

June 16th, 2017

Response to letter to Re: Androgen deprivation therapy and cardiovascular risk: No meaningful difference between GnRH antagonist and agonists.

To The Editor:

We thank Professor Albertsen for his interest to our study.

We do acknowledge that pre-existing cardiovascular events were assessed on a look-back period of 6 months before starting ADT and we observed few events. As regards history of cardiovascular disease, difference in events definition and timing did not allow any fair comparison between our population-based study and the trials meta-analysed by Albertsen et al. [1] However, as regards cardiovascular risk factors (diabetes mellitus, hypertension, lipid-lowering drug use), results were more consistent.

His meta-analysis raised the hypothesis that GnRH antagonists may lower cardiovascular events or death from any cause when compared with agonists predominantly in men with pre-existing cardiovascular disease (around on third of the population) but a significant result was also found in the whole population. In that latter instance, our results were not in line. Notwithstanding a different composite outcome (more focused), we observed a non-significant result with a large confidence interval, reflecting a lack of power (HR = 1.2; 95%CI, 0.7 to 2.1). However, under the assumption of an unbiased analysis, true hazard ratio is almost surely not below 0.7 and could even reach 2.1. Whatever the interpretation we may choose, this is not in line with the hypothesis of a clinical meaningful protective effect of GnRH antagonists.

Sincerely,

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[1] Albertsen PC, Klotz L, Tombal B, Grady J, Olesen TK, Nilsson J. Cardiovascular morbidity associated with gonadotropin releasing hormone agonists and an antagonist. *European urology*. 2014;65(3):565-73.