

Drug May Prevent Prostate Ca in High-Risk Patients

Prostatic intraepithelial neoplasia patients who took toremifene had a 48% drop in prostate cancer risk.

BY JANE SALODOF MACNEIL
Southwest Bureau

ORLANDO — Toremifene citrate, an estrogen blocker approved for the treatment of advanced breast cancer, significantly reduced the incidence of prostate cancer in high-risk patients enrolled in a double-blind, randomized, phase IIb trial.

Investigator David Price, M.D., reported a 48% reduction in prostate cancer risk for high-grade prostatic intraepithelial neoplasia (PIN) patients who took 20 mg of toremifene each day for a full year. Prostate cancer was diagnosed over the course of the 12-month trial in 31.2% of patients in a placebo group, and 24.4% of those on the 20-mg dose.

Cohorts that completed a year of therapy at higher doses of toremifene also showed lower incidence of cancer, but the differences compared with placebo were not statistically significant. The proportion of 12-month biopsies showing prostate cancer was 9% of 88 men still taking 20 mg of toremifene, 14.3% of 91 men taking 40 mg, and 13% of 77 men treated with 60

mg. The highest cancer rate, 17%, was found among 86 men still taking placebo.

Dr. Price, director of urologic oncology and clinical research at Regional Urology, LLC, in Shreveport, La., presented data at the American Society of Clinical Oncology's annual meeting. He identified himself as a consultant to GTx Inc. in Memphis, which sponsored the trial. The company sells the drug, a selective estrogen receptor modulator, under the brand name Fareston for breast cancer and is developing it for prostate cancer under the name Acapodene.

The study enrolled 514 PIN patients at 64 sites across the United States. Researchers randomized 130 men to placebo, 125 to 20 mg of toremifene, 134 to 40 mg, and 125 to 60 mg. Age and prostate-specific antigen levels were similar across the cohorts.

At 6 months, rates of prostate cancer diagnoses were comparable for the 20-mg and placebo groups: 15.7% and 15.9%, respectively. Dr. Price said he believed the 6-month biopsies detected cancers missed at baseline. Consequently, he proposed that

the 12-month biopsy data are more reflective of toremifene's effectiveness.

PIN patients are at substantially higher risk for prostate cancer than are men with high prostate-specific antigen levels, according to Dr. Price. He described PIN as a precancerous condition, comparable with colon polyps, in which abnormal cells are moving toward a malignant state.

"Right now we do not recommend any aggressive treatment for PIN," he said at a press briefing, describing an anxiety-generating watch-and-wait strategy with repeated biopsies as the only option.

"This study documents the natural history of PIN," he added, noting that prior estimates of cancer progression were based on retrospective data. "For the first time in a large prospective fashion, we demonstrated that these patients are truly at risk—that one in three is going to develop prostate cancer [within a year]."

Toremifene was well tolerated, with comparable proportions of patients on the drug (7%-9%) and the placebo (11%) reporting at least one serious adverse event. Its most common side effect, fatigue, occurred in 5% of the group taking 20 mg, the most effective dose, according to the presentation.

Gleason scores in men who developed

prostate cancer were slightly lower (6.1%) in the 20-mg group than in the placebo group (7.4%). Dr. Price interpreted this as evidence that chemoprevention did not make cancers worse than they would have been without the trial.

The preventive effect demonstrated so far is 10-fold greater than that of tamoxifen against breast cancer, according to Dr. Price. Based on the phase IIb data, he estimated daily toremifene use could prevent 6.8 prostate cancers per 100 patients treated per year. He contrasted this with the National Surgical Adjuvant Breast and Bowel Project B-24 trial, in which tamoxifen use prevented 0.71 cancers per 100 patients with ductal carcinoma in situ after 1 year of treatment.

Audience members challenged him to state the actual numbers, and not just percentages, of patients who developed prostate cancer in the trial. He said 16 patients were diagnosed in the placebo group and 12 in the 20-mg cohort.

In a discussion of the trial, Otis W. Brawley, M.D., associate director of the Winship Cancer Institute at Emory University in Atlanta, noted that the absolute difference was only four fewer men developing prostate cancer: "A reduction of four—total." ■

Mayo Study: Prostatectomy Is Best In Clinical Stage T3 Prostate Cancer

BY ALICIA AULT
Contributing Writer

Radical prostatectomy for locally advanced prostate cancer, which generally results in better outcomes than radiation therapy alone, is not often offered. But a 15-year survival rate of 80%—better than for radiation therapy, and equivalent to stage 2 surgery results—was achieved in men with clinical T3 disease who had the procedure, according to results of a long-term study at the Mayo Clinic, Rochester, Minn.

