Vaccine Approved for Prostate Cancer

BY JANE SALODOF MACNEIL

The Food and Drug Administration has approved sipuleucel-T for treatment of advanced prostate cancer in a much-anticipated ruling that marks the first approval of a vaccine for cancer treatment.

The indication is for use in patients with "asymptomatic or minimally symptomatic prostate cancer that has spread to other parts of the body and is resistant to standard hormone treatment," according to the FDA announcement.

At a median follow-up of 3 years, the vaccine was credited with a 4.1-month gain in overall survival, with men on the vaccine living a median of 25.8 months vs. 21.7 months.

Sipuleucel-T will be marketed as Provenge by manufacturer Dendreon Corp.

The company announced the vaccine will be available initially at 50 oncology and urology centers that were approved clinical trial sites. Executives said in an investors' call that they expected to serve 2,000 patients within the first 12 months. Initially, the individually tailored vaccine will be manufactured only in the company's New Jersey facility, but Dendreon plans to add facilities in Atlanta and in Orange County, Calif. by mid-2011.

Pricing has been set at $31,000 per infusion, or a total of $93,000 for the therapy. The company has set up a patient-access program to help men who cannot afford co-payments.

The granting of the indication follows a long and tumultuous review process in which protestors picketed after an FDA advisory committee rejected Dendreon's initial application for the vaccine. Early results from a key trial designed to address issues raised by the panel failed to show an improvement in progression-free survival, but researchers were eventually able to demonstrate that men lived longer when treated with sipuleucel-T.

The pivotal Dendreon-sponsored, phase III IMPACT (Immunotherapy for Prostate Adenocarcinoma Treatment) trial randomized 512 men with metastatic castration-resistant prostate cancer to sipuleucel-T or placebo. At a median follow-up of 3 years, the vaccine was credited with a 4.1-month gain in overall survival, with men on the vaccine living a median of 25.8 months vs. 21.7 months in the control group.

Adverse events occurred in almost all patients, with chills, fatigue, fever, back pain, nausea, joint ache, and headache being common reactions. Most side effects were mild or moderate, but the FDA noted that about a quarter of patients had serious adverse reactions, including some acute infusion reactions and stroke.

"Cerebrovascular events, including hemorrhagic and ischemic strokes, were observed in 3.5% of patients in the Provenge group, compared with 2.6% of patients in the control group," it said.

The company announced that it has committed to conducting "a registry of approximately 1,500 patients to further evaluate a small potential safety signal of cerebrovascular events."

An autologous cellular immunotherapy, sipuleucel-T delivers a patient's own immune cells, extracted via leukapheresis, in a vaccine designed to stimulate an immune response against prostatic acid phosphatase (PAP), an antigen expressed in most prostate cancers. Men received three doses of the vaccine in intravenous injections given at about 2-week intervals.

"The availability of Provenge provides a new treatment option for men with advanced prostate cancer, who currently have limited effective therapies available," said Dr. Karen Midthun, acting director of the FDA's Center for Biologics Evaluation and Research, in the FDA announcement.

The International Society for Biological Therapy of Cancer issued a statement hailing the approval as "a significant advance in the development of biological therapy [also called immunotherapy] for cancer treatment."

Bernard Fox, Ph.D., the society's president, noted that the search for a way to harness the immune system against cancer has lasted more than a century. Dr. Fox had no relevant financial conflicts to disclose. ■

Emily Hayes of the Pink Sheet contributed to this report. The Pink Sheet and this publication are owned by Elseiver.

CLINICAL GUIDELINES FOR FAMILY PHYSICIANS

Prostate Cancer Screening Guidelines

BY NEIL S. SKOLNIK, M.D., AND DANNY MAI, M.D.

Approximately 192,000 men were diagnosed with prostate cancer in 2009, making it the most frequently diagnosed cancer and the second leading cause of cancer death in men. Controversy still remains, however, regarding the benefit of screening with prostate-specific antigen (PSA) testing and overall reduction in mortality. In addition, the preliminary results from two prospective randomized trials—the European Randomized Study of Screening for Prostate Cancer (ERSPC) and the prostate arm of the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial—have shown different mortality reductions (20% vs. none), thus adding to the debate.

