidence demonstrating that 3 years of adjuvant imatinib improves recurrence-free survival and OS versus 1 year in high-risk patients (19). Current guideline recommendations also endorse 3 years of adjuvant imatinib for patients with a significant risk of relapse and imatinib-sensitive genotypes (2,20). In *de novo* metastatic disease, the use of first-line imatinib for all patients is consistent with guideline-based management and reflects the central role of KIT proto-oncogene receptor tyrosine kinase/platelet-derived growth factor receptor alpha (KIT/PDGFR α) inhibition in advanced GIST.

The observed metastatic dissemination pattern, characterized by the predominance of liver and peritoneal involvement and

rare lung or distant lymph node metastases, matches what has been repeatedly reported across large clinical series (21,22). This is clinically relevant because it supports surveillance focused on the liver and peritoneum in high-risk non-gastric disease while acknowledging that extra-abdominal spread, although uncommon, can occur.

Despite the unfavorable baseline risk profile expected for non-gastric primaries, the cohort's long follow-up and low number of deaths suggest that contemporary risk-adapted use of surgery and TKIs can translate into favorable long-term outcomes in real-world practice. These outcomes may, in part, reflect the routine use of a multidisciplinary tumor board at our center (medical oncology and surgery), which facilitates timely imaging review, coordinated decision-making, and consistent surgical planning. However, causal inferences cannot be made in this retrospective analysis.

Although molecular profiling was not systematically available in our cohort, the molecular landscape of GIST is highly relevant when interpreting non-gastric disease. Most GISTs are driven by activating alterations in KIT or PDGFR α , and mutational subtype has predictive as well as prognostic implications (1). KIT exon 11 mutations are the most frequent overall and are generally associated with sensitivity to standard-dose imatinib, whereas KIT exon 9 mutations are relatively enriched in small intestinal GIST and may require dose optimization in the advanced setting (2,23,24). In contrast, PDGFR α -mutant GIST is more typical of gastric primaries and shows primary resistance to imatinib, limiting its relevance to most non-gastric cohorts (25). Rectal and small intestinal GISTs may also include clinically important KIT/PDGFR α wild-type subsets, including neurofibromatosis type 1-associated, B-Raf proto-oncogene, serine/threonine kinase-mutant, or neurotrophic tyrosine receptor kinase-fusion-positive tumors, each with distinct therapeutic implications (26-28). Therefore, the lack of routine molecular annotation in the present study limits our ability to correlate anatomical site, recurrence risk, and TKI sensitivity.

Study Limitations

This observation should be interpreted cautiously; the low number of events limits robust survival modeling and subgroup inference. Moreover, the retrospective design, single-center setting, and missingness in some pathology variables, including risk classification, may introduce bias and constrain generalizability. Comprehensive molecular profiling could not be performed for every patient in routine practice, representing a real-world limitation relevant to many centers both in our country and internationally. Nonetheless, the strength of the present report lies in its granular characterization of non-gastric GIST in both

localized and metastatic presentations within routine care, thereby complementing the evidence base often dominated by mixed-site cohorts or trial-selected populations.

Conclusion

Our real-world data reinforce that non-gastric GIST constitutes a clinically heterogeneous but generally higher-risk subgroup, with metastatic spread predominantly involving the liver and peritoneum. Despite the generally more aggressive biology associated with non-gastric primaries, our findings suggest that, in routine practice, long-term outcomes can be favorable with high-quality surgery and guideline-consistent use of imatinib. Larger multicenter real-world cohorts with standardized molecular annotation are needed to refine prognostication and optimize treatment pathways.

Ethics

Ethics Committee Approval: The study protocol was approved by the Dokuz Eylül University Institutional Ethics Committee of the study center (approval no: 2026/09-12, date: 02.03.2026).

Informed Consent: Given the retrospective nature of the study, the requirement for informed consent was waived in accordance with national regulations and institutional policy.

