Data Back Leaving Early Prostate Ca in Elderly

BY JANE SALODOF MACNEIL
Senior Editor

A population-based review of more than 9,000 older men diagnosed with early-stage prostate cancer supports the controversial strategy of not treating less aggressive disease in the elderly.

Although most of the cancers went untreated, 10 years after diagnosis only 3%-7% of men with low- or moderate-grade disease had died of prostate cancer. Not surprisingly, mortality was higher, 23%, in men with high-grade disease.

"For elderly men, the survival benefit of treatment is most likely modest. The majority of patients died of other complaints or were still alive," Grace Lu-Yao, Ph.D., lead investigator, said during a press Webcast in advance of a symposium on genitourinary cancers that was sponsored by the American Society for Clinical Oncology, the American Society for Therapeutic Radiology and Oncology, and the Society of Urologic Oncology.

Investigators used Medicare claims linked to the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database to identify 9,018 men diagnosed with stage I or II prostate cancer between 1992 and 2002. None had local therapy (surgery or radiation) or hormonal therapy in the 6 months after diagnosis, said Dr. Lu-Yao, an epidemiologist at the Cancer Institute of New Jersey, New Brunswick.

Although 2,675 men received treatment subsequently, long periods without therapy were common. Investigators reported the median interval between diagnosis and start of cancer therapy to be 10.6 years (127 months). About two-thirds of the population was categorized as either dying of other causes or not experiencing a cancer progression for which they were treated with surgery or radiation.

Compared with previous studies reporting higher mortality rates, the new analysis has the advantage of looking at many more men, older men, and men diagnosed in the era of prostate-specific antigen (PSA) screening. Dr. Lu-Yao said more than 5,000 participants were older than 75 years in the study; the median age was 77 years. Nearly two-thirds of the population had T1 disease.

She noted many men were unlikely to have been diagnosed before PSA screening, which can detect prostate cancer 6-13 years before the slow-growing disease is diagnosed clinically. ■

Biopsy Is Discouraged in Men With PSA Less Than 3 ng/mL

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — Men whose prostate-specific antigen levels were less than 3 ng/mL at their initial screenings had a 20-fold lower risk of dying of prostate cancer, compared with men who presented with higher PSA levels in a study that tracked 19,970 men for 12 years.

The 15,582 men who initially presented with PSA levels less than 3 ng/mL and a normal digital rectal exam did not undergo biopsy, Dr. Monique J. Roobol told a symposium on genitourinary cancers.

Biopsy was offered to men with higher screening PSA levels or positive digital rectal exams in the Rotterdam section of the European Randomized Study of Screening for Prostate Cancer. Rescreening was offered after 1, 4, and 8 years. The analysis included all prostate cancers detected at or between screenings.

Of men biopsied because of screening PSA levels of 3 ng/mL or greater, 1% died of prostate cancer. In the group with initial PSA levels less than 3 ng/mL, 700 prostate cancers were subsequently detected, but only eight men (0.05%) died of the disease. To prevent one prostate cancer death, 1,981 men with initial PSA levels less than 3 ng/mL need to be biopsied, an unacceptable rate, said Dr. Roobol of the urology department at Erasmus University, Rotterdam, the Netherlands.

Mounting evidence suggests prostate cancer in men with low PSA levels may be indolent disease with better outcomes than cancer detected in men with higher PSA levels, the researchers said.

New risk markers need to be developed if the few prostate cancer deaths in men with screening PSA levels less than 3 ng/mL are to be prevented, said Dr. Roobol at the symposium, sponsored by the American Society of Clinical Oncology, the American Society for Therapeutic Radiology and Oncology, and the Society of Urologic Oncology. None of 139 men who presented with a PSA level less than 1 ng/mL died of prostate cancer.

Three of the eight men in the no-initial-biopsy group who died of prostate cancer were diagnosed with the disease within a year of initial screening; in two of the three, the PSA level did not change between screening and diagnosis. The other five in the no-initial-biopsy group who died of prostate cancer were diagnosed 2-8 years after initial screening. The time from diagnosis to death for these men ranged from 6 months to 8 years. ■

Cetrorelix Shows Promise in BPH

BY NANCY WALSH
New York Bureau

NEW YORK — A new treatment paradigm for benign prostatic hyperplasia is on the horizon.

During the past 2 decades, there has been a shift in the management of benign prostatic hyperplasia (BPH) away from surgery and toward earlier medical intervention, but standard treatment with the α_1-adrenergic receptor antagonists and the 5α-reductase inhibitors leaves a significant cohort of nonresponders, Dr. Herbert Lepor said at a meeting on adult and pediatric urology sponsored by New York University.

