

CLINICAL UPDATE

Translating Scientific Advances into Clinical Practice

Current Management of GISTs

Charles Blanke, MD
Head, Division of Medical Oncology
University of British Columbia
Vancouver, British Columbia, Canada

H&O What are the treatment goals for patients with gastrointestinal stromal tumors (GISTs)?

CB The treatment goals for GIST patients depend partly on the stage of the disease. These goals can include cure, extension of life without cure, improvement in symptoms or quality of life (Table 1), and prevention—or at least delay—in recurrence after a potentially curative surgery.

H&O Is there a standard of care for GIST management?

CB Patients with resectable GISTs (without significant organ risk) should go to the operating room, with a decision then required regarding the use of postoperative imatinib (Gleevec, Novartis). Unresectable or metastatic GISTs should be treated with imatinib, with the dose varying according to the genetic assessment of the tumor itself. The role and timing of surgery following imatinib are controversial, except in cases of tumors that start out as unresectable but then shrink to the point where they can be safely removed (in which case, surgery is nearly automatic). The standard second-line systemic therapy for GIST patients is sunitinib (Sutent, Pfizer).

Table 1. Symptoms of GISTs

- Gastrointestinal bleeding
- Anemia secondary to insidious bleeding
- Abdominal pain or fullness
- Presence of a palpable mass
- Fatigue
- Dyspepsia
- Dysphagia (for esophageal GISTs)
- Rare obstruction and/or perforation (for colonic GISTs)

GISTs=gastrointestinal stromal tumors.

Data from Sepe PS, Brugge WR. *Nat Rev Gastroenterol Hepatol.* 2009; 6:363-371¹; and Steigen SE, Eide TJ. *APMIS.* 2009;117:73-86.²

H&O About how many GIST patients are resistant to treatment?

CB The average time to resistance to imatinib is about 2 years. However, a small fraction of GIST patients (approximately 11%) start off as resistant to imatinib, and a larger fraction of patients (approximately 25%) never clearly become resistant, at least out to 10 years of therapy.

H&O What are the strategies for adjuvant treatment of patients with GISTs?

CB Imatinib is the only drug that has a proven role in the adjuvant treatment of patients with GISTs. The best dose and duration of therapy remain unknown.

H&O What are the latest trial data in GIST management?

CB The biggest trial with recent data is ACOSOG Z9001 (American College of Surgeons Oncology Group North American Intergroup Phase III trial), which showed that (at least) 1 year of adjuvant imatinib after resection of intermediate or high-risk GISTs delays recurrence.³ Ongoing or planned studies will look at other drugs in the advanced setting, the role of surgery after treatment with tyrosine kinase inhibitors, and the optimal duration of adjuvant therapy with imatinib.

H&O Are adverse reactions a concern with GIST systemic treatments?

CB Not really. All patients have some reactions to systemic therapy, but most of these reactions are relatively benign. New toxicities do not seem to appear when patients are prescribed tyrosine kinase inhibitors for the long-term.

References

1. Sepe PS, Brugge WR. A guide for the diagnosis and management of gastrointestinal stromal cell tumors. *Nat Rev Gastroenterol Hepatol.* 2009;6:363-371.
2. Steigen SE, Eide TJ. Gastrointestinal stromal tumors (GISTs): a review. *APMIS.* 2009;117:73-86.
3. Blackstein ME, Corless CL, Ballman KV, et al. Risk assessment for tumor recurrence after surgical resection of localized primary gastrointestinal stromal tumor (GIST): North American Intergroup phase III trial ACOSOG Z9001. Paper presented at: American Society of Clinical Oncology 2010 Gastrointestinal Cancers Symposium. January 22-24, 2010; Orlando, FL.