and/or hematemesis. Anemia may be reflected in generalized weakness. With larger tumors, abdominal distention and pain may be presenting symptoms. At endoscopy, a nonspecific smooth bulging mass covered by normal mucosa is the most frequent finding. Initial biopsy may not reveal an epithelial neoplasm. EUS both to assess the extent of the neoplasm and to guide biopsy in order to obtain adequate tissue for histology and molecular pathology may be helpful.

Histologically, a spindle cell neoplasm is the most common subtype (~70%), with epithelioid cells making up 20%; 10% of cases are mixed histology. Immunohistochemical stains for the presence of c-kit or CD34 positivity and mutational analysis of *cKIT* and *PDGFRA* should be performed in all patients. These help to distinguish between GISTs and leiomyoma neoplasms. For nonmetastatic primary GISTs, laparoscopic surgical resection, if feasible, is the treatment of choice; because lymph node metastases are unusual, wedge or segmental resection is preferred. Endoscopic resection has been used in selected cases. Neither histology nor the presence of a c*KIT* or *PDGFRA* mutation distinguishes GISTs with clinically malignant phenotype from those that have a benign course. Higher risk tumors (larger size, higher mitotic index) may present with or develop metastatic or locally unresectable disease. For these patients, use of a c-kit tyrosine kinase inhibitor such as imatinib for tumors with *cKIT* mutations offers effective palliation. Avapritinib is used for tumors with certain *PDGFRA* mutations. However, resistance almost invariably develops, and the development of newer agents effective in tumors with secondary mutations is a high priority. For high-risk GISTs, adjuvant therapy with imatinib for 3 years improves relapse-free and overall survival.

■ SMALL-BOWEL NEOPLASMS

Although the number of new cases of small-bowel neoplasms is substantially less than that of gastric neoplasms (in 2020, there were an estimated 11,110 new cases in the United States, representing 3–4% of gastrointestinal malignancies), the spectrum of malignant tumors of the small bowel is similar and includes NETs (carcinoid), adenocarcinomas, lymphomas, and GISTs. Neuroendocrine cancers