

2. Cannistra SA. Chronic myelogenous leukemia as a model of the genetic basis of cancer. *Hematol/Oncol Clin N Am* 1990, 4, 337-357.
3. Daley GQ, Van Etten RA, Baltimore D *et al.* Induction of chronic myelogenous leukemia in mice by the P210^{bcr/abl} gene of the Philadelphia chromosome. *Science* 1990, 247, 824-830.
4. Talpaz M, McCredie KB, Mavligit GM *et al.* Leucocyte interferon-induced myeloid cytoablation in chronic myelogenous leukemia. *Blood* 1985, 62, 689-692.
5. Talpaz M, Kantarjian HM, McCredie KB *et al.* Chronic myelogenous leukemia: Hematologic remission and cytogenetic improvements induced by recombinant alpha A interferon. *N Engl J Med* 1986, 314, 1065-1069.
6. Kantarjian HM, Talpaz M, Gutterman JU. Biologic therapy of chronic myelogenous leukemia. *Oncology* 1987, 1, 35-40.
7. Talpaz M, Kantarjian HM, McCredie KB *et al.* Clinical investigation of human alpha interferon in chronic myelogenous leukemia. *Blood* 1987, 69, 1280-1288.
8. Niederle N, Kloke O, Osieka R *et al.* Interferon alpha-2b in the treatment of chronic myelogenous leukemia. *Semin Oncol* 1987, 14, 29-35 (Suppl. 2).
9. Ozer H. Biotherapy of chronic myelogenous leukemia with interferon. *Semin Oncol* 1988, 15, 14-20 (Suppl. 5).
10. Talpaz M, Kantarjian H, Kurzrock R *et al.* Update on therapeutic options for chronic myelogenous leukemia. *Semin Hematol* 1990, 27, 31-36 (Suppl. 4).
11. Ogura H, Tani K, Kozai Y *et al.* Effects of interferon-alpha in patients with chronic myelogenous leukemia in the accelerated phase: Cytogenetic and molecular studies. *Jpn J Cancer Res* 1990, 81, 682-686.
12. Levy D, Larner A, Chandhuli A *et al.* Interferon-stimulated transcription: Isolation of an inducible gene and identification of its regulatory region. *Proc Natl Acad Sci USA* 1984, 83, 8929-8933.
13. Larner A, Janak G, Cheng YSE *et al.* Transcriptional induction of two genes in human cells by beta interferon. *Proc Natl Acad Sci USA* 1984, 81, 6733-6737.
14. Reich N, Evans B, Levy D *et al.* Interferon-induced transcription of a gene encoding a 15-kDa protein depends on an upstream enhancer element. *Proc Natl Acad Sci USA* 1987, 84, 6394-6398.
15. Kessler DS, Pine R, Pfeffer KM *et al.* Cells resistant to interferon are defective in activation of a promoter-binding factor. *EMBO J* 1988, 7, 3779-3783.
16. Kishi K. A new leukemia cell line with Philadelphia chromosome characterized as basophil precursors. *Leukemia Res* 1985, 9, 381-390.
17. Selden RF, Skoskiewicz MJ, Howie KB *et al.* Implantation of genetically engineered fibroblasts into mice: Implication for gene therapy. *Science* 1987, 236, 714-718.
18. Garver RI, Chytil A, Courteny M *et al.* Clonal gene therapy: Transplanted mouse fibroblast clones express human alpha 1-antitrypsin gene in vivo. *Science* 1987, 237, 762-764.
19. Ogura H, Tani K, Ozawa K *et al.* Implantation of genetically manipulated fibroblasts into mice as antitumor alpha-interferon therapy. *Cancer Res* 1990, 50, 5102-5106.
20. Brack C, Nagata S, Mantei N *et al.* Molecular analysis of the human interferon-alpha gene family. *Gene* 1981, 15, 379-394.
21. Karasuyama H, Melchers F. Establishment of mouse cell lines which constitutively secrete large quantities of interleukin 2, 3, 4 or 5, using modified cDNA expression vectors. *Eur J Immunol* 1988, 18, 97-104.
22. Lee MS, LeMaistre A, Kantarjian HM *et al.* Detection of two alternative bcr/abl mRNA junctions and minimal residual disease in Philadelphia chromosome positive chronic myelogenous leukemia by polymerase chain reaction. *Blood* 1989, 73, 2165-2170.

Acknowledgements—We thank Dr Kiyoshi Kiamura, the 3rd Department of Internal Medicine, Faculty of Medicine, and many attending physicians, Department of Hematology-Oncology, Institute of Medical Science, University of Tokyo, for kindly supplying the clinical data of the patients.

Interferon Alfa-2b in the Treatment of Chronic Myelogenous Leukaemia

Masami Bessho, Nobutaka Kawai and Kunitake Hirashima

ABSTRACT

Recent reports have indicated that alpha interferon can be an effective treatment for patients with chronic myelogenous leukaemia (CML) [1]. In order to evaluate the clinical usefulness of interferon alfa-2b, we treated six patients with chronic phase CML and observed their clinical course.

The patients consisted of four males and two females, aged between 39 and 58 years, who had previously received either treatment with busulfan (four patients) or no therapy (two patients). Interferon alfa-2b was administered intramuscularly at a dose of 3-10 million units (MU)/body, either daily or three times per week, for more than 8 weeks.

All six patients showed a fall in white blood cell count from a mean of $101.8 \times 10^9/L$ (range 15.6-330) before treatment to a mean of $25.7 \times 10^9/L$ (range 4.0-117) after treatment with

interferon alfa-2b. Haemoglobin remained largely unchanged, and platelet counts fluctuated. Two of the six patients also showed a slight reduction in the percentage of Ph⁺-positive clones (to 98% and 96%, respectively).

Complete haematological response was achieved in four patients, partial haematological response in one and no response in one. All six patients are alive at a mean of 69 months (range 38-108 months) from diagnosis and are either in chronic phase (five patients) or post bone marrow transplant (one patient).

Major side effects of alpha interferon included fever, general fatigue, and nausea, but all were tolerable.

In conclusion, alpha interferon was useful for controlling blood cell counts in chronic phase CML patients, with tolerable side effects. Five of six patients achieved long-term haematological remission, and alpha interferon slightly reduced the fraction of Ph⁺-positive clones in two patients.

Correspondence to: K. Hirashima.
K. Hirashima is at the First Department of Internal Medicine, Saitama Medical School, Iruma-gun, Saitama-ken, Japan.
M. Bessho and N. Kawai are at the First Department of Internal Medicine, Saitama Medical School, Iruma-gun, Saitama-ken, Japan.

1. Takaku F. Recombinant interferon α -2b as therapy for hematological malignancies. *Biotherapy* 1989, 3, (6) 1497-1503.