Sipuleucel-T Prolongs Survival in Prostate Cancer

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The immunotherapy sipuleucel-T significantly prolonged survival in a study of 512 men with metastatic castration-resistant prostate cancer, confirming the results of two smaller previous trials of this therapeutic "cancer vaccine," according to the findings of a randomized, placebo-controlled trial.

The experimental treatment increased median survival by 4.1 months and raised the estimated probability of 3-year survival from 23% to 32%, compared with placebo, significant improvements in this population of men with advanced disease, said Dr. Philip W. Kantoff of the Dana-Farber Cancer Institute and Harvard Medical School, Boston, and his coauthors.

As with the previous studies, this trial also showed that sipuleucel-T (Provenge, Dendreon Corp.) did not hinder tumor progression—a paradoxical finding that has yet to be explained, they noted.

Data from the study were pivotal to the Food and Drug Administration's decision earlier this year to approve the immunotherapy for the treatment of asymptomatic or minimally symptomatic castration-resistant prostate cancer.

Dr. Kantoff and his colleagues assessed sipuleucel-T in patients with asymptomatic or minimally symptomatic disease who had an expected survival of at least 6 months. Serum prostate-specific antigen (PSA) levels were 5 ng/mL or more, and serum testosterone levels were less than 50 ng/dL. All had previous androgen-deprivation therapy.

The study subjects were enrolled at 75 medical centers in the United States and Canada, and stratified according to Gleason score, number of bone metastases, and bisphosphonate use.

They were randomly assigned to receive three 1-hour infusions of active drug (341 patients) or placebo (171 patients) every 2 weeks, completing the course of therapy within 1 month. More than 92% of the subjects received all three infusions. Median follow-up was 34 months.

Mortality was approximately 62% with active therapy and 71% with placebo, a relative reduction in the risk of death of 22%. Median survival was approximately 26 months with sipuleucel-T, significantly longer than the 22 months with placebo. Estimated probability of survival at 36 months was approximately 32% with sipuleucel-T, significantly higher than the 23% with placebo.

These benefits were seen across all subgroups of patients, regardless of their status with respect to adverse factors such as high PSA, lactate dehydrogenase, or alkaline phosphatase levels; a greater number of bone metastases; high Gleason score; poor performance status; and the presence of pain.

However, the median time to disease progression, as measured by CT and bone scanning, was not significantly different between the two study groups, at 14.6 weeks for sipuleucel-T and 14.4 weeks for placebo. The reason for this discrepancy is not yet known, but it might be because of "the delayed onset of antitumor responses after active immunotherapy, relative to objective disease progression, which occurred early in this group of patients," Dr. Kantoff and his associates said (N. Engl. J. Med. 2010;363:411-22).

Sipuleucel-T was generally well tolerated, with only three patients not receiving the entire course of treatment because of infusion-related events. "Adverse events that were more frequently reported for sipuleucel-T than for placebo were generally consistent with the release of cytokines," such as chills, fever, fatigue, nausea, headache, flu-like illness, and myalgia. Most of these developed within 1 day of an infusion and resolved within 1-2 days. One grade 4 adverse event, a case of bacteremia associated with the catheter infusion, was reported.

There was no increase in the rate of cerebrovascular events, as has been reported previously with sipuleucel-T, the investigators noted. ■