
EDITORIAL

Teaching Old Prostate Drugs New Tricks In the Battle Against Prostate Cancer

It was my good fortune to serve as Chair Elect of the February 2011 ASCO Genitourinary Cancer Symposium in Orlando. This annual meeting features the latest developments in the world of urologic oncology. Much of this multidisciplinary program is dedicated to the most common solid tumor in men, namely prostate cancer. A major international meeting of this caliber is expected to focus on the most cutting edge research and drug discoveries and it always fulfills that mission. What I found fascinating is that several major clinical trials presented were based on modified uses of older and familiar prostate drugs and the results were very encouraging.

In the management of advanced prostate cancer, continuous androgen ablation to reduce serum testosterone levels is considered the gold standard. While bilateral orchiectomy is occasionally used, most men today achieve a reduction in testosterone levels through the use of LHRH analogues. Leuprolide was the first approved LHRH analogue in the United States in the mid 1980's. Today there are several other LHRH analogues and a new LHRH antagonist available for use in advanced prostate cancer. While approved for continuous use, concerns over a negative impact on quality of life has called this practice into question. The concept of intermittent androgen suppression (sometimes called "hormone holidays" in the lay press) has been reported in numerous preliminary studies to improve quality of life in men while off LHRH analogue therapy. However, concerns exist that survival may not be as good with intermittent hormonal therapy. A phase III randomized trial comparing intermittent versus continuous androgen suppression for patients with PSA progression after radical therapy demonstrated no significant difference in overall survival when comparing the two regimens but improved quality of life when off hormonal therapy.

Bicalutamide is an oral non-steroidal anti-androgen approved in the mid 1990's. It has been used in combination with LHRH analogues for short and long term total androgen blockade. In some countries it is used as a monotherapy for prostate cancer. At this meeting, the initial report of RTOG 9601 was presented. This trial studied the effect of anti-androgen therapy with bicalutamide during and after radiation therapy. With 7 years of follow up, 2 years of anti-androgen monotherapy with bicalutamide during and after radiation therapy to the prostate significantly reduced biochemical recurrence, and the incidence of metastases.

Dutasteride was made available in the US about 7 years ago. It is a 5-alpha reductase inhibitor that reduces intracellular levels of dihydrotestosterone and has been approved as a therapy for symptomatic prostatic hypertrophy. The REDEEM trial included men with low risk disease who were eligible for active surveillance. In this placebo controlled trial, dutasteride delayed the time to prostate cancer progression, increased the number of men with undetectable prostate cancer and perhaps more importantly, the dutasteride treated group showed no evidence of increased Gleason score upgrading. This trial suggests that dutasteride, a benign prostatic hypertrophy medication, may be a useful adjunct to active surveillance. Active surveillance is a growing option for many men with prostate cancer.

In 1941, Charles Huggins and Clarence Hodges provided the first clinical evidence that in men with symptomatic, metastatic prostate cancer that there was a benefit to hormonal therapy. In their pioneering study, bilateral orchiectomy and estrogens proved beneficial. (What is not often discussed is that they also studied the injection of testosterone and noted that it "activated" prostate cancer). This sentinel work was awarded a Nobel prize in medicine in 1966. Many years after their first report, hormonal therapy, either by the reduction in serum testosterone levels or other interference with the androgen pathways, remains the cornerstone of therapy in advanced prostate cancer. The LHRH analogues, bicalutamide, and dutasteride are well established agents with defined FDA indications for either benign or malignant diseases of the prostate. Some type of hormonal mechanism of action is central to all these drugs.

Over the last 60 years, the concept of hormonal manipulation as an effective means to treat prostate cancer remains at the forefront of standard care. These latest 2011 clinical studies show us how we can teach these old prostate drugs new tricks to improve the outcomes of men with varying stages of prostate cancer.

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