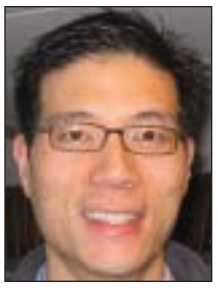
Prostate Cancer Therapy May Up Cardiac Death

BY FRAN LOWRY
Orlando Bureau

ORLANDO — Men aged 65 years or older who received androgen deprivation therapy for localized prostate cancer had an increased risk of cardiovascular death, according to a registry review presented at a symposium on prostate cancer sponsored by the American Society of Clinical Oncology.



Men treated with androgen deprivation therapy had a 2.5% risk of cardiac death at 5 years.

DR. TSAI

Older men who received androgen deprivation therapy had a 3% risk of dying from cardiac causes at 5 years, significantly higher than the 0.9% risk in similarly aged men who did not receive hormone therapy, reported Dr. Henry K. Tsai, of Harvard Medical School, Boston. Androgen deprivation therapy was not associated with a significant increase in the risk of death from cardiac causes in men younger than 65 (1.5% for men on androgen treatment, and 0.3% for men not receiving androgen therapy, he said at the symposium, cosponsored by the Society of Urologic Oncology and the American Society for Therapeutic Radiology and Oncology.

Androgen deprivation therapy, which is commonly used to treat men with prostate cancer, causes weight gain, thus predisposing men to diabetes and the metabolic syndrome. Dr. Tsai and his colleagues at Harvard reviewed data from the CaPSURE (Cancer of the Prostate Strategic Urologic Research Endeavor) database to determine whether the use and duration of this treatment might be linked to a fatal cardiac event. They identified 3,636 men with localized prostate cancer who were treated with surgery, external beam radiotherapy, brachytherapy, or cryotherapy. Of these, 735 received androgen deprivation therapy and 2,901 did not.

The investigators analyzed the cardiac mortality and all-cause mortality, controlling for age and other cardiac risk factors including hypertension, diabetes, body mass index, and smoking.

The median age of the subjects was 64 years at baseline, median duration of hormone therapy in the men who received it was 4.1 months, and median duration of follow-up was 4 years.

Overall, men treated with androgen deprivation therapy had a 2.5% risk of cardiac death at 5 years, compared with 0.6% in men who did not get hormones. That difference was statistically significant, but when the data were analyzed separately for men younger than age 65 and men aged 65 or older, a significant difference in risk was seen only in the older men, Dr. Tsai said.

Limitations of this study included an inability to control for hypercholesterolemia and other coronary artery disease risk factors, as well as the retrospective nature of the analysis.

Nevertheless, the findings point to the importance of a cardiovascular evaluation in men with prostate cancer who are being considered for androgen deprivation therapy. They also underscore the importance of monitoring cardiovascular risk factors in such patients. Further prospective evaluations are needed to corroborate these findings, he added. ■

Toremifene Counters the Adverse Effects of Androgen Deprivation

BY FRAN LOWRY
Orlando Bureau

ORLANDO — Toremifene citrate, a selective estrogen receptor modulator, increased bone mineral density and improved lipid levels in men receiving androgen deprivation therapy for advanced prostate cancer, investigators reported at a symposium on prostate cancer sponsored by the American Society of Clinical Oncology.

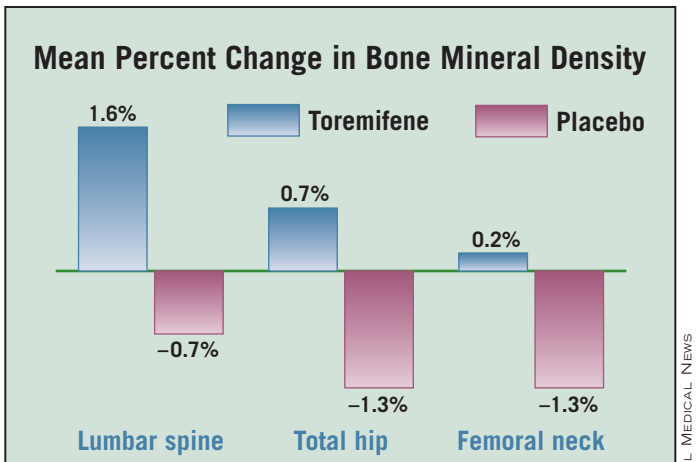
In a planned interim analysis, toremifene (80 mg/day) given orally for 12 months significantly increased BMD in the lumbar spine, hip, and femoral neck in men randomized to the drug. Conversely, men who received placebo experienced decreases in BMD at these sites, said lead investigator Dr. Matthew R. Smith, of the department of medicine at Massachusetts General Hospital and Harvard Medical School, Boston.

