

PROSTATE CANCER

## Dutasteride improves accuracy of diagnosis but may not prevent cancer development

New analyses have been published of data from two large studies of the effect of the 5 $\alpha$ -reductase inhibitor, dutasteride, on prostate cancer development and diagnosis. The REDUCE and CombAT trials investigated the impact of dutasteride on PSA measurements and biopsy rates, respectively.

For the multicenter, double-blind, placebo-controlled REDUCE trial, patients were followed for 4 years, with PSA measurements every 6 months and biopsies performed at 2 and 4 years. Serum PSA concentrations increased between month 6 and study end in 72% of men in the placebo group, compared to only 29% of those in the dutasteride group.

Prostate cancer was more likely to be detected by biopsy in those participants receiving dutasteride who had a PSA increase, compared to those taking dutasteride whose PSA did not rise, and the tumor discovered was likely to be of a higher grade. This suggests that dutasteride improves the diagnostic accuracy of PSA, especially for high-grade cancers.

“Since 5 $\alpha$ -reductase inhibitors like dutasteride can suppress PSA production from BPH and some low grade cancers,

they [therefore] make PSA a better marker for aggressive cancers,” remarks lead author Gerald Andriole, from the Washington University School of Medicine. “A rising PSA in a man receiving one of these drugs is a very strong signal that he is developing an aggressive cancer. By comparison, untreated men often have rising PSA levels (usually due to their growing BPH).”

Similar results were gleaned from the CombAT study, during which the effect of dutasteride alone or in combination with the  $\alpha$ -blocker tamsulosin was assessed. The 4,800 enrollees were also followed for 4 years, with PSA measured annually, and biopsy only carried out if clinically indicated. Dutasteride alone or in combination was associated with a 40% reduction in the relative risk of prostate cancer diagnosis, compared to tamsulosin monotherapy. This probably reflects the 40% reduction in the likelihood of biopsy in these patients.

Despite these positive findings, on 1 December 2010 the FDA turned down an application to extend the license of dutasteride to include use for prostate cancer prevention. The regulator believes that the results may be evidence of an



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increased risk of developing aggressive cancer in men on the drug, and not just a greater chance of diagnosing it. Approval of an agent capable of preventing prostate cancer thus remains elusive.

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**Original articles** Roehrborn, C. G. *et al.* Effect of dutasteride on prostate biopsy rates and the diagnosis of prostate cancer in men with lower urinary tract symptoms and enlarged prostates in the Combination of Avodart and Tamsulosin trial. *Eur. Urol.* doi:10.1016/j.eururo.2010.10.040 | Andriole, G. L. *et al.* The effect of dutasteride on the usefulness of prostate specific antigen for the diagnosis of high grade and clinically relevant prostate cancer in men with a previous negative biopsy: results from the REDUCE trial. *J. Urol.* **185**, 126–131 (2011)