Quality of Life Varies for Prostate Ca Treatments

BY SARA FREEMAN

FROM THE BIENNIAL MEETING OF THE EUROPEAN SOCIETY FOR THERAPEUTIC RADIOLOGY AND ONCOLOGY

BARCELONA – The 3-year results of a nonrandomized trial from Spain reveal different patterns of adverse events after three leading treatments for localized prostate cancer.

Radical retropubic prostatectomy (RRP) was associated with significantly more urinary incontinence and sexual dysfunction than were external beam radiotherapy (EBRT) or brachytherapy, according to charts presented at the meeting.

Brachytherapy, however, was associated with far more irritative and obstructive urinary symptoms than were surgery or EBRT.

The trial was conducted in 11 hospitals throughout Spain, and originally enrolled 435 men with stage T1 and T2 prostate cancer who had received no prior surgical resection or hormonal treatment. The aim of the trial was to compare the health-related quality of life (HRQoL) impact of the three treatments.

Treatment decisions were made jointly by physicians and patients; the analysis covered 123 men who had RRP, 127 who had EBRT, and 123 who had brachytherapy.

HRQoL was assessed using validated questionnaires before and at 1, 3, 6, 12, 24, and 36 months after treatment. The questionnaires included the Medical Outcomes Study 36-Item Short Form, the Functional Assessment of Cancer Therapy (General and Prostate Specific), the Expanded Prostate Cancer Index Composite (EPIC), and the American Urological Association Symptom Index.

This study is important because it takes into account the patients' quality of life before they had any treatment, Dr. Ferran Guedea said at a scientific press briefing. Previously published results showed that despite partial recovery from immediate deterioration in HRQoL, relevant differences persisted with 2 years' follow-up (Int. J. Radiat. Oncol. Biol. Phys. 2008; 72:421-32).

The 3-year results also show that in each treatment group, HRQoL deteriorated immediately after treatment but then rose to varying degrees, said Dr. Guedea, a radiation oncologist at the Catalan Institute of Oncology, L'Hospitalet de Llobregat, near Barcelona.

SF-36 Physical Component scores decreased most dramatically after prostatectomy compared with either radiotherapy technique, but rose in the first 6 months after the procedure before gradually deteriorating over the 3-year follow-up.

EBRT produced lower scores than those for brachytherapy, and these gradually worsened during long-term follow-up, such that they were lower at 3 years than were scores in patients who had undergone surgery.

"RRP caused considerable urinary incontinence and sexual dysfunction," Dr. Guedea observed. He added: "Brachytherapy and EBRT caused moderate urinary irritative-obstructive urinary symptoms and moderate adverse effects on sexual function, and finally, EBRT had very moderate bowel-related adverse events." ■

VITALS

Major Finding: Radical retropubic prostatectomy (RRP) was associated with significantly more urinary incontinence and sexual dysfunction than were other treatments.

Data Source: A 3-year follow-up from a Spanish trial comparing health-related quality of life outcomes after primary radical RRP, external beam radiotherapy (EBRT), and interstitial brachytherapy in 435 patients with localized (T1/2) prostate cancer not given hormonal treatment.

Disclosures: The Spanish National Health System funded the study. Dr. Guedea had no conflicts of interest.

Sipuleucel-T Prolonged Survival in Metastatic Prostate Ca

BY MARY ANN MOON

FROM THE NEW ENGLAND JOURNAL OF MEDICINE

The immunotherapy sipuleucel-T significantly prolonged survival in a study of 512 men with metastatic castration-resistant prostate cancer, confirming the results of two smaller previous trials of this therapeutic "cancer vaccine," according to a report.

The experimental treatment increased median survival by 4.1 months and raised the estimated probability of 3-year survival from 23% to 32%, compared with placebo, significant improvements in this population of men with advanced disease, said Dr. Philip W. Kantoff of the Dana-Farber Cancer Institute and Harvard Medical School, Boston, and his coauthors.

As with the previous studies, this trial also showed that sipuleucel-T (Provenge, Dendreon Corp.) did not hinder tumor progression—a paradoxical finding that has yet to be explained, they noted.

Data from the study were pivotal to the Food and Drug Administration's decision earlier this year to approve the immunotherapy for the treatment of asymptomatic or minimally symptomatic castration-resistant prostate cancer.

