Gastrointestinal stromal tumor: analysis of 146 cases of the center of reference of the National Cancer Institute – INCA

Tumor estromal gastrointestinal: análise de 146 casos do centro de referência do Instituto Nacional do Câncer – INCA

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A B S T R A C T

Objective: To evaluate the treatment of GIST in INCA. **Methods**: We conducted a retrospective analysis of all cases of GIST treated at INCA in the period from 1997 to 2009. **Results**: We analyzed 146 patients with a mean age of 44.5 years and female predominance. The main symptom was abdominal pain. We observed the occurrence of a second primary tumor in 22% of cases and 92% of the immunohistochemistry exams were positive for CD117. The most frequent location was in the stomach and the high-risk group was predominant. Surgery was considered R0 (extensive) in 70% of the cases and the main sites of metastases were liver and peritoneum. Overall survival in two and five years was, respectively, 86% and 59%. There was a significant difference between overall survival (p = 0.29) of the high-risk group versus the other. **Conclusion**: Our patients presented mainly in the form of high-risk disease, with obvious impact on survival. The use of imatinib improved survival of patients with recurrent and metastatic disease. We should study its use in the setting of adjuvant and neoadjuvant therapy to improve results of the high risk group. The creation of reference centers is a need for the study of rare diseases.

Key words: Neoplams. Gastrointestinal stromal tumors. Surgery. Suvivorship. Mesylates.

INTRODUCTION

For decades it was thought that the majority of gastrointestinal mesenchymal tumors arose from the smooth muscle[1], being called "leiomyomas" and "leiomyosarcomas". After the introduction of immunohistochemistry in clinical practice, it was shown that only some of these tumors had features of smooth muscle differentiation, contributing to adoption of the more general term "stromal tumor", proposed by Mazur and Clark[2] in 1983. Later, other authors demonstrated that these tumors also had features of neuronal differentiation[3,4], designating them "plexosarcomas" and "gastrointestinal autonomic nerve tumors".

Only recently it was clarified that this neoplasm is a well-defined disease called GIST, the acronym for gastrointestinal stromal tumor, through the discoveries of its origin from the interstitial cells of Cajal[5] and the expression of c-Kit protein[6].

The interstitial cells of Cajal are responsible for motility[7], show immunophenotypic and ultrastructural features of both smooth muscle and neural differentiation and express the Kit receptor (CD117) similar to gastrointestinal stromal tumor (GIST). The Kit is a transmembrane receptor tyrosine kinase responsible for various cellular functions, among which proliferation, adhesion, apoptosis and cell differentiation[8]. In GIST, a mutation in the Kit gene is responsible for constitutive activation of Kit protein, causing unopposed stimulus for cell proliferation, being implicated in its genesis.

A scientific group was created in INCA in 2007, in order to evaluate and standardize the treatment of this rare tumor in the institution. Since then we noticed an increase in referrals, beginning in 2006 with 18 registered cases/ year, and reaching 37 cases/year in 2009. With this, we created a database with a significant number of patients. In this article we review our experience, with emphasis on the findings of a segment of Brazilian population and, especially, the risk profile and survival.

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METHODS

It was studied all suspected cases of GIST in the period from January 1997 to July 2009. After surveying the cases, was preceded the analysis of medical records and called the surviving patients for medical consultation.

It was studied the demographics, clinical presentation and associated syndromes, such as the presence of second primary neoplasms from the clinical point of view. As to diagnosis, we evaluated the most commonly used imaging tests, namely, computed tomography (CT), magnetic resonance imaging (MRI) and endoscopy.

From the pathological standpoint, we assessed the main prognostic factors, such as size, mitotic index, topography, rupture, metastatic lymph nodes. The classification used was Fletcher's[9] (Table 1). The immunohistochemical profile was performed using a panel of CD117, CD34, vimentin, HHF35, desmin, S100 and ENS.

