

Peginterferon α -2a improved the hepatitis C virologic response in concurrent HIV and chronic hepatitis C virus infections

Authors' response

Dr. Koretz states that translating sustained virologic response (SVR) data into clinical practice is problematic because evidence showing that SVR translates into improved clinical outcome does not exist. We disagree with this statement. According to the recently published Practice Guidelines of the American Association for the Study of Liver Diseases, "The goal of treatment for hepatitis C is prevention of complications of infection, which is principally achieved by eradication of infection" (1). The guidelines go on to state that "Infection is considered eradicated when there is an SVR defined as the absence of HCV RNA in serum by a sensitive test at the end of treatment and six months later." These recommendations were fully endorsed by the Infectious Diseases Society of America.

The link between viral eradication (i.e., SVR) and improved outcomes has been repeatedly demonstrated in follow-up studies. In patients with an SVR, hepatic fibrosis is arrested and reversed, a phenomenon that reduces the rate of progression to cirrhosis (2–6). Several studies have also found an association between eradication of HCV and a reduced incidence of hepatocellular carcinoma or liver failure (7–18).

It is reasonable to critically assess the many studies cited above, to highlight deficiencies in study designs and gaps in knowledge, and to suggest that well-designed prospective studies are required to better define the magnitude of benefit conferred by treatment. It is unreasonable to claim that no evidence exists to link SVR with improved outcomes in patients with hepatitis C. To make such a claim is irresponsible and inconsistent with the tenets of evidence-based medicine and does a disservice to both the physicians who provide care for these patients and to those who struggle to cope with hepatitis C.

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Commentator's reply

The statements of Drs. Torriani and Chung that my commentary is unfair because it claims that there is no evidence linking SVR with improved outcome are based on misinterpretation. The commentary states that there is no evidence from randomized controlled trials with clinically important outcomes. In other words, there is no evidence that treatment reduces the subsequent incidence of liver failure, hepatic cancer, or death. The U.S. Preventive Services Task Force reached the same conclusion (1). Such evidence can only be obtained from randomized controlled trials comparing long-term clinical outcomes in patients randomized to treatment or no treatment. The studies of Drs. Torriani and Chung and their colleagues did not provide such data. In fact, the only such randomized trials were the early treatment trials of standard interferon; those studies were only conducted for about a year, and most of the patients in the control group were subsequently given treatment (so we cannot even do a look-back now to see if there is any difference in outcomes). In a meta-analysis from the Cochrane Collaboration comparing combination therapy (interferon plus ribavirin) with monotherapy (interferon alone), no differences in mortality or liver cancer have been observed (Personal communication, C. Glud).

We should put hepatitis C into perspective. Patients have 2 fundamental questions: "What is the infection going to do to me?", and "If something bad is going to happen, is there anything that can be done to reduce its likelihood?". Society has another issue, namely, the high cost of the treatment (but this is not an individual-patient issue if he or she has a third-party payer).

With regard to the first question, it is now very clear that only a small percentage of infected patients will ever develop liver failure or cancer. Cohort studies, in which the entire population of infected patients is identified at the outset, have shown that < 10% of such patients have serious effects from their illness over the succeeding 20 to 45 years (2–8). Our experience at UCLA has been that only 8 of 90 patients with non-A, non-B posttransfusion hepatitis have developed liver failure from infections obtained in the 1970s [9].) While reports from tertiary care liver centers claim a more severe prognosis, it must be appreciated that such centers do not know what the denominator is—namely, the total number of infected patients from which those referred to them come.

The second issue of concern to patients is the question of treatment. It is true that a small percentage of infected patients will become clinically ill. (It is also true that hepatitis C is the leading indication for liver transplantation, but that is a consequence of the high prevalence of infected patients, so that even a small percentage results in a large absolute number.) What can be done to prevent that?

We know that current therapy can produce SVRs in up to 50% of patients. Proponents of therapy (and the decision analyses that have been published [10, 11]) assume that that translates into a 50% reduction of end-stage liver disease. However, that cannot be true: The occurrence of an SVR is not a random event, with responders having identifiable characteristics, such as infection with nongenotype 1,

a relatively short duration of infection, and little or no fibrosis on biopsy.

Finally, it is disingenuous for Drs. Torriani and Chung to accuse me of performing a disservice to doctors and patients. We currently have a therapy for which we have no definitive data of important clinical benefit. On the other hand, it causes adverse effects in virtually all recipients, severe enough to require cessation of therapy in 10% or so, and death in a few. In addition, it is very expensive. When viewed in that light, it does not make sense to use it. This perspective needs to be provided to doctors and, more important, to patients for an informed decision. The real disservice would be to withhold such information from them.

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