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REVIEW ARTICLE

# Gastrointestinal stromal tumors and synchronous intra-abdominal malignancies: Review of the literature

Alexandros Diamantis, Konstantinos Bouliaris, Grigorios Christodoulidis, Dionysia Vasdeki, Konstantinos Perivoliotis, Konstantinos Tepetes

Department of General Surgery, University Hospital of Larissa, Mezourlo, Larissa, Thessaly, 41110, Greece

## Summary

***Purpose:*** *Gastrointestinal stromal tumors (GISTs) are the most frequent neoplasms of mesenchymal origin affecting the gastrointestinal tract. GISTs quite frequently co-exist with other primary tumors in up to 33% of the cases. Such occurrence has been mainly described in the literature in the form of case reports and rarely of case series which hasn't been sufficient to prove if there is any association between these two entities.*

***Methods:*** *We conducted a review of the current literature regarding the synchronous occurrence of GISTs and other intra-abdominal malignancies. An electronic search of the literature was undertaken using MEDLINE (database provider PubMed). A primary selection of relevant studies was based on the title and abstract, whereas a secondary selection was performed according to the full text of publications.*

***Results:*** *Ten retrospective case series were considered and overall 1108 GISTs patients were included. Synchronous intra-abdominal malignancies were found in 18% of all GISTs patients studied. The mean age was 70,5 years, affecting more the male gender (65%). The mean size of the concurrent GISTs were 18mm while the most common GIST-associated malignancy were gastric adenocarcinomas.*

***Conclusion:*** *The synchronous occurrence of GISTs and other intra-abdominal primary tumors is more common that it has been considered and while it is not yet clear if there is a causal association for the concomitant occurrence of GIST with other malignancies a closer surveillance of GIST patients is needed due to their proved increased prevalence of a second primary tumor especially during the first year after diagnosis.*

***Key words:*** *gastrointestinal stromal tumor, mesenchymal tumors, synchronous malignancies*

## Introduction

Although rare, GISTs are the most frequent neoplasms of mesenchymal origin affecting the gastrointestinal (GI) tract [1-3]. They represent about 0.1-1% of all malignant neoplasms of the GI tract and occur in adults between the 55$^{th}$ and 65$^{th}$ year of life [2-4]. The majority of GISTs manifest as sporadic solitary lesions, but they may develop in a familial fashion, such as in neurofibromatosis and Carney triad [5]. With 50-60%, the majority of GISTs are located in the stomach, but they also involve the small intestine (30-40%), the colon-rectum (5-10%) and rarely the oesophagus (less than 5%) [3,6]. Not frequently, GISTs may occur in extra-GI sites, mainly the mesentery, the omentum and the retroperitoneum.

GISTs have a wide spectrum of presentation from small and benign, incidentally detected nodules, to frankly malignant tumors needing further adjuvant or even neo-adjuvant treatment. KIT (tyrosine kinase receptor c-kit) and PDGFRA (Platelet Derived Growth Factor Receptor Alpha) activating mutations are the oncogenic mechanisms in most cases of sporadic and familial GISTs. Their diagnosis is usually based on the expression of the CD117

*Correspondence to:* Alexandros Diamantis, PhD cand. Department of General Surgery, University Hospital of Larissa, Mezourlo, Larissa, Thessaly, 41110, Greece.
Tel: +30 6948594006, Fax: +30 2413-501559, E-mail: alexandrosdoc@gmail.com
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(90-95%), a membrane-bound receptor of tyrosine kinase, and CD34 (70-80%) [7].

Commonly GISTs co-exist with other primary tumors that can involve either the GI tract or other extra-GI sites. The synchronous occurrence of GISTs with other malignancies varies from 4.5 to 33%, while the most frequent types of GIST-associated malignancies have been GI carcinomas (47%), prostate carcinoma (9%), lymphoma/leukaemia (7%), breast (7%), kidney (6%), lung (5%), female genital tract (5%), carcinoid tumors (3%), soft tissue and bone sarcomas (3%), malignant melanoma (2%) and seminoma (1%) [8]. GISTs with synchronous malignancy of the GI tract have been described to range from 10 to 35%, with the majority of them being adenocarcinomas [1,9-11].

