UPDATE ON CHRONIC MYELOID LEUKEMIA

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Chronic myeloid leukemia (CML) is a pluripotent stem cell disease that is characterized by extreme leukocytosis and granulocytic immaturity, basophilia, often thrombocytosis and splenomegaly.

The causative events in the initiation of CML is a genetic translocation resulting in the fusion of genetic sequences to form the bcr/abl oncogene, which codes for a constitutively active bcr/abl tyrosine kinase that mediates cellular transformation. In more than 90% of patients the bcr fusion gene is associated with a t(9;22)(q34;q11) reciprocal translocation or, as it is known, the Philadelphia translocation, which is the most characteristic feature of CML.

Because the genetic finding in CML is the determinant of the clinical course of this disease – including the almost virtual certainty of blast transformation – the term bcr/abl CML has been broadened to functionally include all myeloproliferative disorders that have this molecular abnormality. In other words, patients who present with, for example, primary thrombocythemia and have the bcr/abl oncogene, will have a similar probability of progressing to blast crisis as classic CML.

Treatment of CML is evolving as new drugs and drug combinations are being applied in clinical trials. For several decades the standard of care for the treatment of CML had been to offer an allogeneic transplant for younger adults who have a histocompatible sibling donor and hydroxyurea and/or alpha-interferon for those who do not have a donor. Therapy with alpha-interferon had become the mainstay of therapy, although in a large proportion of patients the quality of life was severely affected to a greater degree than is often reported.

The advent of imatinib mesylate has altered the standard of care for patients with CML. Phase III data have demonstrated efficacy for newly diagnosed patients with CML or for patients who present with accelerated or blast crisis of CML. The responses are superior to alpha-interferon with far less toxicity. To date there are no data that demonstrate that this therapy may be curative and for younger adults who have a histocompatible sibling donor an allogeneic transplant is often still recommended. However, the precise data on the best recommendations for current therapy of CML are evolving and this may change as the long-term impact of therapy with imatinib mesylate becomes known over the next decade.