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PROSTATE CANCER

# Tipping the balance in favour of degarelix for ADT

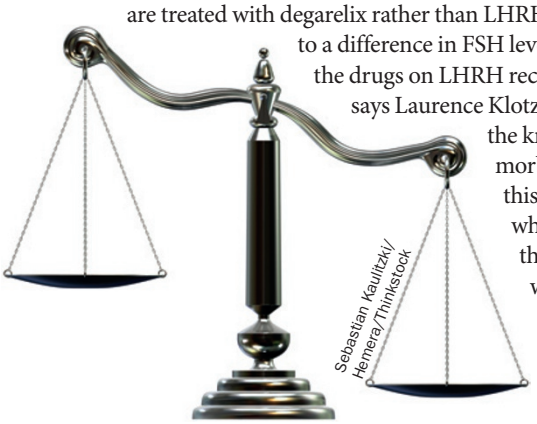
Pooled data from five phase III studies of men with prostate cancer ($n = 1,925$) confirm that androgen deprivation therapy (ADT) with degarelix, a gonadotropin-releasing hormone antagonist, offers superior overall survival and fewer joint-related, musculoskeletal, and urinary tract complications compared with luteinising hormone-releasing hormone (LHRH) agonists, such as leuprolide and goserelin.

Patients in these studies received either 3 months ($n = 67$) or 12 months ($n = 1,458$) of treatment with either degarelix ($n = 1,266$), leuprolide ($n = 201$), or goserelin ($n = 58$). Median follow-up duration was 364 days (ranging from 116–364 days), and was equivalent for the two treatment groups. The mortality rate was threefold greater in the LHRH agonist group (3%; 19 deaths) than in the degarelix group (1%; 18 deaths). However, only a small proportion of these deaths were related to prostate cancer—three in the degarelix group and one in the LHRH agonist group. Approximately half of all deaths in each group were caused by cardiovascular events—including heart failure, cardiac arrest, coronary artery disease, myocardial infarction, and sudden cardiac death—in men with pre-existing cardiovascular disease, suggesting that these men are much more likely to experience fatal cardiovascular complications if they are given LHRH agonists instead of degarelix.

Although adverse events were more commonly reported in men receiving degarelix compared with LHRH agonists (74% and 68%, respectively), this difference can be largely attributed to a greater incidence of injection-site reactions in men treated with degarelix (30% versus <1%). By contrast, rates of joint-related signs and symptoms (mostly arthralgia; 4% versus 5%), musculoskeletal events (8% versus 12%), and urinary tract events (12% versus 18%) were significantly lower in men who received degarelix than in those taking leuprolide or goserelin.

These differences can potentially be explained by the fact that degarelix has a distinct mode of action to LHRH agonists; degarelix causes rapid and sustained testosterone suppression, whereas LHRH agonists trigger an initial testosterone surge that can actually stimulate prostate cancer growth. Furthermore, degarelix offers greater follicle-stimulating hormone (FSH) suppression than LHRH agonists, with implications for tumour growth, bone resorption, and adipocyte regulation.

"The evidence suggests that men with pre-existing cardiovascular disease have a significantly lower risk of subsequent cardiovascular events when they are treated with degarelix rather than LHRH agonists, potentially owing to a difference in FSH levels or to differential effects of the drugs on LHRH receptors in inflammatory cells," says Laurence Klotz, who led the study. "Given the known risk of cardiovascular morbidity in this group of men, this result holds appealing benefit, which must be weighed against the need for monthly injections with degarelix (versus every 3–6 months for the agonists) and patient preference."



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*Melanie Clyne*

**Original article** Klotz, L. *et al.* Disease control outcomes from analysis of pooled individual patient data from five comparative randomised clinical trials of degarelix versus luteinising hormone-releasing hormone agonists. *Eur. Urol.* doi:10.1016/j.eururo.2013.12.063