Rapid Rise of Serum Testosterone Following Discontinuation of Long Term Treatment of Prostate Carcinoma with an LHRH-Agonist

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Introduction

Results

Over the last six years, LHRH-agonists have been successfully used for the treatment of advanced prostate cancer. Testosterone levels identical to castrate levels have been reported after chronic treatment with LHRH-agonists. Long term effects on testicular histology following treatment with an LHRH-agonist and subsequent orchiectomy for disease progression revealed marked decrease in the number of Leydig cells and a partial or total arrest of sperm maturation [1,2]. Short term treatment with an LHRH-agonist indicated a return of plasma testosterone in patients with benign prostatic hyperplasia on discontinuation of the drug [3]. We report on long term treatment (1½ to 3 years) with an LHRH-agonist.

Using the criteria of the National Prostate Cancer Project (NPCP), two of the three patients reported in table 1 had responded to the treatment with a partial response, whereas the third one was rated with stable disease. Four weeks following discontinuation of the last Zoladex injection, in two cases, A. H. and J. S., serum testosterone levels were still in the castrate range (below 50ng/100ml), whereas a third patient exhibited a level already slightly above that cutoff level. Within the next 8 or 12 weeks, the testosterone levels had risen substantially in all three cases (table 1). It is likely that this recovery of serum testosterone is more rapid than the one reported by Tomic et al. [4] following long term treatment with an estrogen.

Material and Method

Discussion

As part of a multicenter phase I and II testing of a long acting LHRH-agonist (ICI 118,630, Zoladex), we have entered 40 patients to the protocols consisting of a monthly s.c. injection of Zoladex, 3.6 mg, following initial treatment with 0.9, 1.8 or 3.6 mg of Zoladex. Three relapsing patients who did not require immediate other treatment were monitored frequently for serum testosterone by radioimmuno-assay when they were removed from Zoladex treatment.

In 'hormone resistant' prostate cancer, it is likely that part of the malignant cells are still sensitive to testosterone deprivation. This conclusion is based mostly on clinical observations such as mixed response to hormone deprivation and especially the observation of unfavorable subjective and objective responses to testosterone administration in patients in remission following endocrine therapy [5]. Hence, rise of serum testosterone may be dysfunctional as remaining hormonally sensitive cells may be induced to proliferate.

Table 1. Development of Testosterone (T) levels in patients treated with Zoladex (ICI 118, 630)

Case

Stage of disease at start of treatment

Length of therapy before relapse (wks)

Response

to

treatment

Plasma Testosterone in ng/100 ml

Before start of Zoladex

Level at time of

last

Development

following

discontinuation

treatment

treatment

with Zoladex

C.B.

B2

156

PR

276

< 30

1 mo: 58.8 8 wk: 150 12 wk: 229

J.S.

D2

88

PR

1070

< 30

1 mo: < 20 6wk: 113

8 wk: 343

A.Z. D2 76 SD 295 < 30 1 mo: < 20

7 wk: 130

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Short Communications!Kurzmitteilungen

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