It has not been clear yet if there is a causal association or coincidence for the concomitant occurrence of GIST with other malignancies, neither its clinical importance has ever been determined. Such occurrence has been mainly described in the literature in the form of case reports and rarely of case series which hasn't been sufficient to prove if there is any association between these two entities.

## Methods

We conducted a review of the current literature regarding the synchronous occurrence of GISTs and other intra-abdominal malignancies. An electronic search of the literature was undertaken using MEDLINE (database provider PubMed). A further search was undertaken including a manual screening of the reference lists of selected articles identified through the electronic search. To identify relevant studies, the following search terms were combined: in the Expanded Medical Subject Headings (MeSH) and key word searches for: gastrointestinal stromal tumors (GISTs), other malignancies, cancers, neoplasms, synchronous, coexistence, coincidence, intra-abdominal. A primary selection of relevant studies was based on the title and abstract, whereas a secondary selection was performed according to the full text of publications.

*Study selection*

All articles located in the initial search strategy had their abstracts and titles independently screened by two authors (A.D. and K.B.) and any discrepancies were resolved after consensus with discussion between K.S. and G.K. and a third senior author (K.T).

All case series analyzing the frequency and the characteristics of GIST patients (minimum 4) with synchronous malignancies were included. We estimated the frequency, the type and the sites of the synchronous intra-abdominal malignancies and any possible causal association between these two entities. All cases series of GISTs with synchronous extra-abdominal malignancies were excluded from the study. We also excluded papers focusing only on the relationship between gastric GISTs and gastric adenocarcinomas. Case reports and small case series (less than 4 cases) were also not included in our study.

The systematic review protocol, the selection process, and reporting were based on the 2009 PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) statement [12].

## Results

In total, 10 retrospective case series were considered analyzing 24-286 GIST patients. In these studies, the authors analyzed in detail the frequency, the type and the site of synchronous malignancies. Overall 1108 patients with GISTs were included (Table 1); of these, there were 202 cases of patients with synchronous intra-abdominal malignancies consisting the 18% of all GIST patients studied. The overall frequency of synchronous intra-abdominal malignancy varied in the different series from 8% to 38% (Figure 1).

**Table 1.** Case series and total cases with GISTs and synchronous intra-abdominal malignancies

| *Author (year) [Ref. no.]* | *Total no. of cases* | *Cases with synchronous intra-abdominal malignancies** |
|---|---|---|
| Agaimy et al (2005) [19] | 97 | 11 |
| Wronski et al (2006) [1] | 28 | 4 |
| Liszka et al (2007) [20] | 82 | 17 |
| Fereira et al (2010) [3] | 43 | 5 |
| Goncalves et al (2010) [21] | 101 | 8 |
| Sevinc et al (2011) [25] | 200 | 17 |
| Giuliani et al (2012) [22] | 24 | 5 |
| Vassos et al (2014) [23] | 86 | 27 |
| Shen et al (2015) [9] | 161 | 61 |
| Du et al (2016) [24] | 286 | 47 |
| Overall | 1108 | 202 |

*case series of GISTs with non intra-abdominal synchronous malignancies were excluded

**Table 2.** Main clinical characteristics and histopathologic features of GISTs and synchronous intrabdominal malignancies

