Imatinib mesylate (Gleevec®, Novartis Pharmaceuticals Corporation, East Hanover, NJ) has revolutionized the treatment of chronic myelogenous leukemia (CML) with marked improvement in survival in all three phases—chronic, accelerated, and blast. Most patients with CML now receive imatinib, which produces complete cytogenetic response in more than 80% of patients. About 10% of patients who initially respond to imatinib subsequently develop resistance. Mechanisms of imatinib resistance in CML include amplification, mutations, and additional chromosomal aberration. To date, more than 30 mutations have been identified in imatinib-resistant CML. Dasatinib and AMN107, second-generation tyrosine kinase inhibitors, are highly effective therapies for patients with CML experiencing imatinib resistance and mutation and offer new options for patients who do not achieve an optimal response to imatinib therapy. Studies found that dasatinib and AMN107 form tighter bonds, overcoming imatinib resistance and producing complete hematologic and cytogenetic remissions. Long-term observations are needed to determine the effectiveness of the treatment. Primary care providers need to follow patients receiving first- or second-generation tyrosine kinase inhibitors because unforeseen toxicity may surface, requiring accurate assessment, evaluation, and management. Oncology nurses will be actively involved in the symptom management of patients. Providing guidelines for symptom management and advanced knowledge of specific test results for monitoring CML may increase positive outcomes.