In light of this uncertainty, the American Cancer Society has revised its 2001 guideline on prostate cancer screening to emphasize discussion with patients to allow them to use their own values to make decisions about screening based on the current available evidence (CA Cancer J. Clin. 2010;60:70-98).

Risk Assessment and Individualized Screening

Patients should be given the opportunity to make an informed decision by being provided with the benefits and risks of screening. Counseling should incorporate the significance of prostate cancer, the potential advantage of early discovery, the strengths and limitations of PSA testing, and the risks of treating cancer. The decision to screen also should integrate the values and preferences of the individual.

Men who are asymptomatic with less than a 10-year life expectancy based on age or comorbid conditions should not be offered screening. Men who are asymptomatic with a life expectancy of at least 10 years should be provided information about screening at an age based on their risk factors. Men are at average risk beginning at age 50 years. Those at high risk (African American men and men with a first-degree relative diagnosed with prostate cancer before age 65) should consider screening starting at age 45. Those who are at considerably higher risk (men with multiple family members diagnosed with prostate cancer before the age of 65) should consider screening at age 40.

Prostate-Specific Antigen Testing

The ACS continues to recommend a PSA level of 4.0 ng/mL as the threshold to recommend biopsy. Health care providers should consider individualized risk assessment and informed decision making for men with a PSA level between 2.5 and 4.0 ng/mL. Sensitivities of PSA screening are approximately 20% and 32% for levels of 4.0 ng/mL and 3.0 ng/mL, respectively. Dropping the threshold from the historical value of 4.0 ng/mL, while increasing cancer detection rate, would decrease the specificity and result in a higher rate of false positives.

The ACS recommends that men with an initial screening PSA level below 2.5 ng/mL can reduce their screening frequency to every 2 years. Those with levels of 2.5 ng/mL and higher should be screened annually. This recommendation comes from several modeling studies that have projected that extending screening to every 2 years would reduce the number of tests and unnecessary biopsies by approximately 50% while retaining 87%-93% of years of life saved. Analysis of a number of data sets showed no considerable enhancement in prostate cancer detection using PSA velocity compared to screening with PSA alone.

Digital Rectal Examination

The current role of the DRE as a screening method for prostate cancer is unclear. Results from case-control studies examining DRE alone have been mixed, and the two randomized trials have not provided evidence supporting it as a screening tool. In particular, an ERSPC subgroup analysis found that the sensitivity and positive predictive value of the DRE were 20% and 8.8%, respectively, in men who had PSA values of less than 3.0 ng/mL. In the same analysis, 17% of prostate cancers were detected by DRE alone (with PSA values below 4.0 ng/mL).

Since the utility of adding DRE to PSA test ing is yet unknown and is likely to be small, the ACS recommends that, for individuals choosing to be screened for prostate cancer, testing should be done with PSA with or without DRE. The addition of DRE may be helpful in decision making for men with PSA levels between 2.5 ng/mL and 4.0 ng/mL.

The Bottom Line

Prostate cancer screening should be offered to an asymptomatic individual of average risk at age 50 years, high risk at age 45, and considerably high risk at age 40. Patients and physicians must weigh the benefits of screening with the potential risks of treatment. PSA testing is recommended with or without DRE and should be performed annually for men whose PSA level is 2.5 ng/mL or greater, and every 2 years for men whose PSA level is less than 2.5 ng/mL. PSA levels greater than 4.0 ng/mL should prompt further evaluation, while PSA levels between 2.5 ng/mL and 4.0 ng/mL should encourage individualized risk assessment integrating additional risk factors for prostate cancer and patient values.

DR. SKOLNIK *(right) is an associate director of the family medicine residency program at Abington (Pa.) Memorial Hospital.* DR. MAI *is a second-year resident in the program. A handheld computer version of this guideline is available at www.redi-reference.com. The authors reported having no relevant conflicts of interest.*