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GIST

(Gastrointestinal Stromal Tumor)

FAQ

The Max Foundation
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FREQUENTLY ASKED QUESTIONS

What is Gastrointestinal Stromal Tumor (GIST)?

A gastrointestinal stromal tumor (GIST) is a rare type of cancer that grows in the supporting (connective) tissue between muscle layers in the digestive (gastrointestinal or GI) tract or close to it. It belongs to the general class of cancers called sarcomas.Most GISTs occur in people over the age of 50. GIST in children and young adults is quite rare.

What is sarcoma?

The name comes from the Greek word "sarkoma" (fleshy growth). These cancers develop from connective tissues that act as supportive frameworks for the organs and structures of the body, such as muscles, tendons, cartilage, fibrous tissue, fat, blood vessels, nerves, and others.

The vast majority of cancers are not sarcomas but carcinomas, which develop from skin-like tissues called epithelial tissues. This includes not only the skin covering the outside of our bodies, but also the skin-like linings of our body cavities and our digestive tracts. Ordinary "stomach cancer" and "colorectal cancer" are carcinomas.

Gastrointestinal stromal tumors (GISTs) should not be confused with these common cancers of the GI tract. Both may occur in the same parts of the body. Distinguishing GISTs from these diseases is important because GISTs behave differently and require particular drugs for treatment.

Why have I developed GIST?

There are no known environmental, behavioural or lifestyle risk factors that are known to cause GIST and hencethere are no preventive strategies. The only exception is for GIST that runs in families (familial GIST), but this is extremely rare, with only about a dozen families reported in the medical literature.

A protein called "KIT", also called CD-117is thought to be one of the major causes of GIST. Normal cells have a limited life span. The KIT protein is located on the surface of normal cells. It sends a signal inside the cells that tells them to grow only as needed. When KIT becomes abnormal, its signal stays on all the time, causing cells to multiply out of control forming a tumor. The longer the cancerous cells live, the more potential they have to become dangerous, and the more likely they are to spread to other parts of the body.

What is KIT?

KIT is the name of both the gene on chromosome and the protein it produces that is thought to be a major cause of GIST.

What are the symptoms of GIST?

When GIST tumors are first discovered, the most common symptoms are:

- Vague abdominal discomfort or pain
- Presence of a palpable abdominal mass
- Feeling of abdominal fullness
- Secondary symptoms resulting from tumor bleeding and associated anemia

How does my doctor diagnose that I have GIST?

GIST is diagnosed after a pathologist tests cells from the tumor. These cells are taken from the tumor by means of a biopsy. A biopsy is a piece of the tumor that is usually obtained with a needle or similar instrument or using an endoscope. The shape and appearance of the tumor cells is then examined under a microscope by a pathologist. The pathologist tests the tumor cells for KIT (CD-117). The vast majority of GISTs test positive for KIT, but a few do not. Other pathology tests can identify GISTs that are not KIT-expression-positive.

Differences among GISTs in the specific gene mutations they show are important in predicting their response to targeted molecular drug treatments. The pathologist can do special Mutation testing to identify these characteristics.

Should I have DNA mutational analysis of my GIST tissue?

Researchers are discovering new information about how the response of GIST patients to drug treatments is related to the particular mutations shown by their tumors. If you are able to have this testing done, it is a good idea. At the very least, try to ensure that adequate pathology samples are kept of your tumor to allow such testing to be done in the future, should you need it. In case of Recurence of disease Mutational analysis should be done again on the new recurrent tumour.

What other investigations will I be subjected to?

Investigations other than the biopsy, are required to stage the disease. The stage helps us in predicting outcome as well as on deciding the best treatment option for your stage. These include a CT scan of the abdomen and/or an MRI scan, an endoscopy (which maybe a colonoscopy or an upper GI scopy). Endoscopic ultrasound is required in selected patients. A PET scan may sometimes be used to clarify ambiguous findings on CT or MRI, or in patients who are being considered for surgery after a course of Imatinib, or in patients with complex metastatic disease.

How does the tumor grow and affect me?

GIST develops in the muscle wall of the digestive tract from special "pacemaker" cells that help move food along the digestive system. Initially small tumors are contained within the muscle wall. As they grow, GISTs usually grow outward from the muscle wall, not inward into the organs of the gastrointestinal tract. The most common location for GISTs is the Stomach, followed by the Small

Intestine, with a few percent occurring in the Esophagus, Colon, and Rectum. Rarely GIST develops in other abdominal sites (including Gallbladder, Liver, Mesentery, Omentum, Pelvic organs).

What is metastatic GIST?