The type of resection performed was classified as R0 if there was no residual disease or microscopic involvement of surgical resection; R1 when there was residual disease; and R2 when there was macroscopic residual disease. The laparoscopic approach was indicated in the INCA gastric tumors smaller than 5cm, according to the routines of the Service.

There was no use of imatinib as adjuvant. This drug is indicated in patients with unresectable or metastatic disease. In cases of risk of non-resectability during operation or major surgical mutilation, neoadjuvant treatment was indicated. In the evaluation of treatment outcomes, we analyzed overall survival and disease-free survival, survival after introduction of imatinib. Treatment with imatinib was ranked neoadjuvant when performed prior to surgery.

We defined overall survival as the interval between first treatment and the last visit or death; disease-free survival as the time interval between surgery and recurrence; survival after introduction of imatinib as the survival of patients with unresectable or metastatic disease who used the drug. We also present survival according to the risk group[9].

The pattern of relapse was assessed by imaging and reoperations, defined as the organ affected. The follow-up of patients was performed by a multidisciplinary team and involved periodic imaging, preferably computed tomography (we could use only CT). The evaluation of mutational analysis was not framed within this line of research and was not reported here.

This study was approved by the direction of INCA and the Ethics Committee of the Institution (SISNEP / CONEP) under number 079/08.

Statistical Analysis

The data obtained in this study concerning the variables overall survival and disease-free time (in months) were analyzed using: A) graphs and tables; B) means, medians, standard deviations, minimum and maximum values; C) Kaplan-Meier method for the determination of the overall survival curve and disease-free time; D) evaluation of the Kruskal-Wallis test for comparison of overall survival times, according to Fletcher risk groups; E) nonparametric Mann-Whitney test to identify significant contrasts regarding overall survival times, according to the aforementioned risk groups. In statistical tests we adopted a significance level of 5% probability ($p = 0.05$).

RESULTS

After the analysis of 204 medical records and patients with suspected gastrointestinal sarcoma, we identified 146 who had the definitive diagnosis of GIST. Ages ranged from six to 86 years with a median of 44.5 years. Female gender predominated with 62.5% of cases.

At presentation, the main clinical symptom reported was abdominal pain (43%), followed by weight loss (10%). Upper gastrointestinal bleeding was reported in the medical charts of 23 patients (15%). The main finding of physical examination was a palpable mass in 17% of cases. In one case there was an association with type 1 neurofibromatosis.

Table 1 - Estimated malignancy potential (Fletcher *et al.*[9]).

Malignancy Risk	Size (Cm)	Mitotic (50hmf)
Very low	< 2	< 5
Low	2-5	< 5
Intermediate	< 5	6-10
	5-10	< 5
High	> 5	> 5
	> 10	Any index
	Any size	> 10

50HMF = 50 high magnification fields (400x).

As for diagnostic imaging, computed tomography was used in 126 cases (86%) and MRI in 13 cases (8.9%). A small percentage (4.7%) of patients had imaging studies performed outside the hospital and were not recoverable for purposes of review. The main radiological finding was an abdominal mass with peripheral hypervascularity and central necrosis.

Endoscopy was performed in 98 cases (66%) and had subepithelial mass as the main finding. Colonoscopy was performed in 33 cases (22%): in the colon an ulcerated lesion was mainly found, and in rectum, a subepithelial mass.

The occurrence of a second primary was 22% (31 cases). The main tumors associated with GIST were adenocarcinoma of the stomach (8 cases), colorectal carcinoma (6 cases), uterine/ovarian cancer (4 cases), breast carcinoma (3 cases), prostate adenocarcinoma (2 cases), carcinoma of the esophagus (2 cases), adrenal neuroblastoma, gallbladder carcinoma, renal carcinoma, meningioma, sarcoma of soft tissues and palate tonsil, one case each.

