HEM/ONC News

By Stuart Schrader

Oblimersen Benefits Relapsed or Chemotherapy-refractory CLL Patients

Dr. Susan O'Brien and colleagues at the University of Texas M. D. Anderson Cancer Center reported positive findings from a phase III study of patients with relapsed or refractory chronic lymphocytic leukemia (CLL) treated with oblimersen (Genasense, Genta). Oblimersen is an antisense agent that inhibits the production of Bcl-2 by binding messenger RNA that produce it. Bcl-2 is often overexpressed in tumors and is associated in CLL with resistance to chemotherapy and decreased survival. The trial treated 241 patients with CLL who had relapsed after a fludarabine-containing chemotherapy regimen or who were refractory to fludarabine. The patients received fludarabine plus cyclophosphamide with or without oblimersen. The findings were published in the March 20 issue of the *Journal of Clinical Oncology*. Complete response or nodular partial response was achieved in 20 (17%) of 120 patients who received chemotherapy plus oblimersen, as compared to 8 (7%) who received chemotherapy alone. Complete response or nodular partial response correlated with extended time to progression and extended survival. Patients who were sensitive to fludarabine achieved the most benefit, results the authors believe "make sense because oblimersen is designed to work alongside chemotherapy." The reported toxicities included frequent thrombocytopenia and rare tumor lysis syndrome and cytokine release reactions. Further study of oblimersen in chemotherapy-sensitive CLL patients is warranted.

Elderly NSCLC Patients Experience Improved Survival With Erlotinib

Elderly non–small cell lung cancer (NSCLC) patients demonstrated prolonged survival when treated with erlotinib (Tarceva, Genentech/OSI). Erlotinib inhibits the epidermal growth factor receptor (EGFR). Dr. David M. Jackman and coworkers at Dana-Farber Cancer Institute treated 80 treatment-naive NSCLC patients at least 70 years of age with erlotinib 150 mg/day until development of significant toxicity or disease progression. Tumor samples were assessed for the presence of somatic mutations to EGFR and the oncogene for the K-Ras protein, and response was assessed every 8 weeks by computed tomography (CT). Eight patients (10%) achieved partial responses and 33 patients (41%) had stable disease for 2 or more months. The median time to progression was 3.5 months, and the median survival time observed was 10.9 months, which exceeded the researchers' predetermined statistical endpoint. Survival rates at 1 and 2 years were 46% and 19%, respectively. EGFR mutations were observed in 9 of 43 patients, and EGFR status was strongly correlated with disease control as well as extended time to progression and survival. Acneiform rash was the most commonly seen toxicity (79%), followed by diarrhea (69%). One patient died as a result of therapy, and 4 patients developed interstitial lung disease grade 3 or higher. Despite these toxicities, there were fewer high-grade toxicities than seen in other trials of systemic chemotherapy in elderly patients with NSCLC. As a result of the findings, erlotinib is considered a first-line treatment option worth further study in elderly patients with NSCLC.

Long-term Cardiovascular Complications Persist for Survivors of Hodgkin Lymphoma

Long-term risk of multiple manifestations of cardiovascular disease in survivors of Hodgkin lymphoma is 5-fold higher than in the general population. With a median follow-up of 20.1 years, investigators from The Netherlands assessed the risk of fatal heart disease in 1,474 five-year survivors of Hodgkin lymphoma treated between 1965 and 1995. The median age at the beginning of treatment was 25.7 years, but 314 patients were 20 years old or younger. At the end of the study 1,017 patients were still alive. It was found that 84% of patients were treated with radiotherapy that included the mediastinum and 29% with radiotherapy and anthracycline-containing chemotherapy. The findings, published in the March 1 issue of *Blood,* included 160 instances of valvular disorders, 134 cases of angina pectoris, 102 cases of myocardial infarction, and 52 cases of congestive heart failure. The median time between beginning of treatment and diagnosis of cardiovascular disease was nearly 19 years, but the risk of myocardial infarction was significantly elevated at 10 years. Among patients under age 20 who received therapy, the risk of developing angina pectoris and congestive heart failure was significantly higher than it was among patients treated at a later age, which led to the conclusion that immature cardiovascular tissue may be more acutely vulnerable to radiation and chemotherapy. Although comparatively fewer young patients with Hodgkin lymphoma are today receiving radiation therapy, and target volumes are reduced with current radiation delivery technologies, it is recommended that young survivors avoid smoking and receive risk reduction from their physicians, including treatment of hypertension and hypercholesterolemia.