

CORRESPONDENCE



Eltrombopag in Thrombocytopenia

TO THE EDITOR: McHutchison et al. (Nov. 29 issue)¹ report that eltrombopag (a thrombopoietin-receptor agonist) raises the platelet count in patients with hepatitis C cirrhosis and thrombocytopenia. Its application in treating interferon-induced thrombocytopenia, however, necessitates that it improve the sustained virologic response. Even among patients with cirrhosis, thrombocytopenia leads to discontinuation of treatment in only 2% of patients.² Of interest, therefore, is the question of whether eltrombopag prevents the reduction in the dose of interferon that partially explains the poor sustained virologic response in cirrhosis.³ McHutchison et al. state that in their study, platelet counts remained higher than the level at which a reduction in the peginterferon dose is recommended (<50,000 per cubic millimeter). The lower end of the range for all eltrombopag groups was below this level, however, at the end of antiviral treatment. The authors' analysis of antiviral-treatment completion also includes five patients whose baseline platelet levels were above the inclusion criterion. If two of these pa-

tients in the 30-mg group completed treatment, then their exclusion would have meant that there was no significant difference from placebo at this dose.

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1. McHutchison JG, Dusheiko G, Shiffman ML, et al. Eltrombopag for thrombocytopenia in patients with cirrhosis associated with hepatitis C. *N Engl J Med* 2007;357:2227-36.
2. Heathcote EJ, Shiffman ML, Cooksley WGE, et al. Peginterferon alfa-2a in patients with chronic hepatitis C and cirrhosis. *N Engl J Med* 2000;343:1673-80.
3. McHutchison JG, Manns M, Patel K, et al. Adherence to combination therapy enhances sustained response in genotype-1-infected patients with chronic hepatitis C. *Gastroenterology* 2002; 123:1061-9.

TO THE EDITOR: In the study of eltrombopag in the treatment of idiopathic thrombocytopenic purpura (ITP), reported by Bussel et al. (Nov. 29 issue),¹ some patients received concomitant medication for ITP, but the authors do not indicate which medication. In patients concomitantly treated with danazol, platelet counts might have increased because of danazol, not eltrombopag.

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1. Bussel JB, Cheng G, Saleh MN, et al. Eltrombopag for the treatment of chronic idiopathic thrombocytopenic purpura. *N Engl J Med* 2007;357:2237-47.

DR. MCHUTCHISON REPLIES: Lawson cites the report by Heathcote et al., which indicates that only 2 to 4% of patients treated with peginterferon

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alfa-2a required a dose reduction for thrombocytopenia.¹ That study, however, excluded patients with baseline platelet counts of less than 75,000 per cubic millimeter and hence does not represent the population studied in our trial or the population targeted in ongoing trials.

Of the five patients with baseline platelet counts that were 70,000 or more per cubic millimeter (with the numbers according to study group listed correctly in Table 1 of our article but incorrectly in the legend for Fig. 1), three initiated and completed the antiviral therapy phase (one in the 30-mg group and two in the 75-mg group). Two patients did not enter the antiviral therapy phase: one (in the 30-mg group) did not enter this phase because of an adverse event, and one (in the placebo group) had insufficient platelets for initiation of antiviral therapy.

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1. Heathcote EJ, Shiffman ML, Cooksley WGE, et al. Peginterferon alfa-2a in patients with chronic hepatitis C and cirrhosis. *N Engl J Med* 2000;343:1673-80.

DR. BUSSEL AND COLLEAGUES REPLY: In our article, Figure 2D shows that patients not receiving concomitant ITP medications had a good response to eltrombopag alone. When we compared patients who received concomitant ITP medications with

those who did not, the response rates were as follows: placebo, 16.7% vs. 9.5%; 30 mg, 44.4% vs. 20.0%; 50 mg, 72.7% vs. 68.8%; and 75 mg, 60.0% vs. 93.8%. Of the patients receiving concomitant ITP medications (6 in the placebo group [21%], 10 in the group receiving 30 mg of eltrombopag [33%], 12 in the 50-mg group [40%], and 10 in the 75-mg group [36%]), the majority were taking corticosteroids (21%, 33%, 37%, and 32%, respectively). Six patients were receiving danazol (one in the placebo group and five in the group receiving 50 mg of eltrombopag). In four of these five patients in the 50-mg group (each of whom had taken danazol for at least 139 days without a response), platelet counts of 171,000, 369,000, 499,000, and 652,000 per cubic millimeter were achieved. After the patients had discontinued eltrombopag (while they were continuing to receive danazol), the platelet counts decreased to 43,000, 5000, 14,000, and 55,000 per cubic millimeter, respectively, indicating that eltrombopag, not danazol, was responsible for these large increases in platelets.

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Chitinase-like Protein and Asthma

TO THE EDITOR: In their descriptive study of a chitinase-like protein in patients with asthma, Chupp et al. (Nov. 15 issue)¹ report elevated levels of YKL-40 (human cartilage glycoprotein 39 and chitinase 3-like 1) in the serum and lungs of patients with asthma. We measured YKL-40 concentrations in serum before and 24 hours after segmental allergen challenge,² as well as in bronchoalveolar-lavage fluid 10 minutes and 24 hours after segmental allergen challenge, in 13 patients with allergic asthma, using the same enzyme-linked immunosorbent assay (Quidel). YKL-40 concentrations were significantly elevated in serum ($P=0.01$) and even more elevated in bronchoalveolar-lavage fluid ($P=0.003$) 24 hours after allergen challenge (Table 1). In addition, levels of YKL-40

in bronchoalveolar-lavage fluid were positively correlated with eosinophil counts 24 hours after allergen challenge ($r_s=0.768$, $P=0.002$). Although the pathogenetic role of YKL-40 in asthma remains unclear, we extend the data from Chupp et al.¹ by showing that YKL-40 concentrations increase in response to allergen challenge predominantly at the site of allergen deposition.

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1. Chupp GL, Lee CG, Jarjour N, et al. A chitinase-like protein in the lung and circulation of patients with severe asthma. *N Engl J Med* 2007;357:2016-27.