GIST cancers begin as localized (single) tumors growing somewhere along the GI tract. Like most cancers, GISTs can shed cancer cells which spread the disease to other sites. This process is called metastasis and the new lesions are called metastases. (The original lesion is called the "primary".) GISTs usually metastasize to nearby sites in the body, such as the peritoneal cavity and liver. GIST metastases growing at these other sites are still GISTs-a liver metastasis, for example, is still a GIST, not a "liver cancer".

How is GIST treated?

The first option is surgery to remove the tumor(s). Surgery cures GIST, especially if the tumor is small and has not spread before being discovered. If the size of the tumour is large and there are certain pathologic features which make the GIST more likely to recur, patients are given a tablet Imatinib for a period of three years or more as per individual case. If the GIST is in a difficult location or large, surgery may be difficult- in these situations patients are offered pre-operative(Neo-adjuvant) Imatinib for a period of 6 to 12 months usually to make the surgery safer.

If the tumor is inoperable, or if GIST returns to the same location (recurs) or spreads to additional locations (metastasizes) after surgery, then drug treatments are available. The two drugs currently approved for inoperable or metastatic GIST are Imatinib and Sunitinib. Imatinib is the drug used first. Sunitinib is approved for GIST patients who are resistant to or intolerant of Imatinib.

GIST is resistant to traditional types of chemotherapy .

Immunotherapy is also being used in some new trials.

Newer drugs Like Masitinib / Pazopanib/ Ponatinib/ Crenolanib are being used in trials world wide for Resistant GIST with good responses in some cases.

What is Imatinib?

Imatinib is a pill that is taken either once or twice daily, depending on the dose. A patient normally takes 400-800 milligrams daily. The tablets should be taken with a meal and a large glass of water. Imatinib is usually taken for as long as patients are benefiting from it unless specified for a period of 3 years post-surgery or more depending on each individual case.

Imatinib is different from traditional chemotherapy in that it is very selective. Traditional chemotherapy kills all cells that are dividing quickly. This is what causes so many of the side effects of traditional chemotherapy. In addition to the cancer cells, this type of chemotherapy also kills many of the body's normal cells. Imatinib only targets the c-kit expressing cells of the tumor GIST,

hence is much more selective and as a result has fewer and less severe side effects.

Common side-effects relating to imatinib are nausea, diarrhea, headaches, leg cramps, fluid retention (commonly around eyes and ankles), itchy rash, visual problems, loss of appetite and can also reduce blood counts and may cause increased risk of infection, bleeding and anaemia.

Imatinib (Glivec)as a drug causes cell death of GIST cells but sometimes it just suppresses cell growth & may not kill all GIST cells .Therefore it is Important to

1. Take daily dose of Glivec, missing the dose can cause mutation.
2. To take the drug for a Longer period of Time,in some cases of Metastatic GIST it should be taken Lifelong.

One should consult his/her medical oncologist about their individual case & Duration of Adjuvant therapy.

What is Sunitinib?

Sunitinib is another drug that is approved in some, but not all countries for GIST that is resistant to Imatinib or for patients that cannot tolerate Imatinib. It is also a pill that is taken every day (37.5 milligrams) or every day for 28 days (50 milligrams) followed by a two week break.

Sunitinib is a tyrosine kinase inhibitor that is similar to Imatinib in some ways. Both drugs inhibit the KIT protein (mutated in 80-85% of GISTs) and the PDGFRα protein (mutated in 5-7% of GISTs).

What should I do if Imatinib stops working for me?

- Make sure the progression is real. Initial treatment with Imatinib can sometimes result in swelling of tumors that are responding to Imatinib. This can be mistaken for progression if the radiologist is inexperienced at reading GIST scans.
- Surgery, RFA or Hepatic artery embolization can be used to treat one or two tumors that are no longer responding to Imatinib.
- The Imatinib dose can be increased up to 800 mg.
- If Imatinib is not working at 800 mg, switch to Sunitinib.
- Don't stop Imatinib too soon.

Even if Imatinib is unable to totally stop tumor growth, it may slow growth. In these cases consideration should be given to continuing Imatinib therapy in the absence of other options.

What medicines should I avoid while I am taking Imatinib?

In general you need to be careful while taking the following medicines with Gleevec. Some of these should be completely avoided after discussion with your doctor.

