Research Highlights

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45th Annual Meeting of the American Society of Hematology San Diego, CA December 6–9, 2003

Clinical Research

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 of 17 evaluable patients had progression-free survival of at least 4 months, and 8 had ongoing progression-free survival at 10 months. Anti-Fab antibodies developed in 5 of 17 patients, and anti-Fab T cell responses were found in 6 of 15 patients. The researchers concluded that the results demonstrate the feasibility, tolerability, and immunogenicity of the vaccine in these patients with non-Hodgkin lymphoma. They recommended further trials of this strategy for idiotype vaccination for patients with non-secreting B cell non-Hodgkin lymphoma.

R115777 Induces Responses in Patients With Myeloid Leukemia

Zarnestra™ (R115777, Johnson and Johnson, New Brunswick, NJ) is a selective oral farnesyltransferase inhibitor that disrupts oncogenic transformation and tumor growth caused by factors such as ras, Rho B, and p53. Researchers presented the results of a multicenter phase II trial of Zarnestra as a single agent in the treatment of acute myelogenous leukemia (AML). A total of 252 adults with refractory (N = 135) or relapsed (N = 117) AML were treated with 600 mg twice a day for 21 days every four weeks. The median survival was 3.1 and 2.1 months for the relapsed and refractory groups, respectively. For those who achieved a partial or complete response (11 of 169 evaluated [6%], 95% confidence interval 3%–11%), the median survival was 12.2 months. The nonhematologic toxicities associated with Zarnestra were fatigue (6%) and hypokalemia (5%). The researchers concluded that Zarnestra as a single agent is able to induce responses in heavily pretreated patients with AML and is well tolerated. A study is under way to examine the effectiveness of Zarnestra for newly diagnosed older adult patients.

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/m^2 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 independence from red cell or platelet transfusions. Thirty-eight patients (24%, 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 hepatic 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.

Basic Research

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.

Mouse Model for Human EVI1 Myelodysplasia Aids in Understanding Molecular Mechanisms

EVI1 is an aggressive oncogene that is inappropriately expressed in patients with acute myeloid leukemia, myelodysplastic syndrome, or chronic myeloid leukemia. The expression of EVI1 disrupts normal differentiation of granulocytes and erythrocytes and favors differentiation of megakaryocytes. Clinical features include cytopenia and dysplasia of one or more hematopoietic cell lineages. Researchers at the University of Illinois at Chicago and the University of Chicago developed a murine model for myelodysplastic syndrome with a very poor prognosis by transplanting murine bone marrow infected with an EVI1-expressing retrovirus into syngeneic recipients. After 10 months, the mice developed pancytopenia and other morphologic features consistent with

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Digital Object Identifier: 10.1188/04.ONF.675-676