The overall recurrence-free probability was 95% at 1 year, and 87% at 5 years from transplantation. The only significant predictors of HCC recurrence were alpha-fetoprotein > 500 ng/mL (P = .003) and microvascular invasion (P = .002). No center-specific differences seen in intention-to-treat survival, post-LT survival, and overall recurrence-free probability of the cohort.

Data from this largest study to date, and the first multicenter study, demonstrated successful downstaging of HCC to within the Milan criteria in almost two-thirds of patients. These results support broader application of this uniform downstaging protocol, concluded Dr Mehta.

SOF Plus GS-5816 Effective in Noncirrhotic, Treatment-Naïve Patients Infected With HCV Genotypes 1 to 6

Written by Brian Hoyle

An oral, once-daily, 12-week, fixed-dose combination of the nucleotide polymerase inhibitor sofosbuvir (SOF) and nonstructural protein 5A (NS5A) inhibitor GS-5816 (ledipasvir) yields high rates of sustained virological response 12 weeks after therapy (SVR12) in noncirrhotic patients infected with genotypes 1 to 6 of hepatitis C virus (HCV). The results of the open-label study were presented by Tram Tran, MD, Cedars-Sinai Hospital, Los Angeles, California, USA.

The prowess of SOF against HCV is known [Jacobson IM et al. *New Engl J Med.* 2013; Lawitz E et al. *New Engl J Med.* 2013]. High SVR following a 12-week GS-5816 regimen in noncirrhotic, treatment-naïve HCV genotype 1 to 6 patients has been described.

In part A of the current study, patients infected with HCV genotype 1 (n = 55), genotype 3 (n = 54), and genotypes 2, 4, 5, and 6 (n = 45) received oral, ribavirin-free, once-daily SOF + GS-5816 25 mg or 100 mg for 12 weeks. SVR12 was consistently high for the 25-mg and 100-mg doses: genotype 1 (26/27, 96% and 28/28, 100%), genotype 2 (10/11, 91% and 10/10, 100%), genotype 3 (25/27, 93% and 25/27, 93%), genotype 4 (7/7, 100% and 6/7, 86%), genotype 5 (25 mg only: 1/1, 100%), and genotype 6 (4/4, 100% and 5/5, 100%). The relatively lower SVR12 for the 100-mg genotype 4 patients reflected the loss of 1 patient to follow-up.

Part B of the study focused on genotype 1 (n = 120) and 2 (n = 103) noncirrhotic, treatment-naïve patients and involved an 8-week treatment with the 25-mg and 100-mg doses of SOF + GS-5816 without or with (1000 to 1200 mg/d) ribavirin.

The primary objective of part B was the evaluation of safety (adverse events [AEs], laboratory abnormalities) and efficacy. The primary efficacy end point was SVR12, with an HCV RNA lower limit of 25 IU/mL.

Demographics of the 4 treatment arms were similar. The completion rate was 98% to 100%, with 1 discontinuation because of an AE in the SOF + GS-5816 25 mg arm and 1 case of noncompliance in the SOF + GS-5816 100 mg + ribavirin arm.

SVR12 in genotype 1 patients receiving the 25-mg dose without and with ribavirin was 87% (26/30; 3 relapses and 1 AE-related discontinuation) and 83% (25/30; 5 relapses), respectively. The respective value for the 100-mg dose was 90% (26/29; 3 relapses) and 81% (25/31; 5 relapses and 1 lost to follow-up). SVR12 in genotype 2 patients receiving the 25-mg dose without and with ribavirin was 77% (20/26; 6 relapses) and 88% (22/25; 2 relapses and 1 lost to follow-up), respectively. The respective value for the 100-mg dose was 88% (23/26; 3 relapses) and 88% (23/26; 3 relapses).

AEs were similar in the 4 arms. The 4 grade 3 to 4 AEs in the SOF + GS-5816 25 mg arm were not treatment related. Relatively frequent AEs mainly comprised fatigue, headache, nausea, and nasopharyngitis. They were manageable.

The 12-week regimen produced SVR12 rates exceeding 90% in all HCV genotypes. The 8-week regimen was less effective, with lower SVR rates and higher relapse rates in HCV genotype 1 and 2 patients. Inclusion of ribavirin did not affect safety and tolerability. SOF 400 mg and GS-5816 100 mg have been coformulated in a fixed-dose combination for a phase 3 study.

Terlipressin and Albumin Combination Therapy Improves Renal Function in HRS-1

Written by Nicola Parry

Thomas D. Boyer, MD, University of Arizona, Tucson, Arizona, USA, presented initial data from A Placebo-Controlled, Double-Blind Study to Confirm the Reversal of Hepatorenal Syndrome Type 1 With Terlipressin [REVERSE; NCT01143246], the largest trial to date in type 1 hepatorenal syndrome (HRS-1) using terlipressin. The results demonstrated that terlipressin plus albumin treatment improved renal function in patients with HRS-1 when compared with albumin alone.

According to Dr Boyer, HRS-1 involves the development of renal failure in patients with liver cirrhosis due