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Antibiotics /antifungal /antiviral

Ketoconazole, Itraconazole, Voriconazole, Ciprofloxacin, Levofloxacin , Clarithromycin, telithromycin, Atazanavir, indinavir, Nefazodone, nelfinavir, ritonavir, saquinavir, Quinine, Mefloquine,

Pain-killers

Diclofenac

Anit-emetic drugs (for vomiting

Aprepitant/fosaprepitant

Anti-diabetic drugs –Monitor sugars closely

Glibenclamide, Rosiglatazone , Pioglitazone , Metformin (decreases imatinib exposure), Nateglinide,

Anti-TB drugs

Rifmapicin

Anti-epileptic drugs

Carbamazepine, Oxcarbamazepine, Phenytoin, Fosphenytoin, Phenobarbital, Primidone,

Cardiac drugs

Clopidogrel (may have to modify dose of clopidogrel), Warfarin – monitor INR closely, Heparin – increases imatinib exposure, Verapamil ,Diltiazem , Nifedipine , Atorvastatin , Simvastatin , Amiodarone , Spironolactone , metoprolol Bisoprolol, Carvediolol (atenolol has no interaction), Captopril , Lisinopril

Steroids

Dexamethasone (decreased level of imatinib)

What is my likely outcome after treatment?

The risk of recurrence or metastasis for a surgically resected GIST depends on its **size** and the **mitotic count.** The mitotic count is a measure of how fast the tumor cells are multiplying.

In general, the smaller the tumor's size at removal and the slower its rate of growth, the better the chance that it will not recur. However, even small GISTs have been known to recur, and no GIST can be categorized as definitely benign.While certain individuals might be cured by

surgical resection of their GISTs, there are no conclusive criteria to guarantee that a GIST tumor is truly benign.Any GIST tumor carries some risk for recurrence of the disease. This can be either at the same site or at distant locations in the body. It may take time to appear at some point in the future. This is the hallmark of a cancerous, malignant behaviour.

Smaller GIST tumours can be successfully treated by Surgery & Adjuvant Imatinib, (depending on the site and pathology), with patients having a good quality of life.

Larger & Metastatic GIST tumours are treated initially with Neo-Adjuvant therapy (Pre Surgery Imatinib) to reduce the size of the tumour given for a period of 6-12 months ,followed by Surgery & then Adjuvant Therapy (Post Surgery Imatinib) which may continue for longer duartions even lifelong in some cases.

It is Important that your Oncologist & Surgeon are GIST Specialist & have a long experience in management of GIST.

How long do I need to follow-up with my doctor after treatment?

GISTs are best categorized into low, intermediate, or high-risk tumors. Factors that predict better outcome include having a stomach GIST, a small tumor size, and low mitotic count. All patients, even those diagnosed with "low risk" GISTs, should have routine medical follow up for several years to monitor for reappearance of the disease.

Conclusion :

GIST is mostly treated Successfully with Imatinib & Surgery ,however some Resistant forms of GIST can also be treated successfully by Newer Drugs & Dosage regimes .

With Newer Drug Trials happening around the World there is Hope for treating Even Resistant GIST.

Early & Prompt Diagnosis & Treatment from a GIST Expert & Adherence to Compliance by the Patient can Result in a Successful Treatment Outcome !

Disclaimer

The Content of this FAQ is not intended to be a substitute for professional medical advice, diagnosis, or treatment. Always seek the advice of your physician or other qualified health provider with any questions you may have regarding a medical condition. Never disregard professional medical advice or delay in seeking it because of something you have read on the FAQ's.

Glossary of terms

Adjuvant therapy	**Drug treatment given after Surgery to prevent recurrence of disease**
Biopsy	is a sample of tissue taken from the body in order to examine it more closely.
Chromosomes	are the structures that hold our genes. These are packages of genetic information contained in every cell of the human body.
CT scan	is a computerised tomography scan. It uses X-rays and a computer to create detailed images of the inside of your body.
DNA	Deoxyribonucleic acid (DNA) is the chemical information database that carries the complete set of instructions for the cell as to the nature of the proteins produced by it, its life span, maturity, function and death.
Endoscopy	is a procedure where the inside of your body is examined internally using an endoscope. An endoscope is a thin, long, flexible tube that has a light source and a video camera at one end. Images of the inside of your body are relayed to a television screen.
Genes	are the working subunits of DNA.
MRI	magnetic resonance imaging (MRI) is a test that uses a magnetic field and pulses of radio wave energy to make pictures of organs and structures inside the body.
Mutation	occurs when a DNA gene is damaged or changed in such a way as to alter the genetic message carried by that gene.
Neo-Adjuvant therapy	**Drug treatment given prior to Surgery to reduce size of tumor**
PET	positron emission tomography (PET) scans are used to produce detailed, three-dimensional images of the inside of the body.
RFA	radiofrequency ablation is a newer, minimally invasive, treatment. (means a doctor uses radiofrequency energy (instead of laser energy) to heat up and damage tumor tissue)

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