Table 2. Abstinence and Mortality

Alcohol Consumption Status (Variable at Day 90)	1-y Mortality			
	n	Odds Ratio	95% CI	*P* Value
Not reduced (ie, still drinking as much as or more than when presented) vs abstinent	478	2.99	1.47 to 6.05	< .001
Reduced drinking but higher than safety limits vs abstinent	478	2.28	1.07 to 4.86	.032
Reduced drinking to lower than safety limits vs abstinent	478	2.17	1.07 to 4.39	.031

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On multivariate analysis, accounting for disease severity and prognosis, the 28-day odds ratio for mortality in the prednisolone group was 0.609 (95% CI, 0.409 to 0.900; $P = .015$), indicating a potential reduction in mortality of about 40%. Neither treatment had any impact on survival beyond 28 days. Infection, in particular lung infection, was more common in prednisolone-treated subjects.

All 4 prognostic scoring systems (ie, DF, Glasgow Alcoholic Hepatitis Score [GAHS], Model for End Stage Liver Disease [MELD], and the Lille model) were significantly associated with prognosis (all $P < .0001$). However, the area under the receiver operating characteristic curves (AUROC) were relatively low ranging from .69 to .74.

Abstinence is a major determinant of survival after 90 days. Compared with patients who reported complete abstinence, the 90-day odds ratio for mortality for those who reduced their drinking to within government guidelines was double. For those who did not reduce their drinking, it was triple (Table 2).

DCV/ASV/BCV Improves Sustained Viral Response in Patients With Chronic HCV GT-1 Infection and Compensated Cirrhosis: UNITY-2 Results

Written by Maria Vinall

Andrew J. Muir, MD, MHS, Duke University School of Medicine, Durham, North Carolina, USA, presented data indicating that treatment with an all-oral fixed-dose combination of daclatasvir (DCV)/asunaprevir (ASV)/beclabuvir (BCV; DCV-Trio) with or without the addition of ribavirin (RBV) is associated with high rates of sustained viral response to treatment 12 weeks after therapy (SVR12) in patients with chronic compensated cirrhosis and hepatitis C virus (HCV) genotype 1 (GT-1) infection.

In a phase 2 trial, combination treatment with DCV/ASV/BCV was associated with SVR12 in > 92% of treatment-naïve patients with GT-1 infection and 100% of patients with GT-4 infection [Hassanien T et al. *J Hepatol.* 2014; Everson GT et al. *AASLD* 2013]. UNITY-2 [NCT01973049] was a randomized phase 3 trial that evaluated DCV/ASV/BCV as a fixed-dose regimen with and without RBV in treatment-naïve (n = 112) and treatment-experienced (n = 90) patients with HCV GT-1 infection and compensated cirrhosis. Adults with chronic HCV GT-1a or 1b infection and confirmed compensated Child-Pugh class A cirrhosis with a platelet count > 50 000/mm^2, international normalized ratio < 1.7, and albumin > 3.5 g/dL were eligible to participate. Patients were randomized to DCV-Trio (DCV 30 mg/ASV 200 mg/BCV 75 mg) with or without blinded RBV and treated twice daily for 12 weeks. The key efficacy variable was SVR12 (HCV RNA < lower limit of quantification [25 IU/mL] target detected/not-detected) in the treatment- naïve and treatment-experienced patients evaluated separately.

Participants were predominately white (> 80%) men (> 60%) between 58 and 60 years of age. Between 70% and 78% of the participants were GT-1a; less than one-third had the favorable IL28B CC GT polypmorphism; 26% of patients had platelets < 100 000/mm^2. Of the 90 treatment-experienced patients, 39% were prior null responders; 9% were partial responders and 18% of patients had relapsed. Nonresponse was characterized as "other" in the remaining 34%.

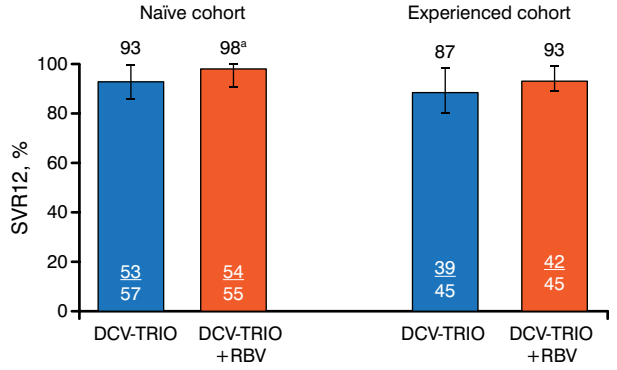
In the treatment-naïve cohort, 93% of patients receiving DCV-Trio only achieved SVR12 compared with 98% of those who received DCV-Trio plus RBV. Results were similar in the experienced cohort (87% and 93%, respectively; Figure 1) and when analyzed by GT-1 subtype (Figure 2).

No clear difference in SV12 was observed between patients who did and did not receive RBV when assessed by platelet count (< vs ≥ 100 000/mm^2), sex, age, baseline HCV RNA, or IL28B GT.

Three patients had on-treatment virologic failure; all were in the treatment-experienced group. Ten patients relapsed (4 treatment-naïve patients; 6 treatment-experienced patients; Table 1). NS5A and NS3 resistance-associated variants (RAVs) did not appear to impact SV12.

Two patients in the DCV-Trio-only group had serious adverse events (AEs) compared with 7 patients receiving

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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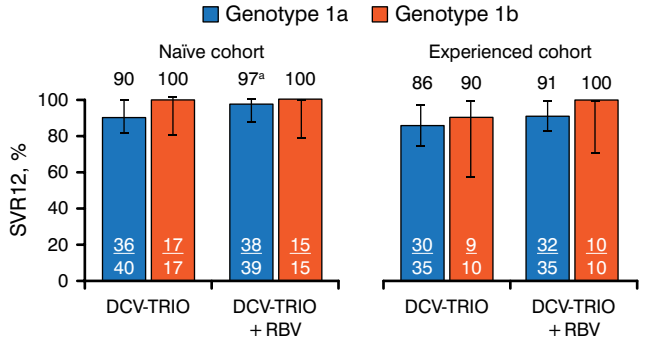
Figure 2. SVR12 by Genotype-1 Subtype



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.

[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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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.