**RESEARCH HIGHLIGHTS FROM THE 38TH ANNUAL MEETING OF THE AMERICAN SOCIETY OF CLINICAL ONCOLOGY MAY 18-21, 2002 ORLANDO, FL**

**CLINICAL RESEARCH**

**Imatinib Mesylate Improves Outcomes for Patients With Chronic Myeloid Leukemia**

The results of a phase III, multicenter trial comparing imatinib mesylate (Gleevec™, Novartis Pharmaceuticals, East Hanover, NJ) with standard therapy for patients with newly diagnosed chronic myeloid leukemia were presented by the International Gleevec Study Group. Imatinib mesylate is a tyrosine kinase inhibitor that interrupts signaling in proliferating cells. The drug has been approved for patients who do not respond to standard interferon therapy and patients who are in accelerated phase or myeloid blast crisis. In this study, 1,106 patients from 16 countries were randomly assigned to groups receiving either imatinib 400 mg per day or interferon (target dose 5 MIU/m² per day) plus cytarabine (20 mg/m² per day for 10 days per month). After six months of therapy, the rates for major and complete cytogenetic responses were 63% and 40% for the imatinib group and 10% and 2% for the interferon group (p < 0.001). The disease progressed in eight patients taking imatinib compared to 57 patients taking interferon. Furthermore, 75% of the patients in the imatinib group showed a significant decrease in the number of cancer cells in their bone marrow compared to 15% in the interferon group. The study results indicated that imatinib mesylate appears to be well tolerated and more effective than standard treatment with interferon.

**Patients With Rare Stomach Tumors Benefit From Imatinib Mesylate**

Researchers from Fox Chase Cancer Center in Philadelphia, PA, and collaborators presented the results of a phase II trial of imatinib mesylate (Gleevec™, Novartis Pharmaceuticals, East Hanover, NJ) for patients with nonresectable or metastatic gastrointestinal stromal tumors. Imatinib mesylate is a tyrosine kinase inhibitor that targets receptors for growth factors that stimulate tumor cell proliferation. Patients (N = 147) were randomized into one of two imatinib groups (400 or 600 mg imatinib mesylate per day). At the time of the study presentation, the patients had been followed for more than six months and 82% had remained in the study. The overall rate of partial response was 54%, and 28% had either minor response or stable disease. Disease progression occurred in 14% of patients. Most (90%) of the adverse effects were mild to moderate, including grade 1 or 2 nausea (54%), diarrhea (51%), periorbital edema (48%), muscle cramps (42.2%), fatigue (38.8%), headache (30.6%), and dermatitis (26%). Severe adverse events (i.e., grade 3 or 4) included edema (3%), gastrointestinal or tumor hemorrhage (5%), abdominal pain (6%), neutropenia (5%), and fluid retention (5%). The researchers concluded that imatinib was effective in treating these patients and the safety profile is acceptable.

**Improved Responses Occur With HuM195 Plus Chemotherapy for Patients With Acute Myeloid Leukemia**

The results of a collaborative, phase III trial of HuM195, an anti-CD33 antibody, were presented by researchers from Weill Medical College of Cornell University in Ithaca, NY. HuM195 targets CD33 receptors on the cell surface of myelomonocytic cells. In this study, 191 adults with acute myeloid leukemia (AML) who were either refractory to standard therapy or had relapsed were randomized to receive mitoxantrone, etoposide, and cytarabine with or without HuM195. HuM195 12 mg/m² was administered as a four-hour infusion on days 7–10 and 19–22. For those treated with HuM195, an overall response rate of 43% resulted, compared to 26% for those who received chemotherapy alone (p = 0.015). Induction mortality rates were 15% and 13% for the HuM195 and control arms, respectively. Toxicities related to HuM195 were mild to moderate fever and chills. Other toxicities were found in both arms of the study: mucositis and diarrhea and hepatic, cardiac, and renal dysfunction. The combination of HuM195 with standard chemotherapy can be safely given and may improve the response for patients with poor prognosis refractory AML.

**Anti-VEGF Antibody Slows Disease Progression in Patients With Metastatic Renal Cancer**

Researchers from the National Cancer Institute in Bethesda, MD, and Genentech, Inc., in San Francisco, CA, examined the effectiveness of an antibody raised against vascular endothelial growth factor (VEGF) for patients with metastatic renal cancer. VEGF is dysregulated and oversecreted because of a genetic mutation in renal carcinoma. As a result, blood vessel growth is enhanced and contributes to tumor growth. Anti-VEGF therapy (bevacizumab) was designed to neutralize VEGF and block tumor cell proliferation. A prospective, double-blind, three-arm trial was initiated to compare the effectiveness of the placebo, low-dose anti-VEGF (3 mg/kg), and high-dose anti-VEGF (10 mg/kg) given every two weeks. A total of 110 patients with renal cell carcinoma were randomized into the three arms. A highly significant prolongation of time to disease progression was found with the high-dose arm compared to the placebo (hazards ratio = 2.3, p = 0.001). The difference between the low dose and placebo showed only borderline significance. Partial response occurred in only three patients (8%, high-dose regimen). At the time of the presentation, 58% of the patients still were living. Both doses of the antibody resulted in minimal toxicity; the most common toxicities were hypertension and asymptomatic proteinuria. This study demonstrated biological activity of bevacizumab as an antiangiogenic agent and suggested that trials with similar agents may be promising.

**Epidermal growth factor receptor (EGFR) commonly is overexpressed in squamous cell head and neck tumors. EGFR is involved in intracellular signaling that leads to cell proliferation and tumor growth. Therapies that target EGFR may, therefore, slow or stop tumor development. Researchers from Yale University School of Medicine in New Haven, CT, presented the results of a collaborative clinical trial by the Eastern Cooperative Oncology Group using C225 (Erbitux™, ImClone, New York, NY), an antibody directed against EGFR. One hundred twenty-one patients with squamous cell head and neck cancer that had not been cured by radiation or surgery were enrolled in the study. The participants had not received prior treatment for metastatic cancer. Patients were assigned randomly to one of two groups: cisplatin plus placebo or cisplatin plus C225 (test dose and reference dose).**

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