

# Response of Imatinib Mesylate in Patients with Gastrointestinal Stromal Cell Tumour

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## Abstract

In this study, the response of Imatinib Mesylate in patients with Gastro-intestinal stromal cell tumour (GIST) was assessed. GIST results from a mutation in one of the receptor protein tyrosine kinases. Imatinib Mesylate, a tyrosine kinase inhibitor, has emerged as a promising new treatment for GISTs. Total 16 cases were reviewed. Diagnosis was based on biopsy and immunohistochemistry. Response assessment was done using CT scans, at a median duration of 4 months.

The median age of the patients was 52 years, Majority were male (n=14). Most common presenting complaint was abdominal pain (n=7). Commonest primary site was stomach (n=7), Liver was the most common organ involved in metastasis (n=8). All patients received Imatinib 400 mg orally, once a day. No mortality was reported during median follow up time of 28 months on Imatinib. There was also either radiological remission (n=5) or response (n=5), in about half of the patients without any serious side effects.

## Introduction

Gastrointestinal stromal cell tumours (GIST) were previously classified as leiomyoma and leiomyosarcoma. Recent studies have established them as a distinct entity. GIST is one of the many subsets of different types of histologies of soft tissue sarcomas and most common mesenchymal neoplasm of gastrointestinal tract; resulting from a mutation in one of the receptor protein tyrosine kinases (KIT, also called CD117).<sup>1</sup> Interestingly this marker is also expressed on inconspicuous population of dendritic-

like cells present in normal gut wall, interstitial cells of Cajal (ICC). ICC plays an important role in gut motility by regulating slow wave contractions. It is widely hypothesized that either GISTs represents neoplastic transformation of ICC or they share common ancestors.<sup>2</sup> GIST tumour had previously been documented to be resistant to conventional chemotherapies. Since KIT activation occurs in the majority of cases of GISTs, in recent years KIT-inhibition has emerged as a promising new treatment for GISTs. Imatinib mesylate, a selective inhibitor of the KIT protein tyrosine kinase, has produced durable clinical benefits and objective anti-tumour responses in most patients with GIST. Multiple clinical trials worldwide have consistently shown the efficacy of Imatinib for patients with GIST.<sup>3</sup> In February 2002 FDA approved Imatinib mesylate for the treatment of patients with KIT (CD117) positive unresectable and/or metastatic malignant GIST.<sup>4</sup> According to western data approximately 3000 GISTs might be diagnosed annually in United States.<sup>5</sup> Population based data from our part of the world is scarce. To our knowledge, our data is the first from Pakistan which showed response assessment of GIST patients on Imatinib.

## Method and Results

Since 2002, a total of 22 diagnosed cases of GIST were registered at The Aga Khan University Hospital, Oncology clinic. Amongst them records of 16 patients were available for review. All available cases of GIST were receiving Imatinib at AKUH. Diagnosis was based on biopsy report and positive CD117 marker on immunohistochemistry. Response assessment of GIST

patients on Imatinib with or without surgery was done with follow up CT scans. Reporting of CT scans was radiologist dependent. Patients were followed up from commencing of Imatinib Mesylate therapy till December 2007. SPSS 14 was used for analysis.

Among 16 patients, 14 were men and 2 were women. Median age was 52 years and age ranged from 38 to 75 years. Out of 16 patients, eight belonged to Sind province (n=8), four to Balochistan province and one was from North West Frontier province. Abdominal pain was the

**TABLE**

<b>Variables</b>	<b>Patients (N=16)</b>
Operable disease	12
Inoperable disease	4
Median size of GIST (cms)	10
Follow up CT assessment (n=13)	
No residual disease/remission	5
Response/regression	5
Progression	3

commonest presenting complaint (n=7). Other complaints included abdominal mass (n=3), gastro-intestinal bleed (n=2) and intestinal obstruction (n=1). Amongst these one patient had anaemia, one complained of dysphagia and one presented with lower urinary tract symptoms. On histological examination spindle cells were most commonly seen (n=8). The minimum size of GIST seen in these patients was 6.5cms and maximum size was 27 cms (median=10 cms). The commonest primary organ for GIST was stomach (n=7). Other primary sites included small intestine (n=3), mesentery (n=1), pancreas (n=1) and retroperitoneum (n=1). Metastatic disease was present at the time of presentation in 12 patients. Liver was the commonest organ involved in metastasis (n=8). Less

common sites of metastasis, included peritoneum, spleen, seminal vesicles and prostate. Out of these, 13 patients had follow up CT scan at a median duration of 4 months (Table). All patients received Imatinib (400 mg orally), once a day. No mortality was reported in patients on Imatinib, during median follow up period of 28 months; three patients were lost to follow up. Side effects of Imatinib were noticed in ten patients. None of the patients reported any serious side effects. Fluid retention was the most frequent side effect leading to facial swelling (n=7). Other side effects were loose stools (n=3), rashes (n=3), muscle cramps and body aches (n=1). Haemoglobin, white cell counts and platelets were checked for each patient on regular three monthly intervals which remained within normal ranges.

## **Conclusion**

GIST patients at our center were mostly men in their 5th decade, from Sind and Balochistan provinces. Majority presented with metastatic disease. Imatinib Mesylate produced either radiological remission or response in more than half of the patients without producing any serious side effects.

## **References**

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