The introduction of the BCR-ABL inhibitor imatinib revolutionized the treatment of patients with chronic myeloid leukemia (CML). However, resistance to imatinib has become a clinically significant issue, limiting its long-term efficacy. Numerous mechanisms have been associated with imatinib resistance, including mutations to the BCR-ABL gene, increased production of BCR-ABL, and activation of BCR-ABL–independent pathways (e.g., SRC-family kinases [SFKs]). Resistance to imatinib has driven the development of second-line therapies, such as dasatinib, a dual BCR-ABL/SFK inhibitor more potent than imatinib at targeting BCR-ABL. Dasatinib is approved for the treatment of patients with imatinib-resistant and -intolerant CML and Philadelphia chromosome–positive acute lymphoblastic leukemia. Nilotinib, an analog of imatinib, more potent than its parent compound, is another approved agent for patients with imatinib-resistant or -intolerant CML in the chronic or accelerated phase. Nurses must be aware of what constitutes a requirement for treatment change and the mechanisms of resistance that inform the choice of second-line agents. Oncology nurses also must ensure that patients have been educated appropriately to understand imatinib resistance and second-line treatment options. This article explores the mechanisms and identification of resistance and treatment options for when resistance occurs, as well as nursing implications.

**At a Glance**

- Resistance to imatinib has become a significant clinical problem and has led to the development of second-line therapies, such as dasatinib and nilotinib.
- Nurses must be aware of what constitutes a requirement for treatment change and the mechanisms of resistance that inform the choice of second-line agents.
- Oncology nurses must ensure that patients are educated appropriately to understand imatinib resistance and available second-line treatment options.

Stephanie Bauer, MSN, FNP-BC, and Edie Romvari, MSN, FNP-BC, are nurse practitioners in the Bone Marrow Transplant Division in the School of Medicine at Washington University in St. Louis, MO. Mention of specific products and opinions related to those products do not indicate or imply endorsement by the Clinical Journal of Oncology Nursing or the Oncology Nursing Society. (Submitted September 2008. Accepted for publication December 31, 2008.)

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