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Editorial

New Drugs for Prostate Cancer?

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PROSTATE CANCER is now the second most common cause of male cancer deaths in the West. Death rates here doubled over the last 20 years and it is predicted that if this increase continues, prostate cancer will be the most common cause of male cancer deaths by the year 2010. Mirroring these changes in incidence has been an increased interest in the treatment of this condition.

Currently, optimal treatment is probably with an LHRH agonist and an anti-androgen. There has been debate over the additional advantages of an anti-androgen. The protagonists of maximal androgen blockade suggest that there is a 7-month survival advantage to treatment with combination therapy as compared with single agent treatment and this leads to a median survival of 3 years in patients with metastatic disease. Although this might be considered to be an advance, in reality, it is only a minor improvement in the patient's prospects and this underscores the significance of the need for new treatments of this condition.

Patients with metastatic prostate cancer have a median period of 14 months from the start of hormonal treatment to marker progression. However, treatment in relapse is generally reserved for symptomatic progression which comes a median of 15 months later. Following symptomatic progression a number of treatments may be offered to the patient with prostate cancer and these include anti-androgen withdrawal, radiotherapy, chemotherapy and further hormonal manipulation. Despite and in spite of all these therapeutic manoeuvres, symptomatic progression is followed by the prospect of a median survival of 7 months. Thus in the context of increasing numbers of patients with prostate cancer and the ultimate inadequacy of all current therapeutic strategies, there is a enormous need for new treatments of this illness.

Retinoids have been used as experimental treatments for patients with cancer for at least 30 years. The original trials of retinoids were unpromising because of toxicity. In this edition of the *European Journal of Cancer* a report of the activity of a new agent, which increases intracellular retinoic acid levels is published (Denis and colleagues, pp. 469–475). Liarozole acts by blocking the hydroxylation of retinoic acid. Retinoic acid acts as a transcription agent through the retinoic acid receptor which is a member of the vitamin D steroid super-receptor family.

Denis and colleagues in this issue of the *European Journal of Cancer* describe their early experience with liarozole in prostate cancer. 100 men with progressive disease were treated in a multicentre study. Treatment was given in one of two dosage regimens and patients were assessed according to their PSA response, prostate size and symptoms. 25 of 85 patients, evaluable by PSA response, improved. However, in 4 of these, this improvement could have been the results of anti-androgen withdrawal. The median survival of patients with a PSA response was 12 or 17 months, depending upon the dosage regimen used and compared with 5–6 months in the non-responders.

Treatment did have toxicity which was mucosal, skin and gut related. The grade of the toxicity was not described according to classical WHO or UICC criteria, but in total, 11 patients had to withdraw from the study because of a drug-related side-effect. Although treatment with liarozole does not exactly provide us with a new penicillin for prostate cancer, at least it does offer the prospect of an addition to the therapeutic armamentarium for this malignancy. It would appear to these observers that there are many similarities between liarozole's side-effects and those of the older retinoids but these would be tolerable should this current report of efficacy be confirmed.

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