Abstract 10088

Diagnosis and Initial Evaluation of Patients With Gastrointestinal Stromal Tumor (GIST): An Observational Study of 1226 Patients

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INTRODUCTION

- Most studies evaluating the treatment of patients with gastrointestinal stromal tumor (GIST) have been based on clinical trials and thus reflect practice patterns at academic referral centers.[1-3]
- A US observational database (reGISTry; clinicaltrials.gov identifier NCT00507273; Novartis study number CSTI571BUS227) was initiated in 2004 to study the management of patients with GIST in community practices in the United States.
  - The study was conducted from August 2005 to December 2010.
  - Preliminary data from this trial that analyzed 882 patients who were enrolled as of March 2009 were previously published.[4]
- The present study was designed to analyze the reGISTry database to characterize methods of diagnosis, variables related to disease assessment, initial treatment of patients, and baseline tumor characteristics.

METHODS

- Details of the reGISTry database have been previously presented.[4]
  - All patients diagnosed with GIST who were currently being treated or followed at each site were eligible for enrollment.
  - The protocol for enrollment of patients and use of data was approved by local institutional review boards, and written informed consent was obtained from all enrolled patients.
  - Since reGISTry documented usual patient care, there were no specific interventions or procedures required.
  - For each patient, reGISTry collected data on demographics; diagnostic history; location, size, and mitotic count of primary lesions and locations of metastases; results of immunohistochemistry and any mutational analyses; treatments administered; and physicians involved in initial GIST diagnosis and treatment management decisions.
  - Information also was collected on treatment management decisions, including basis for choice of surgery or targeted therapy as initial therapy, assessment of patient response to targeted therapy, and changes in therapy.
  - Data were extracted and analyzed every 6 months and summarized using descriptive statistics.
- In this report, we focused on data pertaining to initial diagnosis and treatment decisions.

RESULTS

Patients

- At the time of this analysis (May 2010), 1226 patients were included in the reGISTry database and baseline information had been captured.
- Key baseline patient demographics and characteristics are summarized in **Table 1.**

Table 1. Patient demographics and characteristics

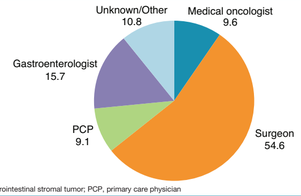
Variable	n (%)
Age, y	
<18	1 (0.1)
18–40	73 (6.0)
41–64	618 (50.4)
≥65	534 (43.6)
Gender	
Male	611 (49.8)
Female	615 (50.2)
Race	
Caucasian	920 (75.0)
African American	196 (16.0)
Asian	33 (2.7)
Hispanic	40 (3.3)
Other	10 (0.8)
Unknown	27 (2.2)
Presenting signs and symptoms at diagnosis	
Symptomatic	1033 (84.3)
Asymptomatic	193 (15.7)
GIST stage at diagnosis	
Localized primary	1014 (82.7)
Metastatic	212 (17.3)

N=1226
GIST, gastrointestinal stromal tumor

Clinicians involved in diagnosis and treatment management decisions

- GIST was most commonly initially diagnosed by surgeons, followed by gastroenterologists (**Figure 1**).
  - Medical oncologists and primary care physicians were the primary source of referral in 10% of the cases.

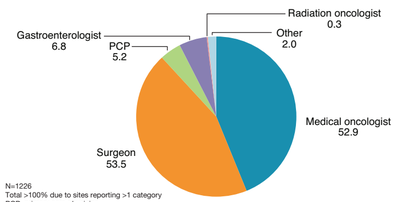
Figure 1. Percentage of clinicians responsible for initial GIST diagnosis



N=1226
GIST, gastrointestinal stromal tumor; PCP, primary care physician

- Primary management decisions were made at time of diagnosis equally by medical oncologists and surgeons (**Figure 2**).

Figure 2. Percentage of clinicians responsible for primary management decisions at diagnosis



N=1226
Total >100% due to sites reporting >1 category
PCP, primary care physician

Biopsy for GIST diagnosis

- Approximately three-quarters of patients were diagnosed by surgical biopsy, with radiologic and endoscopic techniques also used in many patients (**Table 2**).

Table 2. Biopsy type for initial GIST diagnosis[a]

Procedure	n (%)
Interventional radiology	133 (10.8)
Percutaneous FNA	45 (33.8)
Percutaneous core biopsy	88 (66.2)
US-guided	12 (13.6)
CT-guided	79 (89.8)
Endoscopic (FNA)	265 (21.6)
US-guided	121 (45.7)
Surgical	916 (74.7)
Incisional biopsy	60 (6.6)
Intraoperative FNA or core biopsy	29 (3.2)
Excisional biopsy	100 (10.9)
Resection of primary tumor	693 (75.7)
Resection of metastases	34 (3.7)

[a] Sites may have used >1 type of procedure
FNA, fine-needle aspiration; US, ultrasound; CT, computed tomography

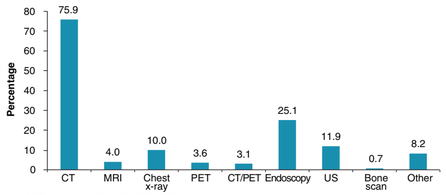
Diagnostic imaging

- A variety of diagnostic imaging techniques were used for initial diagnosis of GIST.
  - Some patients may have had more than 1 type of imaging assessment as part of their diagnostic work-up (**Figure 3**).

