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Melphalan/Prednisone Versus Melphalan/Prednisone Plus Human Alpha Interferon Therapy in Patients with Multiple Myeloma, Stages II and III

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INTRODUCTION

ALPHA INTERFERON alone in untreated patients with multiple myeloma has been shown to achieve a response rate of about 20-30% [1-6]. Furthermore, a synergistic antiproliferative effect has been noted between alpha interferon and melphalan *in vitro* studies with human myeloma cells [7]. The Myeloma Group of Central Sweden (MGCS) therefore undertook a prospective, randomized study, beginning on 1 April 1986, to compare the effectiveness of a combination of melphalan/prednisone (MP) plus human natural alpha interferon with that of a standard MP treatment protocol in patients with myeloma stages II and III.

PATIENTS AND METHODS

A total of 220 patients were entered into the study (Table 1). Of these, 111 were randomized to receive MP and 109 to receive MP plus alpha interferon according to the treatment protocol shown in Figure 1. Patients who responded to therapy were continued on the same doses of MP in both groups but the dose of alpha interferon was changed from 7 million units (MU)/m² intramuscularly for 4 days every third week to 3 MU three days a week. On progression or relapse, patients were changed to therapy with etoposide (vincristin)/doxorubicin (adriamycin)/cyclophosphamide/prednisone (VACP).

Table 1. Pretreatment patient characteristics

	MP	MP + IFN
Total *n*	111	109
Clinical		
Stage II	50	51
Stage III	61	58
Serum creatinine		
< 170 mmol/L	80	84
≥ 170 mmol/L	31	25
M-component		
IgG	56	62
IgA	26	24
BJ	23	21
Non-producer	5	2
IgD	1	–
Patients evaluable for response *n*	91	94

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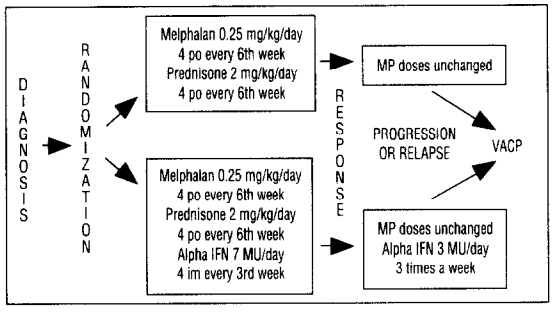

Fig. 1. Treatment protocol.

RESULTS

Response rate

An interim analysis was performed in September 1989, at which time 91 patients in the MP group and 94 patients in the MP/interferon group were evaluable for response. There was a significantly higher response rate in the MP/interferon group as a whole (66%) compared to the MP group (48%) ($P < 0.02$). When the results were analyzed according to disease stage, it was found that a much higher percentage of stage II patients responded to MP/interferon than to MP (76% versus 48%, respectively; $P < 0.01$), while a similar percentage of stage III patients responded (57% versus 49%; NS) (Table 2). It was also found that patients with an IgA M-component responded significantly better to the combined MP/interferon therapy than to MP alone (91% versus 52%, respectively; $P < 0.01$).

Table 2. Response rate (%)

	MP group ($n = 91$)*	MP + IFN group ($n = 94$)*	*P*
Total	48	66	< 0.02
Clinical			
Stage II	48 (20/42)	76 (34/45)	< 0.01
Stage III	49 (24/49)	57 (28/49)	NS
M-component			
IgG	56 (25/45)	62 (31/50)	NS
IgA	52 (11/21)	91 (20/22)	< 0.01
BJ	26 (5/19)	50 (10/20)	NS

*Number of evaluable patients.

Duration of response and survival

The median survival time has not yet been reached. At the time of interim analysis, there was no significant difference in

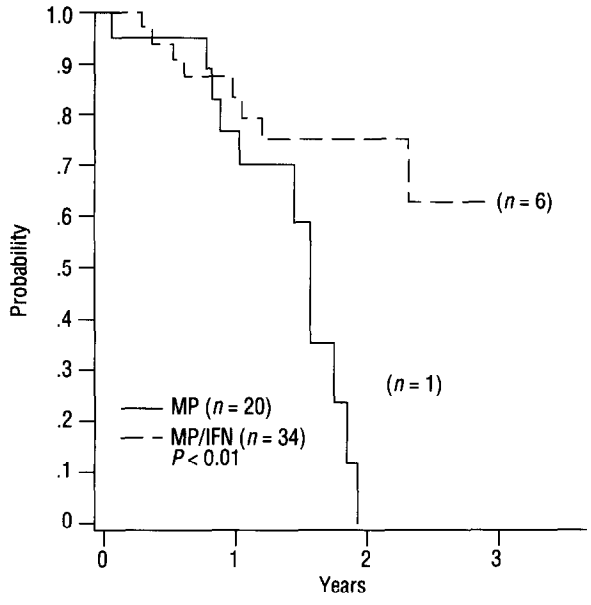

Fig. 2. Duration of response (stage II patients).

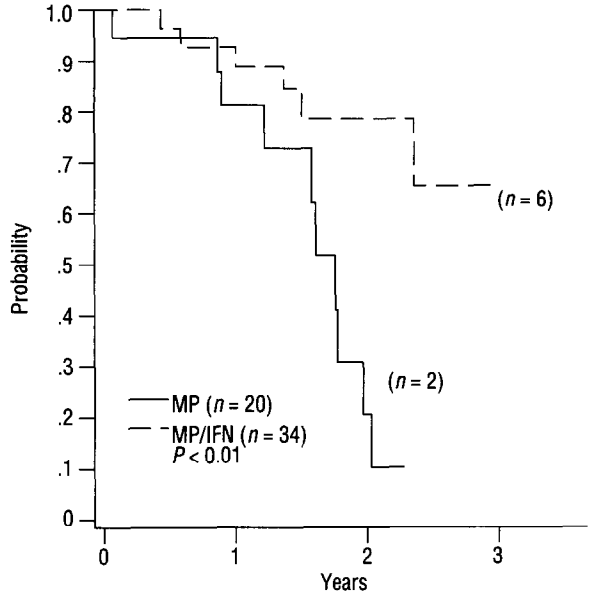

Fig. 3. Survival from response (stage II patients).

response duration or survival between the two treatment groups as a whole (Fig.2). However, the duration of response and survival from response in stage II patients were significantly longer in those receiving MP/interferon (n = 34) than in those receiving MP (n = 20) (Fig. 3; $P < 0.01$).

Dose reduction

There were no major differences in haematological side effects between the two groups. The dose of alpha interferon was reduced during the induction period in 33 patients, including 12 who stopped interferon completely. Reasons for withdrawal from interferon included administrative problems (three), flu-like syndrome (two), myocardial infarction (one), mental confusion (one), congestive heart failure (one), coma with hemiparesis (one), allergic reaction (one), and thrombocytopenia (one).

CONCLUSIONS

Based on the preliminary results of this MGCS study, alpha interferon seems highly promising when given in combination with MP in multiple myeloma patients. The response rate to MP plus alpha interferon in this study is among the highest reported, irrespective of the therapeutic protocols used. The most pronounced effect was seen in patients with a low tumour mass (stage II disease) compared to patients with high-tumour burden (stage III). The observation is still too short to draw conclusions about the effects on survival.

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