In immunohistochemistry, 135 patients expressed positivity for antigen CD117 (92%) and 72 patients for the CD34 (49%). There was positive expression for vimentin (35 cases), HHF35 (8 cases), Desmin (6 cases), S100 (21 cases) and ENS (6 cases). In four patients we could not retrieve the material for immunohistochemistry review and, in seven, they were negative. The seven negative were considered GISTs by the pathologist due to phenotypic expression.

As for location, we found: stomach (80 cases), small intestine (36 cases), colon/rectum (20 cases), extragastrointestinal (14 cases), pelvic mass (2 cases), retroperitoneum (3 cases), pancreas (2 cases) and spleen (1 case).

Surgical treatment was performed in 137 patients. Nine patients underwent biopsy and did a subsequent surgical treatment. Radical surgery was classified as R0 in 70.8%, R1 in 2.9%, R2 in 21.9% and NA in 4.4% (Table 2). The incidental finding of GIST during laparotomy performed for another indication occurred in 17 cases (12%). Laparoscopic approach was performed in 11 patients, successfully in nine cases, conversion being needed in two cases due to the position of the tumor. Both were located in the posterior wall next to the cardia. There was rupture of the tumor in 11 cases. In 24 patients, the disease already had metastases. The main location of isolated metastases was the liver, in 16 cases; liver metastases associated with peritoneal metastasis occurred in one patient and, associated with the spleen, in another. In six cases there was involvement of the peritoneum alone and in one case the metastasis was retroperitoneal.

On histopathologic examination, tumor size was analyzed in 125 cases and ranged in diameter from 0.2 - 77cm with a mean of 11.8cm and a median of 10cm. Counting the number of mitoses per 50HMF was evaluated in 85 cases. In 52 cases it was less than 5/50HMF; in 17 cases it was between 5-10/50HMF; in 16 cases it was higher than 10/50HMF and in 61 cases it could not be assessed. Assessing the risk group, we found that ten patients were very low risk, 14 low-risk, 22 intermediate risk and 69 high risk. In 31 cases we could not make the classification as it was impossible to characterize the mitotic index. In 92 cases lymph nodes were isolated from surgical specimens and in nine cases (9.8%) they were positive. Of these, in six cases the tumor was primary gastric and in three cases from the small intestine. There was a case of multicentric gastric GISTs.

Of the 97 patients operated on with curative intent (R0), 37 (38%) relapsed. The most frequent site of metastasis was the liver, involved in 27 of the 37 cases, followed by the peritoneum in 18 cases (27%). There was isolated liver involvement in 13 patients and of the peritoneum in eight. In the remaining, there were combinations involving the liver, peritoneum, retroperitoneum, local recurrence, lymph nodes, lung, spleen and left adrenal. Treatment of recurrence varied across our sample. Thus, three patients were treated with DTIC (dacarbazine), ten with surgery aimed at resection, three underwent supportive treatment and 21 received imatinib as soon as the drug became available for the Service.

Patients who initially underwent non-curative surgery were treated for palliative purposes. Thus, three patients received DTIC (dacarbazine) or adriamycin, two received therapeutic support, one received radioablation of liver metastasis, in six attempted surgery rescue was carried out and 18 patients were treated with Imatinib. Patients not undergoing treatment with imatinib had a median survival of 31 months, while the ones who received it had a median survival of 46 months.

The assessment of overall survival (Figure 1) showed that 76% of patients were alive in the second year and this rate dropped to 59% in five years.

The analysis of disease-free survival in patients who underwent R0 surgery showed a sharp decline after 18 months (Figure 2).

We performed survival analysis with the sum of the groups considered at lower risk – namely, very low, low and intermediate – versus high risk. We observed a clear difference in survival curves between these two groups

Table 2 - Surgical radicality.

Radicality	Pacients / %
R0	97 – 78.8%
R1	4 – 2.9%
R2	30 – 21.9%
NA	6 – 4.4%

NA = Non-Applicable.

