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.

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

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TABLE I  Patient characteristics (n=587)

<table>
<thead>
<tr>
<th></th>
<th>Indonesia</th>
<th>Korea</th>
<th>China</th>
<th>Thailand</th>
<th>Others*</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numbers of centres</td>
<td>3</td>
<td>4</td>
<td>4</td>
<td>3</td>
<td>12</td>
<td>26</td>
</tr>
<tr>
<td>Number of patients enrolled</td>
<td>81</td>
<td>119</td>
<td>111</td>
<td>41</td>
<td>235</td>
<td>587</td>
</tr>
<tr>
<td>Protocol violations</td>
<td>2</td>
<td>5</td>
<td>3</td>
<td>0</td>
<td>31</td>
<td>41</td>
</tr>
<tr>
<td>Withdrawals (not treatment related)</td>
<td>4</td>
<td>4</td>
<td>8</td>
<td>2</td>
<td>39</td>
<td>57 (9-7%)</td>
</tr>
<tr>
<td>Discontinued (side effects)</td>
<td>0</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>8</td>
<td>12 (2-0%)</td>
</tr>
<tr>
<td>Higher dosage required</td>
<td>0</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>31</td>
<td>37 (6-3%)</td>
</tr>
<tr>
<td>Evaluable patients</td>
<td>75</td>
<td>104</td>
<td>97</td>
<td>38</td>
<td>126</td>
<td>440</td>
</tr>
<tr>
<td>Sex (Male/Female)</td>
<td>53/22</td>
<td>76/28</td>
<td>81/16</td>
<td>28/10</td>
<td>104/22</td>
<td>342/98</td>
</tr>
<tr>
<td>Mean age (y)</td>
<td>27-3</td>
<td>29-4</td>
<td>31-2</td>
<td>29-2</td>
<td>34-3</td>
<td>29-2</td>
</tr>
</tbody>
</table>

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