Journal of Health and Technology
Volume 1, Issue 3, September 2025; pp: 151-157
eISSN: 2455-2852 DOI: 10.65129/health.v1i3.90

RESEARCH ARTICLE

Clinicopathological Study of Gastrointestinal Stromal Tumour

S. Karthikeyan[1] and A. Dhanalakshmi[2]*

Department of Pathology, Coimbatore Medical College, Coimbatore - 641014, Tamil Nadu, India; dhansupath@gmail.com

Abstract

Gastrointestinal Stromal Tumors (GISTs) are the most common mesenchymal neoplasms of the gastrointestinal tract, arising predominantly in the stomach and small intestine. They originate from the interstitial cells of Cajal or related stem cells and are characterized by mutations in the KIT or PDGFRA genes. Clinically, GISTs may present with nonspecific symptoms such as abdominal pain, gastrointestinal bleeding, or may be incidentally discovered. Histologically, they display spindle cell, epithelioid, or mixed morphology, and immunohistochemical staining for CD117 (KIT), DOG1, and CD34 aids in diagnosis. Risk stratification is based on tumor size, mitotic index, and anatomical location. Surgical resection is the primary treatment for localized disease, while targeted therapy with tyrosine kinase inhibitors (e.g., imatinib) is effective in advanced or metastatic cases. Recent advancements in molecular diagnostics and targeted therapy have significantly improved the prognosis of GIST patients.

Keywords: Gastrointestinal Stromal Tumor (GIST); Tyrosine Kinase receptor Inhibitor (TKI); risk classification; prognosis; outcome.

1. Introduction

Gastrointestinal Stromal Tumors (GISTs) are the most common mesenchymal tumors of the gastrointestinal (GI) tract, accounting for approximately 1–2% of all GI malignancies. They arise from the interstitial cells of Cajal or their precursors—specialized pacemaker cells that regulate gut motility. GISTs represent a distinct pathological entity characterized by specific histological, immunohistochemical, and molecular features, setting them apart from other soft tissue or smooth muscle tumors of the gastrointestinal system[1].

The majority of GISTs occur in the stomach (60–70%), followed by the small intestine (20–30%), with rare occurrences in the esophagus, colon, rectum, and even outside the GI tract (Extra- Gastrointestinal Stromal Tumors or EGISTs[2]. Clinical presentation varies widely and depends on tumor size and location, ranging from vague abdominal discomfort and GI bleeding to acute presentations like obstruction or perforation. Some cases are discovered incidentally during imaging or endoscopy for unrelated reasons[3].

Histologically, GISTs show spindle cell, epithelioid, or mixed morphology. Immunohistochemical markers, particularly CD117 (KIT) and DOG1, play a central role in diagnosis[4]. Molecular analysis often reveals mutations in the KIT or PDGFRA genes, which are essential not only for diagnosis but also for guiding targeted therapy. The introduction of Tyrosine Kinase Inhibitors (TKIs), especially imatinib, has revolutionized the management of unresectable, recurrent, or metastatic GISTs[5].

The biological behavior of GISTs can range from benign to highly malignant, making risk assessment vital. Risk stratification is based on tumor size, mitotic activity, and anatomical site[6].With ongoing advancements in molecular pathology and personalized medicine, understanding the pathogenesis and clinical spectrum of GIST is crucial for accurate diagnosis and effective treatment[7].

*Author for correspondence

Article Received on: 01 Jan 2025 Revised on: 15 Feb 2025 Accepted on: 5 March 2025

GISTs are rare neoplasms, accounting for approximately 1–2% of all gastrointestinal tumors. First recognized as a distinct pathological entity in the late 20th century, they were historically misclassified as smooth muscle tumors[8]. The discovery of activating mutations in the KIT proto- oncogene in the late 1990s revolutionized the understanding of GIST biology and led to the development of effective targeted therapies.

These tumors typically occur in individuals over 50 years of age and show no significant gender predilection. Although the stomach is the most common site (60–70%), they can occur anywhere along the GI tract, including the esophagus, small intestine, colon, rectum, and rarely in Extra- Gastrointestinal locations (EGISTs)[8].

