PROSTATE CANCER

Further data on sipuleucel-T immunotherapy

By combining data from two randomized trials, US researchers have provided further information on the safety and efficacy of sipuleucel-T immunotherapy in patients with advanced prostate cancer. D0991 and D0992A had identical study designs, and enrolled a total of 225 patients with metastatic castration-resistant prostate cancer. "Each of the clinical trials provided evidence of survival prolongation," says Celestia Higano, lead author on the paper, "as did the integrated analysis of the two." D0991 has been previously reported; recruitment for D0992A closed early on the basis of early progression results of D0991.

The two trials randomized patients 2:1 to receive either sipuleucel-T immunotherapy—autologous peripheral blood mononuclear cells loaded with a recombinant fusion protein comprising prostatic acid phosphatase and granulocyte–macrophage colony-stimulating factor (an immune activator)—or placebo. The primary end point of the trials was clinical or radiographic disease progression, and overall survival was assessed after 36 months of follow-up. Compared with placebo, sipuleucel-T increased the median time to disease progression from 9.7 to 11.1 weeks, although this difference was not statistically significant. The authors speculate that progression events might in some cases precede the maximal immune response, which can take up to 12 weeks to develop.

More importantly, patients who received sipuleucel-T exhibited a 33% reduction in the risk of death, and a 4.3-month increase in median survival (23.2 versus 18.9 months) compared with placebo. 3-year survival rates were 33% for patients who received immunotherapy compared with 15% for those who received placebo. This effect was robust to adjustment for potential confounders. Overall, the proportion of patients who experienced adverse events was similar in the two groups, but the incidence of chills, pyrexia, headache, asthenia, dyspnea, vomiting and tremor was significantly higher in the immunotherapy arm. The majority of these events were of grade 1 or 2.

On the basis of these and other recently presented data, sipuleucel-T is currently pending approval by the FDA for the treatment of advanced prostate cancer. Dendreon, the manufacturer of sipuleucel-T, provided support for these trials.

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Original article Higano, C. S. *et al.* Integrated data from 2 randomized, double-blind, placebo-controlled, phase 3 trials of active cellular immunotherapy with sipuleucel-T in advanced prostate cancer. *Cancer* **115**, 3670–3679 (2009).