HEM/ONC News

By Stacey Small

Castration-Resistant Prostate Cancer Patients Achieve Delayed Bone Metastases With Denosumab

Subanalyses of the phase III denosumab 147 study were presented on September 25 at the European Multidisciplinary Cancer Congress. Oudard reported that bone metastasis–free survival is prolonged with the use of denosumab (Xgeva, Amgen) in a variety of nonmetastatic, castration-resistant prostate cancer (CRPC) subgroups. The study involved a total of 1,432 men with CRPC who did not have radiologically detectable bone metastases, but were considered to be at high risk for bone metastases because of prostate-specific antigen (PSA) findings (PSA value of ≥8 ng/mL and/or a PSA doubling time of ≥10 months). Patients were randomized to receive monthly subcutaneous denosumab 120 mg or placebo. Compared to placebo, denosumab improved bone metastasis–free survival in patients with the following characteristics: dual PSA risk factors (hazard ratio [HR] 0.83; *P*=.07), a single PSA risk factor (HR 0.87; *P*=.20), a Gleason score of 2–7 (HR 0.85; *P*=.12), and a Gleason score of 8–10 (HR 0.81; *P*=.10). Denosumab significantly increased the median bone metastasis–free survival, which was 29.5 months with denosumab and 25.2 months with placebo (HR 0.85; *P*=.03). This corresponds to a relative risk reduction of 15% (HR 0.85; *P*=.028). The rates of serious adverse events were 46% in both groups. Osteonecrosis of the jaw was not reported in the placebo arm, but it occurred in the denosumab arm at a cumulative incidence of 1.1% in year 1, 2.9% in year 2, and 4.2% in year 3. Hypocalcemia occurred in 1.7% of patients who received denosumab versus 0.3% of patients who received placebo. Other adverse events were similar in both arms. Although denosumab delayed bone metastases, patients who received the drug did not live longer than did those who were given placebo. The median overall survival was approximately 44 months in both groups (HR 1.01; *P*=.91).

Carfilzomib for the Treatment of Relapsed and Refractory Multiple Myeloma

A new drug application has been submitted to the US Food and Drug Administration (FDA) under the accelerated approval process for carfilzomib (Onyx Pharmaceuticals) as a potential treatment for patients with relapsed and refractory multiple myeloma. The request is based on results from the open-label, single-arm, phase IIb study known as 003-A1, which evaluated 266 heavily pretreated relapsed/refractory multiple myeloma patients who had received at least 2 prior therapies, including bortezomib (Velcade, Millennium/Takeda) and either thalidomide (Thalomid, Celgene) or lenalidomide (Revlimid, Celgene). Patients who had less than a 25% response or progressed less than 60 days after therapy were considered refractory. Overall response rate was the primary endpoint; secondary endpoints included duration of response, clinical benefit rate, overall survival, time-to-progression, progression-free survival, and safety. Patients received carfilzomib 20 mg/m^2 for the first cycle, and 27 mg/m^2 for up to 12 cycles. The overall response rate was 24%, with a median duration of response of 7.8 months. The trial was carried out in collaboration with the Multiple Myeloma Research Consortium. If approved by the FDA, carfilzomib could be available in the United States as early as next spring.

Everolimus Plus Exemestane Produces Strongest Data Yet in the Treatment of Estrogen Receptor–Positive Breast Cancer

At the 2011 European Multidisciplinary Cancer Congress, Baselga and colleagues presented data from the pivotal phase III BOLERO-2 (Breast Cancer Trials of Oral Everolimus-2) trial. The study—which was stopped early due to the benefits observed—examined the safety and efficacy of everolimus (Afinitor, Novartis) in combination with exemestane versus exemestane alone in 724 postmenopausal women with estrogen receptor (ER)–positive, human epidermal growth factor receptor 2 (HER2)–negative advanced breast cancer who had previously been treated with and had become refractory to letrozole and anastrozole. Patients who met the study criteria were randomized 2:1 to receive either oral everolimus 10 mg/day (n=485) with a placebo or with oral exemestane 25 mg/day (n=239). A preplanned interim analysis found that everolimus significantly improved progression-free survival, the primary endpoint of the study. Median progression-free survival, as assessed by local investigators, was longer with everolimus plus exemestane than with exemestane alone (6.9 vs 2.8 months, HR 0.43; 95% confidence interval [CI], 0.35–0.54; *P*<.0001). A central assessment analysis also found that the addition of everolimus increased progression-free survival (10.6 vs 4.1 months, HR 0.36; 95% CI, 0.27–0.47; *P*<.0001). Toxicities were similar to those previously reported with everolimus. Stomatitis (7.7%), anemia (5.8%), dyspnea (3.9%), hyperglycemia (4.3%), fatigue (3.7%), noninfectious pneumonitis (3.1%), and increases in liver enzymes (3.1%) were among the most common grade 3/4 adverse events.