

was known. In postmenopausal, hormone-receptor-positive patients with breast cancer, tamoxifen has been the standard of care for years, and the addition of chemotherapy has a small effect, if any, on survival.

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## Peginterferon and Ribavirin for Hepatitis C

**TO THE EDITOR:** In their review of peginterferon and ribavirin for the treatment of hepatitis C, Hoofnagle and Seeff (Dec. 7 issue)<sup>1</sup> do not include data on the association between the consumption of alcohol and both treatment response and disease progression. Level-one evidence of the deleterious effects of alcohol on hepatitis C virus (HCV) RNA levels, on the response to treatment, and on disease progression led the National Institutes of Health and the American Gastroenterological Association to issue position statements advising that “abstinence should be recommended before and during antiviral treatment . . . [since] even moderate alcohol consumption can have a deleterious effect on the progression of liver disease in patients with chronic hepatitis C.”<sup>2,3</sup> Alcohol consumption may explain the marked dichotomy in progression rates that cannot be explained by the HCV genotype.<sup>4</sup> Knowledge of alcohol’s effects on disease progression should provide reassurance to patients who want to alter the outcome of their disease, particularly since data for nondrinkers show a more benign course than the authors suggest.<sup>5</sup> At a population level, targeting alcohol consumption may effectively reduce the excess deaths the authors anticipate.

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**TO THE EDITOR:** The article by Hoofnagle and Seeff would have been more informative if it had indicated the relevance of insulin resistance in chronic hepatitis C. Insulin resistance induces interferon resistance by causing the progression of hepatic fibrosis. The mechanism by which insulin resistance promotes the progression of fibrosis includes steatosis, hyperleptinemia, increased production of tumor necrosis factor  $\alpha$ , and impaired expression of peroxisome-proliferator-activated receptor  $\gamma$ .<sup>1</sup> Insulin resistance has been found to be a common denominator in patients with difficult-to-treat hepatitis C (including those with the risk factors of cirrhosis, obesity, coinfection with the human immunodeficiency virus [HIV], and black race) and is independently associated with a decreased rate of response to peginterferon plus ribavirin.<sup>1,2</sup> Whether the addition of insulin-sensitizing agents will improve the response rate remains to be determined.

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**TO THE EDITOR:** Hoofnagle and Seeff mention that autoimmune diseases are rare side effects of therapy with interferon alfa and ribavirin for hepatitis C, but they do not mention these conditions as possible contraindications. However, the risk