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Review Article

Gastrointestinal Stromal Tumors: A Review of the Disease and Therapeutic Approaches

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Abstract

Gastrointestinal stromal tumors (GISTs) are a formidable form of cancer that arises in the tissues of the gastrointestinal (GI) tract. This review aims to provide insights into GISTs, encompassing their origins, symptoms, diagnostic techniques, and treatment options. GISTs exhibit varying growth rates and predominantly occur in the stomach and small intestine. Genetic factors, particularly specific gene mutations, significantly influence the development of GISTs. Accurate diagnosis is crucial, given the similarity of symptoms with other conditions. Treatment options for GISTs include surgical procedures, targeted therapies, meticulous monitoring, and palliative measures. The ongoing progress of clinical trials promises advancements in therapeutic approaches, offering renewed hope for improved patient outcomes.

Keywords: alzheimer's disease; resonance diagnostics; autonomic nervous system

Introduction

Gastrointestinal stromal tumors (GISTs), a menacing form of cancer, afflict the digestive system, an indispensable component responsible for digestion and nutrient absorption. GISTs manifest diverse growth patterns, spanning from languid to aggressive. While they primarily manifest in the stomach and small intestine, GISTs can also emerge in other regions of the GI tract. This review aims to provide a better understanding of Gastrointestinal Stromal Tumors (GISTs), including their causes, symptoms, methods of diagnosis, and available treatment options.

Etiology and Predisposing Factors:

The precise etiology of GISTs remains elusive; however, scientific research posits that these tumors stem from interstitial cells of Cajal (ICC), found within the muscular layer of the GI wall [1]. Genetic factors play a pivotal role in GIST development, with specific gene mutations serving as key drivers of the disease. Roughly 85% of GIST cases are associated with activating mutations in the KIT gene, while approximately 5-10% of cases are linked to mutations in the PDGFRA gene [2]. In some instances, GISTs can be hereditary, passing through generations, while certain genetic syndromes, such as neurofibromatosis type 1 (NF1) and Carney triad, heighten the risk of GIST development [3].

Clinical Manifestations and Diagnostic Modalities:

Symptoms of GISTs hinge upon the tumor's location and size [4]. Common indicators include gastrointestinal bleeding, abdominal pain, fatigue, dysphagia, and early satiety. However, these symptoms often parallel those of other conditions, underscoring the criticality of an accurate diagnosis [5], [6].

The diagnosis of GISTs necessitates a multifaceted approach, involving physical examinations, meticulous medical history reviews, computed tomography scans, magnetic resonance imaging, endoscopic ultrasonography, and histopathological biopsies [4]. Immunohistochemistry, which employs specific antibodies to identify markers in tissue samples, along with the assessment of the tumor's mitotic rate, plays pivotal roles in confirming the presence of GISTs [4].

Statistics and Data:

- GISTs account for approximately 0.1-3% of all gastrointestinal malignancies [7].

- The average age at diagnosis for GISTs is approximately 60 years [8].

- Roughly 60-70% of GISTs manifest in the stomach, 20-30% in the small intestine, and 10% in other regions of the GI tract [8].

- Up to 15-50% of GISTs have metastasized at the time of diagnosis [9].

- The presence of specific gene mutations, such as KIT exon 11, heightens the risk of recurrence and metastasis [10].

Therapeutic Strategies:

The treatment of GISTs hinges upon various factors, including the tumor's growth rate, size, location, resectability, and extent of metastasis. Four primary treatment modalities exist:

Surgical Resection: Surgically removing GISTs that can be safely excised constitutes a fundamental treatment approach. Laparoscopic techniques may be employed for smaller tumors, while larger tumors necessitate more extensive surgical interventions. In cases where neoplastic cells remain at the tumor's margins, careful monitoring or targeted molecular therapy may be considered [9].

Targeted Molecular Therapy: This treatment modality revolves around utilizing drugs that specifically target cancer cells while minimizing harm to healthy tissues. Tyrosine kinase inhibitors (TKIs), such as imatinib mesylate and sunitinib, serve as common pillars of GIST management. TKIs disrupt signaling pathways vital for tumor growth and may be employed to shrink tumors pre-surgery or control unresectable or metastatic GISTs [11].

