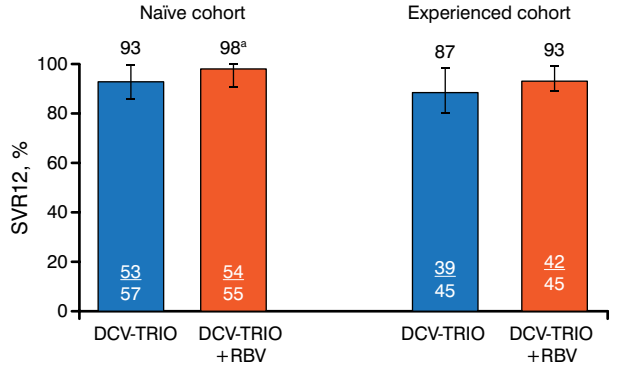
Figure 1. SVR12 in the Modified Intention-to-Treat Population




DCV-Trio, daclatasvir/asunaprevir/beclabuvir; HCV, hepatitis C virus; LLOQ, lower limit of quantification; RBV, ribavirin; SVR12, sustained viral response to treatment 12 weeks after therapy.

[a]One patient with HCV RNA < LLOQ TND at end of therapy and posttreatment week 4 had missing data at posttreatment week 12.

Error bars indicate 97.5% confidence intervals.

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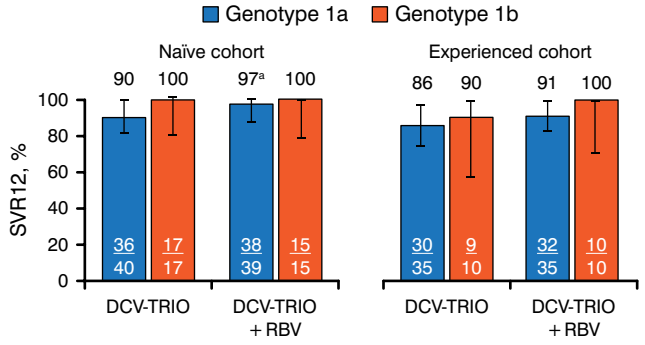
Figure 2. SVR12 by Genotype-1 Subtype




DCV-Trio, daclatasvir/asunaprevir/beclabuvir; HCV, hepatitis C virus; LLOQ, lower limit of quantification; RBV, ribavirin; SVR12, sustained viral response to treatment 12 weeks after therapy.

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Table 1. Virologic Outcomes

| | Treatment Naïve | | Treatment Experienced | |
|---|---|---|---|---|
| | DCV-TRIO (n = 57) | DCV-TRIO + RBV (n = 55) | DCV-TRIO (n = 45) | DCV-TRIO + RBV (n = 45) |
| SVR12 | 53 (93) | 54 (98) | 39 (87) | 42 (93) |
| On-treatment virologic failure | 0 | 0 | 1 (2) | 2 (4) |
| Relapse | 4 (7) | 0 | 5 (11) | 1 (2) |
| Missing data | 0 | 1 (2) | 0 | 0 |

DCV-Trio, daclatasvir/asunaprevir/beclabuvir; RBV, ribavirin; SVR12, sustained viral response to treatment 12 weeks after therapy.

Data are presented as number (%).

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DCV-Trio plus RBV. AEs were similar to those seen in HCV trials and slightly higher among patients receiving RBV.

The all-oral fixed-dose combination of DCV/ASV/BCV with or without RBV was generally safe, well tolerated, and associated with high rates of SVR12. The addition of RBV decreased the frequency of relapse in patients with GT-1a. Baseline RAVs do not appear to impact response.

## Combination DCV/SOF Is Effective in Achieving Sustained Response in Patients With HCV GT-3

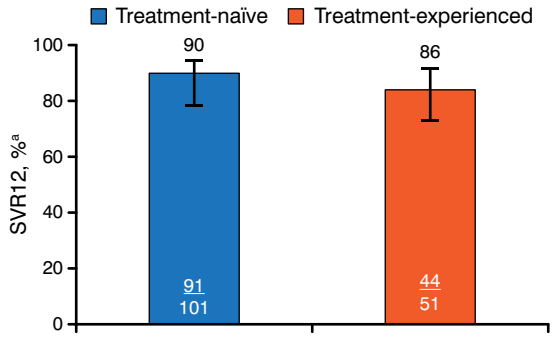
Written by Maria Vinall

Hepatitis C virus (HCV) genotype (GT)-3 is common worldwide and is accompanied by a significant disease burden [Pol S et al. *Liver Int*. 2014]. Among patients with cirrhosis, it is associated with increased risk of fibrosis progression, steatosis, and hepatocellular carcinoma [Nkontchou G et al. *J Viral Hepat*. 2011; Larsen C et al. *J Med Virol*. 2010; Bochud PY et al. *J Hepatol*. 2009]. Current treatment options are limited and require 24-week treatment that includes ribavirin. Results of the Phase III Daclatasvir and Sofosbuvir for Genotype 3 Chronic HCV [ALLY-3; NCT02032901] trial presented by David R. Nelson, MD, University of Florida, Gainesville, Florida, USA, show that oral therapy with the combination of daclatasvir (DCV) and sofosbuvir (SOF) achieves high rates of sustained viral response up to 12 weeks after therapy (SVR12).

