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.