Footnotes

Authorship Contributions

Surgical and Medical Practises: K.C., Ö.Y., Concept: K.C., T.Y., Design: K.C., T.Y., Data Collection or Processing: K.C., Ö.Y., Analysis or Interpretation: K.C., T.Y., Literature Search: K.C., Ö.Y., T.Y., Writing: K.C., Ö.Y., T.Y.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

- Blay JY, Kang YK, Nishida T, von Mehren M. Gastrointestinal stromal tumours. *Nat Rev Dis Primers*. 2021;7(1):22.
- Serrano C, Martín-Broto J, Asencio-Pascual JM, et al. 2023 GEIS guidelines for gastrointestinal stromal tumors. *Ther Adv Med Oncol*. 2023;15:17588359231192388.
- Wang Q, Li M, Bai X, et al. Unraveling the site-specific features in small intestinal stromal tumors: a retrospective study. *BMC Gastroenterol*. 2025;25(1):337.
- Fletcher CD, Berman JJ, Corless C, et al. Diagnosis of gastrointestinal stromal tumors: a consensus approach. *Hum Pathol*. 2002;33(5):459-465.
- Sun X, Sun Y, Xiong R, et al. Hidden risk factors for recurrence of jejunoileal gastrointestinal stromal tumors with low NIH classification: implications for surveillance and adjuvant therapy. *J Transl Med*. 2025;23(1):1156.
- Yang Z, Wang F, Liu S, Guan W. Comparative clinical features and short-term outcomes of gastric and small intestinal gastrointestinal stromal tumours: a retrospective study. *Scientific Reports*. 2019;9(1):10033.
- Alvarez CS, Piazzuelo MB, Fleitas-Kanonnikoff T, Ruhl J, Pérez-Fidalgo JA, Camargo MC. Incidence and survival outcomes of gastrointestinal stromal tumors. *JAMA Netw Open*. 2024;7(8):e2428828.
- Eskitzis P, Michou V, Theoti R, Antoniou A, Tsavlis D, Anastakis D. Unraveling gastric and small intestine gastrointestinal stromal tumors: a review of our current knowledge. *Gastrointestinal Disorders*. 2024;6(4):842-857.
- Adil T, Sagar J, Das P, Jain V. Gastrointestinal stromal tumours: a review on genetics, pathology, risk stratification, clinical characteristics, investigation, and treatment. *EMJ Oncol*. 2016;4(1):113-121.
- Lam TJR, Udonwa SA, Masuda Y, Yeo MHX, Farid Bin Harunal Ras M, Goh BKP. A systematic review and meta-analysis of neoadjuvant imatinib use in locally advanced and metastatic gastrointestinal stromal tumors. *World J Surg*. 2024;48(7):1681-1691.
- Rutkowski P, Gronchi A, Hohenberger P, et al. Neoadjuvant imatinib in locally advanced gastrointestinal stromal tumors (GIST): the EORTC STBSG experience. *Ann Surg Oncol*. 2013;20(9):2937-2943.
- Miettinen M, Lasota J. Gastrointestinal stromal tumors: pathology and prognosis at different sites. *Semin Diagn Pathol*. 2006;23(2):70-83.
- Søreide K, Sandvik OM, Søreide JA, Giljaca V, Jureckova A, Bulusu VR. Global epidemiology of gastrointestinal stromal tumours (GIST): a systematic review of population-based cohort studies. *Cancer Epidemiol*. 2016;40:39-46.
- Muñoz-Medel M, Córdova-Delgado M, Retamal IN, et al. High proportion of wild-type gastrointestinal stromal tumor in a cohort of Chilean patients screened by KIT and PDGFRA exome profiling. *Gastrointest Stromal Tumor*. 2022;5:6.
- Bülbül Doğusoy G; Turkish GIST Working Group. Gastrointestinal stromal tumors: a multicenter study of 1160 Turkish cases. *Turk J Gastroenterol*. 2012;23(3):203-211.
- Selcukbiricik F, Yalçın S, Tural D, et al. Gastrointestinal stromal tumors in Turkey: experiences from 3 centers. *Onkologie*. 2013;36(1-2):18-24.
- Wang L, Ni Z, Xu W, et al. Clinical characteristics and outcomes of gastrointestinal stromal tumor patients receiving surgery with or without TKI therapy: a retrospective real-world study. *World J Surg Oncol*. 2023;21(1):21.
- Hirano H, Naito Y, Nishida T, et al. Epidemiologic features and age-related differences in management among patients with gastrointestinal stromal tumors in Japan: a national cancer registry study. *Cancer Res Commun*. 2025;5(7):1235-1242.
- Joensuu H, Eriksson M, Sundby Hall K, et al. Survival outcomes associated with 3 years vs 1 year of adjuvant imatinib for patients with high-risk gastrointestinal stromal tumors: an analysis of a randomized clinical trial after 10-year follow-up. *JAMA Oncol*. 2020;6(8):1241-1246.

