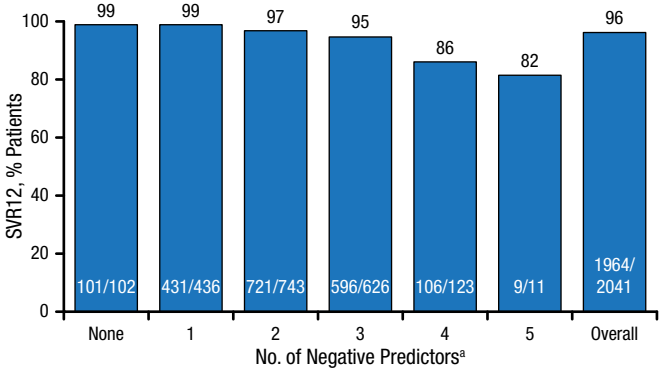
Figure 1. SVR12 Rates per Cumulative Number of Negative Predictors



HCV, hepatitis C virus; SVR12, sustained virologic response for 12 wk.

[a]Negative predictors: HCV genotype 1a, weight ≥ 75 kg, *IL28B TT*, Hispanic/Latino, HCV RNA ≥ 800 000 IU/mL.

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Table 2. Label-Recommended Regimens

	Patients Without Cirrhosis		Patients With Cirrhosis	
	GT1a	GT1b	GT1a	GT1b
Regimen	3D + RBV	3D	3D + RBV	3D + RBV
Duration, wk	12	12	24	12

US product insert and European Union summary of product characteristics–recommended regimens for subjects with GT1 infection.

3D, regimen of 3 direct-acting antivirals (ombitasvir, dasabuvir, and paritaprevir boosted with ritonavir); GT, genotype; RBV, ribovarin.

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The SVR12 rates for the entire cohort by the cumulative number of individual negative predictors are shown in Figure 1.

Among >2000 patients in the studies, 1083 received the label-recommended regimen (Table 2). The overall rate of SVR12 among those patients was 97% (n = 1052), with rates similarly high regardless of whether cirrhosis was present. Only 1 patient with a genotype 1b infection did not achieve SVR12. Of the 31 patients who did not achieve SVR12, 19 (1.8%) had on-treatment breakthrough or posttreatment relapse; 12 (1.1%) discontinued treatment prematurely. Of these 12 discontinuations, 3 were due to adverse events. Of the 22 variables, only body mass index and HCV genotype 1a disease had a negative impact in the multivariate stepwise analysis.

According to Dr Reau, these data suggest that the regimen of 3 direct-acting antivirals with or without ribovarin confers high SVR12 rates and offers an effective treatment option for patients with HCV who present with factors previously thought to have an negative impact on treatment response.

ALLY 2: Daclatavir + Sofosbuvir Effective in Treating HIV/HCV Coinfected Patients

Written by Brian Hoyle

Kenneth Sherman, MD, PhD, University of Cincinnati College of Medicine, Cincinnati, Ohio, USA, presented the findings of ALLY 2 [NCT02032888], a phase 3, randomized, open-label clinical trial, which demonstrated a sustained virologic response for 12 weeks (SVR12) in 97% of patients coinfected with genotypes 1 to 4 hepatitis C virus (HCV) and HIV. Patients were treated with the NS5A inhibitor daclatasvir (DCV) and NS5B inhibitor sofosbuvir (SOF), which allowed for treatment without having to modify the combination antiretroviral therapy (cART) regimen.

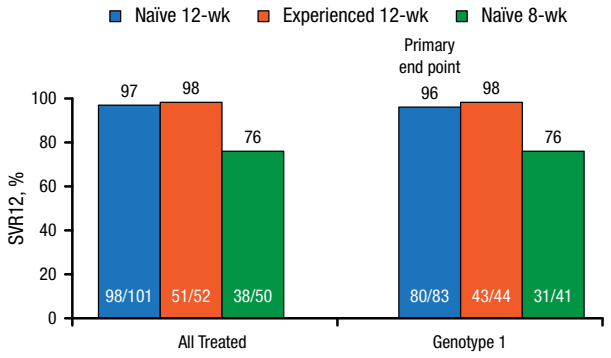
About 130 to 150 million people are infected with chronic HCV worldwide [WHO. http://www.who.int/mediacentre/factsheets/fs164/en/. Accessed June 3, 2015], including an estimated 3 to 4 million in the United States [CDC. http://www.cdc.gov/hepatitis/hcv/statisticshcv.htm. Accessed June 3, 2015]. Up to 20% of people with chronic HCV will develop cirrhosis, with about the same proportion progressing to liver cancer [WHO. http://www.who.int/mediacentre/factsheets/fs164/en/. Accessed June 3, 2015].

HIV/HCV coinfection accelerates progression of HCV liver disease [Macías J et al. *Hepatology.* 2009] and hinders pegylated interferon treatment [Grint D et al. *HIV Med.* 2013]. A treatment regimen directed at HIV/HCV co-infected patients must not compromise cART. The positive efficacy and safety results of the DCV + SOF combination in chronic HCV monoinfection [Sulkowski MS et al. *N Engl J Med.* 2014] prompted ALLY 2, which evaluated the combination treatment in HIV/HCV coinfected patients on a broad range of antiretroviral therapies.