GISTs have a wide spectrum of biological behavior, ranging from benign to highly malignant. Hence, accurate diagnosis, risk stratification, and appropriate treatment planning are crucial. Advances in molecular pathology have enabled subclassification based on mutational status, which guides therapy and prognosis. Understanding the clinicopathological and molecular features of GISTs is essential for improving patient outcomes[9].

2. Aim and Objectives

To study the clinicopathological and immunohistochemical features of Gastrointestinal Stromal Tumors (GISTs), and to evaluate their diagnostic features.

3. Review of Literature

3.1 Historical Perspective

Gastrointestinal stromal tumors were first distinguished as a unique entity in the late 20th century. Prior to that, they were often misclassified as leiomyomas, leiomyosarcomas, or other smooth muscle tumors. Mazur and Clark (1983) first proposed the term GIST for mesenchymal tumors of the GI tract that were neither clearly smooth muscle nor neural in origin[1].

3.2 Cell of Origin

Kind Blom *et al.* (1998) demonstrated that GISTs likely originate from the Interstitial Cells of Cajal (ICCs), based on ultrastructural and immunohistochemical similarities[3]. This finding provided the foundation for understanding GIST as a unique neoplasm.

3.3 Molecular Pathogenesis

The landmark discovery by Hirota *et al.* (1998) revealed activating mutations in the KIT gene in GISTs. Subsequent studies showed that approximately 75–80% of GISTs harbor KIT mutations, while another 5–10% have PDGFRA mutations[11]. These gain-of-function mutations drive tumor growth via constitutive activation of tyrosine kinase signaling pathways[4].

3.4 Immunohistochemistry

Miettinen and Lasota (2001) emphasized the diagnostic value of CD117 (KIT), which is positive in ~95% of GISTs[6]. DOG1, discovered later, has shown high sensitivity and specificity, particularly in KIT-negative tumors. CD34, SMA, and S-100 may also be expressed variably[4].

3.5 Clinicopathological Features

GISTs most frequently arise in the stomach (60%) and small intestine (30%), with rarer involvement of the esophagus, colon, and rectum[3]. Clinical symptoms are nonspecific and may include abdominal pain, GI bleeding, anemia, or palpable mass[2]. Fletcher *et al.* (2002) proposed a risk stratification scheme based on tumor size, mitotic count, and location, which remains widely used[4].

3.6 Treatment Evolution

The introduction of imatinib mesylate, a tyrosine kinase inhibitor, marked a turning point in the treatment of advanced GISTs[5]. Demetri *et al.* (2014) conducted the first clinical trial demonstrating dramatic responses to imatinib in metastatic and unresectable GISTs[14]. Sunitinib and regorafenib were later approved for imatinib-resistant cases[15].

3.7 Recent Advances

Recent research has identified SDH-deficient GISTs, often seen in pediatric patients and syndromic forms (e.g., Carney-Stratakis syndrome), as well as wild-type GISTs without KIT or PDGFRA mutations[12]. Molecular profiling and next-generation sequencing are increasingly used to classify these tumors and guide therapy[10].

3.8 Prognostic Factors

Key prognostic indicators include tumor size, mitotic index, tumor site, presence of tumor rupture, and mutational status[6]. Gastric GISTs tend to have a more favorable prognosis than small intestinal GISTs of similar size and mitotic rate[11].

4. Material and Methods

This is a retrospective study. A total number of 25 cases reported as GIST were analyzed. This study was conducted in Department of Pathology, Coimbatore medical college, Coimbatore during the period of one and half years from September 2023 to April 2025. H&E sections and IHC slides were retrieved for this study. The demographic data like age, sex and sites of GIST were documented. Subtyping of the GIST were done by thorough morphological examination with IHC correlation[16].

5. Results (Including Observations)

In this study, 25 cases of GIST were analyzed out of which 15 were males and 10 were females. The male to female ratio was 3:2. Age group was between 30 to 75 years with mean age being 52 years. The age group was divided into 30-40 years (n=2, 8%), 41-50 years (n=3, 12%), 51-60 years (n=14, 56%), 61-70 years (n=6, 24%). Predominant age group is>50 years (Chart 1, 2). Among these cases 14 cases of GIST were identified in stomach, 7 cases in the duodenum, and 4 cases in the jejunum (Chart 3). Among all the GIST cases 15 cases (60%) were of spindle cell type, 6 cases were (24%) epithelioid cell type and 4 case (16%) were of mixed type (Chart 1 and 3).

