

Practical Management of Dasatinib for Maximum Patient Benefit

Ilene Galinsky, RN, MSN, ANP-C, and Susan Buchanan, MS, PA-C

Dasatinib, an oral inhibitor of multiple tyrosine kinases, including BCR-ABL, Src, and platelet-derived growth factor receptor, was approved for patients with imatinib-resistant or -intolerant chronic myeloid leukemia (CML) or Philadelphia chromosome–positive acute lymphoblastic leukemia (Ph+ ALL). Dasatinib demonstrated efficacy with a well-tolerated safety profile in all phases of CML and Ph+ ALL, which led to its 2006 approval by the U.S. Food and Drug Administration for clinical use. However, although most adverse events are grade 1 or 2, a number of adverse events require management and monitoring to ensure that patients can continue receiving the treatment. This review discusses the appropriate nursing management of key adverse events (cytopenias, fluid retention, bleeding, gastrointestinal toxicity, and cardiotoxicity) to ensure that patients gain maximum benefit from this multitargeted agent.

Chronic myeloid leukemia (CML) is commonly (95%) caused by a genetic abnormality known as the Philadelphia chromosome (Ph), which arises from reciprocal translocation between chromosomes 9 and 22 (Sawyers, 1999). This leads to the formation of a constitutively activated tyrosine kinase, BCR-ABL (Daley, Van Etten, & Baltimore, 1990). CML is characterized by three phases: chronic phase (CP), accelerated phase (AP), and blast-crisis phase (BC). Ph-positive acute lymphoblastic leukemia (Ph+ ALL) accounts for 20%–30% of all adult ALL cases (Ottmann & Wassmann, 2005). Patients with Ph+ ALL generally have a poorer prognosis than those without the cytogenetic abnormality, irrespective of age (Faderl et al., 2000). The age-adjusted incidence rate of CML is 1.5 per 100,000 per year. The incidence of ALL is 1 per 100,000 adults. The rates are based on cases diagnosed from 2002–2006 from 17 Surveillance, Epidemiology, and End Results geographic areas. Eighty-five percent of patients with CML are diagnosed in the CP (Surveillance, Epidemiology, and End Results Program, 1973–2006).

The current standard first-line treatment for patients with CML is imatinib mesylate (Gleevec®, Novartis Oncology), a tyrosine kinase inhibitor that targets BCR-ABL in its inactive conformation. In newly diagnosed patients with CML in CP, those taking imatinib achieved a 98% complete hematologic response and 87% complete cytogenetic response after five years (Druker et al., 2006). The patients also experienced a low level of toxicity and resistance based on five-year follow-up results. However, some patients receiving imatinib developed resistance (24% experienced primary resistance at 18 months, and 17% had secondary resistance at five years) or intolerance (5% of patients discontinued imatinib after 4.5 years as a result of adverse events) (Druker et al.; Ramirez & Di Persio, 2008). Resis-

At a Glance

- ◆ Adverse events related to dasatinib therapy require management and monitoring to maximize patient benefit.
- ◆ Cytopenias, fluid retention, bleeding, gastrointestinal toxicity, and cardiotoxicity require the most vigilance and potential intervention.
- ◆ Nurses should be aware of potential drug-drug interactions with dasatinib.

tance to imatinib arises from a number of different mechanisms, which can be categorized broadly into four groups: decreased intracellular drug levels, increased expression of BCR-ABL, mutations in the ABL kinase affecting drug interaction or kinase activity, and BCR-ABL independent mechanisms (Litzow, 2006). Resistance also can be defined as primary or initial resistance, when patients fail to respond to therapy by distinct time points, and secondary or acquired resistance, when patients develop resistance after initially responding to treatment. Given the poor prognosis of patients with imatinib-resistant CML (Kantarjian,

Ilene Galinsky, RN, MSN, ANP-C, is a leukemia program research nurse practitioner, and Susan Buchanan, MS, PA-C, is an adult leukemia program physician assistant, both at Dana-Farber Cancer Institute in Boston, MA. 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 March 2008. Accepted for publication October 7, 2008.)

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