Tumor location

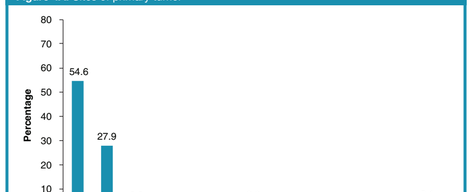
- Primary tumors were typically located in the stomach (55%) and small intestine (28%) (**Figure 4A**).
- Metastases occurred most frequently in the liver (62%), peritoneum (36%), and lymph nodes (10%) and were rare (<1%) in bone (**Figure 4B**).

Figure 3. Imaging methods used for diagnosis of GIST



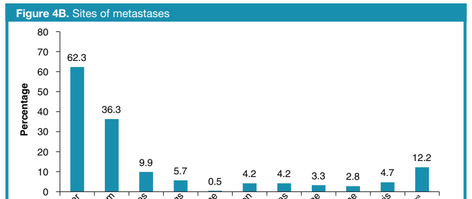
Patients may have had >1 type of imaging assessment
GIST, gastrointestinal stromal tumor; CT, computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography; US, ultrasound

Figure 4A. Sites of primary tumor



Small intestine location included duodenum
GE, gastroesophageal

Figure 4B. Sites of metastases

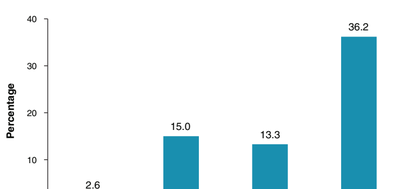


[a] Other category includes ovaries, bladder, adrenal, stomach, and all other sites

Primary tumor characteristics

- Localized primary tumors were characterized based on selected risk assessment criteria (ie, size and mitotic index).
  - More than one-third of patients with localized primary tumor were classified as high risk based on size and mitotic count (**Figure 5**).

Figure 5. Risk assessment (localized primary tumors)



N=1014

Immunohistochemical and mutational analysis

- Immunohistochemistry to determine CD117 (c-KIT) status was performed in 93.3% of patients; positive staining was observed in 97.7% of cases.
- Mutational analysis data were available only in 99 (8%) patients.
- Mutations in *KIT* exon 9 or exon 11 were the most frequently reported (**Table 3**).

Table 3. Mutational analysis

Genotype	n (%)[a]
KIT Exon 9	12 (12.1)
KIT Exon 11	56 (56.6)
KIT Exon 13	0
KIT Exon 17	4 (4.0)
PDGFRA Exon 12	0
PDGFRA Exon 18	10 (10.1)
KIT and *PDGFRA* wild type	17 (17.2)

[a] Based on subset of 99 patients for whom mutational data were available

First treatment

- First treatments are summarized in **Table 4**.
  - First treatment for GIST was primarily surgery in the overall population.
  - Surgical intervention was far less frequently used as initial treatment for metastatic versus localized disease.

Table 4. First treatment for GIST

Treatment	n (%)
Surgery	988 (80.6)
Systemic therapy	212 (17.3)
Radiation therapy	2 (0.2)
Supportive care only	22 (1.8)
Other	2 (0.2)
If surgery	
For primary tumor	897 (90.8)
For metastatic disease	20 (2.0)
For primary and metastatic disease	71 (7.2)
Type of surgery	
Primary tumor	
Gross complete resection	856 (95.4)
Incomplete resection	41 (4.6)
Metastatic disease	
Resection of all known sites of metastatic disease	7 (35.0)
Resection of some, but not all, known sites	12 (60.0)
Resection of some sites and ablation of others	1 (5.0)
Primary and metastatic disease	
Primary	
Gross complete resection	56 (78.9)
Incomplete resection	15 (21.1)
Metastatic disease	
Resection of all known sites of metastatic disease	39 (54.9)
Resection of some, but not all, known sites	32 (45.1)
Resection of some sites and ablation of others	0

N=1226
GIST, gastrointestinal stromal tumor

CONCLUSIONS

- Patients with GIST are initially diagnosed in the community practice setting primarily by surgeons and gastroenterologists, but medical oncologists and primary care physicians diagnose ~20% of cases via image-guided biopsy.
- Initial management decisions are made equally by surgeons and medical oncologists.
  - These data reinforce the need for a multidisciplinary approach in the diagnosis and treatment of GIST.
- Most initial diagnoses were made by means of surgical biopsy or resection.
- Use of genotyping in GIST was low, probably due to the limited number of laboratories with mutational testing available as a clinical test at the time the study was conducted, and the limited recognition of the clinical implications of genotype on imatinib therapy.
  - This is likely to increase with greater availability of molecular analysis as well as increasing data on the therapeutic implications of different genotypes.[5]
- ~36% of reGISTry patients with localized primary tumors were classified as high risk based on tumor size and mitotic index combined.

Acknowledgments

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