The ALLY 2 trial involved 203 patients who were treatment-naïve for HCV (n = 151) or who had been treated previously (n = 52). The treatment-naïve patients were randomized 2:1 to DCV 30/60/90 mg plus SOF 400 mg QD for either 12 weeks (n = 101) or 8 weeks (n = 50). The treatment-experienced patients received 12 weeks of therapy. The standard DCV dose was 60 mg, with the dose being adjusted according to cART: 30 mg in those receiving ritonavir-boosted protease inhibitors and 90 mg when cART included nonnucleoside reverse transcriptase inhibitors, except for rilpivirine. At baseline, the 3 arms were comparable in demographic, clinical, and prior HIV treatment characteristics. The primary end point, SVR12 in the treatment-naïve patients with HCV genotype 1 treated for 12 weeks, was 96% (Figure 1).

Patients with baseline NS5A resistant-associated variants achieved SVR12 at a rate of 96% (22/23) when treated

Figure 1. ALLY 2 Results: SVR12 (Intention to Treat) by Treatment Group



SVR12, sustained virologic response for 12 wk.

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for 12 weeks, and 70% (7/10) when treated for 8 weeks. Treatments did not compromise HIV control, as indicated by the unwavering mean CD4 count and continued HIV virologic suppression throughout the treatment period.

The frequency of serious adverse events was low, occurring in 1.0%, 5.8%, and 0.0% of the naïve/12-week, experienced/12-week, and naïve/8-week arms, respectively. The adverse events commonly comprised fatigue, nausea, headache, and diarrhea. One death occurred after stopping study treatment in the 8-week arm as a result of treatment-unrelated cardiac arrest.

ALLY 2 provides evidence of the efficacy and safety of the DCV + SOF combination in patients coinfected with HIV/HCV, whether or not they had been treated before for HCV. The treatment benefit does not come at the expense of compromised treatment of HIV infection.

TURANDOT: Monoclonal Antibody Effective and Safe in Relieving UC Symptoms

Written by Brian Hoyle

The randomized placebo-controlled double-blind TURANDOT trial [NCT01620255] substantiated the efficacy and safety of a monoclonal antibody that blocks white blood cell adhesion to gut mucosa in the treatment of moderate to severe ulcerative colitis (UC).

As explained by Walter Reinisch, MD, McMaster University Health Centre, Hamilton, Ontario, Canada, inflammatory bowel disease features translocation of white blood cells into the gut mucosa. An important part of this translocation involves the binding of the α4β7 integrin on some white blood cells to the mucosal vascular addressin cell adhesion molecule 1 (MAdCAM-1) receptor on endothelial cells [Feagan BG et al. *N Engl J Med.* 2013; Sandborn WJ et al. *N Engl J Med.* 2013]. Blocking this binding may be beneficial in inflammatory bowel disease. The fully humanized monoclonal antibody PF-00547659 (PF) targets immunoglobulin G2 MAdCAM-1. The antibody does not hamper the immune function of the central nervous system and does not cross-react with vascular cell adhesion protein 1.

In the TURANDOT trial, 357 patients with moderate to severe UC were randomized to subcutaneously delivered placebo or 7.5-, 22.5-, 75-, or 225-mg doses of PF. Doses were given at 0, 4, and 8 weeks in the 12-week trial, with subsequent 24-month follow-up or enrollment in an open-label extension phase. The researchers reported here on the 12-week treatment.

Patients were aged 18 to 65 years, with biopsy-confirmed UC, Mayo endoscopy subscore ≥ 2, active disease beyond the rectum, Mayo score ≥ 6, and failure on or intolerance to ≥ 1 conventional therapy. Exclusion criteria included enteric infection, use of parenteral steroids with a dose of prednisone equivalent > 20 mg, recent biologic therapy, and any history of anti-integrin therapy. The primary efficacy end point was the proportion of patients in clinical remission at week 12, defined as a total Mayo score ≤ 2 points with no individual subscore > 1 point. There were also several secondary efficacy end points, including the proportion of patients with a clinical response at week 12, defined as a decrease in total Mayo score by ≥ 3 points and ≥ 30% decrease in subscore for rectal bleeding of ≥ 1 point or absolute subscore of ≤ 1.

Baseline demographic and clinical characteristics in the 5 arms were comparable. The primary efficacy end point was met, with improved remission in all PF arms compared with placebo at week 12 and with the differences for 7.5, 22.5, and 75 mg of PF being significant when compared with placebo (all $P < .05$; Table 1).

In secondary responses, improvements in clinical response at week 12 for all PF doses (7.5 mg, 38.0%;

Table 1. Primary Efficacy End Point Results: Clinical Remission at Week 12

PF-00547659 Dose, mg	Remission Rate in mITT Population[a], %
0 (placebo)	2.7
7.5	11.3*
22.5	16.7*
75	15.5*
225	5.7

mITT, modified intention to treat.

[a]All subjects randomized and who received at least 1 dose of randomized treatment.

*$P < .05$ vs placebo.