(Figure 3). Although not significant for two years, it was significant (p = 0.001) for five years in the Kruskal-Wallis test. The nonparametric Mann-Whitney test in the fifth year showed p = 0.029.

DISCUSSION

Gastrointestinal mesenchymal tumors are rare and have had different names and classifications[10]. There are no statistics in Brazil, even in the directory of INCA, as for the incidence and mortality from this cancer[11]. Indeed, we believe that the diagnosis of GIST is underestimated, since they represent 80% of mesenchymal tumors of the digestive tract and constitute 5% of all sarcomas[9]. We believe that as more people are submitted to endoscopy and radiology exams, the detection of these tumors increased. In Europe, the annual incidence of 11-14 new cases per million inhabitants is estimated[12].

Considering the Brazilian population of 188 million according to 2006 census, we can expect something arounr 2500 new cases/year. Although there are reports of GIST in the pediatric population, they occur predominantly in middle age (average around 60 years of age) and the occurrence in extreme ages is infrequent. Although there was a slight predominance of females, the literature shows that there is no predilection for sex[13]. There was no difference as to demographics from other reports in the literature.

GIST is asymptomatic in almost 69% of cases, being discovered in routine examinations, autopsies and laparotomies[14]. In symptomatic individuals the most referred complaints are pain and abdominal discomfort, palpable tumors and gastrointestinal bleeding. The main in our study sign was the presence of a palpable mass, a fact confirmed since the beginning of our experience[15]. When we consider the symptoms as a function of the primary site, we have a palpable mass for stomach, small intestine and even colorectal locations[16]. Obviously, this finding suggested to us that we are dealing with advanced disease, which was confirmed by the median tumor size and high percentage of high risk patients, with an impact on overall survival. This was assessed by Hassan[17], who confirmed, in a multivariate analysis, the existence of symptoms associated with worse prognosis.

As for diagnostic imaging, we preferably used computed tomography to have good assessment of the liver and peritoneum, the most frequent sites of metastasis, and due to its good cost/benefit relation. The most important CT findings for diagnosis of gastric GIST are: location in the body/fundus, predominantly extraluminal growth, peripheral hypervascularity with heterogeneous core[18]. In this series we found that these findings are valid for other locations. So, considering this pattern as well-defined, including in the literature[19], we suspect, with good chance of success, the diagnosis of

