SERMs Effective but Underused

Prevention *from page 1*

tice?" said Dr. Gabriel N. Hortobagyi, who was the invited discussant.

Dr. Wickerham echoed this frustration during a press conference. "I see women each week, at a high risk of breast cancer, and I will end up telling one or two of them … all too often … that they have breast cancer. I'd love for that part of my job to go away. These data are a step in that direction," said Dr. Wickerham, chief of the cancer genetics and prevention section at Allegheny General Hospital in Pittsburgh.

The randomized, double-blind federally funded STAR trial included women at least 35 years of age with a 5-year predicted breast cancer risk of at least 1.66% (based on a modified version of the Gail model). Researchers from the NSABP randomized 19,747 women to receive either tamoxifen or raloxifene (JAMA 2006;295:2742-51).

The update includes 19,490 women—9,736 on tamoxifen and 9,754 on raloxifene. The differences in numbers are due to a combination of loss during follow-up or follow-up data becoming available for women who were lost to follow-up in the original report. Women on tamoxifen received 20 mg/day and those on raloxifene received 60 mg/day.

At an average follow-up of 8 years, the relative risk of invasive breast cancer on raloxifene was 1.24 compared with tamoxifen, which was significant. Both drugs reduced the risk of invasive breast cancer by roughly 50% in the original report (median follow-up 47 months).

In this analysis, "we have estimated, however, that this difference in the raloxifene-treated group represents 76% of tamoxifen's chemopreventative benefit, which translates into at 38% reduction in invasive breast cancers," Dr. Wickerham reported.

In the 2006 report, raloxifene (81 events) did not appear to be as effective as tamoxifen (57 events) in preventing noninvasive breast cancer. "Now with additional follow-up, those differences have narrowed," he said. At 8 years, there was no statistical significance between the two groups, with a risk ratio of 1.22. The relative risk of 1.22 favors tamoxifen, but raloxifene preserves 78% of the chemopreventative benefit of tamoxifen. This translates to raloxifene preventing 39% of noninvasive breast cancers.

Raloxifene maintained its toxicity advantage. The relative risk of uterine cancers with raloxifene vs. tamoxifen was 0.55. In addition, there were twice as many hysterectomies for benign disease in the tamoxifen group. This was due in part to an 80% increase in hyperplasia of the endometrium that occurred in women on tamoxifen, Dr. Wickerham said.

KERRI WACHTER/ELSEVIER GLOBAL MEDICAL NEWS

"These data are good news," Dr. D. Lawrence Wickerham commented.

Both drugs increase the risk of thromboembolic complications, but there were significantly fewer of these events in women on raloxifene (154), compared with tamoxifen (202).

Dr. Hortobagyi, director of the breast cancer research program at the University of Texas M.D. Anderson Cancer Center in Houston, identified several factors that may be responsible for limited use of tamoxifen and raloxifene for prevention. He cited misinformation about the drugs, fears about toxicities, limited high-risk prediction tools, lack of a marker or measurement to monitor for risk reduction, cost, and insufficient public and professional education about the drugs.

"There is no perfect drug. Certainly in other areas of preventive medicine, there seems to be greater tolerance for adverse effects for effective preventative interventions," he said, noting a discrepancy between what is considered acceptable risk for other preventative drugs and SERMs. For example, drugs used to prevent hypertension and coronary artery disease have more adverse events and more serious events than do SERMs, he said.

"The adverse effects of SERMs pale in comparison to the complications of and disability caused by breast cancer," Dr. Hortobagyi said. "So the challenge today is how to communicate to the public to enhance the utilization of SERMs and reduce further the incidence of breast cancer." ■

Disclosures: *The study was supported by the National Cancer Institute. Dr. Wickerham reported that he has consulted for Eli Lilly. Dr. Hortobagyi reported no conflicts of interest.*

Vaccine Wins FDA Approval for Advanced 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. Sipuleucel-T will be marketed as Provenge by manufacturer Dendreon.

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 treat the first patient within a week, and aim 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. Executives said they plan to meet with Medicare officials about reimbursement; about three-fourths of the target population is Medicare eligible. The company also has set up a patient-access program to help men who cannot afford copayments.

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," the agency 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.

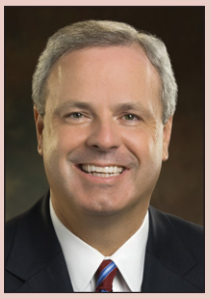
"The availability of Provenge provides a new treatment option for men with advanced prostate cancer, who currently have limited effective therapies available," said Dr. Karen Midthun, acting director of the FDA's Center for Biologics Evaluation and Research, in the FDA announcement. ■

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

MY TAKE

Price Will Be an Issue for Provenge

After a series of ups and downs, the much-debated prostate cancer vaccine Provenge is now FDA approved. Instead of the end of the discussion, the story is likely only beginning. The price is said to be in the $90,000 range for the treatment course (three monthly injections), and that number will further stimulate talk around "how much is it worth, for how long?" and who should receive the therapy.



With other high-priced therapies, such as bevacizumab (Avastin) or cetuximab (Erbitux), the doses are delivered repeatedly, and the overall cost only increases for those patients who are benefiting clinically. In the case of Provenge, the price is basically one size fits all, and there are no predictive tests as to which patients will likely benefit from the vaccine. Coupling the financial concerns with Dendreon's publicly stated manufacturing shortfall (which will limit access), the launch and utilization of this new therapy will be a story to follow closely in this era of health reform.

HOWARD A. BURRIS III, M.D., is chief medical officer and director of drug development at Sarah Cannon Research Institute in Nashville, Tenn., and editor of THE ONCOLOGY REPORT, *which is also published by Elsevier. He has disclosed receiving honoraria from and consulting for nine pharmaceutical companies.*