Gastrointestinal Stromal Tumor (GIST) Fact Sheet

Gastrointestinal stromal tumor (GIST) is found in the gastrointestinal (GI) tract and belongs to a group of rare cancers called soft tissue sarcomas. Sarcomas begin in muscle, fat, fibrous tissue, blood vessels, or other supporting tissue of the body.[1,2]

Although GIST can arise anywhere in the GI tract, they occur most often in the stomach (60 percent) or small intestine (30 percent). The rest are found in the colon, rectum and esophagus.[3]

Facts and Figures About GIST

GISTs are rare tumors, with an estimated incidence of 1.5 per 100,000 per year in Europe.[4]

- The International Union Against Cancer (UICC) recently developed an international "TNM" staging system for GIST, which contains four key pieces of information, including:[5]
    - **T:** The size of the primary tumor, and whether it has spread to nearby organs
    - **N:** The extent of which the cancer has spread to nearby lymph nodes
    - **M:** Whether the cancer has spread, or metastasized, to distant parts of the body
    - **Mitotic rate:** The measure of how fast the cancer cells are growing and dividing

- Historic overall five-year survival rates in patients with GIST were about 25 percent with a median survival of about 19 months.[6]
    - The introduction of imatinib mesylate in 2002 for the treatment of GIST brought the two-year survival rates for patients with metastatic disease to approximately 70 percent.[7]

Biology

- The vast majority of GIST are characterized by expression of a protein receptor called KIT that is involved in cancer growth and development.[8]
- Approximately 80-85 percent of GIST have mutations in KIT.[9]
- Approximately 5 – 8 percent of GIST patients have mutations in another protein receptor called PDGFR, or platelet-derived growth factor receptor.[9]
- It is believed that a deviation, or mutation, in the normal genetic makeup in these two proteins causes the development of GIST in most patients.[10]
- There is growing evidence that KIT mutations impact the course of the disease, especially mutations in KIT exons 9 and 11. Mutational testing is playing an increasing role in the diagnosis and management of GIST.[11]

Risk Factors

- In rare cases, GIST has been diagnosed in many members within the same family. However, most cases of GIST are sporadic, meaning there is no evidence that they are being passed from generation to generation, and they have no apparent cause.[12]
- The majority of people diagnosed with GIST are older than 50.[13]

Diagnosis and Treatment

- GIST is often asymptomatic until it reaches a certain location, grows to a certain size or bleeds.[14] Not infrequently, GIST is discovered incidentally during radiologic imaging for an unrelated condition or as a secondary finding in a surgical resection, which is the removal of all or part of an organ.[15]
- At diagnosis, approximately half of malignant GIST are metastatic.[16]
- The primary treatment for newly diagnosed GIST patients is surgery. Other standard cancer treatments - chemotherapy and radiation - have had limited success in the treatment of GIST.[17]
- The molecular-targeted agent imatinib mesylate was the first systemic therapy to be approved for GIST and is currently the standard of care for first-line treatment of patients with advanced GIST.[17] Imatinib mesylate is also approved for the adjuvant (post-operative) treatment of KIT-positive GIST.[18]
- Although most patients with advanced GIST benefit from imatinib treatment, they may subsequently develop resistance to the agent.[19]
- A multi-kinase inhibitor is approved for patients with GIST after disease progression on or intolerance to imatinib mesylate.[20]

