To the Editor—Six drugs, including IFN, have been approved by the US Food and Drug Administration for the treatment of chronic hepatitis B [1, 2]; in addition, 8 hepatitis B virus (HBV) genotypes (A–H) have been identified. Ample evidence suggests that patients infected with HBV genotype A or B have a better response to IFN-based treatment than do those infected with HBV genotype C or D [3]. In the 15 February 2007 issue of Clinical Infectious Diseases, Zhao et al. [4] assessed the efficacy of a 24-week course of low-dose IFN or pegylated IFN treatment, as well as factors as factors that predicted a sustained response, in Chinese patients with hepatitis B e antigen (HBeAg)–positive chronic hepatitis B. They consistently found HBV genotype B and younger age were independent factors associated with sustained response, and they suggested that a low-dose regimen of IFN treatment may be cost-effective for the treatment of younger patients who are infected with HBV genotype B.

Although it is not ethical to include untreated control subjects in the present report, our previous study, which involved a Taiwanese Han population, revealed that spontaneous annual HBeAg serocconversion rates in patients who were infected with HBV genotype B and C were 15.5% and 7.9%, respectively [5]. Accordingly, the therapeutic efficacy of any anti-HBV agent should be evaluated on the basis of these inherent differences. In the article by Zhao et al. [4], the HBeAg serocconversion rates at the end of follow-up were 33.3% and 12.9% among patients infected with HBV genotype B and those infected with genotype C, respectively. Our independent data similarly indicated that the rates of sustained response to conventional IFN in patients infected with genotype B and those infected with genotype C were 41% and 15%, respectively. In addition, we also found that young age and HBV genotype B infection were positive predictors of a sustained response [6]. Collectively, the rate of IFN-induced HBeAg serocconversion is, in fact, higher than that of spontaneous HBeAg serocversion in HBV carriers at the immune-active phase, especially for young subjects and for those with genotype B infection. These facts further highlight the necessity of early antiviral treatment in this special clinical situation.

Of particular note, patients who are infected with HBV genotype B seem to be more susceptible to IFN-based therapy, regardless of whether pegylated or conventional formulations are used, whereas notable response rates are attained with pegylated IFN (compared with conventional IFN) in HBV genotype C–infected patients [7]. For the treatment of chronic hepatitis C, it is known that hepatitis C virus (HCV) genotype plays an important role in determining the treatment regimen [8]. For example, HCV genotype 1–infected patients should receive a 48-week course of combination therapy with pegylated IFN plus high-dose ribavirin, and genotype 2– or genotype 3–infected patients have a superb response to 24-week courses of combination therapy with low-dose ribavirin. Thus, HBV genotype B is somewhat like HCV genotype 2 or 3, which requires only 24 weeks of low-dose pegylated IFN treatment. In sharp contrast, genotype C acts like HCV genotype 1 in that treatment may require a longer duration of high-dose pegylated IFN. Nevertheless, additional clinical trials that stratify by genotype and treatment regimen are needed to address this issue.

In summary, HBV carriers should undergo routine genotyping to help identify how they can get the greatest benefit from IFN-based therapy and to determine the optimal treatment regimen. This tailoring strategy is also a big step toward individualized therapy for HBeAg-positive chronic hepatitis B in countries where genotype B and C are prevalent.

Acknowledgments

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References
Zanamivir Treatment Is Equally Effective for Both Influenza A and Influenza B

To the Editor—We previously reported that oseltamivir was less effective against influenza B than it was against influenza A in a study of the 2002–2003 influenza season; these findings were similar to those in a report in 2007 by Sugaya et al. [1–3]. However, the effectiveness of another neuraminidase inhibitor, zanamivir, has not been compared between influenza A and influenza B. Therefore, we performed a preliminary study of the effectiveness of zanamivir for the treatment of 67 patients with influenza A and 100 patients with influenza B (with influenza being diagnosed using commercial antigen detection kits) [3, 4] during the 2001–2002, 2002–2003, 2003–2004, 2004–2005, and 2005–2006 seasons (table 1). The percentage of patients who were afebrile at 24 h or 48 h after the first inhalation of zanamivir was analyzed as a parameter of the effectiveness of zanamivir treatment. There was no significant difference between patients with influenza A and patients with influenza B with respect to the percentage of patients who were afebrile at 24 h (49.3% vs. 36%) or at 48 h (79.1% vs. 80%).

In our previous study, the mean duration of fever (±SD) in patients with influenza A and patients with influenza B was 31.2 ± 23.7 h and 47.1 ± 30.8 h, respectively, after the first dose of oseltamivir and 47.9 ± 26.0 h and 65.4 ± 32.8 h, respectively, after the onset of fever [3]. In addition, the mean duration of fever (±SD) after onset of fever was 82.4 ± 36.0 h and 78.3 ± 41.9 h in patients with influenza A and patients with influenza B, respectively, who were not treated with antiviral medicine drugs [3].

Studies of in vitro antiviral activity of oseltamivir or zanamivir against laboratory strains of influenza virus that used culture and enzymatic assays have suggested that influenza B virus is less susceptible than influenza A virus to oseltamivir and zanamivir [5]. However, the reported difference of the mean inhibitory concentration of 50% between influenza A and B viruses was less for zanamivir (2.09 nM vs. 4.15 nM) than it was for oseltamivir (0.73 nM vs. 11.53 nM). These findings may explain our results in a clinical context, showing that oseltamivir is less effective against influenza B than it is against influenza A and that zanamivir is equally effective against both. We are now studying the effectiveness of zanamivir against influenza A and influenza B among a large number of patients identified during the 2006–2007 season. In conclusion, zanamivir is more effective than oseltamivir for the treatment of influenza B.

Acknowledgments

Potential conflicts of interest. All authors: no conflicts.

Table 1. The percentage of afebrile patients at 24 h and 48 h after the first inhalation of zanamivir.

<table>
<thead>
<tr>
<th>Type of influenza</th>
<th>No. of female patients</th>
<th>No. of male patients</th>
<th>Age, mean years ± SD</th>
<th>No. (%) of afebrile patients at 24 h</th>
<th>No. (%) of afebrile patients at 48 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (n = 67)</td>
<td>42</td>
<td>25</td>
<td>37.9 ± 17.5</td>
<td>33 (49.3)</td>
<td>53 (79.1)</td>
</tr>
<tr>
<td>B (n = 100)</td>
<td>61</td>
<td>39</td>
<td>31.6 ± 18.2</td>
<td>36 (36.0)</td>
<td>80 (80.0)</td>
</tr>
</tbody>
</table>

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Halo Sign and Improved Outcome

To the Editor—Greene et al. [1] described baseline chest CT imaging findings from 235 patients with invasive pulmonary aspergillosis who participated in a...