ALLY-3 was a phase 3 trial that evaluated the efficacy and safety of DCV plus SOF in patients chronically infected with GT-3. In this open-label trial, patients received oral DCV 60 mg plus oral SOF 400 mg twice daily for 12 weeks. The primary end point was SVR12 (HCV RNA < lower limit of assay quantification [LLOQ]). The study included treatment-naïve (n = 101) and treatment-experienced (n = 51) adult patients with chronic GT-3 infection and HCV RNA ≥ 10 000 IU/mL. Patients previously treated with NS5A inhibitors were excluded.

Overall, patients had a mean age of approximately 55 years. About two-thirds were men and the majority were white. Between 69% and 75% of the participants had a high viral load (> 800 000 IU/mL) and approximately 21% were cirrhotic as defined by the protocol. About 60% of the participants were non-CC IL28B GT. In the experienced group, about 61% of participants had relapsed, 14% had a null response, and 4% had a partial response. The cause of treatment failure in the remaining 22% was "other." Seven patients in the experienced group had received prior treatment with SOF; 2 were treated with alisporivir.

Figure 1. Primary End Point: Sustained Viral Response to Treatment 12 Weeks After Therapy




Error bars indicate 95% confidence intervals. SVR12, sustained viral response to treatment 12 weeks after therapy.

[a]Hepatitis C virus RNA < lower limit of quantification (25 IU/mL).

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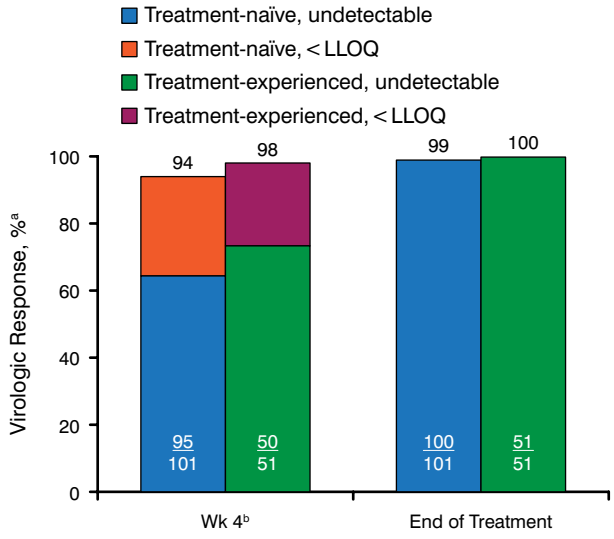
Figure 2. On-Treatment Virologic Response




HCV, hepatitis C virus; LLOQ, lower limit of quantification; SVR12, sustained viral response to treatment 12 weeks after therapy.

[a]Undetectable HCV RNA or HCV RNA < LLOQ (25 IU/mL).

[b]SVR12 rates based on week 4 HCV RNA levels: < LLOQ, target detected, 86%; < LLOQ, target not detected, 91%.

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Treatment with DCV plus SOF was associated with a high rate of SVR12 in both groups (Figure 1).

Figure 2 shows the on-treatment virologic response at week 4 and at the end of treatment for target not detected or target below the level of quantification. By the end of treatment, all but 1 patient were virus negative. Week-4 viral levels did not predict response vs nonresponse.

SVR12 rates were not influenced by sex, age < vs ≥ 65 years, HCV RNA levels, or IL28B polymorphism (CC vs non-CC). Cirrhosis did have a significant influence, regardless of prior treatment status. Overall, only 63% of patients with cirrhosis achieved SVR12 compared with 96% of patients without cirrhosis; rates were similar for treatment-naïve and experienced patients. Among patients with cirrhosis, 34% had portal hypertension (as assessed by platelet counts < 100 000/mm$^2$). Sixteen patients relapsed; 11 of those had cirrhosis. The most common adverse events (> 10% of patients) were headache, fatigue, and nausea; none led to discontinuation.

The combination of DCV plus SOF was safe, well tolerated, and associated with SVR12 rates as high as 96% in patients without cirrhosis. There were no virologic breakthroughs. The resistance analysis for this study is ongoing.

## SOF Plus GS-5816 Effective in Noncirrhotic Patients Infected With HCV GT-3: ELECTRON-2 Final Results

Written by Brian Hoyle

An oral, once-daily, fixed-dose combination of the nucleotide polymerase inhibitor sofosbuvir (SOF) and nonstructural protein 5A (NS5A) inhibitor GS-5816 (ledipasvir) provided for 8 weeks with or without ribavirin to noncirrhotic patients infected with hepatitis C virus (HCV) genotype 3 (GT-3) yields high rates of sustained virological response 12 weeks after therapy (SVR12). The final results of the phase 2 ELECTRON-2 study were presented by Edward Gane, MD, Auckland Clinical Studies, Auckland, New Zealand.

SOF has potent activity against HCV [Jacobson IM et al. *New Engl J Med.* 2013; Lawitz E et al. *New Engl J Med.* 2013]. Unpublished studies presented at the European Association for the Study of the Liver annual meeting have also indicated the anti-HCV activity of GS-5816, and the high SVR following a 12-week regimen in noncirrhotic, treatment-naïve HCV patients. These studies spurred the phase 2, open-label, ELECTRON-2 study evaluating the efficacy and safety of an 8-week regimen of SOF + GS-5816 in noncirrhotic, treatment-naïve patients infected with HCV GT-3. The primary efficacy end point was SVR12 with a lower limit of quantitation of HCV RNA of 15 IU/mL. The primary safety end points were adverse events and laboratory abnormalities.

Subjects received SOF + GS-5816 25 mg (n = 27), SOF + GS-5816 25 mg along with ribavirin (n = 24),