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SHORT COMMUNICATION

Chlorambucil and interferon for low grade non-Hodgkin's lymphoma

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Despite responsiveness to both chemotherapy and radiation therapy, most patients with low grade non-Hodgkin's lymphoma (NHL) die as a consequence of the disease. Chlorambucil (CB) alone yields responses in approximately seventy-five percent of patients with a median duration of first remission of one to two years. However, although subsequent remissions can often be achieved, the characteristic continuous relapse pattern results in a median survival of between five and ten years (Jones *et al.*, 1973; Young *et al.*, 1977; Lister *et al.*, 1978; Rudders *et al.*, 1979; Hoppe *et al.*, 1981; Anderson *et al.*, 1982; Gallagher *et al.*, 1986).

It has been demonstrated that administration of leucocyte or recombinant DNA interferon causes regression of disease in approximately forty per cent of patients with low grade lymphoma (Merigan *et al.*, 1978; Louie *et al.*, 1981; Ozer *et al.*, 1983; Horning *et al.*, 1985; Wagstaff *et al.*, 1986). Combinations of interferon with conventional cytotoxic agents have been investigated in murine models of leukaemia and lymphoma (Chirigos & Peason, 1973; Gresser *et al.*, 1978; Slater *et al.*, 1981; Tozawa *et al.*, 1982; Mowshowitz *et al.*, 1982); longer survival was observed in animals receiving the combination than in those receiving either drug alone. On the basis of these observations it was decided to investigate the concurrent administration of CB and interferon (IFN-α_2) in previously treated patients with low grade NHL.

Twenty-three patients (median age 52 years, range 28–70) with recurrent, low grade NHL (11 follicular, 6 centrocytic, 4 lymphoplasmacytoid, 1 peripheral T cell) and 1 patient with chronic lymphocytic leukaemia received CB and IFN-α_2 as shown in Figure 1. All, except one patient with follicular lymphoma had bone marrow infiltration at the time of treatment.

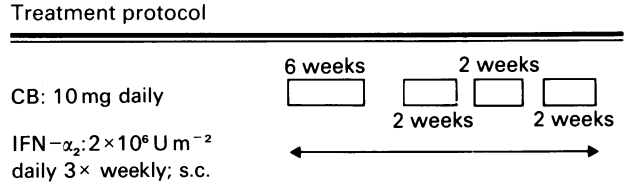

Figure 1

Toxicity Eleven patients completed therapy at full doses with no treatment delay. The reasons for stopping treatment in the remainder were disease progression (5), myelosuppression (5), death due to septicaemia (1) and interferon intolerance (1). Myelosuppression also precluded continuation of CB in two patients at 6 and 12 weeks respectively. The flu-like symptoms experienced by most patients were similar to those previously described with interferon alone (Merigan *et al.*, 1977; Priestman, 1980; Horning *et al.*, 1982; Sherwin *et al.*, 1982). The haematological toxicity was that to be expected in such a patient population treated with CB alone (Table I).

Table I Clinical and haematological toxicity

	No. pts
Fever	12
Lassitude	10
Anorexia	7
Nausea	1
Diarrhoea	2
Erythema at injection site	1
Platelets $<20\times10^9\,l^{-1}$	2[a]
Platelets $<50\times10^9\,l^{-1}$ and Neutrophils $<0.5\times10^9\,l^{-1}$	3[a]
Neutrophils $<1.0\times10^9\,l^{-1}$	2[b]

[a]Treatment stopped due to myelosuppression; [b]Chlorambucil stopped, IFN-α_2 continued.

Response Responses were observed in 14 out of 23 patients overall (1 CR, 13 PR) including 8 out of 11 patients with follicular lymphoma (1 CR, 7 PR). In 4 patients, the combination resulted in a greater degree of clinical response than had previously been observed with CB alone.

This study has demonstrated that it is possible to administer CB and IFN-α_2 on the schedule described to the majority of patients with follicular lymphoma and achieve responses, even if not CR, in approximately three quarters. This is encouraging considering the amount of prior therapy received. A randomised study is currently in progress in previously untreated patients with advanced follicular lymphoma to compare the combination with CB alone.

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