

# Practical Management of Imatinib in Gastrointestinal Stromal Tumors

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Gastrointestinal stromal tumors (GISTs) have an incidence of 7–15 occurrences per million people. Tyrosine kinase inhibitors (TKIs) have significantly improved clinical outcomes as part of multidisciplinary disease management. The authors will review developments in the management of GISTs, including diagnosis, risk stratification, prognosis, and treatment with imatinib. Imatinib is recommended for postsurgical adjuvant therapy and, where appropriate, neoadjuvant therapy. Clinical practice guidelines recommend first-line imatinib for metastatic and unresectable GISTs based on trials showing efficacy at the standard dose (400 mg per day) and at higher doses of 600–800 mg per day. Oncology nurses play a key role in patient management through (a) patient education about GISTs and their treatment including the use of imatinib, (b) timely scheduling of radiologic follow-up to assess treatment response, (c) monitoring treatment adherence, (d) helping to sustain imatinib dose intensity by monitoring toxicities and drug interactions and by counseling patients to prevent treatment interruptions, and (e) collaborating with the multidisciplinary medical team to pursue imatinib dose escalation or other treatment options if patients have primary or acquired mutation-based resistance to imatinib.

**G**astrointestinal stromal tumors (GISTs) are a type of soft-tissue sarcoma, with 4,500–6,000 new cases reported per year in the United States. At the time of diagnosis, about 1,500 of these tumors already have metastasized (American Cancer Society, 2010; Nilsson et al., 2005; Tran, Davila, & El-Serag, 2005; Tryggvason, Gislason, Magnusson, & Jonasson, 2005). Median age at diagnosis is about 60 years and risk is slightly higher in men than in women; about 50% of all cases occur in the stomach, another 33% occur in the small intestine, and the remainder are found in the colon, rectum, or esophagus (Joensuu et al., 2002; Nilsson et al., 2005; Perez et al., 2006; Tran et al., 2005; Tryggvason et al., 2005).

Most GISTs (85%–95%) are driven by oncogenic mutations in either *KIT* or platelet-derived growth factor receptor alpha protein (PDGFR $\alpha$ ). These gain-of-function mutations lead to the constitutive activation of the *KIT* and PDGFR receptors, which result in subsequent cell proliferation and the prevention of apoptosis (programmed cell death) (Fletcher et al., 2002). The observation that most GISTs express *KIT* or PDGFR $\alpha$  led to the

## At a Glance

- ♦ Gastrointestinal stromal tumors (GISTs) are characterized by mutations in the *KIT* proto-oncogene that lead to abnormal expression of a protein, *KIT* receptor tyrosine kinase.
- ♦ Multidisciplinary management of GISTs currently includes targeted therapy with the oral tyrosine kinase inhibitor imatinib.
- ♦ Oncology nurses can help sustain the effectiveness of imatinib therapy by delivering individualized patient education that promotes understanding of the disease and its treatment.

development of the targeted oral therapy imatinib, a tyrosine kinase inhibitor (TKI) (Joensuu et al., 2002). Imatinib inhibits the constitutive activation of *KIT* and PDGFR $\alpha$  tyrosine kinase, which inhibits tumor growth and induces tumor regression (Hirota et al., 1998; Rubin et al., 2001).

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