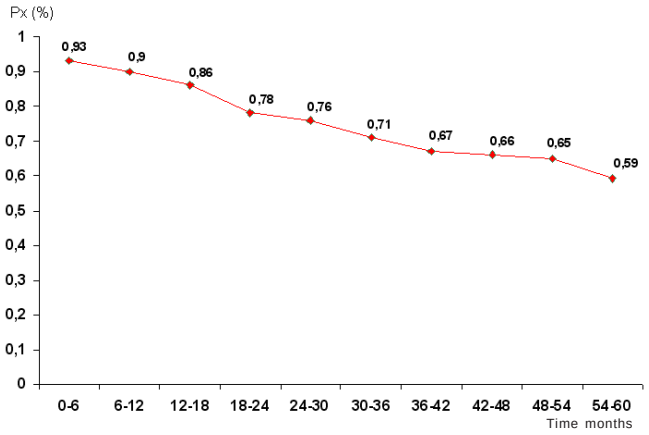

Figure 1 - *Overall survival curve.*

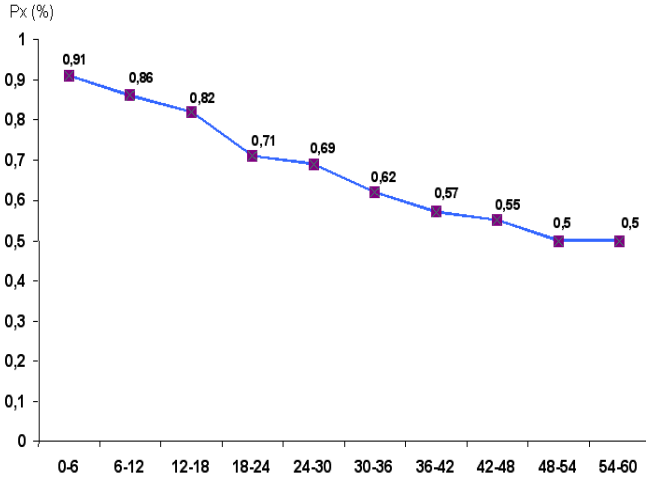

Figure 2 - *Disease-free survival.*

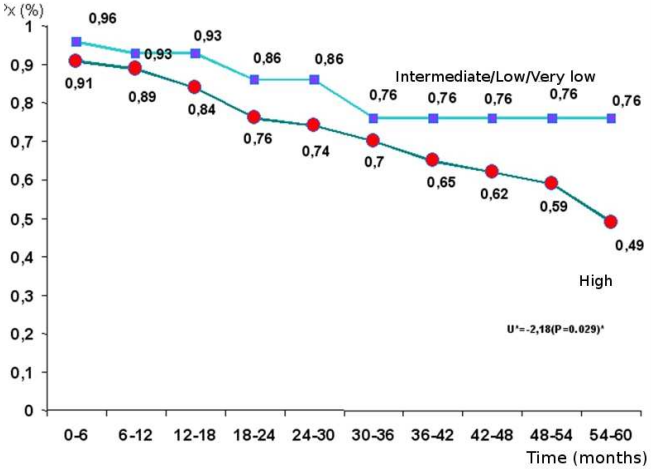

Figure 3 - *Survival according to risk group: High Risk vs. Intermediate + Low + Very Low.*

GIST when faced with abdominal masses who present these characteristics.

Endoscopy and colonoscopy were performed for diagnostic purposes and showed the typical finding of advanced disease: ulceration. In early disease, the lesion

will remain located subepithelially, ulcerating the mucosa, initially by ischemia, and subsequently by direct invasion. Therefore, the conventional endoscopic biopsy is of value only when positive, since the tumor may be situated more deeply. In the endoscopy unit of INCA, the technique was developed to remedy this situation in addition to endoscopic ultrasound. An endoscopic gastrostomy is held with a knife until the tumor is visually reached where, then, the biopsies are performed. Although an alternative proposal, the gold standard is the use of endoscopic ultrasound[20], which only became fully available in our hospital in 2009, and, therefore, was not part of our assessment.

The association of GIST with other tumors is well known and occurs more frequently with gastric adenocarcinoma. Kalmar *et al*.[21] found a higher incidence of synchronous or metachronous gastrointestinal tumors in patients with GIST compared with the normal population[21]. Kawanowa *et al*.[22] studied 100 specimens of stomach resected for adenocarcinoma and identified regions 50 microscopic foci of GIST in 35 of them[22]. In another publication, our group[23] reviewed this issue and described that patients with GIST have mutations that may facilitate the genesis of cancer. In this series, we had a high percentage of such association, but we believe it reflects a bias in the referral to the hospital specialized in oncology.

The main sites were the stomach (60% to 70%), followed by small intestine (20% to 30%), with the esophagus, colon and rectum comprising about 10% of cases and, to a lesser extent, also being found in extragastrointestinal sites of the abdomino-pelvic cavity[24,25]. Our group curiously found a large number of EGISTs (Extragastrointestinal stromal tumors – 14%) when compared to findings in the literature. The EGIST is the GIST outside the gastrointestinal tract, most often located in the retroperitoneum, mesentery and omentum[26,27]. However, it can also be found in the gallbladder, pancreas and rectovaginal septum[28-30].

