Combination Tx Slashes Prostate Cancer Deaths

Interim analysis shows adding radiation to hormone therapy cuts overall risk of death 33%.

BY MICHELE G. SULLIVAN

FROM THE AMERICAN SOCIETY FOR RADIATION ONCOLOGY ANNUAL MEETING

SAN DIEGO – A combination of external-beam radiation and hormone therapy should become the gold-standard treatment for men with locally advanced prostate cancer, if the interim analysis of a large randomized study holds up during its follow-up period.

The study's data safety and monitoring committee recommended releasing the results after an interim analysis found a 43% decrease in the risk of prostate cancer death among the combination group compared with those who received only androgen deprivation, Dr. Malcolm Mason said during a press briefing.

"If the figures from the interim analysis are similar to the final analysis, we would expect a 43% reduction in the chance of death from prostate cancer in men with this [combination regimen]," said Dr. Mason, head of oncology and palliative medicine at Cardiff University, Wales, and the study's primary author.

"This would translate into a reduction in the chances of death from prostate cancers in many thousands of men worldwide," Dr. Mason said.

The study comprised a total of 1,205 men who were treated from 1995 to 2005.

The preplanned interim analysis included data that were collected up through the end of 2008. The median follow-up at that point was 6 years. Final results are expected in either 2011 or 2012, according to Dr. Mason.

Extrapolating the results out to the final 10-year follow-up would give a disease-specific death rate of 15% with the combination regimen and 23% with hormone therapy alone.

The groups were evenly split between the two treatment regimens: 602 men received androgen deprivation therapy only, which consisted of bilateral orchidectomy or lifelong luteinizing hormone–releasing hormone (LHRH) agonist. The remainder of the patients (603 men) had a combination of androgen deprivation therapy and external-beam radiation (65-69 Gy to the prostate and/or seminal vesicles, with or without pelvic nodes).

The majority of the participants had T3 or T4 cancer (1,057); 119 had T2 cancer with a prostate-specific antigen level of more than 40 mcg/L; and the rest had T2 cancer with a lower PSA level (more than 20 mcg/L) and a Gleason score of 8 or higher.

None of the patients in the study had metastatic disease.

The primary end point was overall survival. Secondary end points were disease-specific survival, time to progression, and quality of life.

At the time of the interim data analysis, full follow-up information was available on 90% of the patients. At that time, 320 (26.5%) had died from any cause: 175 in the hormone therapy–only group (55%) and 145 in the combination therapy group (45%). The addition of radiation therapy to hormone therapy resulted in a significant 33% decrease in the overall risk of death (hazard ratio 0.77, $P = .033$).

Deaths from prostate cancer and/or treatment numbered 140: 89 (63.5%) in the hormone therapy–only group and 51 (36%) in the combination therapy group.

This translated to a significant 43% reduction in the risk of dying from prostate cancer (HR 0.57, $P = .001$).

Extrapolating these data out to the final 10-year follow-up point, the researchers predicted that the rate of disease-specific death would be 15% with a combination of hormone therapy and radiation therapy and 23% with hormone therapy alone – again a statistically significant difference.

Toxicity rates of grade 2 or higher and gastrointestinal toxicity were similar in both arms of the study, with proctitis occurring in 1% of the hormone therapy group and 2% of the combination therapy group.

"In addition to the significantly decreased risk of dying from prostate cancer, the toxicity was not a major issue," Dr. Mason observed during the press briefing.

"For both of these reasons, we feel that these results are practice changing, and that the treatment standard for men with high-risk prostate cancer who are fit to undergo radiation therapy should be a combination of hormone therapy and radiation therapy," according to Dr. Mason. ■

VITALS

Major Finding: Compared with hormone therapy alone, a combination of androgen deprivation and pelvic radiation significantly reduced the chance of prostate cancer death by 43% in men with locally advanced disease.

