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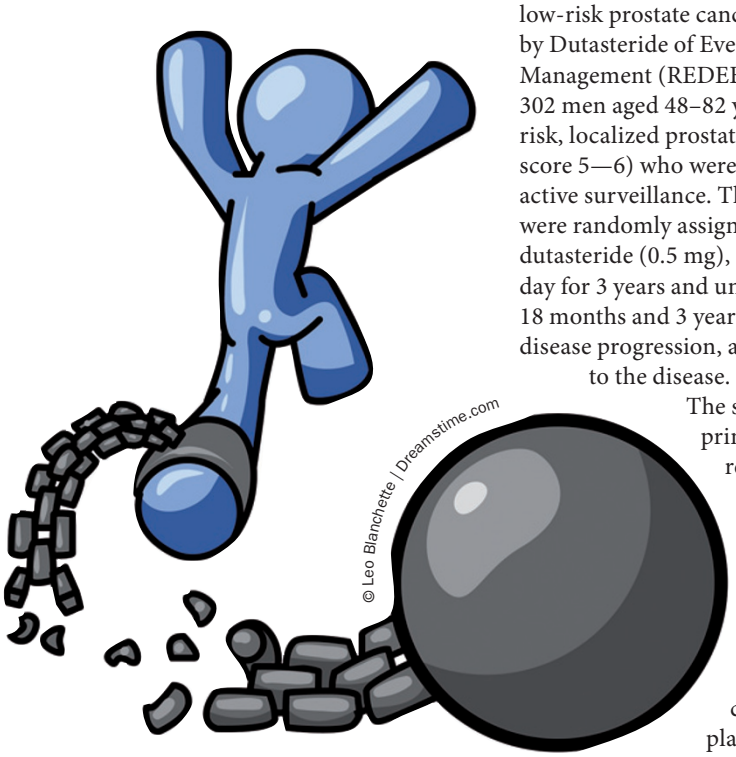
UROLOGICAL CANCER

# Are we redeemed from aggressive treatment for prostate cancer?

Although prostate cancer is a slow progressing disease for which life expectancy is much higher than in other types of cancer, 3% of men diagnosed with this malignancy still die from it, which translates into approximately 10,000 deaths from prostate cancer every year in the UK alone. Treatment for prostate cancer is often aggressive and involves prostatectomy and radiotherapy, so it is very important to assess whether treatment is really needed or if the disease is not progressing quickly and the patient could be spared the consequences of these therapies. To that end, watchful waiting as a form of active surveillance has been implemented as common practice in men with low-risk prostate cancer (Gleason score of <6 and prostate-specific antigen [PSA] concentration of less than 10 ng/ml), so that they can decide whether or not they want to be treated. However, some long-term studies have shown that radical prostatectomy carried out at this stage still saves more lives than watchful waiting. So the question remains, is there a way to improve watchful waiting to help stop prostate cancer from progressing?




Dutasteride is a 5-α-reductase inhibitor that blocks the conversion of testosterone to dihydrotestosterone. Because it leads to a reduction of the prostate volume and a decrease in levels of PSA, dutasteride was approved by the FDA in 2010 for treatment of benign prostatic hyperplasia in men with an enlarged prostate.

Encouraged by the results of a previous study that had assessed the effects of dutasteride in reducing prostate cancer events (REDUCE), Neil Fleshner and colleagues sought to investigate whether dutasteride could decrease the rate of prostate cancer progression in men with low-risk prostate cancer. The Reduction by Dutasteride of Events in Expectant Management (REDEEM) study included 302 men aged 48–82 years with low-risk, localized prostate cancer (Gleason score 5—6) who were undergoing active surveillance. The participants were randomly assigned to receive dutasteride (0.5 mg), or placebo, once a day for 3 years and underwent biopsies at 18 months and 3 years to measure time to disease progression, and anxiety related to the disease.

The study met its primary end point, reduction of risk of pathological or therapeutic progression, as dutasteride significantly delayed prostate cancer progression compared with placebo. After 18 months of treatment, 32 (23%) of the 144 men in the dutasteride group had disease progression compared with 50 (35%) of the 145 men in the placebo group. After 3 years, 54 (38%) men in the dutasteride group had prostate cancer progression (pathological or therapeutic) compared with 70 (48%) in the control arm. In addition, a greater proportion of men treated with dutasteride (36% versus 23%) showed no evidence of cancer detected in their final biopsy compared with men who received placebo, although this difference was not statistically significant. There were no prostate cancer-related deaths and no metastatic events in any of the two groups.

The adverse events reported were also similar between the two groups, although more men in the dutasteride group experienced drug-related adverse effects compared with those given placebo (24% versus 15%). These toxic effects were mainly sexual dysfunction (impotence or decreased libido) or breast enlargement and tenderness.

Does this mean that dutasteride can redeem men with low-risk prostate from aggressive treatments in the future? Would the men in the trial that benefited from taking dutasteride have ever needed treatment anyway? Because prostate cancer is a disease that progresses very slowly, long-term results will be needed to answer these questions. In the meantime, the REEDEM study suggests that dutasteride could be a beneficial adjunct to active surveillance for men with low-risk prostate cancer, delaying their time to initiation of primary therapy.

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