HEM/ONC News

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Bortezomib Plus Dexamethasone Is Superior to Vincristine, Doxorubicin, and Dexamethasone as Induction Therapy in Newly Diagnosed Multiple Myeloma

Results from Intergroupe Francophone du Myélome (IFM) 2005-01, a phase III trial reported by Harousseau and colleagues in the September 7 issue of the *Journal of Clinical Oncology*, showed that the combination of bortezomib (Velcade, Millennium) and dexamethasone was superior to the combination of vincristine, doxorubicin and dexamethasone (VAD) as induction before stem cell transplantation in newly diagnosed multiple myeloma. The study population consisted of 482 patients who were randomly assigned to receive VAD (n=121), VAD plus dexamethasone, cyclophosphamide, etoposide, and cisplatin (DCEP) consolidation (n=121), bortezomib plus dexamethasone (n=121), or bortezomib plus dexamethasone plus DCEP followed by autologous stem cell transplantation (n=119). Complete response/near complete response (CR/nCR) rate was the primary endpoint. The postinduction CR/nCR rate (35% vs 18.4%), at least very good partial response rate (54.3% vs 37.2%), and overall response rate (78.5% vs 62.8%) were higher in patients receiving bortezomib plus dexamethasone compared to those receiving VAD; response rates in patients who did and did not receive DCEP consolidation were similar. Median progression-free survival (PFS) was higher in patients receiving bortezomib plus dexamethasone compared to those receiving VAD (36 vs 29.7 months). The frequency of adverse events was similar across groups, with the exception of hematologic toxicities and toxicity-related deaths, which occurred more frequently in patients receiving VAD. Peripheral neuropathy during induction through first transplantation was, however, more frequent in those receiving bortezomib plus dexamethasone.

Trastuzumab/Chemotherapy Combination Effective in HER2-positive Advanced Gastric or Gastroesophageal Junction Cancer

In the August 28 issue of the *Lancet*, Bang and colleagues reported the results of ToGA (Trastuzumab for Gastric Cancer), a phase III, open-label, randomized controlled trial, which evaluated trastuzumab (Herceptin, Genentech) in combination with chemotherapy as first-line treatment of HER2-positive advanced gastric or gastroesophageal junction cancer. The study recruited 594 patients from 24 countries in 122 centers. Patients were randomized to receive chemotherapy consisting of capecitabine plus cisplatin or fluorouracil plus cisplatin every 3 weeks for 6 cycles (n=296) or chemotherapy in combination with intravenous trastuzumab (n=298). The primary endpoint was overall survival. Of 594 patients, 584 were evaluated in the primary analysis. Median overall survival was approximately 2 months longer in those receiving trastuzumab plus chemotherapy compared to those receiving chemotherapy alone (13.8 vs 11.1 months; *P*=.0046). Nausea, vomiting, and neutropenia were the most frequently reported adverse events in both groups. The incidence of grade 3/4 adverse events and cardiac adverse events was similar in both groups. The findings suggest that trastuzumab combined with chemotherapy is an option for patients with HER2-positive advanced gastric or gastroesophageal junction cancer.

Phase III Study Finds Adjuvant Gemcitabine Comparable to Fluorouracil for Resected Pancreatic Cancer

In the European Study Group for Pancreatic Cancer-3 trial, Neoptolemos and colleagues studied gemcitabine (Gemzar, Eli Lilly) versus fluorouracil plus folinic acid in the adjuvant setting following complete resection of pancreatic cancer. The phase III open-label trial was conducted at 159 centers in 17 countries. A total of 1,088 patients were randomized to receive 6 months of standard fluorouracil plus folinic acid (n=551) or 6 months of gemcitabine (n=537). Patients were followed for a median of 2 years. At the time of analysis, 753 patients had died; median survival was similar in both groups (23 months in the fluorouracil group and 23.6 months in the gemcitabine group). Interim survival estimates and interim PFS rates at 12 and 24 months were comparable in both groups. Furthermore, median PFS was the same in both groups (14 months). In the safety analysis, it was demonstrated that serious adverse events related to treatment were reported by twice as many patients receiving fluorouracil. Stomatitis and diarrhea were more prevalent in patients receiving fluorouracil, whereas hematologic toxicities were more frequent in the gemcitabine group. Although the study, reported in the September 8 issue of the *Journal of the American Medical Association,* found that gemcitabine did not improve overall survival, it did validate the possibility of alternative treatment with fluorouracil in pancreatic cancer patients who cannot tolerate gemcitabine.