Data Source: A randomized phase III trial in 1,205 patients, 6 years after treatment,

Disclosures: The trial was sponsored by the National Cancer Institute of Canada's Clinical Trials Group, the U.K. Medical Research Council, and the Southwest Oncology Group in the United States. Dr. Mason reported no financial disclosures with regard to the trial. One of the coauthors (Matthew Sydes) is an employee of the U.K. Medical Research Council.

Androgen Deprivation Use Paralleled Reimbursement Trends

BY MARY ANN MOON

FROM THE NEW ENGLAND JOURNAL OF MEDICINE

For men with prostate cancer, use of gonadotropin-releasing hormone agonists rose dramatically in the 1990s, when Medicare reimbursement for the drugs was highly profitable for physicians, and dropped just as dramatically after 2004, when reimbursement was drastically lowered, according to an analysis of Medicare data.

The recent reductions in use were most profound among patients for whom the drugs were probably not beneficial and therefore inappropriate. In contrast, among the types of patients for whom the GnRH agonists' benefit has been established, use did not change with reimbursement level, said Dr. Vahakn B. Shahinian of the University of Michigan, Ann Arbor, and his associates.

"Our findings suggest that reductions in reimbursement may influence the delivery of care in a potentially beneficial way, with even the modest changes in 2004 [in reimbursement policy] associated with a substantial decrease in the use of inappropriate therapy," they noted.

The investigators used data from the Surveillance, Epidemiology, and End Results (SEER) Medicare database on older cancer patients to test their hypothesis that, given the 50% cut over 2 years in reimbursement to physicians administering the GnRH agonists, the use of the androgen deprivation therapy "would decline markedly for indications for which there was limited evidence of efficacy" but would continue to be used for truly evidence-based indications.

The researchers categorized the use of androgen-deprivation therapy in 54,925 prostate cancer patients seen from 1994 through 2005 as inappropriate, appropriate, or discretionary – the last category being for therapy of uncertain benefit because of insufficient evidence or because reasonable alternatives were available.

VITALS

Major Finding: The use of GnRH agonists as androgen deprivation therapy for prostate cancer rose dramatically from the 1990s until 2004, an interval in which Medicare reimbursement for the drugs was profitable for physicians. It then declined markedly in 2004 and 2005, when the government's reimbursement policy was changed and use of the drugs was no longer as profitable.

Data Source: A cohort study using data on 54,925 patients with prostate cancer who were enrolled in the SEER database 1994-2005.

Disclosures: This study was funded by the American Cancer Society. Dr. Shahinian reported working as a consultant to Amgen.

"Reimbursement for GnRH agonists per monthly dose fell from $356 in 2003 to $311 in 2004 and to $176 in 2005," Dr. Shahinian and colleagues noted.

The rate of inappropriate use of the drugs increased steadily from 30% in 1994 to a peak of 45% in 2002, then dropped precipitously, according to the analysis. "In the inappropriate-use group, there was a dramatic drop in rates … from 39% in the fourth quarter of 2003 to 30% in the first quarter of 2004, with a continued decline to 22% by the end of 2005," the researchers said (N. Engl. J. Med. 2010;363:1822-32).

In the discretionary-use group, the rate of use also was highest in 2003, "gradually declined in 2004, and dropped more markedly in 2005," they added. Rates of use did not decline in the appropriate-use group.

"These findings are consistent with previous research on the influence of financial incentives on the delivery of health care," the investigators said, adding that "Financial incentives are most likely to have an effect on physicians' behavior in cases in which medical uncertainty exists, as opposed to cases in which care is clearly lifesaving."

The authors acknowledged that a guideline change by American Society of Clinical Oncology in 2004 may have influenced physicians to reach for GnRH for localized high-risk disease.

Additionally, it is possible that increasing recognition of the adverse effects of androgen-deprivation therapy may have contributed to some of the reductions in use of the drugs.

One major study published in 2005 demonstrated a link between the treatment and fracture risk. Since the changes in reimbursement policy roughly coincided with this publication, "it is difficult to separate out the contributions of these influences," the researchers noted.

The corollary to their findings is that reimbursement policies should be carefully crafted to avoid inadvertently providing incentives for care for which no clear benefit has been established, they added. ■