Rituximab Plus Cyclophosphamide, Doxorubicin, and Etoposide May Increase Survival

Rituximab (Rituxan®, Genentech, South San Francisco, CA) is a monoclonal antibody directed against the CD20 protein on the surface of normal and malignant B lymphocytes. An international trial examined 29 patients receiving combination therapies with cyclophosphamide, doxorubicin, and etoposide (CDE) for the treatment of AIDS-related non-Hodgkin’s lymphoma. CDE was administered as a continuous 96-hour infusion, and rituximab 375 mg/m² was given either a) prior to each cycle of CDE, or b) on day eight and day one prior to cycle 1, just prior to cycles 3 and 5, and then on days 28 and 35 after the last cycle. The overall response rate was 86% (83% complete response). Toxicities included grade 3 or 4 neutropenia (79%), anemia (45%), thrombocytopenia (34%), and bacterial infections (34%). The overall survival and progression-free survival at two years were 80% and 79%, respectively.

Autologous Stem Cell Transplantation and High-Dose Chemotherapy May Improve Survival

A study of 11 patients with lymphoma (five with Hodgkin’s disease; six with non-Hodgkin’s disease) suggests autologous progenitor cell transplantation may be feasible for relapsed AIDS-related lymphoma. Therapy included etoposide, methylprednisolone, cisplatin, and cytarabine (ESHAP) (n = 9) and granulocytecolony stimulating factor (n = 10), followed by acquisition of peripheral blood progenitor cells. Conditioning prior to transplantation consisted of carmustine, vincristine, cytarabine, and melphalan for five patients; the other six patients had this regimen plus total body irradiation. Ten of the patients received highly active antiretroviral therapy. Good engraftment occurred in all patients. The median times to granulocyte and platelet recovery were 12 and 11 days, respectively. Complete remission occurred in seven patients (64%). No major opportunistic infections occurred. This study indicates the need for additional research to identify toxicity and efficacy of autologous stem cell transplantation in these patients.

Stanford V Regimen May Increase Survival for Patients With Newly Diagnosed Hodgkin’s Disease

Data from a European trial (France and Italy) of the Stanford V regimen (doxorubicin, vinblastine, mechloretamine, vincristine, bleomycin, etoposide, and prednisone) involving 46 patients with AIDS who also had newly diagnosed Hodgkin’s disease demonstrated 68% (n = 39) complete remission, with 68% of the group remaining disease-free at two years. All patients received G-CSF 5 mcg/kg per day on days 3–13 and 17–26 of each cycle. Triple-drug antiretroviral therapy, including a protease inhibitor and prophylaxis against Pneumocystis carinii and candida, also were administered. Although these data suggest that the Stanford V regimen may be more efficacious than ABVD (adriamycin, bleomycin, vincristine, and dacarbazine), in prior trials with ABVD for Hodgkin’s disease, patients with AIDS did not receive highly active antiretroviral therapy. The Stanford V regimen is currently under evaluation as part of the AIDS Malignancy Consortium.

Epidemiological and Clinical Research Study Reports AIDS-Related Malignancies in the United States

The Centers for Disease Control and Prevention sponsored the Adult and Adolescent Spectrum of Disease Study involving 19,684 people infected with HIV in the United States between 1994 and 1997. The case-rates (per 1,000 person-years) of Kaposi’s sarcoma (KS) and primary central nervous system lymphoma fell significantly; the case-rate of immunoblastic lymphoma fell but returned to levels found prior to the initiation of highly active antiretroviral therapy (HAART). For other types of lymphomas and Hodgkin’s disease, the case-rates increased. KS declined 50% in people taking HAART, and no decrease was observed in those on no therapy, monotherapy, or dual therapy.

Targeted Antisense Therapy Shows Promise in Melanoma Treatment

Researchers at Ohio State University and Genta, Inc. conducted the study. Twenty patients with refractory or relapsing acute leukemia were treated with Genasense plus fludarabine, ARA-C, and G-CSF. Of the 20 patients, 9 (45%) had disease response and 7 of the responders had complete remission. Clinical doses of Genasense ranged from 4–7 mg/kg per day. Pharmacokinetic analysis showed that Genasense plasma levels were at the biologically relevant target level (1 mg/ml) after 24-hour infusion. Toxic effects of the combination chemotherapy included central nervous system bleeding (one patient), fever, nausea, emesis, hypocalcemia, hypophosphatemia, and fluid retention. None were dose-limiting, and the side effects were not necessarily attributable to Genasense. The maximum tolerable dose was not reached. This study supports the safety of Genasense and suggests that future trials at 7 mg/kg per day are warranted.

Overexpression of Bcl-2, a protein that inhibits programmed cell death (apoptosis), contributes to drug resistance in patients with acute leukemia. Genasense™ (Genta, Inc., Berkeley Heights, NJ) reduces (downregulate) expression of Bcl-2 protein, was tested in a phase I trial as a possible strategy for overcoming drug resistance. Researchers at Ohio State University and Genta, Inc. conducted the study. Twenty patients with refractory or relapsing acute leukemia were treated with Genasense plus fludarabine, ARA-C, and G-CSF. Of the 20 patients, 9 (45%) had disease response and 7 of the responders had complete remission. Clinical doses of Genasense ranged from 4–7 mg/kg per day. Pharmacokinetic analysis showed that Genasense plasma levels were at the biologically relevant target level (1 mg/ml) after 24-hour infusion. Toxic effects of the combination chemotherapy included central nervous system bleeding (one patient), fever, nausea, emesis, hypocalcemia, hypophosphatemia, and fluid retention. None were dose-limiting, and the side effects were not necessarily attributable to Genasense. The maximum tolerable dose was not reached. This study supports the safety of Genasense and suggests that future trials at 7 mg/kg per day are warranted.