| *Author (year)* | *Cases with synchr. intrabdominal malignancies** | *Gender (%)* | *Mean age, Years* | *GIST* | | | *Other intrabdominal malignancies* |
|---|---|---|---|---|---|---|---|
| | | | | Location (%) | Mean size (mm) | Risk stratification (%) | Location (No of patients) |
| Agaimy et al (2005) [23] | 11 | M (55)<br>F (45) | 77 | Stomach (73)<br>Small intestine (27) | 28 | Very low and Low (100) | Stomach (4)<br>Rectum (2)<br>Liver (2)<br>Pancreas(1)<br>Lymph nodes (1)<br>Diffuse (1) |
| Wronski et al (2006) [1] | 4 | M (25)<br>F (75) | 68 | Stomach (100) | 15 | Very low and Low (100) | Stomach (3)<br>Colon (1) |
| Liszka et al (2007) [22] | 17 | M (59)<br>F (41) | 62 | Stomach (35)<br>Small intestine (47)<br>Oesophagus (8) | NA | Very low and Low (82)<br>Intermediate and High (18) | Stomach (5)<br>Colon (5)<br>Rectum (2)<br>Pancreas (5) |
| Fereira et al (2010) [3] | 8 | M (50)<br>F (50) | 71 | Stomach (62,5)<br>Small intestine (25)<br>Mesentery (12,5) | 26 | Very low and Low (75)<br>Intermediate and High (25) | Stomach (3)<br>Colon (2)<br>Rectum(1)<br>Kidney (1)<br>Ovaries (1) |
| Goncalves et al (2010) [24] | 5 | M (20)<br>F (80) | 57 | Stomach (60)<br>Small intestine (40) | 25 | Very low and Low (60)<br>Intermediate and High (40) | Stomach (2)<br>Colon (2)<br>Oesophagus (1) |
| Giuliani et al (2012) [26] | 5 | M (80)<br>F (20) | 71 | Stomach (80)<br>Small intestine (20) | 7 | Very low and Low (100) | Colon (3)<br>Rectum (1)<br>Prostate (1) |
| Vassos et al (2014) [27] | 27 | M (67)<br>F (35) | 73 | Stomach (70)<br>Small intestine (22)<br>Oesophagus (4)<br>Rectum (4) | 17 | Very low and Low (92)<br>Intermediate and High (8) | Stomach (7)<br>Oesophagus (4)<br>Colon (4)<br>Pancreas (5)<br>Rectum (5)<br>Prostate(1)<br>Liver(1) |
| Sevinc et al (2011) [25] | 17 | M (65)<br>F (35) | 62 | Stomach (53)<br>Small intestine (41)<br>Colon (6) | NA | Very low and Low (76)<br>Intermediate and High (24) | Stomach (9)<br>Colon (3)<br>NHL (1)<br>Periampullary (1)<br>Prostate (1)<br>Endometrium (1)<br>Spermatic cord (1) |
| Shen et al (2015) [9] | 61 | M (70)<br>F (30) | 70 | Stomach (95)<br>Small intestine (3)<br>Other (2) | NA | Very low and Low (93)<br>Intermediate and High (7) | Stomach (30)<br>Oesophagus (28)<br>Rectum (3) |
| Du et al (2016) [28] | 47 | M (62)<br>F (38) | NA | Stomach (92)<br>Small intestine (6)<br>Other (2) | 7 | Very low and Low (89)<br>Intermediate and High (11) | Stomach (27)<br>Oesophagus (12)<br>Colon (7)<br>Pancreas (1) |

*Cases with non intrabdominal synchronous malignancies were excluded. NA: not available, NHL:Non Hodgkin Lymphoma

