

CORRESPONDENCE



Peginterferon Alfa-2a and Ribavirin in Latino and Non-Latino Whites with Hepatitis C

TO THE EDITOR: Rodriguez-Torres and colleagues (Jan. 15 issue)¹ state that the rate of response to standard therapy for hepatitis C virus (HCV) infection was lower among Latino white patients than among non-Latino whites. We have concerns about the selection of patients, because in the Latino group at baseline, higher percentages of patients had cirrhosis and an alanine aminotransferase quotient of more than 3. These characteristics might indicate more advanced disease.² Furthermore, the rates of obesity and diabetes, which are risk factors for the lack of a sustained viral response,¹ were higher in the Latino group. If the aim of the study was to ascertain whether a lower response to therapy derived from a Latino ethnic background, the two patient groups should have been selected in such a way that they would have had the same severity of disease and the same rates of risk factors.

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1. Rodriguez-Torres M, Jeffers LJ, Sheikh MY, et al. Peginterferon alfa-2a and ribavirin in Latino and non-Latino whites with hepatitis C. *N Engl J Med* 2009;360:257-67.
2. Di Bisceglie AM, Shiffman ML, Everson GT, et al. Prolonged therapy of advanced chronic hepatitis C with low-dose peginterferon. *N Engl J Med* 2008;359:2429-41.

TO THE EDITOR: Rodriguez-Torres and coworkers show that the rates of sustained virologic response among patients infected with HCV genotype 1 were lower among Latino whites than among non-Latino whites. Their study gives rise to the hypothesis that host factors may influence the response to antiviral nucleosides and nucleotides. In 2006, my colleagues and I reported three cases of natu-

rally occurring resistance of hepatitis B virus (HBV) to adefovir in association with the novel resistance mutation rtI233V,¹ whereas others have observed that patients who are infected with this mutant strain have a good response to adefovir.² New data from a French group confirm that host factors influence the response to these classes of antiviral drugs,³ but one can only speculate on such factors. With all the published data taken together, it is rather likely that distinct parts of the host metabolism, such as uptake, intracellular processing, and phosphorylation of antiviral agents, act in concert with mutations in the enzymes targeted by the antiviral drug and thus lead to reduced rates of response to therapy. Consequently, not only mutations in the viral genome but also host factors that are putatively involved in therapy failures need to become the focus of future research.

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1. Schildgen O, Sirma H, Funk A, et al. Variant of hepatitis B virus with primary resistance to adefovir. *N Engl J Med* 2006;354:1807-12.

THIS WEEK'S LETTERS

- 1907 Peginterferon Alfa-2a and Ribavirin in Latino and Non-Latino Whites with Hepatitis C
- 1908 Blood Oxygen on Mount Everest
- 1911 Mortality Attributable to Smoking in China
- 1911 Endometriosis
- 1912 Vitamin D Deficiency in Critically Ill Patients

2. Curtis M, Zhu Y, Borroto-Esoda K. Hepatitis B virus containing the I233V mutation in the polymerase reverse-transcriptase domain remains sensitive to inhibition by adefovir. *J Infect Dis* 2007;196:1483-6.
3. Carrouée-Durantel S, Durantel D, Werle-Lapostolle B, et al. Suboptimal response to adefovir dipivoxil therapy for chronic hepatitis B in nucleoside-naïve patients is not due to pre-existing drug-resistant mutants. *Antivir Ther* 2008;13:381-8.

THE AUTHORS REPLY: Malgarini and Pimpinella inquire about the difference in baseline characteristics between the Latino and non-Latino white patients and the effect that these differences might have on the ability to conclude that the two groups have different responses to peginterferon alfa-2a and ribavirin. In designing our study, we took into consideration factors that could affect the response in the Latino versus non-Latino white patients with chronic HCV infection. These factors included black race and the presence or absence of cirrhosis, alcohol and drug abuse, human immunodeficiency virus infection, and other forms of liver disease, including hepatitis A and B. We limited the proportion of patients with cirrhosis in both ethnic groups. One of our goals was to identify factors that are predictive of a response in each group, in addition to investigating the overall difference between the two groups. As we noted in our article, we performed a multivariable logistic-regression analysis to evaluate the effects of baseline prognostic factors, such as the body-mass index, on the probability of a sustained virologic response. As

we show in Figure 2C of our article, the difference in sustained virologic response between Latino whites and non-Latino whites remained significant, and ethnic background was the strongest predictor of a response after adjustment for other significant factors. Therefore, we can confidently conclude that Latino whites have a lower rate of response to standard therapy for HCV than do non-Latino whites.

Schildgen shares his research findings regarding the altered host response to adefovir in HBV infection. We cannot make any relevant association between the findings in hepatitis B and those in hepatitis C, because they are very different diseases caused by biologically distinct viruses. In our article, we alluded to the fact that the difference in response rates between Latino whites and non-Latino whites could be due to dissimilar host factors, including genetic and immune characteristics; however, our objective — to explore whether there is a difference in the rate of response — has been achieved. Further research is needed to define the molecular mechanisms of this difference.

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Blood Oxygen on Mount Everest

TO THE EDITOR: Grocott et al. (Jan. 8 issue)¹ measured arterial blood gases in healthy climbers breathing ambient air on Mount Everest. The authors acknowledge the potential confounding influence of the subjects' use of supplemental oxygen before the sampling of blood gases, but further medication history is not provided. Apart from oxygen, a variety of medications, including acetazolamide, inhaled salmeterol, dexamethasone, sildenafil, and tadalafil, have been used by healthy climbers as prophylaxis against altitude-related illnesses.² Use of these medications may affect the physiological response and subsequent blood gas values in hypoxic, hypobaric conditions, particularly with respect to the pulmonary vasculature and the oxygen-hemoglobin dissociation curve.

In addition, the subjects' hemoglobin concentrations at 8400 m, and hence their arterial oxygen content, were estimated from the hemoglobin values measured at 5300 m. It is plausible that this calculation underestimates the hemoconcentration in the subjects at 8400 m that is likely to have occurred as a result of further dehydration and hypothalamic-renal effects,³ resulting in an underestimate of the subjects' true arterial oxygen content at the Balcony on Mount Everest.

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1. Grocott MPW, Martin DS, Levett DZH, McMorrow R, Windsor J, Montgomery HE. Arterial blood gases and oxygen content in climbers on Mount Everest. *N Engl J Med* 2009;360:140-9.