Nature Reviews Urology **10**, 679 (2013); published online 19 November 2013; doi:10.1038/nrurol.2013.268

PROSTATE CANCER

Cardiovascular morbidity risk lower for ADT with GnRH antagonists than GnRH agonists

For men with prostate cancer and pre-existing cardiovascular disease, androgen deprivation therapy (ADT) with gonadotropin-releasing hormone (GnRH) antagonists results in half as many cardiac events—defined as arterial embolic or thrombotic events, haemorrhagic or ischaemic cerebrovascular conditions, myocardial infarction, and other ischaemic heart disease—as treatment with GnRH agonists, according to pooled data from six phase III prospective randomized trials of 2,328 men.

For men without pre-existing cardiovascular disease, treatment with a GnRH agonist was no different to a GnRH antagonist in terms of the incidence of cardiac events or death from any other cause. However, for men with pre-existing cardiovascular disease, significantly fewer (8% versus 11.8%) cardiac events were experienced by patients receiving a GnRH antagonist (degarelix; $n = 1{,}491$) compared with a GnRH agonist (leuprolide or goserelin; $n = 837$). The absolute risk reduction during the first year of treatment was 3.8% for these men, with a number needed to treat of 26.

> “We were surprised to see a difference between GnRH agonists and antagonists”

In their discussion of the study, the authors hypothesize that ADT with GnRH agonists increases the risk of atherosclerotic plaque rupture by destabilizing established vascular lesions via T-cell activation. GnRH antagonists suppress both luteinizing hormone and follicle-stimulating hormone (FSH), whereas GnRH agonists primarily suppress luteinizing hormone. As FSH receptors are thought to have a role in endothelial cell function, lipid metabolism, and fat accumulation, this difference in hormone activity could perhaps explain the reduced cardiovascular risk in men receiving GnRH antagonists compared with GnRH agonists.

“The study was primarily a hypothesis-generating idea,” explains Peter Albertsen, lead author of the study. “We were surprised to see a difference between GnRH agonists and antagonists. As the finding only occurred in men with pre-existing cardiac disease, we are looking at mechanisms of plaque formation and destabilization.” Studies of animal models and further randomized clinical trials are needed to validate these findings.

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Original article Albertsen, P. C. *et al.* Cardiovascular morbidity associated with gonadotropin releasing hormone agonists and an antagonist. *J. Urol.* doi:10.1016/j.eururo.2013.10.032