Dr. Kantoff and his colleagues assessed sipuleucel-T in patients with asymptomatic or minimally symptomatic disease who had an expected survival of at least 6 months. Serum PSA levels were 5 ng/mL or more, and serum testosterone levels were less than 50 ng/dL. All had previous androgen-deprivation therapy.

The subjects were enrolled at 75 medical centers in the United States and Canada, and stratified by Gleason score, number of bone metastases, and bisphosphonate use. They were randomized to receive three 1-hour infusions of active drug (341 patients) or placebo (171 patients) every 2 weeks, completing the course of therapy within 1 month. More than 92% of the subjects received all three infusions. Median follow-up was 34 months.

Mortality was about 62% with active therapy and 71% with placebo, a relative reduction in the risk of death of 22%. Median survival was about 26 months with sipuleucel-T, significantly longer than the 22 months with placebo. Estimated probability of survival at 36 months was about 32% with sipuleucel-T, significantly higher than the 23% with placebo.

These benefits were seen across all subgroups of patients, regardless of their status with respect to adverse factors such as high PSA, lactate dehydrogenase, or alkaline phosphatase levels; a greater number of bone metastases; high Gleason score; poor performance status; and the presence of pain.

However, the median time to disease progression, as measured by CT and bone scanning, was not significantly different between the two study groups, at 14.6 weeks for sipuleucel-T and 14.4 weeks for placebo. The reason for this discrepancy is not yet known, but it might be because of "the delayed onset of antitumor responses after active immunotherapy, relative to objective disease progression, which occurred early in this group of patients," Dr. Kantoff and his associates said (N. Engl. J. Med. 2010;363:411-22).

Sipuleucel-T was generally well tolerated, with only three patients not receiving the entire course of treatment because of infusion-related events. "Adverse events that were more frequently reported for sipuleucel-T than for placebo were generally consistent with the release of cytokines," such as chills, fever, fatigue, nausea, headache, flu-like illness, and myalgia. Most of these developed within 1 day of an infusion and resolved within 1-2 days. One case of bacteremia associated with the catheter infusion was reported.

There was no increase in the rate of cerebrovascular events, as has been reported previously with sipuleucel-T, the investigators noted. ■

VITALS

Major Finding: Risk of death was cut by 23%, median survival was prolonged by 4 months, and estimated 3-year survival was improved by 9% with sipuleucel-T, compared with placebo, in men who had metastatic castration-resistant prostate cancer.

Data Source: A multicenter double-blind randomized clinical trial involving 512 patients.

Disclosures: Dendreon Corp., the maker of sipuleucel-T, sponsored the study, which was designed, conducted, and analyzed by Dendreon employees in collaboration with clinical investigators. Coauthors also reported ties to AstraZeneca, Centocor Ortho Biotech, Celegen, Millenium, Sanofi-Aventis, Novartis, Natrogen Therapeutics, Merck, Pfizer, Johnson & Johnson, Amgen, Ferring, and Endo Pharmaceutical.

VIEW ON THE NEWS

Why No Evidence of Antitumor Effect?

The current study findings raise questions as to why survival improved even though there was no evidence of an antitumor effect.

"It is hard to understand how the natural history of a cancer can be affected without some apparent measurable change in the tumor, either evidence of tumor shrinkage or at least disease stabilization reflected in a delay in tumor progression," said Dr. Dan L. Longo.

"This lack of tumor effect raises concern that the results could have been influenced by an unmeasured prognostic variable that was accidentally imbalanced in study-group assignment," he added.

In the future, researchers may need to account for other factors that have recently been discovered to affect prognosis--such as statin use, duration of the first off-treatment interval, and circulating tumor cells, Dr. Longo said.

He also noted that the high cost of sipuleucel-T therapy may curtail its use.

"The manufacturer has set the cost of a 1-month course of sipuleucel-T at $93,000, or $23,000 per month of survival advantage," he noted.

DAN L. LONGO, M.D., *a deputy editor of the New England Journal of Medicine, is an internist and oncologist at the National Institutes of Health's Biomedical Research Center, Baltimore. These comments are taken from his editorial accompanying Dr. Kantoff's article (N. Engl. J. Med. 2010; 363:479-81).*