Imatinib Is Superior to Interferon Alpha Plus Cytarabine for Patients With Chronic Myeloid Leukemia

Researchers from the University of Chicago presented a summary of the International Randomized Interferon Versus STI571 Study comparing the efficacy of imatinib (STI571, Gleevec™, Novartis Pharmaceuticals, East Hanover, NJ) monotherapy and interferon plus AraC (cytarabine) for chronic myeloid leukemia. Imatinib inhibits the Bcr-Abl tyrosine kinase that is important in cell proliferation in Philadelphia-chromosome-positive chronic myeloid leukemia. A total of 1,106 patients aged 18–70 were randomized into groups receiving imatinib 400 mg per day (n = 553) or interferon (target 5 μm2 per day subcutaneously) plus AraC (target 20 mg/m2 SC for 10 days every month) (n = 553). The study arms were balanced in terms of risk. Median follow-up was 14 months. Criteria allowed crossover based on intolerance or treatment failure. Statistically significant differences (p = 0.001) were found between the two arms (imatinib and interferon plus AraC) as follows: Complete hematologic response was 94.4% and 54.6%, respectively; major cytogenetic response was 82.6% and 20.3%, respectively; complete cytogenetic response was 67.8% and 7.4%, respectively; and 12-month progression-free survival was 97.2% and 80.3%, respectively. The researchers concluded that for patients with newly diagnosed, chronic-phase, chronic myeloid leukemia, imatinib is superior to interferon plus AraC in terms of all the endpoints examined.

Imatinib Offers Quality-of-Life Advantages Compared to Interferon Alpha Plus Cytarabine

Although interferon alpha has been shown to induce relatively high hematologic response rates for patients with chronic myeloid leukemia, the improvement occurs at a cost in quality of life. A significant number of patients withdraw from interferon therapy within six months. Researchers from the International Randomized Interferon Versus STI571 Study Group presented data comparing the effects of imatinib (STI571, Gleevec™, Novartis Pharmaceuticals, East Hanover, NJ) monotherapy and interferon plus AraC (cytarabine) on quality of life for patients with chronic myeloid leukemia. Quality of life was assessed using the Functional Assessment of Cancer Therapy–Biologic Response Modifiers instrument at baseline, monthly for six months, and then every three months. The primary endpoint was the Trial Outcome Index (TOI), a composite of physical, functional, and treatment-specific subscales. Of the 1,067 patients who were eligible, 83% completed at least six of the nine assessments. For the imatinib group, TOI scores remained stable relative to the baseline, whereas the interferon plus AraC group demonstrated a significant decline in scores. The researchers concluded that imatinib offers a clear advantage over interferon in terms of quality of life during therapy.

Peptide Vaccination Can Induce Remission in Patients With Acute Myelogenous Leukemia

Researchers from the University of Texas M.D. Anderson Cancer Center presented the results of a phase I trial of a novel agent designed to induce a specific immune response against leukemia cells. PR1 peptide is a nine amino acid HLA-A2 restricted peptide derived from proteinase three. T-cell immunity to PR1 correlates with cytogenetic remission in chronic myeloid leukemia patients treated with interferon or bone marrow transplantation. Nine patients with several types of leukemia were enrolled in the study and treated in cohorts of three at three different dose levels: 0.25 mg, 0.5 mg or 1 mg of PR1 in incomplete Freund’s adjuvant subcutaneously. None of the patients developed antibodies to PR1. Adverse events included a cutaneous injection reaction (grade two) in one patient at dose level three that resolved after one week and mild fatigue in four patients. At the time of the report, one patient at dose level two and three patients at dose level three were in complete remission. PR1-specific cytotoxic T lymphocytes were induced in all four patients with complete remission. The researchers concluded that this study is the first direct evidence that peptide vaccination of patients with leukemia can induce specific immunity against leukemia cells and lead to remission.

Proteasome Inhibitor Bortezomib Represents a Novel Treatment for Multiple Myeloma

Cell proliferation requires the activation of intracellular regulatory proteins by proteasomes. Significantly, the proteasome activates NF-κB, a protein important in regulating cancer cell division. The results of a multicenter trial of the selective proteasome inhibitor bortezomib (Velcade™, Millennium Pharmaceuticals, Cambridge, MA) for patients with relapsed or refractory multiple myeloma were presented. Patients received 1.3 mg/m2 IV push on days 1, 4, 8, and 11 of a 21-day cycle for up to eight cycles. For some patients, dexamethasone was added after two or four cycles. Patients were enrolled in two cohorts (n = 78 and 124). For cohort one (n = 78), the overall response rate was 32%, and of these, 27% had major responses (4% complete and 23% partial). The mean duration of complete or partial responses had not been reached at 10.2 months. The responders showed evidence of improved hemoglobin, performance status, quality of life, and levels of non-M protein immunoglobulins. Bortezomib may be a novel potential therapy for patients with relapsed or refractory multiple myeloma.

Rituximab Can Overcome BCL2-Associated Drug Resistance

Rituximab is a monoclonal antibody directed against the CD20 protein located on the surface of normal and abnormal B lymphocytes. The drug can be used to treat B-cell lymphomas because the normal cells that may be destroyed by the antibody are replaced by new cells and the abnormal cells are permanently destroyed. Researchers from France presented the results of a study comparing the effectiveness of cyclophosphamide, hydroxydoxorubicin, vincristine, and prednisone (CHOP) versus rituximab plus CHOP (R-CHOP) in the treatment of elderly patients with diffuse large B-cell lymphoma (DLBCL). The objective of this study was to determine whether rituximab would improve outcomes for patients whose tumors expressed BCL2 protein, known to be