HEM/ONC News

By Stacey Small

Afatinib Increases Progression-Free Survival in Patients With Non–Small Cell Lung Cancer

Results from 2 clinical trials, LUX-Lung 1 and LUX-Lung 2, examining the investigational compound afatinib (BIBW 2992, Boehringer Ingelheim) were recently presented at the 35th Congress of the European Society for Medical Oncology (ESMO) in Milan, Italy. Findings from the LUX-Lung 1 phase IIb/III trial suggested that afatinib, an irreversible epidermal growth factor receptor (EGFR) and HER2 tyrosine kinase inhibitor, was highly active in late-stage patients with non–small cell lung cancer (NSCLC). In the LUX-Lung 2 phase II trial, afatinib had promising activity in advanced NSCLC patients with a mutated EGFR. The LUX-Lung 1 trial compared afatinib to placebo in NSCLC patients whose disease had progressed after treatment with chemotherapy and a first-generation EGFR tyrosine kinase inhibitor (TKI; erlotinib [Tarceva, Genentech/OSI] or gefitinib [Iressa, AstraZeneca]). The LUX-Lung 2 trial studied advanced NSCLC patients with EGFR mutations who were either chemotherapy naïve or had received one course of chemotherapy. In both trials, afatinib significantly delayed tumor progression and even caused tumor shrinkage. In LUX-Lung 1, afatinib patients had a disease control rate of 58% versus 19% for those on placebo. Progression-free survival (PFS) in these patients increased from 1.1 months to 3.3 months. In LUX-Lung 2, afatinib patients had a PFS of 14 months. The overall response rate (ORR) of LUX-Lung 1 afatinib patients was 11% compared to 0.5% in placebo patients, and LUX-Lung 2 patients had an ORR of 61%. Afatinib substantially improved lung cancer–related symptoms, such as cough and dyspnea. Diarrhea and rash were the most common side effects in both studies.

Brentuximab Vedotin (SGN-35) Induces Durable Remissions in Relapsed/Refractory CD30-Positive Lymphomas

In the November 4 issue of the *New England Journal of Medicine*, Younes and colleagues reported data from a phase I, open-label, multicenter, dose-escalation study of brentuximab vedotin (SGN-35, Seattle Genetics), an antibody-drug conjugate consisting of the antitubulin agent monomethyl auristatin E attached to a CD30-specific monoclonal antibody. The 42 evaluable patients had relapsed/refractory CD30-positive hematologic cancers, primarily Hodgkin lymphoma and anaplastic large-cell lymphoma. Patients had previously received a median of 3 chemotherapy regimens, and 73% had undergone autologous stem-cell transplantation. The dosage of brentuximab vedotin varied from 0.1 to 3.6 mg/kg, administered every 3 weeks. Tumor regression occurred in 86% of evaluable patients. Among the 17 patients who achieved an objective response, there were 11 complete remissions. An objective response was observed in 50% of the 12 patients who received the regimen of 1.8 mg/kg, which was identified as the maximum tolerated dose. The median duration of response was 9.7 months or longer. Brentuximab vedotin was well tolerated; most adverse reactions were grade 1 or 2. Fatigue, fever, diarrhea, nausea, neutropenia, and peripheral neuropathy were the most common adverse events.

Phase III Study Accelerates Dasatinib Approval for Early Chronic Myeloid Leukemia

On October 28, 2010, the FDA announced the expanded approval of the oral kinase inhibitor dasatinib (Sprycel, Bristol-Myers Squibb) for first-line treatment of chronic-phase Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML). Approval was granted based on data from the DASISION (Dasatinib versus Imatinib Study In Treatment-Naive CP-CML Patients) study, an open-label, phase III head-to-head international trial (N=519) of dasatinib and imatinib (Gleevec, Novartis) that appeared in the June 17 issue of the *New England Journal of Medicine*. Patients were randomized to receive daily treatment with 100 mg dasatinib or 400 mg imatinib. Analysis 1 year after baseline demonstrated significantly greater confirmed complete cytogenetic response and major molecular response rates in the dasatinib group than in the imatinib group (76.8% vs 66.2%; P=.007 and 52.1% vs 33.8%; P<.0001, respectively). Dasatinib also showed a faster response time (3.1 months for complete cytogenetic response, 6.3 months for major molecular response) than imatinib (5.6 months for complete cytogenetic response, 9.2 months for major molecular response). Grade 3/4 anemia was reported in 10% of dasatinib patients versus 7% of imatinib patients. Neutropenia was observed in 21% of dasatinib patients and 20% of imatinib patients. Thrombocytopenia was more common in dasatinib patients (19% vs 10%).