HEM/ONC News

By Stacey Small

FDA Approves Life-Extending Ipilimumab in Metastatic Melanoma Patients

On March 25, the US Food and Drug Administration (FDA) approved ipilimumab (Yervoy, Bristol-Myers Squibb) 3 mg/kg to help extend survival in patients with unresectable or metastatic melanoma. The approval was based on results from a randomized, double-blind, phase III study involving 676 patients with unresectable stage III or IV melanoma who had disease progression while receiving therapy for metastatic disease. Results were published by Hodi and colleagues in the August 19 issue of the *New England Journal of Medicine*. The primary endpoint was overall survival. Patients were randomly assigned in a 3:1:1 ratio to receive ipilimumab plus glycoprotein (gp) 100 (n=403), ipilimumab alone (n=137), or gp100 alone (n=136). The ipilimumab groups were given the drug every 3 weeks for up to 4 treatments. A median overall survival of 10 months was observed in the ipilimumab plus gp100 treatment group, compared with 6.4 months among patients receiving gp100 alone (hazard ratio [HR] for death, .68; $P<.001$). Patients treated with ipilimumab alone had a median overall survival of 10.1 months (HR for death compared to gp100 alone, 0.66; $P=.003$). Overall survival did not differ between the ipilimumab groups (HR with ipilimumab plus gp100, 1.04; $P=.76$). Immune-related adverse events, especially those affecting the skin and gastrointestinal tract, were the most commonly observed toxicities associated with the study drugs, and occurred in approximately 60% of patients treated with ipilimumab and 32% of patients treated with gp100.

Bevacizumab in Combination With Standard Chemotherapies Improves Progression-Free Survival in Breast Cancer: RIBBON-1 Trial Results

Results from the phase III RIBBON-1 (Regimens in Bevacizumab for Breast Oncology) trial were reported in the March 7 advanced online issue of the *Journal of Clinical Oncology*. Robert and coworkers evaluated the safety and efficacy of bevacizumab (Avastin, Genentech) when added to several standard chemotherapy regimens as first-line treatment in patients with human epidermal growth factor receptor 2 (HER2)-negative, locally recurrent, metastatic breast cancer (MBC) or MBC previously untreated with chemotherapy. Progression-free survival (PFS) was the primary endpoint. Before patients were randomized, they were assigned to receive one of the following chemotherapy regimens: capecitabine (2,000 mg/m^2 for 14 days), taxane-based (nab-paclitaxel 260 mg/m^2, docetaxel 75 or 100 mg/m^2), or anthracycline-based (doxorubicin or epirubicin combinations [doxorubicin/cyclophosphamide, epirubicin/cyclophosphamide, fluorouracil/epirubicin/cyclophosphamide, or fluorouracil/doxorubicin/cyclophosphamide]) administered every 3 weeks. Patients were then randomized to receive additional treatment with bevacizumab (15 mg/kg every 3 weeks) or placebo. A parallel analysis examined 2 independently powered cohorts based on the type of chemotherapy administered (capecitabine or combined taxane/anthracycline). A total of 1,237 patients were enrolled (capecitabine cohort, n=615; taxane/anthracycline cohort, n=622). The addition of bevacizumab significantly improved median PFS in both the capecitabine cohort (from 5.7 to 8.6 months; HR, 0.69; 95% confidence interval [CI], 0.56–0.84; $P<.001$) and the taxane/anthracycline cohort (from 8.0 to 9.2 months; HR, 0.64; 95% CI, 0.52–0.80; $P<.001$). Safety was similar to that observed in prior bevacizumab trials. Differences in overall survival between the placebo arm and bevacizumab-containing arms were not statistically significant.

The Addition of an Alkylating Agent to Standard Chemotherapy in Primary Central Nervous System Lymphoma

Ferreri and colleagues investigated the addition of an alkylating agent to standard chemotherapy in patients with primary central nervous system lymphoma (PCNSL). The study, published in the March issue of The Oncologist, evaluated the efficacy of methotrexate (MTX) and cytarabine (araC) plus the alkylating agent thiotepa (MAT regimen). Based on earlier experience with this combination, the dose of araC was half that used in the standard regimen to minimize toxicities. A total of 20 PCNSL patients received the MAT regimen and were analyzed for treatment tolerability, activity, and efficacy. Results were compared with previously reported data for the standard MTX/araC combination. A complete response occurred in 4 patients (clinical response rate, 20%; 95% CI, 3–37%), and a partial response was observed in 3 patients (overall response rate, 35%; 95% CI, 15–55%). At a median follow-up of 26 months, 15 patients experienced treatment failure, and 16 patients died. The 2-year overall survival was 24% ±9%. Grade 4 hematologic toxicity was common; 60% of patients required dose reduction. Infection occurred in 20% of patients, grade 4 nonhematologic toxicity occurred in 15%, and toxic death occurred in 5%. Investigators concluded that the tolerability observed with the MAT regimen was similar to that seen with traditional MTX/araC combinations. The reduced araC dose used in the MAT regimen was associated with remarkably lower efficacy, thus obscuring any possible benefit of thiotepa. The recommended dosage of araC in PCNSL is 4 doses of 2 g/m2 per course.