Re: Association of Treatment with 5α-Reductase inhibitors with Time to Diagnosis and Mortality in Prostate Cancer

Sarkar RR, Parsons JK, Bryant AK, et al

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Expert's summary:
In this population-based cohort study of 80 875 patients with prostate cancer from the Veterans Affairs Health Care System, 8587 (10.6%) were taking 5α-reductase inhibitors (5-ARIs) at the time of diagnosis [1]. Compared to non-users, 5α-ARI users had longer delays from first elevated prostate-specific antigen (PSA; corrected for the effect of the drug) to prostate biopsy, presented with more high-grade, lymph node–positive metastatic disease, and had worse prostate cancer–specific and all-cause mortality. 5-ARI use was associated with delayed prostate cancer diagnosis and greater mortality among men who underwent PSA screening.

Expert's comments:
We are told that 5-ARIs prevent prostate cancer and do not increase the risk of high-grade disease [2]. If this were true, why did the men in this study who were treated with 5-ARIs develop high-grade, lethal disease? Sadly, this is because we have not been told the full truth. There is no 5α-reductase enzyme in normal or malignant prostatic epithelial cells; it is located in the stroma. Because higher-grade cancers (Gleason >6) have little stroma, 5-ARIs have no effect in reducing Gleason 7–10 disease. 5-ARI treatment reduces the production of PSA by the stroma in benign prostatic hyperplasia. To correct for this effect, men treated with a 5-ARI must multiply their level by 2.0 for the first 2 yr, by 2.3 for years 2–7, and by 2.5 after year 7 [3]. If patients do not know this, they will not realize they may need a biopsy and might miss the opportunity of being diagnosed with curable disease. This explains the findings in this study.

In the original publication from the Prostate Cancer Prevention Trial, which was a randomized, placebo-controlled trial evaluating finasteride for the prevention of prostate cancer, the authors reported a 25% reduction in prostate cancer prevalence and a 68% increase in high-grade disease [2]. Although the authors have argued that the increase in high-grade disease was an artifact, in 2011 the US Food and Drug Administration reported on their independent reanalysis of the study and found that the original published article was severely flawed [4]. They concluded that in the clinical setting, if 150–200 men were treated with a 5-ARI, there would be a reduction in only three to four Gleason 6 cancers, no reduction in Gleason 7, and an increase in one new case of Gleason 8–10 disease. Sarkar et al [1] suggest that their results "include the possibility that 5-ARIs inherently increase the risk of high-grade cancer".

When I first prescribe 5-ARIs, I explain to patients the importance of having their PSA measured regularly for as long as they are taking the drug. I tell them why they need to know those numbers and if their PSA ever increases they need a biopsy. In patients taking a 5-ARI, PSA levels should continue to go down for as long as they are taking them. If their PSA ever goes up at all, the risk of cancer is increased by a factor of three and the risk of high-grade disease by a factor of six [5]. Urologists need to know the full truth about drugs that have lethal potential.

Conflicts of interest: The author has nothing to disclose.

References

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Re: Detection of Individual Prostate Cancer Foci via Multiparametric Magnetic Resonance Imaging

Johnson DC, Raman SS, Mirak SA, et al

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Experts' summary:
The authors performed a retrospective analysis of 588 patients with 1213 pathologically confirmed tumour foci, with lesion-specific results from multi-parametric magnetic resonance imaging (mpMRI) co-registered with whole-mount pathology (WMP) prostatectomy specimens. The primary objective was to determine the per-lesion detection rate for prostate cancer (CaP) foci by mpMRI.

mpMRI demonstrated sensitivity of 45% for all CaP, and 65% for clinically significant CaP (csCaP). Multifocality was associated with a higher risk of missing CaP foci, with at least one csCaP focus missed by mpMRI in almost 50% of patients.