20. Casali PG, Abecassis N, Aro HT, et al. Gastrointestinal stromal tumours: ESMO-EURACAN clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2018;29(Suppl 4):iv68-iv78.
21. Yang DY, Wang X, Yuan WJ, Chen ZH. Metastatic pattern and prognosis of gastrointestinal stromal tumor (GIST): a SEER-based analysis. *Clin Transl Oncol*. 2019;21(12):1654-1662.
22. Yu X, Liang X, Wen K. Clinical characteristics and prognosis of gastrointestinal stromal tumors with rare site metastasis (Review). *Oncol Lett*. 2022;24(6):453.
23. Künstlinger H, Huss S, Merkelbach-Bruse S, et al. Gastrointestinal stromal tumors with KIT exon 9 mutations: update on genotype-phenotype correlation and validation of a high-resolution melting assay for mutational testing. *Am J Surg Pathol*. 2013;37(11):1648-1659.
24. Gastrointestinal Stromal Tumor Meta-Analysis Group (MetaGIST). Comparison of two doses of imatinib for the treatment of unresectable or metastatic gastrointestinal stromal tumors: a meta-analysis of 1,640 patients. *J Clin Oncol*. 2010;28(7):1247-1253.
25. Szucs Z, Thway K, Fisher C, et al. Molecular subtypes of gastrointestinal stromal tumors and their prognostic and therapeutic implications. *Future Oncol*. 2017;13(1):93-107.
26. Qian H, Yan N, Hu X, Jiang J, Cao Z, Shen D. Molecular Portrait of GISTs associated with clinicopathological features: a retrospective study with molecular analysis by a custom 9-gene targeted next-generation sequencing panel. *Front Genet*. 2022;13:864499.
27. Hostein I, Faur N, Primois C, et al. BRAF mutation status in gastrointestinal stromal tumors. *Am J Clin Pathol*. 2010;133(1):141-148.
28. Cao L, Tian W, Zhao Y, et al. Gene mutations in gastrointestinal stromal tumors: advances in treatment and mechanism research. *Glob Med Genet*. 2024;11(4):251-262.

Reader Questions

Based on the manuscript: “Not All GISTs are Gastric: A Single-center Cohort of Non-gastric GIST”

1. Which anatomical site was the most common non-gastric primary gastrointestinal stromal tumor (GIST) in this study?

- A. Esophagus
- B. Colon
- C. Small intestine
- D. Rectum

Correct Answer: C. Small intestine

2. Which metastatic site was observed most frequently among patients who developed metastatic disease?

- A. Lung
- B. Bone
- C. Liver
- D. Brain

Correct Answer: C. Liver

3. Which risk stratification system incorporates primary tumor location in addition to tumor size and mitotic activity?

- A. AJCC TNM staging
- B. NIH Consensus criteria
- C. AFIP (Miettinen-Lasota) classification
- D. WHO classification

Correct Answer: C. AFIP (Miettinen-Lasota) Classification

4. According to this study, what was the estimated 10-year overall survival?

- A. 54%
- B. 68%
- C. 74%
- D. 86%

Correct Answer: D. 86%

5. What was the standard first-line systemic treatment for all patients with metastatic GIST in this cohort?

- A. Regorafenib
- B. Sunitinib
- C. Imatinib
- D. Ripretinib

Correct Answer: C. Imatinib