6. Discussion

In this retrospective study of 25 Gastrointestinal Stromal Tumors (GISTs), the clinicopathological profile closely parallels the global epidemiological and pathological trends, with a few distinctive local observations.

Demographic Profile

The mean age was 52 years, with a predominance in patients over 50 years of age. This finding is in agreement with international literature, where GIST typically present in the fifth to seventh decades of life. The male-to-female ratio was 1.5:1, suggesting a

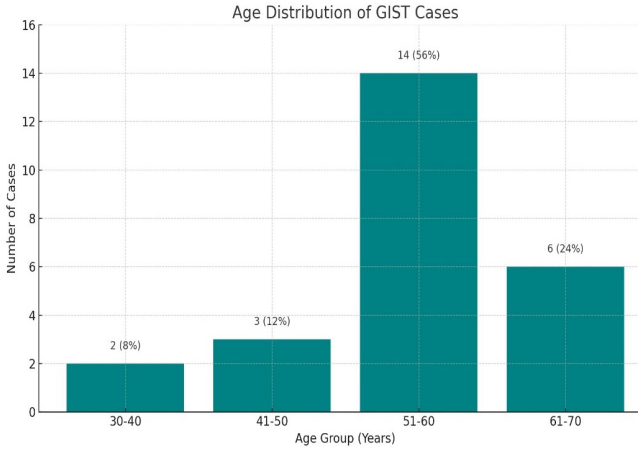

Chart 1. Age distribution of a study group.

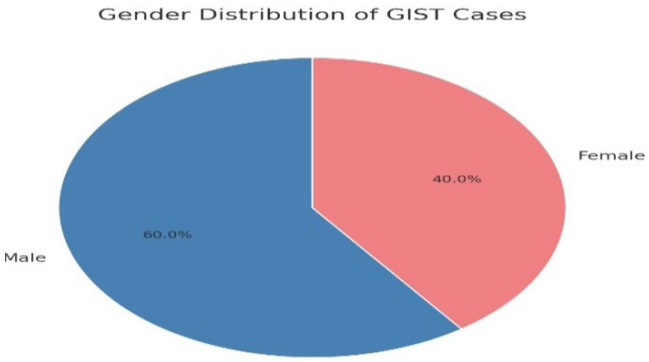

Chart 2. Sex Distribution of a study group.

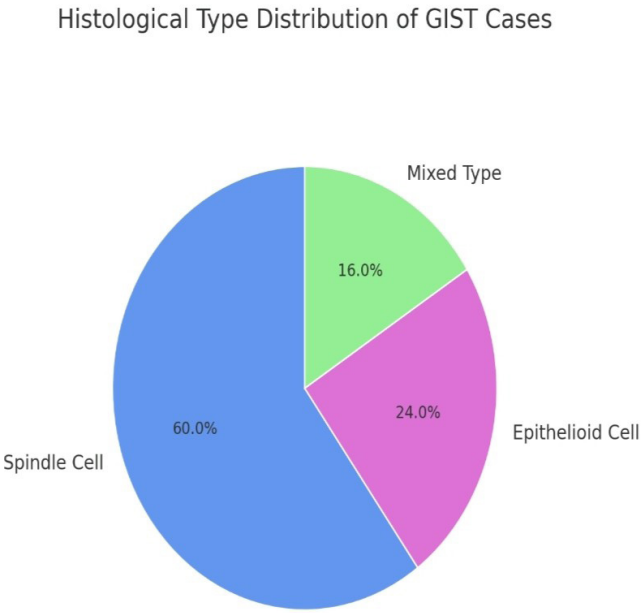

Chart 3. Histological type distribution of GIST cases.

