

# Identification of Side Effects Associated With Intolerance to BCR-ABL Inhibitors in Patients With Chronic Myeloid Leukemia

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Clinical intolerance occurs when the toxicity of a medication outweighs its clinical benefit. Early recognition of clinical intolerance to BCR-ABL inhibitors used for chronic myeloid leukemia (CML) is important for maximizing patient benefit. In CML, most side effects associated with BCR-ABL inhibitor therapy are mild and easily managed, so recognizing, monitoring, and addressing serious side effects may ensure optimal outcome. However, a subset of patients will be intolerant to first-line imatinib. Patients who experience unresponsive grade 3 or any grade 4 nonhematologic side effects to imatinib may require discontinuation and switching to second-line therapies, such as dasatinib or nilotinib, after identification of intolerance. The most common side effects associated with dasatinib and nilotinib are hematologic and generally are reversible with dose adjustment. Pleural effusions are more common with dasatinib use and may be managed by dose interruption and reduction. Both drugs possess warnings regarding QT prolongation, but nilotinib carries a black box warning for QT prolongation and sudden death.

**C**hronic myeloid leukemia (CML) is a hematologic disorder accounting for 15%–20% of all adult leukemias (Ault, 2007). The disease course of CML is usually triphasic, most often initiating in a chronic phase (CP), which is asymptomatic in 40% of patients (Alvarez, Kantarjian, & Cortes, 2007). Patients may progress to an accelerated phase (AP) and ultimately to blast phase (BP). The disease is characterized by the presence of the Philadelphia chromosome (Ph), a reciprocal translocation between chromosomes 9 and 22. The resulting fusion protein from Ph, called BCR-ABL, functions as a constitutively active tyrosine kinase and is responsible for the pathophysiology of CML (D'Antonio, 2005). The treatments of choice for patients with CML are tyrosine kinase inhibitors that target BCR-ABL and mitigate its activity. BCR-ABL inhibitors currently approved by the U.S. Food and Drug Administration (FDA) for the treatment of CML include imatinib, dasatinib, and nilotinib. All BCR-ABL inhibitors are associated with side effects that require early recognition, vigilance, and appropriate treatment to ensure

## At a Glance

- ◆ Oncology nurses need to recognize, monitor, and manage serious BCR-ABL inhibitor-associated side effects to help ensure optimal patient outcomes.
- ◆ Educating patients about potential side effects is vital and patients should be advised not to delay reporting them.
- ◆ A change in treatment may be required for a small subset of patients who develop clinical intolerance to BCR-ABL inhibitor-associated side effects.

optimum outcomes. Oncology nurses play an integral role in that process; however, even with the best patient care, therapy-related toxicity is unavoidable and may require adjustments or an alternative therapeutic strategy.

Clinical intolerance to one of the available BCR-ABL inhibitors occurs when the toxicity of the medication outweighs the clinical

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