**Therapeutics**

**Peginterferon α-2a alone or combined with lamivudine increased response rates more than lamivudine alone**


**Question**
In patients with hepatitis B e antigen (HBeAg)--negative chronic hepatitis B, how do peginterferon α-2a monotherapy, peginterferon α-2a plus lamivudine, and lamivudine monotherapy compare for efficacy and safety?

**Methods**
Design: Randomized controlled trial (Peginterferon Alfa-2a HBeAg-Negative Chronic Hepatitis B Study).
Allocation: Concealed.*
Blinding: Blinded [clinicians, data collectors, and outcome assessors]*
Follow-up period: 72 weeks.
Setting: 54 sites in 13 countries.
Patients: 552 patients (mean age 40 y, 85% men) who had been negative for HBeAg and positive for anti--hepatitis B e antibody and hepatitis B surface antigen for ≥ 6 months, had a hepatitis B virus (HBV) DNA level > 100 000 copies/mL, a serum alanine aminotransferase (ALT) level > 1 but ≤ 10 times the upper limit of the normal range, and had findings on liver biopsy in the previous 24 months consistent with chronic hepatitis B.
Intervention: Peginterferon α-2a, 180 µg once weekly, plus oral placebo once daily (n = 186); peginterferon α-2a, 180 µg once weekly, plus lamivudine, 100 mg once daily (n = 180); or lamivudine, 100 mg once daily (n = 184) for 48 weeks.

**Outcomes:** Normalization of ALT levels, suppression of HBV DNA levels to < 20 000 copies/mL, and adverse events.

**Patient follow-up:** 97% (intention-to-treat analysis).

**Main Results**
Patients who received peginterferon α-2a monotherapy or peginterferon α-2a plus lamivudine had greater normalization of ALT levels and greater suppression of HBV DNA levels to < 20 000 copies/mL, but also had an increased rate of having ≥ 1 adverse event, than did patients who received lamivudine monotherapy (Table).

**Commentary**
Chronic HBV infection affects about 350 million people worldwide, including 1.25 million in the United States (1). HBV increases risk for cirrhosis, hepatic decompensation, and hepatocellular carcinoma (2). About 5000 people die each year from complications of HBV (2).

The study by Marcellin and colleagues highlights the importance of identifying patients with chronic hepatitis B who are antiviral-naive (3). Several antiviral combination therapies have been approved by the U.S. Food and Drug Administration for treatment of chronic HBV infection.

Single-drug therapy for patients with HBeAg–negative hepatitis B e antigen appears to be a better choice for single-drug, long-term treatment.

Various combination therapy trials are ongoing, and their results should be watched for further advances in therapy.

**References**

The availability of safe and easy-to-use drugs for HBV infection is important. Interferon α-2b, lamivudine, and adefovir dipivoxil have all been approved by the U.S. Food and Drug Administration for treatment of chronic HBV infection.

Single-drug therapy for patients with HBeAg–negative hepatitis B e antigen appears to have poor response and can lead to drug resistance. Both interferon and lamivudine, used in this study, are associated with side effects and development of resistance if used for the long term. For these reasons, adefovir appears to be a better choice for single-drug, long-term treatment.

**Conclusions**
In patients with hepatitis B e antigen–negative chronic hepatitis B, peginterferon α-2a monotherapy and peginterferon α-2a plus lamivudine increased rates of normalization of alanine aminotransferase levels and suppression of hepatitis B virus DNA levels to < 20 000 copies/mL, but also increased adverse events compared with lamivudine monotherapy.

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*See Glossary.
†Information provided by author.

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<th>RRI (95% CI)</th>
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<td>Normalization of alanine aminotransferase levels</td>
<td>P vs L</td>
<td>59% vs 44%</td>
<td>34% (10 to 65)</td>
<td>7 (4 to 21)</td>
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<td>P + L vs L</td>
<td>60% vs 44%</td>
<td>35% (11 to 66)</td>
<td>7 (4 to 20)</td>
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<td>Suppression of hepatitis B virus DNA levels to &lt; 20 000 copies/mL</td>
<td>P vs L</td>
<td>43% vs 29%</td>
<td>47% (11 to 95)</td>
<td>8 (5 to 27)</td>
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<td></td>
<td>P + L vs L</td>
<td>44% vs 29%</td>
<td>51% (14 to 100)</td>
<td>7 (5 to 21)</td>
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≥ 1 adverse event:

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<thead>
<tr>
<th>RRI (CI)</th>
<th>NNH (CI)</th>
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<td>P vs L</td>
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