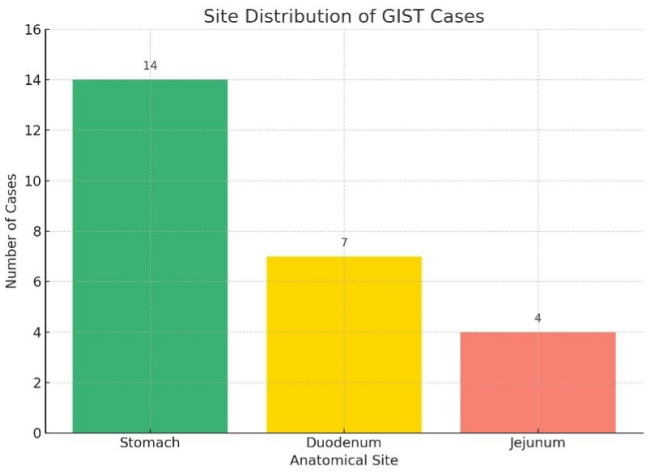

Chart 4. Site of GIST in our study group.

modest male predominance, which has been variably reported in earlier studies (Chart 2).

6.1 Anatomical Distribution

The stomach was the most frequent site (62%), followed by the small intestine (38%; including duodenum and jejunum). This distribution is consistent with previous reports where 60–70% of GISTs occur in the stomach and about 20–30% in the small intestine. The relative predominance of gastric tumors in this series may also reflect a more favorable biological behavior, as gastric GISTs are generally associated with better outcomes than small intestinal counterparts. (Chart 4).

6.2 Histomorphological Features

Spindle cell morphology was the most common subtype (60%) (Figure 1, 2) followed by epithelioid (24%) (Figure 3, 4) and mixed type (16%). (Figure 5, 6) This pattern is consistent with established data, where spindle cell type is the predominant histological variant. Epithelioid morphology, while less common, is important as it may correlate with specific mutational backgrounds (such as PDGFRA mutations) and altered therapeutic response.

6.3 Immunohistochemistry

Immunohistochemical confirmation was achieved using DOG1 and CD117, (Figure 7) the two most sensitive and specific markers for GIST. DOG1 positivity was observed in almost all subtypes, reaffirming its diagnostic utility, particularly in CD117-negative cases (Table 1). CD117 showed slightly lower detection

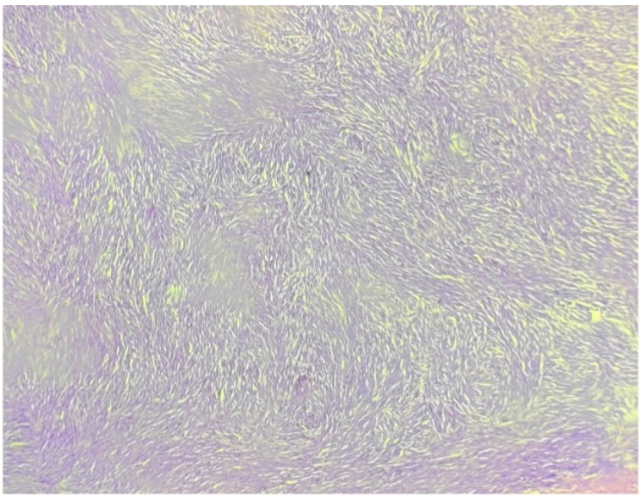

Figure 1. GIST spindle cell type low power.

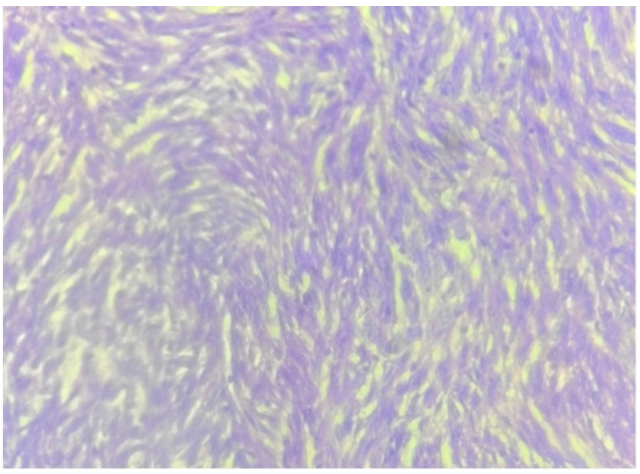

Figure 2. GIST spindle cell type high power.

