A Once-Daily Dasatinib Dosing Strategy for Chronic Myeloid Leukemia

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The BCR-ABL inhibitor imatinib is standard first-line therapy for patients with chronic myeloid leukemia (CML) and has revolutionized treatment of these patients. However, resistance and intolerance to the agent have emerged as major clinical issues (Ramirez & DiPersio, 2008). In the pivotal phase III Immediate Risk-Stratification

Chronic myeloid leukemia (CML) is a clonal myeloproliferative disorder of hematologic stem cells and accounts for 15% of adult leukemias (Jemal et al., 2007). CML is characterized by the abnormal multiplication of one or more lines of bone marrow cells, including myelocytic, erythroblastic, and megakaryocytic cells (Sawyers, 1999). The disease follows a triphasic course consisting of a relatively benign chronic phase (CP); a transitional, accelerated phase (AP); and the rapidly fatal blast phase (BP) (Sawyers). Progression from CP to BP usually occurs within three to five years if the disease is untreated (Sawyers).

The underlying molecular lesion of CML is the product of the Philadelphia chromosome (Ph), an aberration that results from the exchange of genetic material between the BCR and ABL genes on chromosomes 9 and 22, respectively. The resulting new chromosome produces a BCR-ABL fusion protein that causes development and progression of CML (Faderl et al., 1999; Sawyers, 1999). Imatinib (Gleevec®, Novartis Oncology) was the first BCR-ABL–targeted treatment for CML (Druker et al., 1996). As a result of its impressive activity and relatively mild toxicity profile compared to previous treatment options, such as interferon alpha and cytarabine, imatinib has become the standard first-line therapy for CP CML and has revolutionized the treatment of the disease (Soverini, Martinelli, Iacobucci, & Bacarani, 2008). Nonetheless, the therapeutic breakthrough with tyrosine kinases does not represent a curative strategy for CML. That would require the selective destruction of mutated stem cells, a therapeutic modality that currently remains elusive.

Despite significant improvements in the physical function, well-being, and quality of life of patients with CML treated with imatinib (Hahn et al., 2003), resistance and intolerance to this agent have emerged as substantial clinical issues (Ramirez & DiPersio, 2008). In the pivotal phase III Immediate Risk-Stratification

At a Glance

- Imatinib, a first-line treatment for chronic myeloid leukemia (CML), is associated with resistance and intolerance, necessitating second-line treatment options.
- A new 100 mg once-daily dose of dasatinib, the first available second-line CML treatment, has demonstrated similar efficacy and improved safety as other doses in patients with chronic phase CML.
- Dasatinib 70 mg twice daily remains the approved dosing regimen in patients with advanced CML or Philadelphia chromosome–positive acute lymphoblastic leukemia.