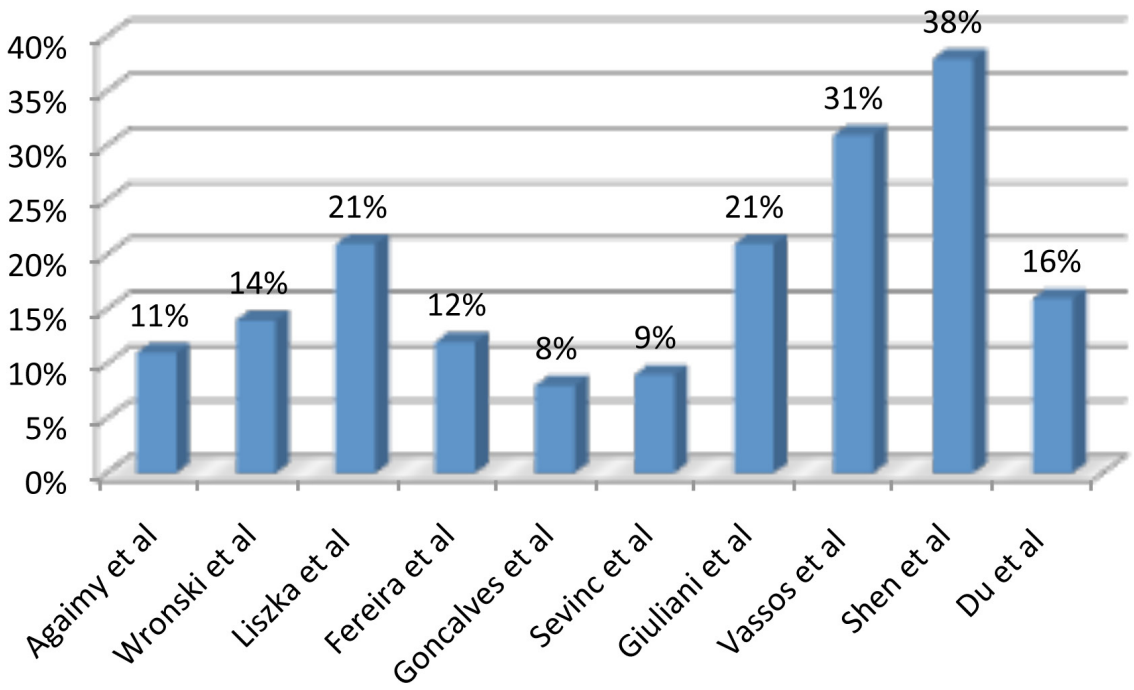


**Figure 1.** Frequency of occurrence of GISTs and synchronous intra-abdominal malignancies. Case series of GISTs with non-intra-abdominal synchronous malignancies were excluded.

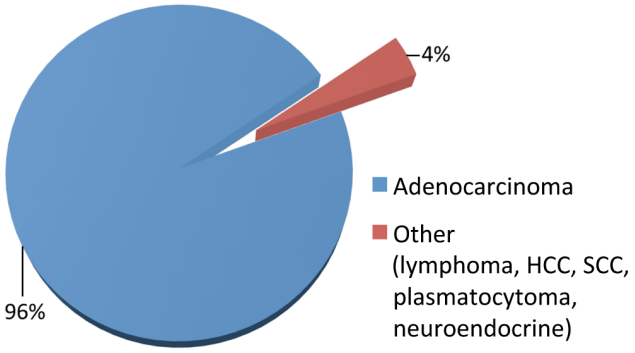


**Figure 2.** Type of synchronous intra-abdominal malignancies (%).

The main clinical and pathological features of patients with synchronous intra-abdominal malignancies are summarized in Table 2. The mean age of the patients involved was 70,5 years, affecting more frequently the male gender (65%). Data on prognostic groups of GISTs were available for all patients with synchronous intra-abdominal malignancies. The majority of them had small size, with no or low mitotic activity, diagnosed as either very low or low risk for malignant potential and most commonly located in the stomach (87%). Mean GIST size was 18mm (range 7-44). The most common GIST-associated malignancies were gastrointestinal carcinomas mainly located in the stomach (123 patients) and in the oesophagus (44 patients). Other common sites of synchronous malignancies were colon, rectum and the pancreas, while more unusually sites affected were prostate, ovaries, kidneys and the liver. The most common type of cancers encountered were adenocarcinomas (96%), while unusual histogenetic categories included lymphoma (3 patients), squamous cell carcinoma (SCC, 2 patients), neuroendocrine tumor (2 patients), plasmatocytoma and hepatocellular carcinoma (HCC) (1 patient) (Figure 2).

