PROSTATE CANCER

Degarelix controls serum alkaline phosphatase better than leuprolide

Gonadotropin-releasing hormone (GnRH) receptor agonists, such as leuprolide, are the most commonly used androgen deprivation therapy (ADT) agents in patients with advanced prostate cancer, but are associated with an initial testosterone surge that can stimulate cancer growth. GnRH receptor antagonists, such as degarelix, are a new class of ADT agents that have been shown to achieve castrate levels of testosterone faster than GnRH agonists and without the initial testosterone surge.

“...ALP suppression was significantly greater in the degarelix group than in the leuprolide group...”

Alkaline phosphatase (ALP) is a serum marker of bone turnover that is found at high levels in patients with bone metastases. GnRH agonists have been reported to decrease serum ALP levels, but the effects of the newer GnRH antagonists on this bone marker are unknown. Schröder and colleagues analyzed data from a randomized, phase III trial to compare changes in serum ALP levels during treatment with leuprolide or degarelix.

This analysis included 408 patients with prostate cancer (of any stage) who

were randomly allocated to receive either degarelix at a starting dose of 240 mg followed by a monthly maintenance dose of 80 mg ($n = 207$), or leuprolide 7.5 mg monthly ($n = 201$) for 1 year. Baseline characteristics did not differ significantly between groups, although serum ALP levels were highest in patients with metastatic disease compared to those with localized or locally advanced disease, and in patients with serum PSA levels ≥ 50 ng/ml compared to those with PSA levels < 50 ng/ml.

In patients with localized or locally advanced disease, serum ALP remained at or around baseline levels throughout the 12-month study. In the subgroup of patients with metastatic disease, however, an initial increase in serum ALP levels, peaking at 1 month, was followed by a decrease to sub-baseline levels at 2 months in those treated with degarelix and at 3 months in patients who received leuprolide. ALP levels began to rise back towards baseline values from around 9 months in the leuprolide group, whereas degarelix-treated patients maintained their reduced ALP levels until the end of the study; at 12 months, ALP suppression was significantly greater in the degarelix group than in the leuprolide group ($P = 0.014$).

Patients with a serum PSA level ≥ 50 ng/ml showed similar serum ALP

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responses to those with metastatic disease (initial ALP peak at 1 month followed by an extended trough), with a late rise in ALP levels from about 10 months in patients treated with leuprolide compared to stable, maintained suppression in those treated with degarelix.

The authors conclude that, compared to leuprolide, degarelix treatment might lead to improved, sustained control of serum ALP levels in patients with metastatic prostate cancer or a high PSA level, potentially delaying skeletal metastasis and disease progression and improving survival. The consequences of ALP suppression, however, will need further examination in randomized trials.

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Original article Schröder, F.H. *et al.* Changes in alkaline phosphatase levels in patients with prostate cancer receiving degarelix or leuprolide: results from a 12-month, comparative, phase III study. *BJU Int.* **106**, 182–187 (2010)