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.

## Survival in Advanced Cervical Cancer Is Significantly Improved With the Addition of Gemcitabine

Dueñas-González and colleagues conducted a phase III, open-label, randomized study investigating the addition of gemcitabine to concurrent cisplatin chemoradiotherapy and as adjuvant chemotherapy with cisplatin in patients with locally advanced cervical cancer. The study, published in the March 28 advanced online issue of the *Journal of Clinical Oncology*, sought to determine whether PFS at 3 years could be improved with the addition of gemcitabine compared with the current standard of care. A total of 515 chemotherapy- and radiotherapy-naïve patients with stage IIB to IVA disease were randomized to receive either gemcitabine plus cisplatin and concurrent external beam radiotherapy (EBRT), followed by brachytherapy and adjuvant treatment with gemcitabine and cisplatin (259 patients) or cisplatin and EBRT, followed by brachytherapy without adjuvant treatment (256 patients). The 3-year PFS was significantly improved in the gemcitabine arm versus the control arm (74.4% vs 65%; *P*=.029). Patients in the gemcitabine arm also experienced improved overall PFS (*P*=.0227; HR, 0.68; 95% CI, 0.49–0.95), overall survival (*P*=.0224; HR, 0.68; 95% CI, 0.49–0.95), and time to progressive disease (*P*=.0012; HR, 0.54; 95% CI, 0.3–0.79). Grade 3/4 toxicities occurred more frequently in the gemcitabine arm than the control arm (86.5% vs 46.3%; *P*<.001), but they were clinically manageable. Two patients in the gemcitabine arm died, possibly due to treatment toxicity.