Chronic Myeloid Leukemia (CML) Fact Sheet

Leukemia is a cancer that begins in the bone marrow (the soft inner part of some bones), but in most cases, moves into the blood. It can then spread to other parts of the body, such as organs and tissues. Chronic myeloid leukemia (CML), one of the four main types of leukemia, is a slow-growing blood cancer that starts in bone marrow cells called myeloid cells --- the cells that become white blood cells, red blood cells or platelets. Once these blood-forming cells are affected by leukemia, they do not go through their normal process of maturing. Ultimately, these immature cells build-up in the bone marrow, blood and body tissues and crowd out the normal blood cells needed to fight infection and promote blood clotting.

A hallmark of CML is an abnormal chromosome known as the Philadelphia Chromosome, a genetic or DNA related abnormality that initiates a series of events leading to the development of what is called a Bcr-Abl translocation. This translocation results in an abnormality of an enzyme known as tyrosine kinase causing CML cells to grow and reproduce rapidly. The Philadelphia chromosome is found in over 90 percent of CML patients.

Facts and Figures

- Worldwide, there was an estimated 351,000 new cases of leukemia overall and approximately 257,000 related deaths in 2008.
- CML accounts for 15 percent of all leukemia cases.
- In 2007, it was estimated that approximately 7,000 people were diagnosed with leukemia in the United Kingdom (UK). The following year, there were approximately 4,350 deaths in the UK.
- The estimated five-year survival rate of patients diagnosed with CML between 2001 and 2007 was 57 percent. More recent studies evaluating the impact of imatinib on survival found that the estimated eight-year event free survival rate in treated patients has increased to 81 percent.
  - In the UK, the five-year survival rates for leukemia patients have more than tripled since the early 1970’s.
- Leukemia is diagnosed more commonly in adults than children, and the average age of a CML patient is 66 years old.
  - The risk of being diagnosed with CML increases with age and is slightly higher in males than in females.

Phases of CML

The phases of CML are based on the number of immature white blood cells that are seen in the blood or bone marrow.

- **Chronic phase CML** occurs when less than 10 percent of the cells are immature. Patients in the chronic phase typically have very mild symptoms, if any. Most patients are diagnosed in the chronic phase.
- **Accelerated phase CML** is characterized by an increased number of immature cells (up to 20 percent), as well as other fluctuations in white blood cell and platelet counts. Patients in the accelerated phase may have symptoms including fever and weight loss.
- **Blast phase CML**, the most advanced phase of the disease, is an aggressive form of leukemia and typically means the immature cells have spread beyond the bone marrow to the tissues and organs. The number of immature cells found in the bone marrow or blood exceeds 20 percent, and patients often experience symptoms of fever, weight loss and decreased appetite.

Diagnosis

Up to 20 percent of CML patients are asymptomatic at the time of diagnosis, and the disease is usually detected following a medical examination for another condition or as part of a routine checkup. In addition, many of the signs and symptoms of CML, including fatigue, shortness of breath, and weight loss, are common to other illnesses.

A diagnosis of CML is usually made with information from blood and bone marrow tests, including blood cell counts, blood chemistry studies and bone marrow sampling (bone marrow aspiration and biopsy). A cytogenetic analysis is a test in which cells in a sample of blood or bone marrow are viewed under a microscope to look for certain changes in the chromosomes, such as the Philadelphia chromosome.
Treatment

- Originally, chemotherapy was the main treatment of CML, and was used to kill cancer cells that grow and divide through the bloodstream. Following chemotherapy, doctors sometimes would recommend stem cell transplantation, particularly in younger patients, as a way to restore healthy, blood-making bone marrow stem cells.

- More recently, drugs that inhibit tyrosine kinases have become the standard of care since the approval of imatinib in 2001. Imatinib, the first approved therapy of this kind specifically targeted the Bcr-Abl tyrosine kinase, was successful in achieving meaningful responses in patients for many years. However in some cases, CML develops resistance to therapy that focus strictly on the inhibition of the Bcr-Abl tyrosine kinase.

- Newer therapies are now targeting the inhibition of both Src and Abl tyrosine kinases to help overcome treatment resistance, as overexpression of the Src family of tyrosine kinases have been implicated in resistance to certain therapies and CML progression.

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