

Durability of a sustained virologic response in patients with chronic hepatitis C treated with peginterferon and ribavirin

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A Sustained virologic response is durable in patients with chronic hepatitis C with peginterferon alfa-2a and ribavirin.

Swain MG, Lai MY, Shiffman ML, Cooksley WG, Zeuzem S, Dieterich DT, Abergel A, Pessôa MG, Lin A, Tietz A, Connell EV, Diago M

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The current standard therapy for chronic hepatitis C virus (HCV) infection is the combination of pegylated interferon and ribavirin. The ultimate goal of treatment in patients with chronic HCV infection is to completely eradicate HCV in infected hosts, and prevent liver-related morbidity and mortality. However, these goals are difficult to measure and it takes long time to assess the achievement of these goals. A sustained virologic response (SVR) has been used as a surrogate marker of these ultimate goals in treatment of chronic hepatitis C. An SVR is defined as undetectable serum HCV RNA at 24 weeks after the end of treatment. To be a useful surrogate marker, achievement of SVR should result in the reduction of liver-related morbidity and mortality, complete eradication of HCV in infected hosts, and no late virologic relapse.

Achievement of SVR has been associated with improvement in liver histology and health-related quality of life, as well as a reduced risk of hepatocellular carcinoma and liver-related mortality.¹⁻³ The survival of patients who achieved SVR was

reported to be comparable to that of general population, matched for age and sex.⁴ However, the development of hepatocellular carcinoma was reported despite achievement of SVR in patients with chronic hepatitis C and advance fibrosis.⁵

There is some debate as to whether achievement of SVR results in complete eradication of HCV. In a study of 2089 patients with chronic hepatitis C from 3 clinical trials, hepatic HCV RNA was found to correlate with serum HCV RNA in all cases, and 98% of sustained virologic responders had undetectable hepatic HCV RNA.⁶ Several small studies have described patients who achieved SVR but have residual HCV RNA detected in peripheral blood mononuclear cells with highly sensitive reverse transcription and nested polymerase chain reaction assays.^{7,8} Whether these findings represent a replication-competent virus or have any clinical significance is unclear.

Several small studies reported SVR achieved with conventional interferon alone or in combination with ribavirin was durable. In these reports, serum HCV RNA remained undetectable in 92-100% of patients who achieved SVR with 2 to 13 years of follow-up.^{4,5,9-12} However, there are limited data on the durability of SVR achieved with peginterferon in patients with chronic hepatitis C. Swain et al. studied the durability of SVR achieved with peginterferon in 1343 patients.¹³ They analyzed the durability of SVR in large cohort of patients who were enrolled in one of 9 randomized controlled clinical trials,¹⁴⁻²² which evaluated

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Abbreviations: HCV, hepatitis C virus; SVR, sustained virologic response

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the efficacy of peginterferon alfa-2a alone or in combination with ribavirin. Total 1343 treatment-naïve patients who achieved SVR and had at least one post-baseline HCV RNA evaluation were assessed. One thousand three hundred thirty one of 1343 patients (99.1%) remained HCV RNA undetectable in serum at mean of 3.9 years after completion of treatment. The durability of SVR in this study was independent of patient characteristics such as HCV mono-infection, HCV-HIV co-infection, or ALT level. The durability of SVR also appeared to be unaffected by the type of treatment. HCV RNA was detected in the serum of 12 patients who obtained SVR in their original studies at mean of 666 days after completing treatment. Among the 12 patients with reappearance of HCV RNA, there were no baseline or treatment factors associated with reappearance of HCV RNA including HCV genotype, sex, age, race, risk factor for infection, or baseline viral load. It was unknown whether these cases reflect relapse or re-infection because of the paucity of paired samples. The findings of this study were comparable with those reported from smaller studies with conventional interferon.

There was one domestic report on the durability of interferon-based therapy in patients with chronic hepatitis C.²³ In this study, 73 patients who achieved SVR with conventional interferon or peginterferon in combination with ribavirin were included. HCV RNA reappeared in 8 of 73 (11%), but persistent viremia remained only in one patient (1.4%). Transient positive tests probably represent false-positive test, and the durability of SVR in Korean patients with chronic hepatitis C appears to be similar with those reported in other studies.

In conclusion, this study showed SVR achieved with peginterferon alfa-2a alone or in combination with ribavirin is durable in 99% of patients for at least 4 years after completion of therapy and is independent of patient or treatment characteristics.

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