Idiotype Vaccine for Non-Hodgkin Lymphoma Shows Promise

Researchers from Freiburg University Medical Center in Germany developed a novel production strategy for individual idiotype vaccines using anchored reverse transcriptase polymerase chain reaction cloning of variable segments of the idiotype genes for antibody transcripts from lymphoma biopsies. Recombinant idiotype Fab fragments were expressed in E. coli and purified. Vaccine production was successful in 89% of attempted cases via this strategy. Eighteen patients with B cell non-Hodgkin lymphoma who had relapsed after chemotherapy received repeated intradermal vaccinations with 0.5–1.65 mg Fab fragment mixed with a lipid-based adjuvant over two to four weeks. Injections of 150 micrograms of granulocyte macrophage–colony-stimulating factor (GM-CSF) were given subcutaneously at the vaccination site immediately after each immunization. Mild fever and fatigue were common and attributed to the GM-CSF. Ten patients had high levels of anti-GM-CSF antibodies. Fourteen patients (78%) had tumor regressions, which were considered durable for at least four years. The median survival was 18 months, with 10 patients ongoing regremission at 18 months. A phase II trial using an idiotype vaccine in these patients with non-Hodgkin lymphoma is under way.

Gemtuzumab Ozogamicin Induces Responses in Patients With CD33-Positive Acute Myeloid Leukemia

The Mylotarg Study Group presented the results of a phase II study of gemtuzumab ozogamicin (Mylotarg®, Wyeth, Madison, NJ) for the treatment of patients with acute myeloid leukemia (AML). Gemtuzumab ozogamicin is an antibody therapy that targets CD33-positive leukemic cells. In this study, 157 patients aged 60 years or older who were in their first relapse were treated with 9 mg/m² via IV on days 1 and 15. All patients received the first dose, 117 received the second dose, and 4 received a third dose. In this study, a remission was characterized as 5% or fewer leukemic blast cells in the bone marrow, 9 g/dl or less hemoglobin, 1,500/microliter or fewer absolute neutrophil count, and 9 g/dl or less hemoglobin. The median survival was 3.1 months (95% confidence interval = 18, 32) achieved remission, with 35% lasting 12 months or longer. The median relapse-free survival was 6.8 months. The most common toxicities were fever (13%), sepsis (15%), chills (11%), pneumonia (8%), and mucositis (3%). The infection rate was 29%, and hematologic toxicities occurred with elevated aspartate aminotransferase (16%), alanine aminotransferase (8%), and bilirubin (29%). Two patients (1%) developed fatal hepatic veno-occlusive disease. The researchers concluded that gemtuzumab ozogamicin as a single agent for older patients with CD33-positive AML has a potential benefit with an acceptable toxicity profile.

Syndecan-1 May Be a Novel Target for Multiple Myeloma Treatment

Syndecan-1 (CD138) is a transmembrane proteoglycan found on the surface of most myeloma plasma cells. It accumulates in the blood and bone marrow of patients with myeloma, and high levels indicate poor prognosis. Researchers from the Arkansas Cancer Research Center and Myeloma Institute for Research and Therapy in Little Rock developed a myeloma cell line that produced a soluble form of syndecan-1. These cells could invade to a level four times deeper than control cells in an in vitro cell invasion assay. The percentage of invasive cells was three times higher in the syndecan-1–producing cells than in controls (15% versus 5%). Control or syndecan-1–producing cells also were injected subcutaneously into seven-week-old immunodeficient mice (N = 9). Eight weeks later, the mice that received the syndecan-1–producing cells were more likely to have metastases in the femur contralateral to the injection site compared to controls (78% versus 33%). Abdominal metastases were more common in the mice that received the syndecan-1–producing cells (67% versus 11%). The researchers also found that the microvessel density was higher in the primary tumors of mice that received the syndecan-1 cells (p < 0.00001). They concluded that syndecan-1 promotes tumor invasion and metastasis. Syndecans enhance growth and dissemination of myeloma cells, in part, by promoting angiogenesis. Modulation of blocking of syndecans may be an important new therapeutic approach.