Among the limitations for α-blockers are safety concerns in patients with low blood pressure and orthostatic hypotension. The α-reductase inhibitors also have a slow onset of action and undesirable side effects, including loss of libido and erectile dysfunction. Moreover, compliance with daily regimens has been low, Dr. Lepor said.

A new approach to the medical management of lower urinary tract symptoms (LUTS) secondary to BPH uses a gonadotropin-releasing hormone (GnRH) antagonist such as cetrorelix. Unlike the GnRH agonists used for prostate cancer, GnRH antagonists lower serum testosterone only partially and in a dose-dependent manner.

The GnRH antagonist is used to reach a level of androgen suppression that will shrink the prostate and improve clinical symptoms without the side effects associated with complete testosterone suppression, said Dr. Lepor, professor and Martin Spatz chairman of the department of urology at the university.

In phase II studies evaluating various doses, regimens, and two different formulations of cetrorelix, statistically significant differences from baseline and compared with placebo were seen on the primary end point of International Prostate Symptom Score (IPSS) at week 12. In one of these trials, 140 patients were randomized to receive cetrorelix acetate in four doses of 5 mg or 10 mg at 7-day intervals, two doses of 10 mg at 14-day intervals, or placebo. Improvements on IPSS of three to four symptom units were already noted at week 4. Mean baseline flow rate was about 9 ng/mL and rose to about 13 ng/mL in those in the active treatment groups.

With regard to prostate size, the results were not significant, although there was a trend to decrease in prostate volume. Testosterone levels during the 4-week injection period showed decreases of about 25%, and returned to baseline after the last injection. There was no effect on erectile function.

A second phase II trial randomized 250 patients to placebo or cetrorelix pamoate in two doses of 30 mg, three doses of 30 mg, one of 60 mg followed by another of 30 mg, or 60 mg followed by 60 mg. Doses were given at 14-day intervals. The results echoed those in the previous trial, with statistically significant dose-related improvements reported on the IPSS and on urinary flow rates, and responses persisting out to 120 days. In none of the groups were castration-level testosterone suppression or associated adverse effects seen.

A phase III study randomizing patients with BPH and voiding symptoms to cetrorelix pamoate is underway. Dr. Lepor disclosed he is a consultant to Æterna Zentaris Inc., the study sponsor. ■

Family History Does Not Predict Outcome From Prostate Cancer

LOS ANGELES — Dad had prostate cancer. So did a brother. Does this mean a worse prognosis for the patient?

To answer this, researchers compared rates of freedom from biochemical failure in a retrospective study of 1,738 men treated with low-dose-rate brachytherapy alone or combined with external beam radiotherapy or hormone ablation. A history of prostate cancer in one or more first-degree relatives did not predict worse biochemical outcomes at 5 years, said Dr. Christopher A. Peters of Mount Sinai School of Medicine, New York, at the annual meeting of the American Society for Therapeutic Radiation and Oncology.

A patient with a family history of prostate cancer won't do any worse because of that history.

DR. PETERS

High-risk men with a positive family history had significantly better biochemical control (94% vs. 80% of men with no family history). In intermediate-risk patients, there was a trend toward better control in those with a positive family history (100% vs. 93%). Low-risk patients with a family history of prostate cancer had an actuarial freedom-from-biochemical-failure rate (95%) similar to those without a family history.

Family history was not a significant predictor, however, when its impact was weighed with that of other factors in a multivariate analysis. The only significant factors affecting prostate-specific antigen (PSA) failure at 5 years were use of hormone therapy, a biologically effective radiation dose >150 Gy, initial PSA level, and Gleason score.

"You can confidently say to the patient, 'You would not do any worse [because] you have your family history,' " Dr. Peters said in an interview.

He and his coauthors identified 2,652 consecutive patients with clinically localized prostate cancer who were treated with low-dose-rate brachytherapy alone or in combination with external beam radiotherapy or hormone ablation from 1992 to 2005. They found family history information for 1,738 of these patients, among whom 187 men (11%) had a first-degree relative with prostate cancer. The minimum follow-up for inclusion in the study was 2 years; median follow-up was 5 years.

Patients with a family history of prostate cancer were younger (median 65 years), compared with those with no history (67 years). Those without a family history also had significantly fewer low-dose implants (2.7% vs. 10.8%). Both findings were statistically significant.

—Jane Salodof MacNeil