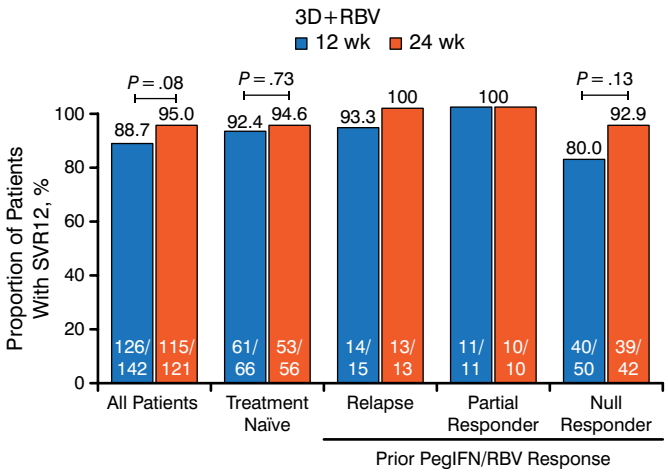
Figure 1. SVR12 Rates in Cirrhotic HCV1a-Infected Treatment-Naïve and Treatment-Experienced Patients Treated for 12 or 24 Weeks



3D, 3-drug direct-acting antiviral regimen; HCV1a, hepatitis C virus genotype 1a; PegIFN, pegylated interferon; RBV, ribavirin; SVR12, sustained virologic response at week 12.

P=.009, respectively). Adverse events and event-related discontinuation were similar for both treatment durations.

This pooled analysis of 4 phase 3 trials of patients infected with HCV genotype 1a indicates that the rate of SVR in noncirrhotic patients treated with the 3D regimen may be enhanced by addition of RBV. In addition, in patients with cirrhosis, extension of 3D + RBV to 24 weeks may be warranted, especially for those who were prior null responders to peginterferon/RBV.

HCV–Infected Patients With Compensated Cirrhosis Benefit From 12-Week, Once-Daily, Oral Combination of LDV and SOF

Written by Brian Hoyle

The once-daily, oral, 12-week regimen using a single tablet combination of the nonstructural protein 5B (NS5B) inhibitor sofosbuvir (SOF; 400 mg) and the NS5A inhibitor ledipasvir (LDV; 90 mg) with or without ribavirin (RBV) produces high sustained virologic response 12 weeks after conclusion of treatment (SVR12) in hepatitis C virus (HCV)-infected patients with compensated cirrhosis, according to Marc Bourlière, Hôpital Saint Joseph, Marseilles, France. Inclusion of RBV can boost the SVR12 at the expense of increased adverse events and declined hemoglobin count. The LDV plus SOF regimen, recently approved by the Food and Drug Administration for the treatment of chronic HCV genotype 1 infection, is safe and well tolerated in cirrhotic patients.

The present study used pooled data from the phase 2 LONESTAR trial [Lawitz E et al. *Lancet* 2014], phase 2 ELECTRON and ELECTRON-2 trials [NCT01260350], phase 3 GS-US-337-0113 [NCT01975675], phase 3 ION-1 trial [Afdhal N et al. *N Engl J Med.* 2014], phase 3 ION-2 trial [Afdhal N et al. *N Engl J Med.* 2014], and phase 3 SIRIUS trial [NCT02073656]. The primary end point after a 12- or 24- week treatment with LDV plus SOF ± RBV was SVR12.

Of the 513 HCV infected patients, 161 were treatment naïve and 352 were treatment experienced. They were comparable at baseline concerning mean age, gender, ethnicity, mean body mass index, proportions of interleukin 28B (IL28B) CC genotype and genotype 1a, mean HCV RNA, and laboratory data. The majority (68%) of treatment-experienced patients had a prior failure of protease inhibitor therapy. SVR12 was high overall and in the 12- and 24-week groups.

Twenty of the 513 patients (3.9%) failed to achieve SVR12. Of these, 18 relapsed, 1 was lost to follow-up, and 1 died (likely from an infection). SVR12 was not influenced by age, treatment duration, and/or the absence/presence of RBV, with the exception of treatment-experienced patients treated for 12 weeks with LDV plus SOF. Genotype in both the absence and presence of RBV was not influential. For treatment-experienced patients, prior failure of protease inhibitor therapy was not influential. Lower SVR12 was noted in patients with a platelet count $< 75 \times 10^3$ per µL.

The inclusion/absence of RBV had no effect on the frequency of adverse events in general and on grade ≥ 3 adverse events. RBV was associated with more adverse events that prompted discontinuation (n = 3, 1% vs n = 38, 15%) and decline of hemoglobin to < 10 g/dL (n = 1, < 1%, versus n = 26, 10%). Adverse events occurring in more than 10% overall and in either patient group predominantly included headache, fatigue, asthenia, insomnia, and nausea. The presence of RBV was associated with a greater prevalence of pruritus and rash.

The pooled data revealed an SVR12 of 96% overall. In treatment-experienced patients, the 12-week LDV plus SOF regimen produced a 90% SVR12. The rate was boosted to ≥ 96% by the inclusion of RBV at the expense of more frequent adverse events and hemoglobin decline. The LDV plus SOF combination is thus judged to be safe and effective for HCV-infected patients with compensated cirrhosis. The similar findings from the 12- and 24-week treatments indicate that the shorter treatment period is acceptable.