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Interferon Alfa-2b in Stage A Untreated B-Chronic Lymphocytic Leukaemia Patients

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INTRODUCTION

ALTHOUGH THE anti-neoplastic effect of alpha interferon is generally accepted, experience with this agent in B-chronic lymphocytic leukaemia (B-CLL) is limited [1-5]. In a previous study, we observed a 50% response rate to interferon alfa-2b administration in previously untreated B-CLL patients in early-stage disease [3]. We performed the present randomized clinical trial in order to re-evaluate our observations and to compare the results in relation to dose and schedule of interferon administration.

PATIENTS AND METHODS

Thirty-four patients were included in the trial, 19 male and 15 female, with a mean age of 62 years (range 44-77). The mean duration of follow up before treatment was 16 months (range 1-60 months).

Patients were allocated to one of four treatment groups: control (no treatment) (n = 8); interferon alfa-2b 1.5 million units (MU) per day (n = 8); interferon 1.5 MU three times a week (t.i.w.) (n = 10); or interferon 3 MU t.i.w. (n = 8). Criteria for response are shown in Table 1.

Table 1. Response criteria

Complete response:	Restoration of palpable disease and haematological parameters to normal.
Partial haematological response:	Reduction of blood lymphocytes by ≥ 50% of pretreatment values.
Minor haematological response:	Reduction of blood lymphocytes by < 50% of pretreatment values.
Stable disease:	No change in clinical and haematological findings.
Negative response:	Further increase in blood lymphocytes or size of palpable disease.
Progressive disease:	Change of clinical stage from A to B or C.

Therapy was administered for a period of 3 months, after which the dose of interferon was modified according to response: patients with complete response (CR) and partial haematological response (PHR) were given two-thirds of the initial dose, and those with minor haematological response (MHR) were given one-third of the initial dose. In patients with stable disease (SD), negative response (NR) or progressive disease (PD), treatment was discontinued.

For statistical analysis of the results, Student's t test and paired t test were used.

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RESULTS

Response

Mean haematological values before and after 3 months' alpha interferon therapy are shown in Table 2. White blood cell and lymphocyte counts fell significantly in the 1.5 MU/day group ($P < 0.001$) and the 3 MU t.i.w. group ($P < 0.05$) but not in the control or the 1.5 MU t.i.w. group. Overall, there was no change in haemoglobin or polymorphonuclear cell counts in any of the groups, while patients on interferon experienced a minor fall in platelet count.

Table 2. Mean haematological values pre and post 3 months' interferon therapy

	Controls		1.5 MU/day		1.5 MU/t.i.w.*		3 MU/t.i.w.†	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Hgb g/dL	13.6	13.4	14.1	13.2	14.3	13.4	13.7	12.7
WBC x 10^9/L	27.6	32.6	41.8	28.1	33.4	33.0	122.8	72.8
PMN x 10^9/L	5.0	4.6	5.2	4.2	3.9	4.0	5.8	8.5
Lymphocytes x 10^9/L	21.6	27.6	34.9	22.7	28.1	27.1	113.5	62.6
Platelets x 10^9/L	206.0	222.6	183.8	171.3	164.1	139.0	199.0	139.0
P value	< 0.1		< 0.001		< 0.1		< 0.05	

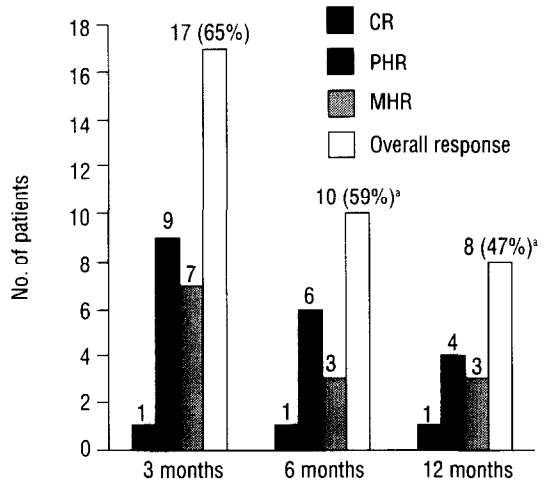
PMN = polymorphonuclear cells. WBC = White blood cells. Hgb = Haemoglobin
P values refer to WBC and lymphocytes.
*Therapy was discontinued at 4 weeks in one patient.
†Therapy was discontinued at 8 and 11 weeks in two patients.

Response at completion of 3 months' interferon therapy are shown in Table 3. Overall, 17 of the 26 interferon-treated patients achieved a response, including one CR, nine PHRs and 7 MHRs. Bone marrow pattern and degree of infiltration remained unchanged after interferon therapy. In one patient with NR who developed severe autoimmune haemolytic anaemia and thrombocytopenia, we observed an increased number of erythroid precursors and megakaryocytes.

Table 3. Response at completion of 3 months' interferon therapy

Treatment arm	Response					
(no. of patients)	CR	PHR	MHR	Stable	NR	Progression
1.5 MU/day (8)		4	2	1	1	
1.5 MU/t.i.w. (10)	1	2	3	1	3	
3.0 MU/t.i.w. (8)		3	2		2	1

After 12 months of follow up, eight of the 17 original responders had maintained their response (one CR, four PHRs and three MHRs) (Fig. 1).



[a]Percentages refer to the 17 initial responders

Fig. 1. Follow-up of responders.

Toxicity

Adverse effects included weight loss (20 patients), flu-like syndrome (12 patients), temporary increase or appearance of lymph nodes (10 patients), massive increase of lymph nodes while in MHR (two patients), relapse of herpes zoster (one patient), and severe anaemia and thrombocytopenia (one patient).

CONCLUSIONS

Interferon alfa-2b is effective in early stages of B-CLL. More than 50% of our patients responded, with a rapid response in nine and a slow continuous response in eight patients.

The most prominent change in mean lymphocyte values was observed in the group receiving 1.5 MU interferon daily and this was statistically more significant compared to the changes observed in the group receiving 1.5 MU or 3 MU interferon t.i.w. Whether this is due to the effect of continuous low-dose alpha interferon or to the inclusion in this group of individuals with high lymphocyte counts is not clear. At 12 months, the results obtained during the first month were sustained in half of the patients.

Toxicity is evident but well tolerated by most patients.

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Alpha Interferon in Patients with Progressive and/or Recurrent Hodgkin's Disease*

Benjamin Koziner

INTRODUCTION

SEVERAL SMALL studies have suggested that patients with Hodgkin's disease may be sensitive to therapy with alpha interferon [1-5]. We therefore undertook a study to determine the therapeutic efficacy and toxicity of recombinant interferon alfa-2b in six patients with progressive and/or recurrent Hodgkin's disease.

PATIENTS AND METHODS

Inclusion criteria for the study were as follows: histologically confirmed Hodgkin's disease; progressive or recurrent disease after first-line and salvage chemotherapy, with or without radiotherapy; measurable disease; adequate renal, hepatic and bone marrow function; a life expectancy of more than 3 months; and Eastern Cooperative Oncology Group performance grades of 0, 1 or 2.

Patient characteristics, including disease stage, histological diagnosis, and previous therapy, are shown in Table 1. All patients had received between three and five different salvage programmes, with no disease-free interval preceding administration of interferon. Two patients (1 and 5) had extranodal involvement and all had B symptoms.

Treatment consisted of interferon alfa-2b 5 million units

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