Statistics and Data:

Tyrosine kinase inhibitors, such as imatinib mesylate, have significantly revolutionized outcomes for patients with advanced or metastatic GISTs. Response rates of approximately 80-85% have been observed, accompanied by notable improvements in overall survival [12].

Vigilant Observation:

For small, asymptomatic GISTs with a slow growth rate, a strategy of meticulous monitoring may be employed. Regular monitoring of tumor progression takes place, with treatment interventions initiated only upon evidence of growth or symptom onset [13].

Palliative Supportive Care:

Palliative care aims to alleviate symptoms and enhance the quality of life for individuals with GISTs. Radiotherapy may be considered for cases where extensive tumors have disseminated, providing relief from associated pain and discomfort [14].

Statistics and Data:

- The 5-year survival rate for localized GISTs stands at approximately 83% [15].

Clinical Trials and Prospective Horizons:

Clinical trials occupy a central role in understanding and treating GISTs. These trials explore innovative treatment approaches, evaluating their safety and efficacy. Patients may opt to participate in clinical trials to access novel treatment options and contribute to the development of improved therapies [16].

Statistics and Data:

- Ongoing clinical trials investigate novel targeted therapies, immunotherapies, and combination treatments for GISTs [16]. (**List1**, by MAYO CLINIC https://www.mayo.edu/research/clinical-trials/diseases-conditions/gastrointestinal-stromal-tumor-(gist)/)

Conclusion:

Gastrointestinal stromal tumors (GISTs), a formidable cancer type, manifest within the digestive system. While the precise cause remains unknown, genetic factors and specific gene mutations, such as KIT and PDGFRA, exhibit strong associations with an increased risk of GIST development. Due to symptom overlap with other conditions, accurate diagnosis assumes paramount importance. Treatment options for GISTs encompass surgical procedures, targeted therapies, meticulous monitoring, and palliative care. Tyrosine kinase inhibitors, such as imatinib mesylate, have significantly transformed outcomes for patients with advanced or metastatic GISTs. Ongoing clinical trials incessantly explore novel treatment strategies, offering renewed hope for improved outcomes in individuals grappling with GISTs.

List1 (GIST Clinical Trials, MAYO Clinic)

(https://www.mayo.edu/research/clinical-trials/diseases-conditions/gastrointestinal-stromal-tumor-(gist)/)

1. **A Drug-drug Interaction Study of Avapritinib and Midazolam to Treat Unresectable or Metastatic GIST**
    a. *Location:* Jacksonville, FL
    b. *Purpose:* Investigating the impact of Avapritinib on the pharmacokinetics of Midazolam in patients with unresectable or metastatic GIST and other advanced solid tumors.
2. **Expanded Access Program of Ripretinib (DCC-2618) for the Treatment of Patients With Advanced GIST**
    a. *Locations:* Jacksonville, FL; Rochester, MN; Scottsdale/Phoenix, AZ
    b. *Purpose:* Providing early access to ripretinib for patients with locally advanced unresectable or metastatic GIST who have received prior FDA-approved therapies.
3. **A Study of XmAb ®18087 in Subjects with NET and GIST**
    a. *Locations:* Scottsdale/Phoenix, AZ; Jacksonville, FL; Rochester, MN
    b. *Purpose:* Evaluating the safety and tolerability of XmAb18087 in subjects with advanced neuroendocrine tumors (NET) and GIST.
4. **(Peak) A Phase 3 Randomized Trial of CGT9486+Sunitinib vs. Sunitinib in Subjects With GIST**
    a. *Locations:* Scottsdale/Phoenix, AZ; Jacksonville, FL; Rochester, MN
    b. *Purpose:* Assessing the effectiveness of CGT9486 in combination with sunitinib to treat GIST.
5. **A Study of DCC-2618 vs. Sunitinib in Advanced GIST Patients after Treatment with Imatinib**
    a. *Locations:* Scottsdale/Phoenix, AZ; Jacksonville, FL; Rochester, MN
    b. *Purpose:* Comparing the effectiveness of DCC-2618 to sunitinib in GIST patients who progressed on or were intolerant to first-line anticancer treatment with imatinib.
6. **Early Detection of Broken Hearts in Cancer Patients (Rochester, MN)**
    a. *Purpose:* Detecting cardiotoxicity caused by certain cancer treatments early, allowing for timely intervention.
7. **A Study of Disease Risk Caused by Tumor Particles Getting into the Blood from Endoscopic Ultrasound Guided Fine Needle Aspiration**
    a. *No Locations*
    b. *Purpose:* Assessing the risk of cancer spread due to tumor particles entering the bloodstream during biopsy procedures.
8. **An Early Access Program (EAP) for Avapritinib in Patients with Locally Advanced Unresectable or Metastatic GIST**
    a. *Locations:* Rochester, MN; Scottsdale/Phoenix, AZ; Jacksonville, FL
    b. *Purpose:* Providing early access to avapritinib for GIST patients.
9. **A Phase 3 Study to Evaluate Efficacy and Safety of Masitinib in Comparison to Sunitinib in Patients with GIST After Progression with Imatinib**
    a. *Locations:* Jacksonville, FL; Rochester, MN
    b. *Objective:* Comparing the efficacy and safety of masitinib at 12 mg/kg/day to sunitinib at 50 mg/day.
10. **Phase 3 Study of DCC-2618 vs Placebo in Advanced GIST Patients Who Have Been Treated With Prior Anticancer Therapies**

