HEM/ONC News

By Stacey Small

Rindopepimut for Newly Diagnosed EGFRvIII-Positive Glioblastoma: Mature Survival Data from the ACTIII Trial

Mature overall survival (OS) data from ACT III, a multicenter, single arm, phase II clinical trial of rindopepimut (CDX-110) in patients with newly diagnosed epidermal growth factor receptor variant III (EGFRvIII)-positive glioblastoma were presented by Lai and associates at the 16th annual meeting of the Society for Neuro-Oncology in Orange County, California. The ACT III trial evaluated rindopepimut in combination with radiation plus temozolomide (Temodar, Schering Corp.) in patients with newly diagnosed glioblastoma that expressed EGFRvIII. Sixty-five patients were enrolled in the study. Tumors had been surgically removed in all patients. Approximately 3 months after diagnosis and following treatment with standard chemoradiation, patients began vaccination with rindopepimut in combination with standard of care temozolomide therapy. As previously reported, the primary endpoint was met, with 66% of patients progression-free at 5.5 months after enrollment (approximately 8.5 months from the time of diagnosis). The median OS was 24.6 months from the time of diagnosis, which was significantly better than the median OS for a cohort of patients with tumors expressing the EGFRvIII oncogene who were selected to match major ACT III eligibility criteria (15.2 months). At 4 months, the OS rate was 52% for ACT III patients versus 6% for the matched EGFRvIII-positive cohort. Both temozolomide-sensitive patients as well as temozolomide-resistant patients experienced the reported progression-free survival (PFS) and OS benefits. Rindopepimut was generally well tolerated. Toxicities occurring in at least 10% of patients included injection site reactions, fatigue, rash, nausea, and pruritus. Efficacy and safety data were consistent with previous, smaller studies of rindopepimut in glioblastoma.

Approval of Asparaginase *Erwinia Chrysanthemi* for ALL Patients With Hypersensitivity to Asparaginase Agents

On November 18, 2011, the US Food and Drug Administration (FDA) granted orphan drug approval to asparaginase *Erwinia chrysanthemi* (Erwinaze, EUSA Pharma) for the treatment of acute lymphoblastic leukemia (ALL) in patients with hypersensitivity to the already approved, *Escherichia coli (E. coli)*-derived, asparaginase agents. The safety and efficacy of asparaginase *Erwinia chrysanthemi* were assessed in 2 clinical trials, which helped the drug earn approval. The first trial, known as Study 1, involved 58 patients with ALL who were unable to continue receiving *E. coli*-derived asparaginase agents due to allergic reactions. The main efficacy endpoint was attainment of sustained serum asparaginase activity levels of 0.1 International Units/mL or higher, which has been shown to correlate with asparagine depletion (asparagine <0.4 µg/mL or 3 µM), and to serum levels that predict clinical efficacy. Samples were available from 48 patients, who achieved this threshold through level of asparaginase activity. Safety data were compiled from 58 patients in Study 1 (median age, 10 years) and from 574 patients in the Erwinaze Master Treatment Protocol (EMTP; median age, 9 years). Anaphylaxis, hypersensitivity, and urticaria were among the most common nonhematologic and noninfectious adverse events, occurring in 17% of patients. Grade 3/4 allergic reactions occurred in 9% of Study 1 patients and in 5% of EMTP patients. Asparaginase *Erwinia chrysanthemi* is contraindicated in patients who have experienced pancreatitis, thrombosis, or hemorrhage while receiving prior L-asparaginase therapy.

Ruxolitinib Earns FDA Approval for Myelofibrosis

Ruxolitinib (Jakafi, Incyte) received FDA approval on November 16, 2011 for the treatment of intermediate- or high-risk myelofibrosis (MF), including primary MF, post-polycythemia vera MF, and post-essential thrombocythemia MF. The oral Janus kinase (JAK) 1 and JAK2 inhibitor is the first drug to be approved for this condition. Two randomized phase III trials, which demonstrated that patients treated with ruxolitinib experienced significant reductions in splenomegaly, were the basis for its approval. A total of 309 patients with primary MF, post-polycythemia vera MF, and post-essential thrombocythemia MF were randomized to receive ruxolitinib or placebo in the COMFORT-I (Controlled Myelofibrosis Study With Oral JAK Inhibitor Treatment) trial. The primary endpoint was met, as 41.9% of patients who received ruxolitinib experienced at least a 35% reduction in spleen volume at 24 weeks, compared with 0.7% of patients who received a placebo (P<.0001). Additionally, 45.9% of patients in the ruxolitinib arm reported a reduction in symptoms, compared with 5.3% of patients in the placebo arm. In the COMFORT-II trial, ruxolitinib was compared to best available therapy in 219 patients with primary MF, post-polycythemia vera MF, and post-essential thrombocythemia MF. This trial also met its primary endpoint, as 28.5% of patients in the ruxolitinib arm experienced at least a 35% reduction in spleen volume at 48 weeks, compared with no patients who received best available therapy (P<.0001). Thrombocytopenia and anemia were the most common adverse events in both studies; they were considered manageable and rarely led to cessation of treatment with ruxolitinib. Bruising, dizziness, and headache were among the most common nonhematologic adverse events.