Eur J Cancer, Vol. 27, Suppl. 4, p. S26, 1991
Printed in Great Britain

0277-5379/91 $3.00 + 0.00

A Multicentre Study of a Randomized Therapeutic Protocol in Previously Untreated Patients with Ph[1]-positive Chronic Myelogenous Leukaemia: Interferon Alfa-2b and Hydroxyurea with or without Cytosine Arabinoside, Preliminary Results

François Guilhot, Jean-Pierre Lamagnère, Jean Luc Harousseau, Hervé Tilly, Philippe Casassus, Norbert Ifrah, Henri Rochant, Francis Bauters, Gerard Dine and Joseph Tanzer

INTRODUCTION

RECENT STUDIES have shown that interferons can induce complete haematological responses (CHR) and even complete cytogenetic responses (CCR) in chronic myelogenous leukaemia (CML) patients [1]. Moreover, Sokal demonstrated that the proportion of Ph[1]-positive mitoses can be reduced with cytosine arabinoside (Ara-C) alone [2]. Preliminary data [3] suggest a high incidence of haematological remissions and cytogenetic responses with the combination of alpha interferon, hydroxyurea (HU) and low-dose Ara-C.

The aims of this study were to compare the efficacy of alpha interferon plus low-dose Ara-C versus alpha interferon alone in the maintenance phase of interferon-treated CML patients.

PATIENTS AND METHODS

Patients

A total of 138 patients (78 male, 60 female), aged between 17 and 70 years, were entered into the study. All patients were in chronic phase and had the characteristic t(9;22) translocation. The spleen was enlarged in 59% of patients. Pretreatment assessments included complete blood count and differential, serum lactate dehydrogenase and vitamin B_{12} levels, LAP score, and bone marrow cytogenetic analysis. The percentages of patients in each risk group (Sokal classification) were identical in the two arms. Patients were followed up every 3 months for clinical and haematological evaluation and bone marrow cytogenetic analysis.

Treatment protocol

In the induction phase, all patients received interferon alfa-2b starting at 5 million units (MU)/m² per day subcutaneously (s.c.) plus hydroxyurea 50 mg/kg per day orally until stable haematological response was achieved. After 3 months, patients were randomized to receive either interferon alfa-2b alone at a dose of 5 MU/m² per day (or lower, according to side effects), or the same dose of interferon alfa-2b plus low-dose Ara-C (10 mg/m² per day s.c. for 10 days each month).

Correspondence to: F. Guilhot.
F. Guilhot is at the Hôpital Jean Bernard La Milétrie, 86021 Poitiers, France.

Response criteria

CHR was defined as disappearance of symptoms and signs, including splenomegaly, with a decrease in white blood cell count to less than 10 x 10^9/L, normal differential cell counts, and platelet counts less than 350 x 10^3/L. Cytogenetic response was classified according to three grades: minimal response (35-95% Ph[1]-positive metaphases), partial response (5-34% Ph[1] -positive metaphases), and complete response (total elimination of the Ph[1]-positive clone).

RESULTS

Cytogenetic response

In low- and intermediate-risk patients, interferon plus Ara-C achieved cytogenetic responses in 57% of patients compared to 32.5% of patients in the interferon alone group. Overall, 53% of patients receiving combined maintenance therapy achieved a cytogenetic response, compared to 39% on single-agent interferon.

Haematological remission

Haematological remission was better maintained with combined interferon plus Ara-C than with interferon alone, but the difference was not significant.

CONCLUSIONS

Alpha interferon plus Ara-C was more effective than interferon alone in achieving cytogenetic responses in low- and intermediate-risk patients. Overall, a greater cytogenetic response was achieved with the combination. However it is too early to draw any conclusion on the effect of the addition of Ara-C.

1. Talpaz M, Kurzrock R, Kantarjian HM, Gutterman SU. In: [eds]. *Important Advances in Oncology*. Philadelphia: JB Lippincott 1988, 297-321.
2. Sokal JE. Prognosis in chronic myeloid leukaemia: Biology of the disease vs treatment. *Baillière's Clin Hematol* 1987, 1, 907-929.
3. Guilhot F, Dreyfus B, Brizard A, Huret JL, Tanzer J. Cytogenetic remission in chronic myelogenous leukemia using interferon alfa-2b and hydroxyurea with or without low-dose cytosine-arabinoside. *Leukemia Lymphoma* 1991, 4, 49-55.