GIST is typically characterized by immunohistochemical expression of c-Kit (CD117), a transmembrane receptor tyrosine kinase present in the interstitial cells of Cajal (ICC), which are located in the myenteric plexus of the muscular layer of the intestine and act as gastrointestinal pacemakers. Thus, considering the source cell, the expression of c-Kit also present in EGISTs should not be expected. One histogenesis hypothesis is that GISTs and EGISTs would have originated from a common precursor of ICCs and smooth muscle[27]. Another hypothesis suggests that EGIST originates from a mural GIST with extensive extramural growth, resulting in possible loss of connectivity to the intestinal wall[31]. Our high number of EGISTs can find a better explanation in the second hypothesis. In a review on EGISTs, awaiting publication[32], the average size of these tumors was 18cm above the group total (11.8cm), characterized by their larger size and, therefore, the likelihood of loss of contact with the gastrointestinal tract and adherence or fixation to other organs.

The diagnosis of GIST is confirmed by its clinical presentation, typical cellular morphological characteristics and positive immunohistochemical essay for c-Kit (CD117). However, some tumors, around 4%, have clinical and pathologic features consistent with GIST, but do not express Kit protein. Heinrich *et al*.[33] demonstrated that this group (c-kit negative GIST) is mutated in other receptor tyrosine kinase with activities similar to Kit (Activated Platelet-Derived Growth Factor Receptor – PDGFRá), representing an alternative pathway in the pathogenesis of this neoplasm. More recently the antigen DOG1 (Discovered On GIST 1) has been incorporated in the immunohistochemical panel when CD117 is negative. This antigen showed high specificity and sensitivity, being positive in over 91% of overall cases of GIST, and positive in more than half of CD117 negatives[34-36].

The prediction of biological behavior of GISTs is problematic because, despite the identification of numerous variables in the literature able to suggest their evolution, the findings are conflicting, with no consensus[15,37-40]. Hence, we have avoided the term "benign" and GIST was classified according to the malignant potential based on the two most relevant prognostic factors recognized in the literature[9].

Table 1 has the merit of easy memorization and is still used, but does not include a known high prognostic value, the location of the primary. Miettinem and Lasota reshaped the prognostic table with this new data, allowing to infer the risk of recurrence based on size, mitotic index and location of the primary tumor[41]. The study showed that the more distal the tumor in the gastrointestinal tract is the worst prognosis, the stomach being therefore of better prognosis and the colon and rectum displaying a worse one. In our analysis, we did not use it because we believe that it would divide the population in many subgroups with few members, which would hinder or render impossible any comparison. Our population draws attention to the high percentage of high risk (69/146 = 47%) which was probably underestimated due to the group sent in which we could not evaluate the mitotic index. Thus, this percentage is mainly due to the size, and corroborates our publications[37,42] showing that we tend to perform late detection. The initial publication of DeMatteo[24] showed that size greater than 10cm accounted for 19% of cases and had a negative impact on survival, considered then (2000) a negative prognostic factor. Other international series[17,43-45] confirm that this finding applies to both pre and post imatinib eras.

The mitotic index is another prognostic factor considered vital, and according to some reports it is currently considered to be the main one[46-48]. The difficulty related to mitotic index is the reproducibility among examiners, and here lies the main criticism to the nomogram proposed by the group at the Memorial Sloan-Kettering Cancer Center

as a behavior-predictor criterion[49]. The reason is that, in this model, there is too much impact on calculated survival, when we consider two individuals with lesions at all similar, except that one has four mitoses per high magnification field and the other has five. Different factors inherent to the tumor have prognostic impact in GIST, as: tumor necrosis, type of mutation, Ki-67, mucosal invasion, tumor perforation and histological type[13,15,46-48,50]. But undoubtedly the main at the moment are: mitotic index, size, location of the primary, type of mutation and tumor rupture.