[1] Cancer.net. Gastrointestinal Stromal Tumor - GIST Available at: http://www.cancer.net/patient/Cancer+Types/Gastrointestinal+Stromal+Tumor+-+GIST. Accessed May 9, 2012.
[2]American Cancer Society. Sarcoma – Adult Soft Tissue Cancer. Available at: http://www.cancer.org/cancer/sarcoma-adultsofttissuecancer/detailedguide/sarcoma-adult-soft-tissue-cancer-soft-tissue-sarcoma. Accessed Aug. 8, 2012.
[3] National Cancer Institute. General Information About Gastrointestinal Stromal Tumors Treatment. Available at: http://www.cancer.gov/cancertopics/pdq/treatment/gist/HealthProfessional/page1. Accessed July 12, 2011.
[4] Casali PG , Jost L, Reichardt P, et al. Gastrointestinal stromal tumours: ESMO Clinical Recommendations for diagnosis, treatment and follow-up. Annals of Oncology. 2010: 21(5):v98-v102.
[5]International Union Against Cancer. TNM Classification of Malignant Tumours. Seventh Edition. 2010: 76-81.
[6] Gold JS, van der Zwan SM, Gonen M et al. Outcome of metastatic GIST in the era before tyrosine kinase inhibitors. Ann Surg Oncol. 2007;14(1):134-142.
[7] Antonescu CR, Besmer P, Guo T, et al. Acquired resistance to imatinib in gastrointestinal stromal tumor occurs through secondary gene mutation. Clin Cancer Res. 2005;11:4182-4190.
[8] Heinrich MC, Corless CL, Demetri GD, et al. Kinase mutations and imatinib response in patients with metastatic gastrointestinal stromal tumor. J Clin Oncol. 2003;21:4342-4349.
[9] Fletcher J, Liegl-Atzwanger B, et al. *Virchows Arch*. 2010; 456:111-127.
[10] American Cancer Society. Do we know what causes gastrointestinal stromal tumors? Available at: http://www.cancer.org/Cancer/GastrointestinalStromalTumorGIST/DetailedGuide/gastrointestinal-stromal-tumor-what-causes. Accessed Aug. 8, 2012.
[11] National Comprehensive Cancer Network Task Force. NCCN Task Force Report: Optimal management of patients with gastrointestinal stromal tumor (GIST) – Update of the NCCN Clinical Practice Guidelines. J NCCN 2007; 5(Supp 2)
[12] Cancer.net. Gastrointestinal Stromal Tumor – GIST: Risk Factors. Available at: http://www.cancer.net/patient/Cancer+Types/Gastrointestinal+Stromal+Tumor+-+GIST?sectionTitle=Risk%20Factors. Accessed Aug. 8, 2012.
[13] American Cancer Society. What are the key statistics about gastrointestinal stromal tumors? Available at: http://www.cancer.org/Cancer/GastrointestinalStromalTumorGIST/DetailedGuide/gastrointestinal-stromal-tumor-key-statistics. Accessed May 9, 2012.
[14] American Cancer Society. How are gastrointestinal stromal tumors diagnosed? Available at: http://www.cancer.org/cancer/gastrointestinalstromaltumorgist/detailedguide/gastrointestinal-stromal-tumor-diagnosis. Accessed Aug. 8, 2012.
[15] American Cancer Society. Can gastrointestinal stromal tumors (GIST) be found early? Available at: http://www.cancer.org/cancer/gastrointestinalstromaltumorgist/detailedguide/gastrointestinal-stromal-tumor-detection. Accessed Aug. 8, 2012.
[16] Stamatakos M, Douzinas E, et al. Gastrointestinal Stromal Tumor. *World Journal of Surgical Oncology*. 2009;7(61): 1477-7819-61.
[17] Cancer.net. Gastrointestinal Stromal Tumor – GIST: Treatment. Available at: http://www.cancer.net/patient/Cancer+Types/Gastrointestinal+Stromal+Tumor+-+GIST?sectionTitle=Treatment. Accessed July 12, 2011.
[18] GLEEVEC (imatinib mesylate) Prescribing Information. Novartis.
[19] Heinrich MC, Maki RG, Corless CL et al. Primary and secondary kinase genotypes correlate with the biological and clinical activity of sunitinib in imatinib-resistant gastrointestinal stromal tumor. J Clin Oncol. 2008;26: 5352-5359.
[20] SUTENT (sunitinib malate) Prescribing Information. Pfizer Inc.