Treatment of chronic hepatitis C with recombinant interferon alfa-2b

M Piazza, R Orlando, G Tosone, D Tiseo, M C D Conte, F Minervini, G Santoro, F Scordino, D Vitale

Department of Infectious Diseases, II Medical School, University of Naples, Italy
M Piazza
R Orlando
G Tosone
D Tiseo
M C D Conte
F Minervini
G Santoro
F Scordino
D Vitale
Correspondence to: Professor M Piazza, Department of Infectious Diseases, II Medical School, University of Naples, Naples, Italy.

Abstract
In a study of 87 patients with chronic hepatitis C, 12 months' treatment with interferon alfa-2b at a dose of 6 million units (MU) three times per week seemed to be more effective than treatment with 3 MU three times a week for two months plus 1.5 MU three times a week for 10 months in increasing the percentage of long term responders. The percentage of patients in whom alanine aminotransferase activities returned to normal was highest in the 6 MU group, as was the percentage of responders who sustained this normal activity after treatment. Side effects were moderate and self-limited in most patients.
(Gut 1993; supplement: S128-S129)

The efficacy of three different treatment schedules of recombinant interferon (IFN) alfa-2b (INTRON A, Schering-Plough) was evaluated in patients with chronic hepatitis C virus (HCV) infection.

TABLE Patient characteristics before treatment

	Group A (n=30)	Group B (n=24)	Group C (n=33)
Male/female	23/7	19/5	25/8
Mean age (y) (range)	49 (18-60)	47 (18-62)	48 (18-59)
Liver histology:			
Chronic persistent hepatitis	6	9	7
Chronic active hepatitis	22	13	24
Chronic lobular hepatitis	1	1	1
Cirrhosis	1	1	1
Alanine aminotransferase (IU/l)	110-75	118-48	109-69
White blood cell count ($\times 10^9/l$)	4-98	5-05	4-89
Platelets ($\times 10^{11/l}$)	1-50	1-49	1-51

Figure 1: Percentage of patients with normalisation of serum alanine aminotransferase activities.

Patients and methods
For inclusion in the trial, patients had to be aged between 18 and 65 years, with a white blood cell (WBC) count $>3 \times 10^9/l$, platelets $>1 \times 10^{11/l}$, and serum alanine aminotransferase (ALT) activities twice the upper limit of normal for nine months. They were also required to have a histologically proved diagnosis of chronic persistent hepatitis, chronic active hepatitis, chronic lobular hepatitis or compensated cirrhosis, and to be positive for antibodies to hepatitis C virus (anti-HCV) on second generation ELISA (ELISA II, Ortho).
Patients were excluded if they had a history of drug or alcohol abuse; cardiac, renal, or respiratory failure; or positivity for antibodies to HIV or autoimmune antibodies (antinuclear, antimitochondrial, or anti-liver-kidney microsomal-1).
All patients received recombinant interferon alfa-2b for 12 months, according to the following schedule:
Group A: 6 million units (MU) intramuscularly three times weekly for 12 months.
Group B: 3 MU three times weekly subcutaneously for 12 months.
Group C: 3 MU three times weekly subcutaneously for two months followed by 1.5 MU TIW for 10 months.
Clinical and laboratory parameters were evaluated every 15 days for the first two months, and then at monthly intervals. A return of alanine aminotransferase (ALT) activities to normal during IFN treatment was considered a complete response.
Patient characteristics before beginning treatment are shown in the Table. No significant differences were observed between the three study groups in respect of age, sex, or biochemical and histological features.
STATISTICAL ANALYSIS
Data were evaluated using the χ^2 test and Student's *t* test.
Results
After 12 months, the percentage of patients with normal ALT activities (responders) was highest in group A (70%) and lowest in group C (48%) (Fig 1). Furthermore, the percentage of responders with ALT rebound after treatment was stopped was highest in group C (56.2%) and lowest in group A (19%), a statistically significant difference ($p < 0.05$) (Fig 2). The percentage of responders whose

Figure 2: Percentage of responders with alanine amino transferase (ALT) rebound on stopping treatment.

ALT activities remained normal six months after treatment stopped was 81% in group A, 64.3% in group B, and 43.8% in group C.

None of the responders lost anti-HCV antibodies.

The side effects were moderate and self limited in most patients (asthenia occurred in 40 patients, flu like syndrome in 28, alopecia in 16, granulocytopenia in 21, thrombocytopenia in 16 and arthromyalgias in 10). Doses were reduced for a short period in five patients (two in group A, two in group B, and one in group C) as a result of granulocytopenia and thrombocytopenia.

Conclusions

Twelve months' treatment with recombinant interferon alfa-2b at a dosage of 6 MU three times weekly seemed to be more effective than treatment with 3 MU three times weekly for two months plus 1.5 MU three times weekly for 10 months in increasing the percentage of long term responders. This regimen was well tolerated with no appreciable toxicity.