## Discussion

GISTs are the most common soft tissue sarcomas of the GI tract, resulting most commonly from KIT or PDGFRA activating mutations [13]. They can arise anywhere along the GI tract, but they are more frequently located in the stomach (60%) and small intestine (30%). Less usual sites are the rectum, duodenum, colon and the oesophagus [4]. Approximately 5% of all gastrointestinal tumors have a hereditary etiology [14]. Most known heritable syndromes associated with GISTs are caused by germline mutation in C-KIT, PDGFRa, neurofibromin 1 and succinate dehydrogenase subunits [5,6]. Individuals with this kind of mutations can frequently develop multiple benign and malignant tumors. However, these syndromes account for only 5% of the cases with the rest 95% considered as sporadic. These tumors have a wide spectrum of characteristics, ranging from benign, small, incidentally detected nodules to frankly malignant tumors [15]. Surgery is still the primary treatment

of choice for patients with localized or potentially resectable metastatic lesions.

Commonly GISTs are incidentally detected during imaging studies, operation or examination of the resected specimens. In this setting GISTs co-exist with other primary tumors that can involve either the GI tract or other extra-GI sites. The synchronous occurrence of GISTs with other malignancies varies in the current literature from 4.5 to 33%.

Multiple studies showed that patients with sporadic GISTs may develop synchronous or metachronous malignancies with frequencies much higher than the often cited 1-in-9 lifetime chance of developing 2 primary cancers [4,16]. In one large population-based study of 6112 GIST patients, 1047 (17.1%) of them had additional cancers occurring either before or after the diagnosis of GIST [27]. In the same study Murphy and his colleagues [17] presented a significant increase in the cancer rates. GIST patients had a 44% increased prevalence of cancer occurring before and a 66% increased relative risk after the GIST diagnosis respectively [17]. The maximum increase occurred within the first year before and after the GIST diagnosis, suggesting a much closer surveillance of GIST patients versus the general population. Kalmar et al. [18] also found that the frequency of malignant neoplasm among GIST patients (21.7%) is more than 5 times higher than the incidence in the general population (4%, $p<0.001$). In this setting, Rodriquenz et al. suggested that GIST could be considered as a "sentinel tumor" and surveillance not only for GIST but also for second malignancies is an important compound of the management of GIST patients, particularly in the first year after diagnosis [19].

The major types of GIST-associated cancers were gastrointestinal carcinomas (47%), lymphoma/leukemia (7%), and carcinoma of prostate (9%), breast (7%), kidney (7%), lung (5%), female genital tract (5%) and carcinoid tumors (3%). Less usual cancers included soft tissue and bone sarcomas (3%), malignant melanoma (2%) and seminoma (2%) [8].

In our review, we analyzed the current literature on the association of synchronous GISTs and other intra-abdominal malignancies, especially of the GI tract. The frequency of the synchronous development of other intra-abdominal malignancy was found to be 18%, demonstrating the relatively high risk of a synchronous second cancer among the GIST patients. The vast majority of the GISTs were found incidentally during histopathologic evaluation of gastric carcinoma specimens or intraoperatively during a laparotomy for other malignancies.

The present study showed a very high incidence of patients with GISTs located in the stomach (87%) co-existing with other malignancy of the abdomen and most usually adenocarcinomas of the GI tract and especially the upper GI (stomach, oesophagus). Beside the obvious bias of the location more extensive epidemiological and statistical analyses are needed to reveal a possible causal association. Kawanowa et al. found that microscopic GISTs can be found in 35% of stomach specimens resected due to gastric cancer, suggesting a possible underestimation of the actual annual incidence of GISTs and, as a consequence, the incidence of synchronous tumors [20].

Tumors with smaller size and very low or low risk of malignant potential are more frequently found in patients with synchronous malignancies, supporting the theory that the GIST itself in these patients has little effect on the overall survival and patient prognosis. Although tumor size and mitotic rate are used to assess the risk of metastasis of GISTs, it is quite difficult to predict their biologic behavior; small GISTs (<2cm) may be asymptomatic and non-malignant on the day of diagnosis, although nobody can deny the potential for malignant transformation [4]. Consequently, GISTs should be excised when incidentally discovered during surgery for other malignancy and if needed targeted therapy with TKI inhibitors (imatinib) should be considered. Surgical exploration in these patients should be careful and comprehensive.