In a second interim analysis of lipid results, toremifene significantly decreased total cholesterol by an average of 7.1%, and also decreased LDL cholesterol by 9.0% and triglyceride levels by 20.1%. The total cholesterol: HDL cholesterol ratio dropped an average of 11.7%, whereas HDL cholesterol levels increased by 5.4%, Dr. Smith said at the symposium, which was cosponsored by the Society of Urologic Oncology and the American Society for Therapeutic Radiology and Oncology.

Androgen deprivation therapy, either with bilateral orchiectomy or treatment with GnRH agonists, is the mainstay of treatment for metastatic prostate cancer. This therapy has also become routine for many men with nonmetastatic disease. But the treatment is not without considerable side effects, including an increased risk of fracture and cardiovascular disease.

Currently, about a third of the estimated 2 million prostate cancer survivors in the United States receive treatment with GnRH agonists, and this expanded use in a greater proportion of men—especially in those who have long life expectancies—has heightened concerns about these deleterious effects, Dr. Smith said.

In the study, 1,392 men aged 50 years and older who were on androgen deprivation therapy for metastatic disease were randomly assigned to toremifene or placebo for 2 years. These analyses were done at the midpoint of the randomized, controlled trial; BMD and changes in lipid profiles were secondary end points. The primary end point, vertebral fractures in the two arms, will be analyzed at the end of 2 years. ■



Elsevier Global Medical News

Alternative Male Contraceptive Options Are in Development

BY ROBERT FINN
San Francisco Bureau

SAN FRANCISCO — Condoms and vasectomy remain the only options for male contraception, but that may change within a few years if promising methods under investigation pan out in clinical trials, Sharon Myoji Schnare said at a meeting on contraceptive technology sponsored by Contemporary Forms.

Ms. Schnare, a nurse-practitioner, and nurse-midwife at the South Kitsap Family Care Clinic in Port Orchard, Wash., highlighted five of the most promising approaches:

► **Reversible inhibition of sperm under guidance (RISUG).** This method of male contraception involves vas deferens injections of styrene maleic anhydride in the solvent dimethyl sulfoxide. Currently in phase 3 trials, RISUG seems to be highly effective and is regarded by many as the most promising of the male contraceptives. No pregnancies have been reported from men who were treated as long ago as 10-15 years. Primate studies indicate that this method may be reversible, but there have been no official reversibility tests in humans.

RISUG inhibits fertility by providing a partial physical block to sperm transport through the vas deferens and stripping membranes from the sperm that make it through, making it impossible for them to fuse with the oocyte.

Skilled practitioners can complete the no-scalpel procedure in about 15 minutes, with the only immediate side effects being a slight, painless swelling of the testes. Although viable sperm can be found for up to 3 months after vasectomy, RISUG seems to produce infertility in as little as 10 days afterward.

► **Adjudin (also called AF-2364).** This is an analogue of an old anticancer drug called lonidamine that is conjugated to follicle-stimulating hormone (FSH). Lonidamine alone is known to cause kidney damage and its' bioavailability is extremely low. But conjugated to FSH, small amounts of the drug go directly to the Sertoli cells of the testes, the only cells in the male body with FSH receptors. The sperm made by these cells are incapable of fertilizing an egg. Adjudin is currently in phase 2 human trials.

► **The Intra Vas Device (IVD).** This device is composed of a set of two flexible silicon plugs, 1 inch long and either 1.2 mm or 1.4 mm in diameter. The plugs are inserted in the vas deferens, separated by a small space, and they physically block the passage of sperm.

The no-scalpel procedure can be performed by anyone experienced in vasectomy. It's expected to cost about $1,000, which is comparable to a vasectomy. Unlike a vasectomy, however, reversal would theoretically be simpler and less expensive. In May 2006, the Food and Drug Administation approved human trials with this device, and if all goes according to plan, approval is expected in Europe, Canada, and the United States by 2010.

► **Suppression of spermatogenesis with transdermal testosterone gels plus various progestins.** In one such study, 100 mg per day of testosterone gel and 300 mg per 3 months of depot medroxyprogesterone acetate (DMPA) resulted in dramatic decreases in spermatogenesis in 90% of the 44 men who were tested. There were no serious adverse events and only minimal changes in weight, lipids, and PSA.

► **Several gene-therapy strategies under consideration.** Some researchers hope to target genes controlling sperm development; others, the genes that control the sperm's entry into the oocyte; and still others, the genes that control the sperm's tail and affect motility.

For more information, Ms. Schnare suggested visiting www.malecontraceptives.org. Contemporary Forms and this news organization are both wholly owned subsidiaries of Reed Elsevier. ■