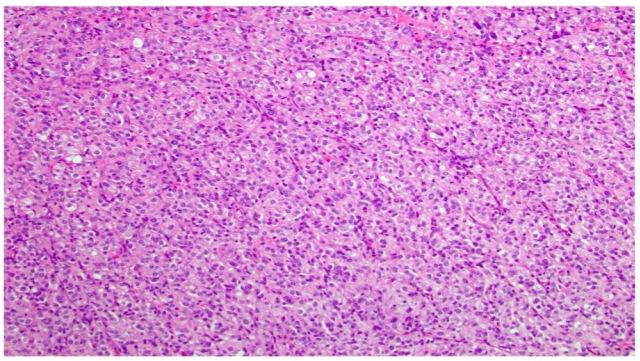

Figure 3. GIST epithelioid cell type low power.

rates, which may be due to antigenic variability or fixation-related issues. The findings underline the complementary role of DOG1 and CD117 in routine diagnostic practice.

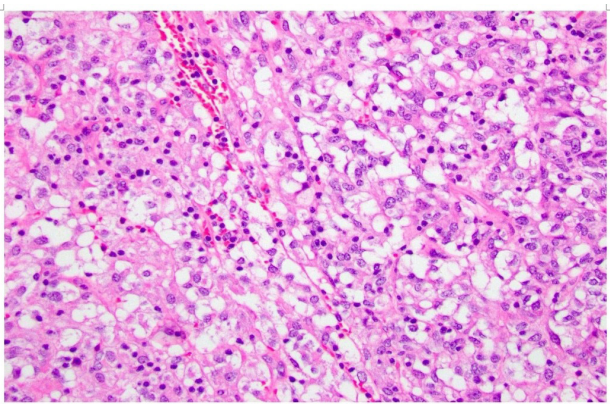

Figure 4. GIST epithelioid cell type high power.

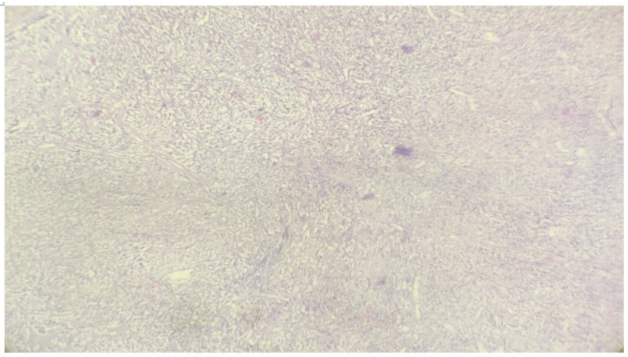

Figure 5. GIST mixed cell type low power.

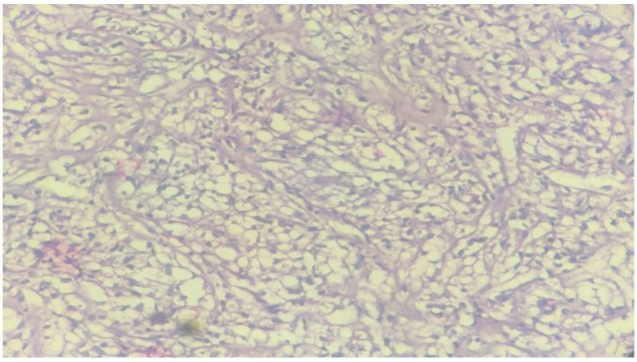

Figure 6. GIST mixed cell type high power.

6.4 Clinical Implications and Risk Stratification

Although formal risk stratification (tumor size, mitotic index, rupture status) was not possible in this study due to incomplete mitotic count data, the predominance of gastric site and spindle cell morphology suggests that many cases may fall into the low-to-intermediate risk categories. However, the higher frequency of small intestinal GISTs (38%) in this cohort also highlights the possibility of a significant subset with higher malignant potential. For optimal prognostic evaluation and therapeutic planning, future studies must integrate