An additional challenge has been to determine whether the incidental lesion found is a GIST or a metastasis/recurrence of a known malignancy. In the case where a suspicious lesion is found, especially on the walls of the digestive tract, physicians should carefully resect it and apply the appropriate surgical technique, after pathological examination and histological confirmation.

The mean age in the group of patients with synchronous malignancies was higher in all cases series studied. The higher age of patients with a second malignancy compared to the mean age of all patients with GIST is also consistent with a mere coincidence, as most of these non-GIST tumors are more common with increasing age.

The high frequency of second tumors in GIST patients could also possibly suggest an unknown common molecular mechanism. Determining whether GISTs coexisting with other tumors share similar genetic mutations or signaling pathways is an active area of research. Although the synchronous occurrence of GISTs and other abdominal malignancy seems to be just a coincidence, the development of these tumors may involve common carcinogenic agents. Maiorana et al. suggested that

a single carcinogenic agent might interact with 2 neighboring tissues, inducing development of tumors of different histotypes in the same organ [10]. This assumption [10] was made after experimental evidence where Cohen and his colleagues proved that oral administration of N-methyl-N-nitro-N-nitrosoguanidine combined with aspirin or stress induced synchronous formation of leiomyosarcoma and adenocarcinoma in the rats' stomach [21].

Clinicopathological profiles and molecular analysis of the KIT/PDGFRA genes did not produce any positive association between synchronous GISTs and gastric cancer [22]. Until today no underlying connections have been found between GISTs and synchronous intra-abdominal malignancies [23-25].

## Conclusion

The synchronous occurrence of GISTs and other intra-abdominal primary tumors is more common that it has been considered, with the majority of them being found incidentally during surgery performed for other malignancy [26-28]. Even though coincidence may be the answer, the hypothesis of gene mutations or the same carcinogenic agent resulting in two tumors of different origin cannot be excluded. Further research based on large populations and cancer registries and on molecular mechanisms, and more animal experiments are required to elucidate probable association between GISTs and other intra-abdominal malignancies. In addition, despite the fact that the prognosis of these patients is mainly determined by the other malignancy and not by the GIST, all physicians must be aware of possible synchronicity, recognize the gastrointestinal tumor and apply the proper therapeutic protocol to the patient. Last but not least, new follow up protocols should be addressed for the closer surveillance of GIST patients due to their recently proved increased prevalence of a second primary tumor, especially during the first year after diagnosis.

## Conflict of interests

The authors declare no conflict of interests.

## References


1. Wronski M, Ziarkiewicz-Wroblewska B, Gornicka B et al. Synchronous occurrence of gastrointestinal stromal tumors and other primary gastrointestinal neoplasms. World J Gastroenterol 2006;12:5360-2
2. AbdullGaffar B. Gastrointestinal stromal tumors and extra-gastrointestinal tract neoplasms. South Med J 2010;103:1004-8.
3. Ferreira SS, Werutsky G, Toneto MG et al. Synchronous gastrointestinal stromal tumors (GIST) and other primary cancers: Case series of a single institution experience. Int J Surg 2010;8:314-7.
4. 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;29:52-68.
5. Stratakis CA, Carney J. A. The triad of paragangliomas, gastric stromal tumours and pulmonary chondromas (Carney triad), and the dyad of paragangliomas and gastric stromal sarcomas (Carney–Stratakis syndrome): molecular genetics and clinical implications. J Intern Med 266:43-52.
6. Ponti G, Luppi G, Martorana D et al. Gastrointestinal stromal tumor and other primary metachronous or synchronous neoplasms as a suspicion criterion for syndromic setting. Oncol Rep 2010;23:437e-44.
7. Pidhorecky I, Cheney RT, Kraybill WG, Gibbs JF. Gastrointestinal stromal tumors: current diagnosis, biologic behavior and management. Ann Surg Oncol 2000;7:705e-12.
8. Agaimy A, Wünsch PH, Sobin LH et al. Occurrence of other malignancies in patients with gastrointestinal stromal tumors. Semin Diagn Pathol 2006;23:120-9
9. Shen C, Chen H, Yin Y et al. Synchronous occurrence of gastrointestinal stromal tumors and other digestive tract malignancies in the elderly. Oncotarget 2015;6:8397-406.
10. Maiorana A, Fante R, Maria Cesinaro A et al. Synchronous occurrence of epithelial and stromal tumors in the stomach: a report of 6 cases. Arch Pathol Lab Med 2000;124:682-6.
11. Lin M, Lin JX, Huang CM et al. Prognostic analysis of gastric gastrointestinal stromal tumor with synchronous gastric cancer. World J Surg Oncol 2014;12:25.
12. Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 2009;6:e1000097.
13. 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.
14. Nilsson B, Bumming P, Meis-Kindblom JM et al. Gastrointestinal stromal tumors: the incidence, prevalence, clinical course, and prognostication in the preimatinib mesylate era-a population-based study in western Sweden. Cancer 2005;103:821-9.

