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Human Interferon-Beta in the Treatment of Non-Hodgkin Lymphoma *

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A. Introduction

Interferon has potent antiviral, antiproliferative, and immunomodulating properties [9, 10]. Leukocyte and fibroblast interferon have been applied in the treatment of human malignancies. Due to the limited availability of interferon, only small numbers of patients have been treated so far. According to the literature a total of 106 patients with malignant lymphomas have been treated, including five patients with Hodgkin's disease, 65 patients with multiple myeloma, nine patients with acute lymphatic leukemia, 14 patients with chronic lymphatic leukemia, nine patients with nodular poorly differentiated lymphocytic non-Hodgkin lymphoma, and four patients with diffuse histiocytic non-Hodgkin lymphoma. Eight of the 106 patients achieved complete remission and 56 showed partial regression [1, 2, 4, 5, 7, 8, 12–15].

A relatively good response was observed with non-Hodgkin lymphoma of favorable prognosis, with 15 partial regressions and two complete remissions out of 23 patients. These results encouraged us to study the effect of fibroblast interferon (Hu-IFN-beta) in patients with non-Hodgkin lymphoma of low-grade malignancy. We describe our results obtained with ten patients. Preliminary results have been reported recently [6].

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B. Materials and Methods

Partially purified human fibroblast interferon was produced by Dr. Rentschler GmbH und Co., D 7958 Laupheim, Federal Republic of Germany. It was supplied in lyophilized form at a specific activity of 2.5×10^6 IU/mg protein. Freshly dissolved material was applied by intravenous infusion over a period of 30–60 min.

Between October 1980 and August 1981 ten patients entered the study. Their diagnoses were designated according to the Kiel classification [11]. All patients were in advanced stages of their disease, with cytostatic and radiation pretreatment. Such treatment was omitted for at least 1 month prior to interferon application.

C. Treatment Evaluation

Physical examinations took place at weekly intervals; spleen size and lymph node index were recorded. The development of the disease was documented by chest roentgenograms, CT scans, and bone marrow histology. Response was evaluated according to the criteria suggested by the International Union Against Cancer [7].

D. Dosage Schedule

Patients received induction therapy with 4.5×10^6 IU i.v. daily for 4 weeks and thereafter 9×10^6 IU i.v. daily for 2 weeks. After this dose increment consolidation therapy was started, with 4.5×10^6 IU i.v. 3

	n	Result after						
		Induction and increment				Consolidation		
		CR	PR	SD	PD	CR	PR	PD
CLL	1	–	–	–	1	–	–	–
PCLL	1	–	–	–	1	–	–	–
IC	4	–	–	2	2	–	–	2
CC	1	–	–	–	1	–	–	–
CB/CC	3	–	–	2	1	1	1	–
Total	10	–	–	4	6	1	1	2

Table 1. Results of treatment of ten patients with advanced non-Hodgkin lymphoma

CLL, chronic lymphatic lymphoma; PCLL, prolymphocytic leukemia; IC, immunocytoma; CC, centrocytic lymphoma; CB/CC, centroblastic/centrocytic lymphoma; CR, complete remission; PR, partial remission; SD, stable disease; PD, progressive disease

times per week. Interferon treatment was abandoned when patients fulfilled the criteria for progressive disease [7].

E. Results and Discussion

Ten patients with advanced non-Hodgkin lymphoma of low malignancy were treated with Hu-IFN-beta. One patient had chronic lymphatic leukemia, one patient had prolymphocytic leukemia, four patients had lymphoplasmocytoid immunocytoma, one patient had centrocytic lymphoma, and three had centroblastic/centrocytic lymphoma. All patients were pretreated with chemotherapy and in some cases with irradiation. The outcome of the treatment is summarized in Table 1. During induction and increment therapy six out of ten patients had progressive disease and four out of ten had stable disease; two of the latter developed progressive disease after 1 and 3 months of consolidation therapy, respectively.

In one patient with centroblastic/centrocytic lymphoma, preexisting minimal bone marrow infiltration disappeared, as evidenced by biopsies on both iliac crests. We rated this response as complete remission. In a second patient with centroblastic/centrocytic lymphoma, bone marrow involvement disappeared, while the lymph node enlargement remained constant. We rated this response as partial remission. It is possible that we missed small nodular lymphatic infiltrates in the bone marrow. Therefore these two cases of good response based solely involvement must be viewed with reservation.

All patients experienced the known reversible interferon side effects: fever, chills, malaise, fatigue, and headache. Some patients showed a reversible drop of absolute granulocyte counts.

These results, namely the achievement of only one partial remission and one questionable complete remission out of ten patients are rather disappointing, particularly when compared with the promising data of Merigan et al. [13] and Gutterman et al. [7]. The reasons for these discrepancies are unknown. The differences may in part be due to the use of IFN-beta instead of IFN-alpha [3]. The poor response of the patients described in this study cannot be explained by a lack of stimulation of natural cytotoxicity or by the production of antibodies to interferon. All patients responded with a significant increase of NK-cell activity with peak values 1–7 days after interferon administration and a subsequent drop during prolonged interferon application. No patient developed antibodies against interferon.

We can conclude that IFN-beta certainly does not cause rapid effective tumor regression. It may exert a moderate response or a stabilization of the disease.

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