PROSTATE CANCER

Hormone therapy dosing regimen affects development of castration resistance

Testosterone-based (T-based) dosing of hormone therapy is associated with a lower risk of developing castration resistance than a calender-based schedule, according to a study published in the February issue of *Urology*. "Patients in the T-based group had a 35% lower rate of treatment failure than those receiving calender-based dosing" says Jeremy Blumberg, lead author of the study.

Although androgen suppression using luteinizing hormone releasing hormone (LHRH) agonists is one of the main treatment options for patients with prostate cancer, the most appropriate dosing regimen is unclear. Traditionally, a calender-based schedule has been used, whereby patients receive LHRH agonist at regular intervals estimated to provide continuous androgen suppression. In T-based dosing, LHRH agonist is administered only when serum testosterone increases above a certain threshold. Alternatively, an intermittent regimen has been suggested, whereby dosing is triggered when PSA level rises.

Researchers identified 692 men in the Kaiser Permanente Southern California Cancer Registry who received LHRH agonist therapy as primary treatment between 2003 and 2006. 325 patients had received a calender-based dose every 3 months, 252 men were re-dosed whenever their serum testosterone rose above 50 ng/dl, and 115 were classified as receiving intermittent dosing, although the PSA level at which treatment was instigated was at the discretion of the attending clinician. All patients received 22.5 mg leuprolide acetate each dose, and had their PSA measured every 3 months.

Men who received T-based dosing were at a significantly lower risk of treatment failure (defined as two consecutive increases in PSA level after the last dose of LHRH agonist without a decrease in any subsequent PSA measurement) than those in the calender-based group (hazard ratio = 0.65; $P = 0.02$). Intermittent dosing was associated with a slightly lower risk of developing castration resistance than a calender-based schedule, but it was not statistically significant (hazard ratio = 0.80; $P = 0.30$).

Having used T-based dosing to treat his patients for many years, Blumberg highlights the economic benefits. "Most patients don't require re-dosing for at least 6 months and in many cases longer—this has amounted to tremendous cost-savings, in the order of millions of dollars."

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Original article Blumberg, J. M. *et al*. Early development of castrate resistance varies with different dosing regimens of luteinizing hormone releasing hormone agonist in primary hormonal therapy for prostate cancer. *Urology* **77**, 412–416 (2011)