15. Gupta P, Tewari M, Shukla HS. Gastrointestinal stromal tumor. Surg Oncol 2008;17:129-138.
16. Pandurengan RK, Dumont AG, Araujo DM et al. Survival of patients with multiple primary malignancies: a study of 783 patients with gastrointestinal stromal tumor. Ann Oncol 2010;21;2107-11.
17. Kawanowa K, Sakuma Y, Sakurai S et al. High incidence of microscopic gastrointestinal stromal tumors in the stomach. Hum Pathol 2006;37:1527-35.
18. Yan Y, Li Z, Liu Y, Zhang L, Li J, Ji J. Coexistence of gastrointestinal stromal tumors and gastric adenocarcinomas. Tumor Biol 2013;34:919-27.
19. Agaimy A, Wuensch PH. Gastrointestinal Stromal Tumours in Patients with Other-Type Cancer: A Mere Coincidence or an Etiological Association? A Study of 97 GIST cases. Zeitschrift für Gastroenterologie 2005;43:1025-30.
20. Liszka Ł, Zielińska-Pajak E, Pajak J, Gołka D, Huszno J. Coexistence of gastrointestinal stromal tumors with other neoplasms. J Gastroenterol 2007;42:641-9.
21. Gonçalves R, Linhares E, Albagli R et al. Occurrence of other tumors in patients with GIST. Surg Oncol 2010;19:e140-3.
22. Giuliani J, Marzola M, Indelli M et al. Gastrointestinal Stromal Tumors and Other Malignancies: a Case Series. J Gastrointest Cancer 2012;43:634-7.
23. Vassos N, Agaimy A, Hohenberger W, Croner RS. Coexistence of gastrointestinal stromal tumours (GIST) and malignant neoplasms of different origin: Prognostic implications. Int J Surg 2014;12:371-7.
24. Du J, Shen N, He H-S, Fu X-L, Wang J-Z, Mao C-Z. Synchronous gastrointestinal cancer and gastrointestinal stromal tumors: a single-institution experience. World J Surg Oncol 2016;14:130.
25. Sevinc A, Seker M, Bilici A et al. Co-existence of gastrointestinal stromal tumors with other primary neoplasms. Hepatogastroenterology 2011;58:824-30.
26. Rodriquenz MG, Rossi S, Ricci R et al. Gastrointestinal stromal tumors (GISTs) and second malignancies. Medicine 2016;95:e4718.
27. Murphy JD, Ma GL, Baumgartner JM et al. Increased risk of additional cancers among patients with gastrointestinal stromal tumors: A population-based study. Cancer 2015;121;2960-7.
28. Cohen A, Geller SA, Horowitz I, Toth LS, Werther JL. Experimental models for gastric leiomyosarcoma. The effects of N-Methyl-N'-Nitro-N-Nitrosoguanidine in combination with stress, aspirin, or sodium taurocholate. Cancer 1984;53:1088-92.
29. Kalmar K, Tornoczky T, Poto L et al. Gastrointestinal stromal tumors in a single institute: is there an association to other gastrointestinal malignancies? Magyar Sebészet 57 (2004) 251e256.