Many men with clinical T3 disease are told they can't be helped by surgery and are often referred to the clinic for second opinions, senior investigator Horst Zincke, M.D., director of urooncologic surgery at the clinic, told FAMILY PRACTICE NEWS.

Principal investigator John Ward, M.D., now of the Naval Medical Center, Portsmouth, Va., along with Dr. Zincke and other colleagues, conducted a retrospective study of 5,652 men who had radical prostatectomy for confirmed prostate cancer from 1987 to 1997 (a period when prostate-specific antigen [PSA] testing came into use).

Of those, 15% (842) had the surgery for clinical stage T3. Median follow-up was 10.3 years. Survival was compared with men who had prostatectomy for stage 2 disease during the same period as well as with published results for radiation therapy (BJU Int. 2005;95:751-6).

Reports in the literature indicate a 79% survival at 5 years for T3 disease treated with radiation alone, Dr. Zincke said in the interview. And, he and his colleagues noted, studies have also shown that cancer can persist in 14%-91% of men given radiotherapy.

The Mayo study found that survival rates with surgery were 95% at 5 years, 90% at 10 years, and 79% at 15 years. During those same periods, 85%, 73%, and 67% of patients, respectively, were free of local or systemic disease recurrence after surgery.

Although 21% of T3 patients were given neoadjuvant hormone therapy, that intervention had little impact on the grade, stage, or rates of margin positivity, and did not affect progression-free or cancer-specific survival, the authors said.

The fact that survival, complication, and incontinence rates were similar to those for surgery for T2 disease, including a 75% rate of erectile dysfunction, reflected "the infrequent use of a nerve-sparing technique," the authors reported. Perioperative mortality was the same as for T2 patients.

Experts continue to debate T3 disease management, and surgery has declined significantly in the United States; only about 6% of T3 patients undergo radical prostatectomy, according to the authors. At the Mayo Clinic, the number of patients receiving the procedure has dropped from 25.3% of T3 patients in 1987 to 2.8% in 2001. The decline may partly be due to overstaging by PSA results—in this study, 27% were clinically overstaged, the authors said.

And surgeons have gotten more wary of operating when they believe the cancer is extracapsular, Dr. Zincke said.

While the Mayo results were good, they may not be repeated everywhere, he said. The best candidates are patients in their 40s to 60s who have early extracapsular disease, Dr. Zincke said. With those men, "we know we can take the cancer out without causing increased morbidity," he said. ■

Metaanalysis Links Some STDs To High Prostate Cancer Risk

BY DAMIAN McNAMARA
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NEW ORLEANS — Specific sexually transmitted diseases are associated with prostate cancer, most significantly so, according to a metaanalysis.

Prostate cancer is the most common cancer in American men and is estimated to account for one-third of all new cases of cancer in men this year. It is the second leading cause of cancer-related death in this group and will be responsible for an estimated 30,000 deaths this year, according to the American Cancer Society.

Sexually transmitted diseases (STDs) cause inflammation of the prostate, which might increase the risk for malignancy, Marcia L. Taylor, M.D., said at the annual conference of the Society of Teachers of Family Medicine.

A previous metaanalysis of 17 case-control studies showed an association (odds ratio 1.44) between and increased risk of prostate cancer and history of any STD infection in men (Epidemiology 2002;13:72-9). "But there were study limitations," said Dr. Taylor of the Medical University of South Carolina. The researchers, for example, did not include human papillomavirus (HPV) or a subgroup analysis of specific STDs.

To determine more specific as-

sociations, Dr. Taylor and her colleagues performed a Medline search of published reports from 1966 to August 2004. They found 29 case-control studies that demonstrated an association between prostate cancer and any STD or gonorrhea, syphilis, or HPV.

There was a statistically significant association between any STD and an increased risk of prostate cancer (OR 1.48) based on 6,022 cases in the 29 studies. Similarly, researchers found a statistically significant association between gonorrhea and prostate cancer (OR 1.39), based on 2,241 cases in 11 studies; and between HPV and prostate cancer (OR 1.52), based on 2,305 cases in 10 studies.

The association between syphilis and prostate cancer, based on 2,254 cases in seven case-control studies, did not reach statistical significance (OR 1.42).

Some studies included in the metaanalysis controlled for confounding variables, and some did not. Researchers, for example, did not account for exposure to multiple STDs or patients with asymptomatic infection.

Recall bias is another possible limitation. "Most used patient history for documentation of STDs, and not all patients may have been forthcoming," Dr. Taylor reported. ■