   a. *Locations:* Jacksonville, FL; Rochester, MN
   b. *Objective:* Comparing the efficacy of DCC-2618 to placebo in patients who have received prior anticancer therapies.
11. **A Study to Evaluate the Effect of Ripretinib on the Pharmacokinetics of a CYP2C8 Probe Substrate in Patients With Advanced GIST (Jacksonville, FL)**
   a. *Objective:* Assessing the impact of Ripretinib on the pharmacokinetics of a CYP2C8 Substrate.
12. **A Study of THE-630 in Patients With Advanced Gastrointestinal Stromal Tumors (GIST) (Jacksonville, FL)**
   a. *Objective:* Assessing the safety, effectiveness, and pharmacokinetics of THE-630 in participants with advanced GIST.
13. **Collection of Tissue, Blood Samples, and/or Cystic Fluid in Patients with Benign, Premalignant and/or Malignant Gastrointestinal (GI) Disease (Scottsdale/Phoenix, AZ)**
   a. *Objective:* Establishing a biospecimen bank for gastrointestinal disease research.
14. **A Study to Evaluate the Safety and Tolerability of DCC-2618 in Patients with Advanced Malignancies (Jacksonville, FL)**
   a. *Objective:* Investigating the safety, tolerability, pharmacokinetics, and preliminary antitumor activity of DCC-2618.
15. **(VOYAGER) Study of Avapritinib vs Regorafenib in Patients With Locally Advanced Unresectable or Metastatic GIST (Scottsdale/Phoenix, AZ; Jacksonville, FL; Rochester, MN)**
   a. *Objective:* Comparing avapritinib and regorafenib in advanced GIST patients.
16. **Factors Contributing to Delay in Diagnosis of Bone/Soft Tissue Sarcoma (Rochester, MN)**
   a. *Objective:* Identifying factors contributing to delayed diagnosis of sarcoma.
17. **Study of the Safety, Pharmacokinetics and Efficacy of EDO-S101 in Patients With Advanced Solid Tumors (No Locations)**
   a. *Objective:* Investigating the safety and efficacy of EDO-S101 in advanced solid tumors.
18. **Collection of Sarcoma Tissue Study (Scottsdale/Phoenix, AZ)**
   a. *Objective:* Creating a comprehensive tissue bank for sarcoma research.
19. These 18 clinical trials encompass a wide spectrum of research areas, from treatment effectiveness to early detection, safety, and efficacy. These trials make a substantial contribution to the ongoing efforts in combating Gastrointestinal Stromal Tumors (GIST) and other complex medical conditions.

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