Clinical Journal of Oncology Nursing  •  Volume 13, Number 5  •  Suboptimal Responses to Imatinib

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First-line treatment for chronic myelogenous leukemia (CML) is imatinib, but some patients do not respond or develop resistance to the drug, leading to suboptimal responses. Dasatinib and nilotinib are approved second-line compounds for patients experiencing imatinib failure. In a prospective comparison of dasatinib with high-dose imatinib in patients who did not respond to first-line imatinib, dasatinib was more effective and well tolerated. Nilotinib also is effective, but cross-intolerance does occur in a substantial number of patients. This article explores the importance of suboptimal response to imatinib and the appropriate second-line therapy as well as nursing implications for caring for patients with CML.

Chronic myelogenous leukemia (CML) is a clonal hematopoietic stem cell disorder accounting for approximately 20% of all adult leukemia cases, with an estimated 5,050 new cases per year (American Cancer Society, 2009). The initial chronic phase (CP) can be asymptomatic and, if left untreated, CML progresses to an accelerated phase (AP), then to fatal blast crisis (BC) over the course of three to five years (Sawyers, 1999). In the United States, the age-adjusted incidence rate for CML is 1.5 per 100,000 people per year, and the median age at diagnosis is 66 years (National Cancer Institute, 2007). From 1999–2005, the five-year relative survival rates were 53.3% overall (Leukemia and Lymphoma Society, 2009). With the introduction of imatinib in newly diagnosed patients with CML, survival rates after five years is 89% (Druker et al., 2006). For a more comprehensive review of CML, see D’Antonio (2005).

At the cellular level, the distinguishing feature of CML is the Philadelphia chromosome (Ph), created by the exchange (t[9:22] translocation) of genetic material between chromosomes 9 and 22 (Nowell & Hungerford, 1960; Rowley, 1973). The creation of the Ph chromosome leads to the formation of the Bcr-Abl tyrosine kinase signal transduction protein, which underlies the pathophysiology of CML (Bartram et al., 1983; Groffen et al., 1984; Lugo, Pendergast, Muller, & Witte, 1990).

CML may be cured by bone marrow stem cell transplantation, but few patients can receive the procedure because of the difficulty in finding matched donors and morbidity and mortality concerns, particularly for older adults (National Comprehensive Cancer Network [NCCN], 2009). Furthermore, patient outcomes deteriorate with disease duration (Davies et al., 2001). Therefore, most patients rely on effective drug therapy.

The treatment of CML improved dramatically with the introduction of tyrosine kinase inhibitors (TKIs) directed against Bcr-Abl, thereby specifically targeting the pathophysiology of CML. The first such compound to be introduced as treatment for CML was imatinib in 2001, which has become a paradigm of targeted cancer therapies (Druker et al., 1996). In the key IRIS (International Randomized Study of Interferon and STI571) phase III clinical study, imatinib was associated with significantly longer progression-free survival (PFS) compared with the previous standard, interferon-α plus cytarabine (O’Brien et al., 2003). Estimated rates of overall survival after 54 months of

At a Glance
- Suboptimal responses to first-line imatinib in patients with chronic myelogenous leukemia are associated with poorer patient outcomes.
- High-dose imatinib, a current recommended second-line treatment for patients responding suboptimally to initial imatinib therapy, only benefits a minority of patients temporarily.
- Dasatinib and nilotinib, approved second-line treatments for patients experiencing failure of first-line imatinib therapy, may be used to treat suboptimal responders.

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Digital Object Identifier:10.1188/09.CJON.537-542