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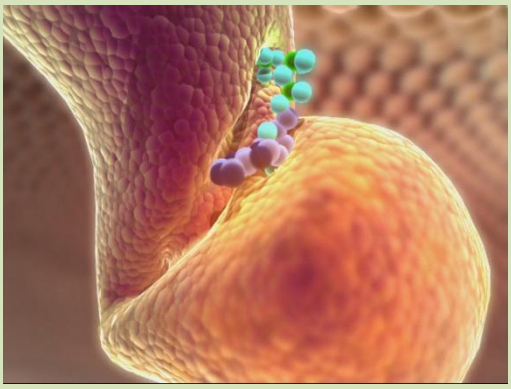
Gastrointestinal Stromal Tumors (GIST)

ABOUT GIST

Gastrointestinal stromal tumor, or GIST, is a rare, life-threatening cancer of the gastrointestinal (GI) tract, also known as the digestive system. Most GISTs develop in the stomach or small bowel. GIST is often difficult to diagnose and to treat because it may not cause any physical symptoms [1].



ATP binds to a pocket in the mutated KIT causing abnormal cell growth

It is believed one of the major causes of GIST is an abnormal form of the c-kit gene. The c-kit gene is present in all cells, and in GIST, the c-kit gene has undergone mutation causing abnormal cell division and tumor growth [1]. Approximately 95% of GIST express the KIT protein and stain positive for KIT in immunohistochemical tests[2].

Diagnosis of GIST can be challenging - recent research has shown people with rare cancers are two times more likely than those with common cancers to receive multiple diagnoses before physicians are able to accurately identify their disease[3]. To help get the most information and best advice about their disease, patients with GIST should work with their treating physicians to form personal multidisciplinary teams, which should include a surgeon, oncologist and pathologist[4].

ADJUVANT VS. METASTATIC DISEASE

Adjuvant GIST

Although complete surgical removal is possible in most patients with primary GIST, meaning that the tumors are found at the original site of development and have not spread to other locations, many patients develop tumor recurrence or metastasis following surgery and survival following recurrence is poor. Median time to recurrence after surgical removal of high-risk primary GIST is about two years[5].

Metastatic GIST

Metastatic GIST is when the tumors have spread to distant parts of the body. Data shows the 5-year survival rate for these patients at initial diagnosis to be about 13%[1].

DISEASE INCIDENCE

The exact number of people diagnosed with GIST each year is not known. In the EU and the US individually, the incidence of GIST is estimated to be more than 5,000 cases each year[1,2,6].

Most people diagnosed with GIST are older than 50, but these tumors can occur at any age[1]. GIST is slightly more common in men[1].

DISEASE PROGRESSION

Upon diagnosis, doctors use several means to assess how GIST might progress. Factors they take into account include the size of the tumor, where the primary tumor was found, mitotic rate, tumor rupture and patient demographics[1].

Mitosis is a type of cell division, and the mitotic rate is a measure of how fast cancer cells are growing and dividing, found by a ratio of the number of cells in mitosis to the total number of cells. In cancer, a high mitotic rate indicates that a tumor is rapidly growing and dividing, and therefore is more aggressive. It is a marker used in other cancers, such as skin cancer, and is discovered by

viewing the tumor's behavior under a microscope and measured by high-powered fields[1].

In GIST, tumor rupture is strongly associated with tumor recurrence, making patients who experience this at high risk[7].

References

1. American Cancer Society. Cancer Reference Information. Detailed Guide for Gastrointestinal Stromal Tumors. http://www.cancer.org/acs/groups/cid/documents/webcontent/003103-pdf.pdf. Accessed December 2012.
2. Joensuu H. Current perspectives on the epidemiology of gastrointestinal stromal tumors. European Journal of Cancer Supplements. March 2006; Volume 4, Issue 3: 4-9.
3. CURE Rare Cancer Survey: Data on file: Novartis Pharma AG. East Hanover, NJ, USA.
4. Demetri GD, Benjamin RS, Blanke CD, et al. NCCN task force report: management of patients with gastrointestinal stromal tumor (GIST) - update of NCCN clinical practice guidelines. J Natl Compr Cancer Network, 2007; 2(suppl 1):S1-S26.
5. DeMatteo RP, et. al. Two hundred gastrointestinal stromal tumors: recurrence patterns and prognostic factors for survival. Ann Surg. 2000 Jan; 231(1):51-8.
6. The World Factbook. European Union Population. CIA.gov; November 2012. Available at: https://www.cia.gov/library/publications/the-world-factbook/geos/ee.html. Accessed December 2012.
7. Rutkowski P et al., Validation of the Joensuu risk criteria for primary resectable gastrointestinal stromal tumour e The impact of tumour rupture on patient outcomes. Eur J Surg Oncol. 2011