Prostate cancer drug reduces testosterone levels in as little as 3 days

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More than 95 per cent of men who took degarelix for prostate cancer saw their testosterone levels fall dramatically as early as three days after they started treatment, according to a paper in the December issue of *BJU International*.

They also experienced much greater falls in their prostate-specific antigen (PSA) levels at 14 and 28 days than men taking leuprolide.

Researchers from Canada, the USA, France, Denmark and the Netherlands studied 610 men as part of the Phase Three trial, randomly assigning them to one of three study groups.

"Androgen deprivation hormone therapy is an effective response to prostate cancer, but the drugs that are most widely used cause an initial rise in testosterone - the hormone we are trying to reduce - when the patient first takes them" explains lead author Dr Laurence Klotz from the Division of Urology at the University of Toronto, Canada.

"We prefer to avoid this biochemical surge as it can stimulate the prostate cancer cells and exacerbate a number of clinical symptoms, such as spinal cord compression and bone pain. It could also result in more rapid growth of microscopic disease that is present in the patient but is too small to be detected.

"Degarelix is a new gonadotrophin-releasing hormone (GnRH) antagonist. It works by binding to, and blocking, the GnRH receptors in

the pituitary gland, reducing the amount of LH and FSH hormones that are released. This leads directly to a rapid fall in testosterone."

Group one (207 patients) received an injection of 240mg of degarelix in month one, followed by a maintenance dose of 80mg every month for eleven months and group two (202 patients) received 240mg of degarelix in month one followed by a maintenance dose of 160mg for eleven months.

The third group (201 patients) received a monthly 7.5mg dose of leuprolide, which is a GnRH agonist.

At the start of the trial the study participants had a median testosterone level of 3.93 ng/mL. The aim was to reduce this to 0.5ng/mL or less at all monthly measurements from day 28 to day 364.

Eight out of ten study participants completed the trial (504 patients) between February 2006 and October 2007, with similar drop-out and exclusion rates in all three groups.

The key findings were impressive:

Three days after starting their treatment regimes, 96.1 per cent of the patients on 240/80mg degarelix and 95.5 per cent of the patients on 240/160mg degarelix had achieved a testosterone level of 0.5ng/mL or less. In contrast, median testosterone levels in the leuprolide group had increased by 65 per cent by day three, but had reduced by day 28.

At the end of the study period, 98.3 per cent of the 240/160mg degarelix group and 97.2 per cent of the 240/80mg degarelix group had achieved a testosterone level of 0.5ng/mL or less. The figure for the leuprolide group was 96.4 per cent.

PSA levels fell much faster in the degarelix groups when measured at 14 and 28 days – by 64 per cent and 85 per cent in the degarelix 240/80mg group, 65 per cent and 83 per cent in the 240/160mg degarelix group and 18 per cent and 68 per cent in the leuprolide group.

The hormonal side-effects experienced by the three treatment groups were similar to previously reported effects for androgen deprivation hormone therapy.

Patients receiving degarelix were much more likely to experience injection-site reactions than those receiving leuprolide (40 per cent compared to one per cent).

However degarelix patients suffered fewer urinary tract infections than those in the leuprolide group (three per cent versus nine per cent) together with fewer joint pains and chills (four per cent versus nine per cent).

"More than 2,000 patients have now taken part in clinical trials for degarelix and there have been no signs of immediate or late-onset systemic allergic reactions, in contrast to other reported trials of other GnRH antagonists" points out Dr Klotz.

"The aim of the study was to show that degarelix was not inferior to leuprolide when it came to maintaining low testosterone levels over a one-year treatment period. We have conclusively shown that this is the case.

"However, we have also demonstrated that degarelix - which is an antagonist - offers an advantage, in that it reduces testosterone and PSA levels very quickly. It doesn't cause the initial surge of testosterone seen with agonist drugs like leuprolide - the other drug featured in this study.

"This is relevant as biochemical surges in testosterone can stimulate the

prostate cancer cells and cause unpleasant side effects for patients. They may also require further drug therapy to counteract the effects of agonist drugs like leuprolide."

Source: Wiley