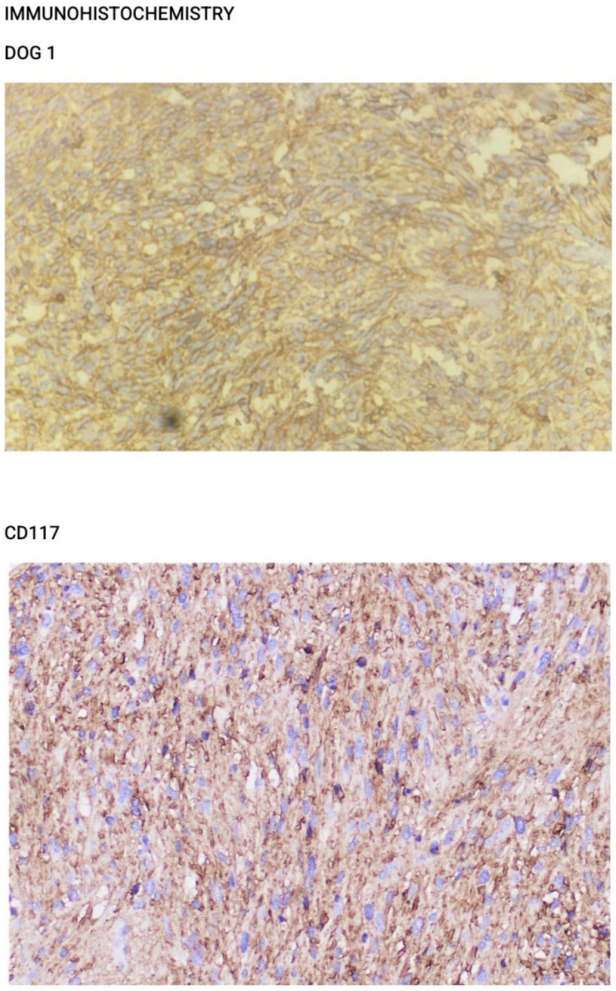

Figure 7. GIST immunohistochemistry DOG 1, CD11.

Table 1. IHC markers Expression in cases of GIST

Histological Subtype of GIST	DOG1 Positive	CD117 Positive
Spindle Cell Type	8	6
Epithelioid Cell Type	3	2
Mixed Cell Type	3	2

Out of 25 cases immunohistochemistry was done for 15 cases

8 cases of spindle cell type GIST in which 8 cases show DOG 1 postivity, 6 cases show CD117 positivity.

4 Cases of epithelioid cell type GIST in which 3 cases show DOG 1 postivity, 2 cases show CD117 positivity.

3 cases of mixed cell type GIST in which 3 cases show DOG 1 postivity, 2 cases show CD117 positivity.

mitotic activity and size-based risk stratification schemes.

6.5 Comparison with Literature

The clinicopathological features in this study—older age at diagnosis, male predominance, gastric site predilection, spindle morphology dominance, and consistent DOG1/CD117 immunoreactivity—are in strong concordance with major published series. The slightly higher proportion of epithelioid/mixed variants may reflect referral patterns or population differences.

6.6 Limitations

The main limitations of this study include small sample size, retrospective design, and absence of detailed risk stratification parameters such as tumor size cut-offs, mitotic activity, and follow-up data. Furthermore, molecular profiling (KIT/PDGFRA mutations, SDH status) was not performed, which restricts correlation with therapeutic and prognostic implications.

7. Summary and Conclusion

This clinicopathological study of 25 cases of GIST reinforces the established trends in demographic distribution, anatomical predilection, and histomorphological features. Gastric GISTs with spindle morphology formed the majority, and immunohistochemical confirmation with DOG1 and CD117 proved highly reliable for diagnosis.

The findings highlight the importance of thorough histopathological examination combined with IHC in establishing a definitive diagnosis. Future studies incorporating mitotic index, tumor size, rupture status, and molecular profiling are essential for accurate risk stratification and personalized management. Strengthening these aspects will enable better prognostic assessment and improved therapeutic decision-making, particularly regarding the role of adjuvant tyrosine kinase inhibitor therapy.

