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Fax Communication

Suramin for Prostatic Cancer: a Phase I/II Study in Advanced Extensively Pretreated Disease

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SURAMIN inhibits the activity of several growth factors. Prostate cancer was the first human tumour against which antitumour activity was demonstrated. In this preliminary report of a phase I/II study the antitumour activity of suramin is confirmed with four short partial responses in nine patients. Suramin is a polysulphonated naphthylurea that was first introduced for the treatment of trypanosomiasis [1]. Recently, suramin has been shown to block the binding of a range of tumour growth factors *in vitro* [2]. Clinical responses have been reported in HIV related lymphomas and sarcomas [3]. A further report suggested activity in advanced prostatic cancer [4]. Our aim was to establish a safe treatment schedule of high-dose intravenous suramin by monitoring serum drug levels [5], and to detect antitumoural activity in a limited population of heavily pretreated patients with advanced prostatic cancer.

PATIENTS AND METHODS

Nine patients with advanced, metastatic prostatic cancer entered the study. All had been pretreated with bilateral orchiectomy and additional hormonal and/or chemotherapeutic drugs and had progressive disease. A test dose of 200 mg suramin intravenously was given to detect allergic reactions. Blood samples were taken before the start of treatment and at 1/2, 2, 3, 4, 8, 12 and 24 h for the measurement of serum drug levels and for pharmacokinetic evaluation. None of the patients had adverse reactions other than transient, mild pyrexia (less than 38°C).

A continuous loading infusion of suramin was then started at 425 mg/m^2 day until plasma levels reached 200 μg/ml. Serum chemistry, prostate specific antigen, prostate acid phosphatase, alkaline phosphatase, liver function, cortisol, and blood cytology and coagulation were regularly. Additional loading infusions were given, whenever possible on an out-patient basis, when plasma levels dropped below 130 μg/ml to attain 200 μg/ml.

The only suitable objective response for all patients was serum PSA.

RESULTS

Nine patients received an average mean dose of 12.1 g (9–23) over a mean of 4.6 weeks (1–13). Loading infusions were stopped at a plasma level of around 200 μg/ml after an average of 9 days. In only four patients did their general condition allow additional infusions to be given.

All patients had low-grade pyrexia during the first days of treatment. Seven patients had a non-specific papular skin rash. In only one patient did the rash last more than 3 days and be of sufficient severity to require specific treatment.

Severe blood coagulation disorders did not occur, but suramin infusions were interrupted whenever prothrombin time increased more than 50%. No adrenal, liver or neurological toxicity was observed.

None of the nine patients achieved normalization of serum prostate specific antigen levels (complete response); there were four partial responses (prostate specific antigen reduction greater than 50%); five were non-responders. None of the responses lasted for more than a few weeks. After a mean follow up period of 9 weeks, seven of nine patients had died, all of malignancy.

CONCLUSIONS

Serial plasma level measurements revealed important inter- and intraindividual differences in the suramin dose needed to reach high plasma levels. Levels above 160 μg/ml were difficult to maintain without close monitoring and carefully adapted dosages. In contrast, under 130 μg/ml, drug levels only slowly decreased, with a half-life of at least several weeks. No major adverse reactions were experienced in these circumstances.

On the basis of preliminary reports in other diseases [6] it could be argued that higher levels with accompanying increased side-effects are needed to optimize the response rate. In this small group of heavily pretreated patients with poor prognostic factors, only short lasting, partial responses were obtained in 4/9 patients using this treatment schedule. More prolonged phase I studies are needed to define the pharmacokinetics of the drug and to determine its subsequent optimal use in phase II studies.

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