Intermittent hormone therapy for prostate cancer inferior to continuous therapy

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Many men with metastatic, hormone-sensitive prostate cancer live longer on continuous androgen-deprivation therapy (also known as hormone therapy) than on intermittent therapy, according to a seventeen-year study led by SWOG, a cancer research cooperative group funded by the National Cancer Institute (NCI).

Men with newly diagnosed metastatic prostate cancer are usually either surgically castrated or given medications to suppress the production of male hormones that drive their cancer. The treatment can help keep the disease at bay temporarily, but in the majority of patients the cancer will relapse and contribute to the patient's death.

Surgical castration is permanent but "medical castration" provides men the potential advantage of receiving therapy intermittently. A halt in this therapy is followed in time by a rise in testosterone levels. Scientific data suggested that intermittent treatment may delay the cancer relapse, and that the rise in testosterone may result in an improvement in the patient's quality of life.

These data provided the rationale for the phase III clinical trial SWOG-9346, the largest such study to date in men with metastatic, hormone-sensitive disease. Results of this study demonstrate that intermittent androgen-deprivation (AD) therapy is not as good as continuous hormone therapy with regard to patient longevity.

The findings are to be presented today at the plenary session of the American Society for Clinical Oncology's (ASCO's) annual meeting by the study's principal investigator, Maha Hussain, M.D., F.A.C.P., of the University of Michigan Comprehensive Cancer Center.

"Based on these results," Hussain says, "we can conclude that intermittent AD is not as effective as continuous AD in men with metastatic prostate cancer."

Clinical researchers from the SWOG network, with funding from the NCI, led an international team in conducting the study at more than 500 sites, enrolling 3,040 men with hormone-sensitive, metastatic prostate cancer between 1995 and 2008.

All men got an initial course of androgen-deprivation treatment for seven months. The 1,535 eligible men whose prostate-specific antigen (PSA) level dropped to 4 ng/mL or less by the end of those seven months were then assigned at random to stop therapy (the intermittent therapy group) or continue therapy (the continuous therapy group).

Those randomized to the intermittent therapy arm had their treatment suspended until their PSA rose to a predetermined level, at which time they started another seven-month course of androgen-deprivation therapy, cycling on and off therapy in this way as long as their PSA levels continued to respond appropriately during the "on" cycle.

Men on continuous therapy had a median overall survival time of 5.8 years from the time of randomization, with 29 percent of these men surviving at least 10 years. Those on intermittent therapy had a median overall survival time of 5.1 years, with 23 percent surviving at least 10 years from the time they were randomly assigned to a treatment arm.

The researchers found, in additional analyses, that men with "minimal disease" (disease that had not spread beyond the lymph nodes or the bones of the spine or pelvis) did significantly better on continuous therapy, while men with "extensive disease" (disease that had spread beyond the spine, pelvis, and lymph nodes or to the lungs or liver) seemed to do about as well using either treatment approach.

Additional analyses indicated that the median overall survival time for those with minimal disease was 7.1 years on continuous androgen-deprivation therapy compared to only 5.2 years on intermittent treatment. Patients with extensive disease had median overall survival times of 4.4 years on continuous therapy and 5.0 years on intermittent therapy.

"In the past when it came to using hormone therapy in this disease, doctors viewed the disease as one entity and adopted a 'one size fits all' approach," Hussain says. "Based on this study's findings, it seems that one size does not necessarily fit all."

Trial researchers also compared quality-of-life measures across the two study arms during the first 15 months following patient randomization, including measures of sexual function (impotence and libido), physical and emotional function, and energy level. They found improved sexual function in men who received intermittent therapy as compared to those on continuous therapy. A second presentation at an ASCO Poster Discussion session (morning of June 4th, Poster #25) reports on these preliminary quality-of-life findings from SWOG-9346 (Abstract #4571, CM Moinpour, DL Berry, et al).

"Though we see potential quality-of-life benefits with IAD," Hussain says, "from a medical perspective, the primary findings of the study demonstrating that IAD is inferior with regard to overall survival should be the primary consideration in counseling all patients who are interested in intermittent therapy and particularly those with minimal disease."

In brief: 1,535 men with metastatic, hormone-sensitive prostate cancer were randomized to intermittent androgen-deprivation (AD) therapy or continuous AD therapy after seven months of androgen deprivation.

- When overall survival times were compared, intermittent AD was inferior to continuous AD.
- For the subset of patients with minimal disease, continuous AD was superior to intermittent AD.
- For patients with extensive disease, overall survival was comparable between intermittent and continuous AD.
- A number of quality-of-life measures got higher scores in the intermittent AD arm than the continuous AD arm.

Prostate cancer statistics: More than 240,000 men in the United States will be diagnosed with prostate cancer in 2012, according to the American Cancer Society, and more than 28,000 will die of the disease.

More information: Reference: Hussain, M et al, "Intermittent (IAD) vs Continuous Androgen Deprivation (CAD) in Hormone Sensitive Metastatic Prostate Cancer (HSM1PC) Patients (pts): Results of S9346 (INT-0162) an International Phase III Trial." American Society of Clinical Oncology Annual Meeting, June 1-5, 2012, Chicago, abstract No. 4.

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