HEM/ONC News

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Sipuleucel-T Extends Survival in Metastatic Prostate Cancer Patients

According to study findings reported in the July 29 issue of the *New England Journal of Medicine*, sipuleucel-T (Provenge, Dendreon) significantly prolongs survival in men with metastatic, castrate-resistant prostate cancer. These findings corroborate the results of previous trials of this immunotherapy. Dr. Philip W. Kantoff and colleagues evaluated sipuleucel-T in patients with asymptomatic or minimally symptomatic disease with an expected survival of at least 6 months. The patients (n=512) were enrolled at 75 centers in the United States and Canada; stratification was conducted according to Gleason score, number of bone metastases, and bisphosphonate use. The patients were randomly assigned to receive 3 one-hour infusions of either sipuleucel-T (n=341) or placebo (n=171) every 2 weeks. Median follow-up was 34 months, and more than 92% of patients received all 3 infusions. The analysis showed that median survival was approximately 26 months in patients receiving sipuleucel-T compared to 22 months in those receiving placebo. Mortality was approximately 62% in the sipuleucel-T group compared to 71% with placebo. Although there was a survival benefit seen in patients on active therapy, the time to disease progression was not significantly different between those receiving sipuleucel-T and placebo (14.6 vs 14.4 weeks, respectively). Sipuleucel-T was well tolerated overall; patients receiving the immunotherapy reported chills, fevers, fatigue, nausea, headache, flu-like illness, and myalgia. One grade 4 event of bacteremia associated with catheter infusion was reported. The study findings have raised questions as to why survival improved when there was no evidence of antitumor effect, which evoked concerns that the findings may have been influenced by a prognostic variable that was not taken into consideration.

Induction With Bortezomib Plus Dexamethasone Improves Patients With t(4;14) Myeloma

In the July 19 issue of *Journal of Clinical Oncology*, a retrospective analysis of newly-diagnosed multiple myeloma patients found that induction with bortezomib (Velcade, Millennium Pharmaceuticals) and dexamethasone (Vel/Dex) given before high-dose melphalan and stem cell transplantation was associated with improved survival in myeloma patients with t(4;14) but not in patients with del(17p) cytogenetics when compared to induction with vincristine, doxorubicin, and dexamethasone (VAD). The group of patients receiving Vel/Dex induction (n=507) was treated during the study and according to protocol after it closed; patients were given 4 courses of 1.3 mg/m^2 bortezomib on days 1, 4, 8, and 11. The VAD group (n=512) was also treated with induction therapy within the same period. In those patients treated with Vel/Dex induction, 106 had t(4;14) abnormalities and 54 had del(17p) abnormalities in more than 60% of plasma cells. In the patients receiving VAD induction (n=217), 98 had t(4;14) abnormalities and 119 had del(17p) abnormalities in more than 60% of plasma cells. The findings showed that among patients with t(4;14) cytogenetics, those treated with Vel/Dex had longer event-free survival compared to those treated with VAD induction (28 vs 16 months; $P<.001$); Vel/Dex treated patients also had a higher 4-year overall survival rate (63% vs 32%; $P<.001$). However, differences in survival were not observed in patients with the del(17p) abnormality.

American Society of Clinical Oncology (ASCO) Updates Guidelines on Endocrine Therapy for Women With Hormone Receptor–Positive Breast Cancer

In the July 12 issue of *Journal of Clinical Oncology*, the ASCO guidelines were updated to include aromatase inhibitors as a treatment option for adjuvant endocrine therapy for hormone receptor–positive breast cancer. A recent publication of 12 trials of endocrine therapy caused ASCO to update its clinical practice guidelines. In the new guidelines, the Update Committee recommends that postmenopausal women with hormone receptor–positive breast cancer should consider adding aromatase inhibitor therapy at some point during adjuvant therapy, either as primary therapy for 5 years, sequential therapy for 2–3 years after receiving tamoxifen for 2–3 years, or extended therapy for 5 years after 5 years of tamoxifen. Although the reduction in risk of recurrence with aromatase inhibitor therapy has been modest, and overall survival benefit for aromatase inhibitors versus tamoxifen has only been reported in 2 trials, the panel stated that the recommendation to incorporate aromatase inhibitors was warranted, since breast cancer recurrence is of importance. The panel also suggested being cautious with the concurrent use of CYP2D6 inhibitors and tamoxifen because of drug-drug interactions. Furthermore, the panel also encourages consideration of adverse event profiles, patient preferences, and preexisting conditions when deciding on an adjuvant endocrine therapy.