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Interferon and Dexamethasone in Multiple Myeloma Patients Refractory to Chemotherapy*

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INTRODUCTION

THE TREATMENT of refractory myeloma represents an important and challenging problem [1]. Both *in vitro* and *in vivo* studies have shown that interferons have anti-tumoral activity in myeloma patients [2,3]. Moreover, the combination of alpha interferon and prednisone has an additive inhibitory effect on myeloma colony formation [4]. Based on these observations, we conducted a pilot study in order to investigate the effectiveness of the combination of alpha interferon and high-dose dexamethasone in patients with refractory myeloma [5].

PATIENTS AND METHODS

Thirty-two patients (15 male, 17 female) with refractory multiple myeloma were included in the study: nine cases were primarily resistant; 17 cases were secondarily resistant after an initial response; and six cases had relapsed on cessation of therapy.

The treatment schedule was as follows: a) induction (3 months) - interferon alfa-2b 4 million units (MU)/m^2 subcutaneously (s.c.) three times per week (t.i.w.) and 4-day pulses of 25 mg/m^2/day of dexamethasone with intervals of 4 days during the first month, 10 days during the second month, and 15 days during the third month. Thus, a total of eight pulses were given during this induction phase; b) maintenance - interferon alfa-2b 2 MU/m^2 s.c. t.i.w. and dexamethasone 25 mg/m^2 for 4 days every 3 weeks.

Criteria for objective response (OR) included a 50% decrease in serum M-component and/or > 90% decrease in light chain proteinuria; disappearance of plasmocytomas; resolution of anaemia and hypercalcaemia; improvement in performance status (ECOG); and no increase in lytic lesions. A partial response (PR) included a 25-50% reduction in serum M-component plus the other criteria as for OR.

Lymphocyte subsets (CD4, CD8) were determined in 14 patients by flow-cytometry before and 3 months after initiation of interferon therapy.

RESULTS

Of the 32 patients included in the study, 22 completed the 3 months' induction therapy, six were considered early deaths (all with poor performance status - PS 3 or 4), and in four patients there was a major protocol violation.

Response

Of the 22 evaluable patients, seven achieved an OR (31.8%), eight a PR (36.4%) and the remaining seven (31.8%) were treatment failures. Four of the seven OR patients showed a reduction in bone marrow plasma cells to less than 5%. Follow up of the seven patients with OR shows that four remain in remission on maintenance treatment at 20+, 17+, 6+ and 4+ months, respectively, while the other three relapsed after 6, 12 and 14 months. Three of the eight patients with PR remain stable at 22+, 13+ and 10+ months, respectively.

Response to treatment was independent of the duration of disease prior to study entry, previous treatment, age, sex, M-component and the reason for inclusion in the protocol. Indeed, a high proportion of responses (five out of nine) were found among primarily resistant patients. On the other hand, performance status clearly influenced the response.

Interestingly, five out of 11 patients who were previously refractory to a treatment regimen comprising similar high-dose dexamethasone together with vincristine, BCNU and doxorubicin responded to the interferon/dexamethasone combination.

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Lymphocyte subsets

Analysis of changes in the distribution of T-cell subsets according to response to therapy showed an increase in the absolute number of CD4 cells in all four patients studied with OR, while in the seven patients with PR, the lymphocyte evolution was heterogeneous; and all three patients who failed to respond to interferon/dexamethasone showed a progressive decrease in CD4 cells (Fig. 1).

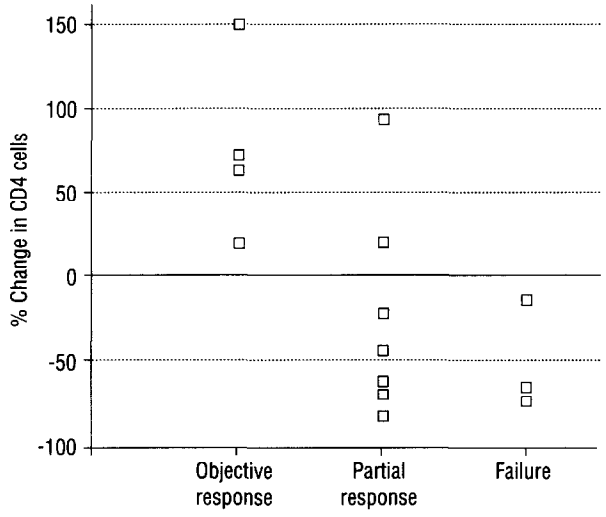

Fig. 1. Percentage increase and decrease in absolute number of CD4 + cells after alpha interferon treatment according to response to therapy.

Toxicity

The protocol was generally well tolerated, with only four patients discontinuing therapy due to adverse effects (confusion, hepatic toxicity, hyperglycaemia, and evolution to overt plasma cell leukaemia). Moderate flu-like symptoms were reported by 51% of the patients, and severe confusion and neuropathy occurred in two patients but resolved on temporary discontinuation of interferon and did not reappear during maintenance treatment. Two further patients required dose reduction for granulocytopenia and thrombocytopenia.

CONCLUSIONS

The present results indicate that the combination of interferon alfa-2b and dexamethasone is effective in the treatment of refractory multiple myeloma patients, including both primarily resistant cases and patients previously resistant to dexamethasone. Although a larger series of patients and a longer follow up is needed to evaluate the long-term efficacy, the use of this combination appears to be a promising therapeutic approach for patients with refractory myeloma.

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Maintenance Treatment of Multiple Myeloma with Alpha Interferon versus an Alternating Schedule of Alpha Interferon and Chemotherapy

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INTRODUCTION

RECENT STUDIES indicate that treatment with alpha interferon, either alone [1] or in combination with chemotherapy [2], can prolong the plateau phase in patients with multiple myeloma. The aim of the present study is to compare the efficacy of alpha interferon versus alternate monthly cycles of alpha interferon and chemotherapy, in maintaining the remission obtained by various chemotherapy

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