8. References

1. Mazur MT, Clark HB. Gastric stromal tumors. Reappraisal of histogenesis. Am J Surg Pathol. 1983; 7:507-19. https://doi.org/10.1097/00000478-198309000-00001 PMid:6625048.
2. Rammohan A, Sathya Nesan J, Rajendran K, et al. A gist of gastrointestinal stromal tumors: A review. World J Gastrointestinal Oncol. 2013; 5:102-12. https://doi.org/10.4251/wjgo.v5.i6.102 PMid:23847717 PMCid: PMC3708046.
3. Kind Blom LG, Remotti HE, Aldenborg F, *et al.* Gastrointestinal pacemaker cell tumor (GIPACT): gastrointestinal stromal tumors show phenotypic characteristics of the interstitial cells of Cajal. Am J Pathol. 1998; 152:1259-69.
4. Fletcher CD, Berman JJ, Corless C, *et al.* Diagnosis of gastrointestinal stromal tumors: a consensus approach. Hum Pathol 2002; 33:459-465
5. Hirota S, Isozaki K, Moriyama Y, *et al.* Gain-of-function mutations of c-kit in human gastrointestinal stromal tumors. Science. 1998; 279:577-80. https://doi.org/10.1126/science.279.5350.577 PMid:9438854.,
6. Miettinen M, Sobin LH, Lasota J. Gastrointestinal stromal tumors of the stomach: a clinicopathologic, immunohistochemical, and molecular genetic study of 1765 cases with long-term follow-up. Am J Surg Pathol. 2005; 29(1):52-68. [PubMed]
7. Corbin KS, Kindler HL, Liauw SL. Considering the role of radiation therapy for gastrointestinal stromal tumor. Onco Targets Ther. 2014; 7:713-8. https://doi.org/10.2147/OTT.S36873 PMid:24872712 PMCid:PMC4026585.
8. Wu PC, Langerman A, Ryan CW, *et al.* Surgical treatment of gastrointestinal stromal tumors in the imatinib (STI-571) era. Surgery. 2003; 134:656-65. https://doi.org/10.1016/S0039-6060(03)00315-5
9. Benjamin RS, Casali PG. Adjuvant imatinib for GI stromal tumors: When and for how long? J Clin Oncol. 2016; 34:215-8. https://doi.org/10.1200/JCO.2015.64.0102 PMid:26644523.
10. DeMatteo RP. Nano neoadjuvant therapy of gastrointestinal stromal tumor (GIST). Ann Surg Oncol. 2009; 16:799-800. https://doi.org/10.1245/s10434-009-0316-9 PMid:19169754.
11. Demetri GD, Reichardt P, Kang YK, *et al.* Efficacy and safety of regorafenib for advanced gastrointestinal stromal tumors after failure of imatinib and sunitinib (GRID): an international, multicenter, randomized, placebo controlled, phase 3 trial. Lancet. 2013; 381:295-302.
12. Eisenberg BL. The SSG XVIII/AIO trial: results change the current adjuvant treatment recommendations for gastrointestinal stromal tumors. Am J Clin Oncol. 2013; 36:89-90. https://doi.org/10.1097/COC.0b013e31827a7f55 PMid:23334483.
13. Gronchi A, Blay JY, Trent JC. The role of high dose imatinib in the management of patients with gastrointestinal stromal tumor. Cancer. 2010; 116:1847-58. https://doi.org/10.1002/cncr.24944 PMid:20166214.
14. Heinrich MC, von Mehren M, Demetri GD, *et al.* A phase

2 study of ponatinib in patients (pts) with advanced gastrointestinal stromal tumors (GIST) after failure of tyrosine kinase inhibitor (TKI) therapy: Initial report. J Clin Oncol. 2014; 32:10506. https://doi.org/10.1200/jco.2014.32.15_suppl.10506

15. Mulet-Margalef N, Garcia-Del-Muro X. Sunitinib in the treatment of gastrointestinal stromal tumor: patient selection and perspectives. Onco Targets Ther. 2016; 9:7573-82. https://doi.org/10.2147/OTT.S101385 PMid:28008275 PMCid: PMC5171199.
16. Beltran MA, Cruces KS. Primary tumors of jejunum and ileum as a cause of intestinal obstruction: a case control study. Int J Surg. 2007; 5:183-91. https://doi.org/10.1016/j.ijsu.2006.05.006 PMid:17509501.