Low dose interferon alfa-2b for chronic hepatitis B in Asian countries

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Abstract
In a study of low dose interferon alfa-2b in 587 patients expected to show a good response to treatment, 76-87% patients in different countries had alanine aminotransferase activities returned to normal after four months' treatment, 49-72% were negative for hepatitis B virus (HBV)-DNA, 51-66% were negative for hepatitis B e antigen (HBeAg), and 44-62% were anti-HBe positive. These effects were maintained after nine to 12 months' follow up. Side effects were mild, but led to discontinuation of treatment in 12 patients.
(Gut 1993; supplement: S99-S100)

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Figure Treatment schedule.
TIW=three times weekly.

TABLE I Patient characteristics (n=587)

	Indonesia	Korea	China	Thailand	Others*	Total
Numbers of centres	3	4	4	3	12	26
Number of patients enrolled	81	119	111	41	235	587
Protocol violations	2	5	3	0	31	41
Withdrawals (not treatment related)	4	4	8	2	39	57 (9.7%)
Discontinued (side effects)	0	3	1	0	8	12 (2.0%)
Higher dosage required	0	3	2	1	31	37 (6.3%)
Evaluable patients	75	104	97	38	126	440
Sex (Male/Female)	53/22	76/28	81/16	28/10	104/22	342/98
Mean age (y)	27.3	29.4	31.2	29.2	34.3	29.2

*Others are centres in Hong Kong, Japan, Malaysia, and Taiwan.

The aim of this study was to evaluate the efficacy and degree of tolerance to low dose interferon alfa-2b (INTRON A) in carefully selected Asian patients with chronic hepatitis B virus (HBV) infection. The rationale for the protocol was based on previous publications describing the type of patients who should show a good response to interferon alfa-2b treatment.¹⁻⁸

Patients and methods

Investigators were asked to include only those patients with a potentially favourable response to interferon alfa-2b. To be enrolled in the study, therefore, patients had to have been infected later in life, and be under 50 years of age, negative for antibodies to HIV (anti-HIV), and without delta or hepatitis C virus superinfection. They were also required to have serum alanine aminotransferase (ALT) activities at least twice the upper limit of normal, with low viral replication — that is, low HBV-DNA titres, and a medium to high histology activity index for chronic hepatitis B.

Corticosteroids were given for six weeks in a reducing dose, followed by a two to four week rest period, and then four months of low dose interferon alfa-2b, according to the schedule shown in the Figure.

Results

Five hundred and eighty seven patients were enrolled from eight different Asian countries and a total of 26 centres. Of these, 440 patients (342 males and 98 females, mean age 29.2 years) were suitable for evaluation treatment of efficacy and tolerance. Of the 147 patients who were not suitable, 57 withdrew because of effects not related to treatment, 41 were not suitable because of protocol violations, 37 required higher dosages, and 12 discontinued treatment because of side effects. Patient characteristics for the 587 enrolled are shown in Table I.

After four months of treatment with interferon alfa-2b, 76-87% of patients in different countries had regained normal serum ALT activities, 49-72% were negative for HBV-DNA, 51-66% were negative for hepatitis B e

TABLE II Effects of INTRON A (3 million units (MU)) after four months of treatment

	Indonesia	Korea	China	Thailand	Others*	Total
Number of patients	75	104	97	38	126	440
Male/female	53/22	76/28	81/16	28/10	104/22	342/98
ALT (%)						
Returned to normal	87	82	87	76	85	76–87%
No change	13	18	13	24	15	13–24%
HBV-DNA (%)						
No change	13	27	24	28	21	13–28%
Decreased	15	16	18	12	30	12–30%
Negative	72	57	58	60	49	49–72%
HBeAg (%)						
No change	8	20	16	29	23	8–29%
Decreased	26	29	32	16	26	16–32%
Negative	66	51	52	55	51	51–66%
Anti-HBe (%)						
Negative	38	56	55	48	52	38–56%
Positive	62	44	45	52	48	44–62%
HBsAg (%)						
Negative	5	4	2	5	3	2–5%

*Others: Hong Kong, Japan, Malaysia, and Taiwan.

TABLE III Effects of INTRON A (3 million units) after nine to 12 months of treatment

	Indonesia	Korea	China	Thailand	Others*	Total
Number of patients (%)	22	64	42	20	91	239 (54%)
Male/female	11/11	54/10	36/6	12/8	75/16	188/51
ALT (%)						
Returned to normal	77	75	77	90	84	75–90%
No change	23	25	23	10	16	10–25%
HBV-DNA (%)						
Increased	Not	28	30	15	16	15–30%
Decreased	yet	18	18	25	26	18–26%
Negative	available	54	52	60	58	52–60%
HBeAg (%)						
Increased	0	17	24	15	23	0–24%
Decreased	32	25	20	31	17	17–32%
Negative	68	58	56	54	60	54–68%
Anti-HBe (%)						
Negative	30	52	53	48	48	30–53%
Positive	70	48	47	52	52	47–70%
HBsAg (%)						
Negative	18	8	7	10	9	7–18%
Positive	82	92	93	90	91	82–93%
Histology (%)						
No repeat	50	57	60	40	40	40–60%
Improved	36	38	30	60	24	24–60%
No change	14	5	10	0	36	0–36%

*Others: Hong Kong, Japan, Malaysia, and Taiwan.

TABLE IV Side effects during treatment

Minor side effects (% patients)	Side effects which caused the treatment to be discontinued (n=12)
Flu like symptoms (fatigue, fever, headache, myalgia)	Hair loss
During first 2 weeks	Severe flu like symptoms
During later treatment	Loss of weight and appetite
Loss of appetite (temporary)	Skin rash
Nausea (temporary)	
Hair loss (after 2–3 months)	
Depression, irritability, dizziness	

antigen (HBeAg) and 44–62% were anti-HBe antibody positive (Table II). These effects were consistent between the populations of different Asian countries and were maintained after nine to 12 months' follow up (Table III). Three to six months after treatment, the rate of hepatitis B surface antigen (HBsAg) loss had increased from 2–5% to 7–18% in different countries, and 24–60% of patients also showed improvements when the liver was examined histologically.

Side effects were generally mild but led to discontinuation of treatment in 12 patients (not included in the efficacy results) (Table IV).

Conclusions

Although only those patients who were considered to be good candidates for interferon alfa-2b treatment were included in this study, the results indicate that a considerable number of Asian patients do respond to low dose interferon alfa-2b treatment.

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