HEM/ONC News

By Stacey Small

Addition of Chemotherapy to Radiotherapy Reduces Locoregional Recurrence of Muscle-Invasive Bladder Cancer

Results from a multicenter, randomized study by James and associates demonstrated that patients with muscle-invasive bladder cancer who received fluorouracil and mitomycin-C along with radiotherapy had a significant reduction in locoregional recurrence compared with patients who received radiotherapy alone. A total of 360 patients were enrolled in the study, which was published in the April issue of *The New England Journal of Medicine*. Patients who were randomized to receive chemoradiotherapy were administered fluorouracil 500 mg/m^2 daily during fractions 1–5 and 16–20 of radiotherapy, and mitomycin-C 12 mg/m^2 on day 1. The primary endpoint was locoregional disease-free survival. The median follow-up was 69.9 months. At 2 years, rates of locoregional disease-free survival were significantly higher in the chemoradiotherapy group compared with the radiotherapy group (67% vs 54%). Patients in the chemoradiotherapy group were significantly less likely to have progression (hazard ratio [HR], 0.68; 95% confidence interval [CI], 0.48–0.96; *P*=.03). Patients in the chemoradiotherapy group were slightly more likely than radiotherapy patients to experience grade 3/4 adverse events during treatment (36% vs 27.5%; *P*=.07), but not during follow-up (8.3% vs 15.7%; *P*=.07). Five-year overall survival rates were also higher among patients in the chemoradiotherapy group (48% vs 35%, respectively).

Improved Survival for High-Risk GIST Patients With Extended Imatinib Treatment

According to a study in the March 28 online issue of *JAMA*, 36 months of imatinib (Gleevec, Novartis) treatment following surgery for patients with *KIT*-positive gastrointestinal stromal tumor (GIST) resulted in longer recurrence-free survival (RFS) and OS compared with 12 months of imatinib treatment. This randomized, phase III trial by Joensuu and colleagues included 400 patients undergoing surgery for *KIT*-positive GIST. Patients were considered at high risk of recurrence, based on modified National Institutes of Health Consensus Criteria. Patients were randomized to receive either 12 or 36 months of imatinib 400 mg daily. Adjuvant therapy was started within 12 weeks postoperatively. The median follow-up was 54 months. Patients who received 36 months of imatinib had significantly longer RFS compared with patients assigned to imatinib for 12 months (HR, 0.46; 95% CI, 0.32–0.65; *P*<.001; 5-year RFS, 65.6% vs 47.9%, respectively). Patients assigned to longer imatinib treatment also had longer OS (HR, 0.45; 95% CI, 0.22–0.89). The 5-year survival for patients assigned to 36 months of imatinib was 92%, compared with 81.7% among patients assigned to 12 months of imatinib. Adjuvant therapy was generally well tolerated, although there were patients in both groups who discontinued imatinib for reasons other than GIST recurrence (25.8% in the 36-month group vs 12.6% in the 12-month group).

Origin of Acute Myeloid Leukemia Linked to Founding Clones and Subclones that Cause Myelodysplastic Syndrome

In order to identify the somatic mutation specific to secondary acute myeloid leukemia (AML), Walter and coworkers performed whole-genome sequencing of 7 paired samples of skin and bone marrow in 7 patients with secondary AML. To establish whether the specific somatic mutations were present at that stage, the investigators then genotyped marrow samples obtained during the antecedent myelodysplastic syndrome (MDS) stage from each patient. The entire clonal structure of each pair of samples from the MDS to the AML stage was analyzed in order to identify recurrent mutations. Regardless of the myeloblast count, there was an approximate 85% clonality between MDS and AML cells from paired bone marrow samples. An antecedent founding clone was observed in each case, containing 182–660 somatic mutations. A new subclone with hundreds of new mutations was also observed to be emerging from the founding clone. At least 1 mutation in a coding gene was present in all founding clones and subclones. Published in the March issue of *The New England Journal of Medicine*, the study results suggest that AML evolves from the cells that cause MDS after these cells have undergone multiple cycles of mutations and clonal selection.