Complete surgical resection is the standard treatment for GIST. It is the only modality capable of providing cure. R0 resection (no residual disease) is one of the most important influences for treatment outcome (disease-free interval and survival), and is achieved in around 40% to 60% of all cases of GIST and in more than 70 % in cases of non-metastatic disease [13,17,43,51,52]. The primary goal of surgery is complete resection and the type of resection will depend on the location and size of the tumor. The lesion with suspected invasion of adjacent organs should be treated by *en bloc* resection of the affected organ. It is mandatory that the negative resection margins get checked by examination of intraoperative frozen section, because the presence of residual disease negatively influences survival[48,53]. The ideal extent of surgical margin is not, but there is consensus that wide margin resections of the lesion are not necessary. Thus, depending on location and tumor size, segmental resection of the organ can be employed. It takes a meticulous surgical technique to prevent tumor rupture during surgery because the tumor capsule breaks easily and can result in neoplastic dissemination and poor prognosis[47,53,54].

Nodal metastasis is a rare event[24], there being no data in the literature indicating the conduction of systematic lymphadenectomy[52]. Our experience showed almost 10% of lymph node involvement, confirming our previous publication[55], in which we justify a selective approach to lymphadenectomy when the surgeon suspects the presence of macroscopically positive lymph nodes. This view is based on the experience of another group[56].

A laparoscopic resection was initially considered inappropriate in the treatment of GIST for risk of rupture of the tumor[57], but in 2006 our group has proposed its judicious use. In our study, we performed laparoscopic resection in tumors smaller than 5cm, all successfully. Currently, laparoscopic resection is deemed a valuable tool and should be considered when feasible and risk-free[58].

The presence of recurrence is frequent, despite complete surgical resection of the primary tumor. In the experience of the MD Anderson Cancer Center, only 10% of patients were free of disease after ten years of follow-up[53]. The initial pattern of relapse involves predominantly the peritoneum and liver. In the cases of the Memorial Sloan-Kattering Cancer Center, 40% of patients undergoing potentially curative surgery (R0) developed recurrence, with involvement of the peritoneum in 50% of cases and the liver in 75%, and median survival of 15 months after salvage surgery[53].

Our findings confirm the worldwide evidence of liver and peritoneum as the main sites of metastases. The remaining sites occurred only in cases of disseminated disease and never in isolation. The median survival of 69% in five years should be considered very good, but includes patients treated with imatinib and therefore should not be compared with the findings of a series treated with resection alone, as DeMatteo's[24], who had 35 % or Ng[53] to 28%. When compared to similar series in which we find variation of 63%[46] to 84%[45], we can consider that in fact we should look in a stratified manner, because the risk factors will certainly be very different between these populations and ours. When analyzing survival stratified by risk group, we found a significant difference (p = 0.029), with worse survival for the high-risk group. Disease-free survival showed a more noticeable drop after 18 months of follow-up and had no *plateau*, or it will occur after the fifth year. The similarity between the survival curve of the high risk group, which accounts for nearly half the population, and the disease-free survival curve called our attention. Our explanation lies in this population probably contaminating the curve and determining worse findings.

The discovery of STI571 (imatinib mesylate [Glivec®], Novartis, Basel, Switzerland) has revolutionized the treatment of cancer therapy by being the first to act specifically on the molecular changes responsible for the etiology of cancer. The knowledge of mutations (with a gain of Kit gene function) in the genesis and progression of GIST enabled the development of drugs with a defined molecular target that interferes with the tyrosine kinase receptor Kit.

The encouraging results with the first case studies led to the implementation of phase I and II[59,60], showing that imatinib mesylate had significant activity in patients with advanced GIST, achieving partial response rate of 53.7%, stable disease in 27.9% and toxicity grade 3 and 4 (bleeding, abdominal pain and electrolyte disturbances) in 21.1% of cases.

In the past, some types of treatment were used to control unresectable metastatic disease, such as radiotherapy, systemic or intraperitoneal chemotherapy and hepatic artery chemoembolization, without evidence of benefit[61].

