

Bullseye! Targeting CML

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and Robert L. Redner, MD

Follow the captivating development of kinase inhibitors and the revolution in management and monitoring of chronic myelogenous leukemia (CML) in the Education Session on CML being chaired by Charles L. Sawyers, MD. This session is held today from 7:30 to 9:00 a.m. and again at 2:00 p.m.

Neil Shah, MD, PhD, will highlight the future of kinase inhibitor therapy in chronic phase CML. The successes of imatinib have not been universal. Four percent of responders per year develop resistance. Some patients fail to ever achieve a hematologic or cytogenetic response. These patients often respond to second-generation ABL kinase inhibitors such as the FDA-approved dasatinib and nilotinib and, in clinical trials, bosutinib. The third-generation ABL kinase inhibitors such as aurora kinase inhibitors may be appropriate for patients who harbor the BCR-ABL/T315I mutation.

Next, Susan Branford, PhD, will address the all-important issue of monitoring response to therapy. Response can be evaluated at the molecular and cytogenetic level. Major molecular response (MMR) defined by real-time quantitative PCR (RQ-PCR) analysis of the peripheral blood correlates with progression-free survival and freedom of progression. Does this mean that we can now shield the patient from routine surveillance bone marrow biopsies? Not necessarily. Dr. Branford will suggest continued monitoring of bone marrow sample cytogenetics in those patients who have not achieved or have lost an MMR. She will also advocate the standardization of RQ-PCR techniques. Dr. Branford agrees with the need for detection of resistant mutations of BCR-ABL, which may soon become a tool to choose between therapeutic options.

What about blast-crisis CML? Jerald Radich, MD, will caution us never to let it occur. Currently, there are many genes and signaling pathways that are responsible for the progression from chronic-phase to blast crisis. Unfortunately, while complete cytogenetic response for early chronic phase CML patients on imatinib is as high as 80 percent, that for blast crisis falls to about 20 percent. Dr. Radich will explain that the search for the “progression gene” has been difficult. He imagines that, in the near future, patients could be tested for a small set of 20 progression-participating genes and will spotlight the potential roles of SOCS2, PRAME, Wnt/b-catenin signaling, and altered microRNA expression. In the meantime, however, Dr. Radich will urge intense control of BCR-ABL early on in the treatment of CML.

What happens when imatinib is combined with chemotherapy in the Ph+ ALL pediatric population? Find out its impact on event-free survival when Kirk Schultz, MD, details the results from his protocol at the Plenary Session on Sunday at 1:30 p.m.