Currently, without any doubt, patients with recurrent or metastatic disease should be treated by imatinib according to the algorithms ESMO[52] and NCCN[62].

The surgical approach to metastatic disease is currently limited to investigational studies in patients with stable resectable disease or responsive to treatment with imatinib[63-65]. Those who display disease progression in the presence of the drug will only have surgery indication in very restricted situations[52,62].

The long-term monitoring of patients with high-risk GIST who underwent surgical resection indicates that

only the isolated resection is usually not able to provide healing in a high percentage. In our group, only 50% of patients were alive in the fifth year. In order to improve survival in this group, lines of research are underway to clarify these issues. The phase III, multicenter, randomized study, also sponsored by the American College of Surgeons (ACOSOG-Z9001)[66] aimed to answer if there is a benefit in the long term with the use of adjuvant imatinib in GIST operated patients with high/intermediate risk. In its first post-closure review[67], the study showed a definite gain of disease-free survival at one year. The group of bone sarcoma and soft tissue of the EORTC[66] is also evaluating the results of adjuvant therapy with imatinib and is designed to allocate 400 cases to the trial. The trial of the Scandinavian Sarcoma Group (SSGXVII)[66] expects to complete its multicenter, randomized study with 80 cases of GIST divided into two arms (400mg of adjuvant imatinib for 12 or 36 months).

The rationale of neoadjuvant therapy with imatinib is to increase the number of unresectable cases converted for resection (pharmacological tumor reduction) and optimize the response to imatinib after surgical cytoreduction, reducing the chances of local recurrence and distant metastasis, prolonging disease-free interval and overall survival. Neoadjuvant treatment with imatinib is also being tested in studies such as the RTOG-S0132[66] in order to assess the impact of this approach in progression-free survival and objective response rate. In our own institution we have in place a study called CONVERT 1, in which we administer imatinib for three months preoperatively.

Our patients present mainly in the form of high-risk disease, with obvious impact on survival. The use of imatinib improved survival of patients with recurrent and metastatic disease. We should study its use in the setting of adjuvant and neoadjuvant therapy to improve the rates of the high-risk group. The creation of reference centers is a need for the study of rare diseases.

We know how difficult it is to study rare diseases in our midst and we think that this is only possible by creating centers of excellence that make possible the gathering of cases to conduct a study. The analysis of data collected retrospectively is always criticized and it becomes more difficult when different centers contribute. However, we believe that, although with limitations, this type of work has value and should be encouraged.

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R E S U M O

Objetivo: *Avaliar os resultados do tratamento de GIST no INCA.* ***Métodos****: Análise retrospectiva de todos os casos de GIST tratados no INCA no período de 1997 a 2009.* ***Resultados****: Analisamos 146 pacientes, com média de idade de 44,5 anos e predomínio do sexo feminino. O principal sintoma foi dor abdominal. Tivemos ocorrência de segundo primário em 22% dos casos e na imuno-histoquímica, 92% foram positivos para CD117. A localização mais frequente foi estômago e predominou o grupo de alto risco. A cirurgia foi R0 (extenso) em 70% e os principais sítios de metástases foram fígado e peritônio. A sobrevida global foi, respectivamente, em dois e cinco anos de 86% e 59%. Houve significante diferença entre a sobrevida global (p=0,29) do grupo de alto risco versus os demais.* ***Conclusão****: Os nossos pacientes apresentam-se principalmente sob forma de doença de alto risco com repercussão óbvia na sobrevida. O uso de Imatinib melhorou a sobrevida dos pacientes com doença metastática e recidivada. Devemos estudar seu uso no cenário de adjuvância e neoadjuvancia visando melhorar os índices do grupo de alto risco. A criação de centros referenciais é uma necessidade para o estudo de doenças pouco frequentes.*

Descritores: *Neoplasias. Tumores do estroma gastrointestinal. Cirurgia. Sobrevida. Mesilatos.*

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