


Non-NS5A Inhibitor, Sofosbuvir-Containing Regimen-Experienced, Genotype 1 Patients With Compensated Cirrhosis

Recommended regimens listed by evidence level and alphabetically for:

Non-NS5A Inhibitor, Sofosbuvir-Containing Regimen-Experienced, Genotype 1 Patients With Compensated Cirrhosis^a

RECOMMENDED	DURATION	RATING 
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg) for genotype 1a patients	12 weeks	I, A
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) ^b , regardless of subtype	12 weeks	IIa, B
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) for genotype 1b patients	12 weeks	IIa, B

^a For [decompensated cirrhosis](#), please refer to the appropriate section.

^b This is a 3-tablet coformulation. Please refer to the prescribing information.

Recommended Regimens

Sofosbuvir/Velpatasvir/Voxilaprevir

The phase 3, open-label, randomized clinical trial POLARIS-4 compared a 12-week course of the daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100mg) to 12 weeks of sofosbuvir/velpatasvir in non-NS5A inhibitor DAA-experienced patients ([Bourliere, 2017](#)). Overall, 69% of patients were previously exposed to sofosbuvir plus ribavirin ± peginterferon, and 11% were exposed to sofosbuvir plus simeprevir. Cirrhosis was common, 46% in both study arms. SVR12 rates for patients with genotype 1 infection were 97% (76/78) for sofosbuvir/velpatasvir/voxilaprevir and 90% (60/66) for sofosbuvir/velpatasvir. Only sofosbuvir/velpatasvir/voxilaprevir met the prespecified efficacy (SVR12) threshold of 85%. The vast majority of patients had experienced prior treatment failure with a sofosbuvir plus simeprevir regimen. Overall, there was 1 relapse in the sofosbuvir/velpatasvir/voxilaprevir arm compared to 15 virologic failures (14 relapses, 1 virologic breakthrough) in the sofosbuvir/velpatasvir group. The single patient who experienced relapse in the sofosbuvir/velpatasvir/voxilaprevir arm did not have treatment-emergent RASs; 9 of the patients with relapse in the sofosbuvir/velpatasvir arm developed NS5A treatment-emergent RASs. This study supports sofosbuvir/velpatasvir/voxilaprevir as a recommended regimen for the treatment of patients with a history of treatment failure with a sofosbuvir-containing DAA regimen, regardless of the presence of cirrhosis.

Glecaprevir/Pibrentasvir

In the EXPEDITION-1 study, 146 patients with genotype 1, 2, 4, 5, or 6 infection and compensated cirrhosis were treated with the daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) administered as three 100 mg/40 mg fixed-dose combination pills for 12 weeks ([Forns, 2017](#)). Of these patients, 25 patients were previously treated with interferon or peginterferon ± ribavirin and 11 were previously treated with sofosbuvir and ribavirin ± peginterferon. Overall, 99% (145/146) of patients achieved SVR 12. The single patient who did not respond to therapy had genotype 1a infection and relapsed at post-treatment week 8. None of the patients enrolled in the EXPEDITION-1 trial were previously treated with simeprevir plus sofosbuvir. However, 12 weeks of glecaprevir/pibrentasvir was evaluated in patients with NS3/4A treatment failure in the MAGELLAN-1 trial, which included simeprevir plus sofosbuvir treatment failures ([Poordad, 2017](#)); ([Poordad, 2017b](#)).

Sofosbuvir/Velpatasvir

As described in the discussion of sofosbuvir/velpatasvir/voxilaprevir, the POLARIS-4 trial included a 12-week arm of the daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) in non-NS5A inhibitor DAA-experienced patients ([Bourliere, 2017](#)). While only sofosbuvir/velpatasvir/voxilaprevir met the overall prespecified efficacy (SVR12) threshold of 85%, this was primarily driven by treatment failure in patients with genotype 1a or 3 infection. Forty-four patients with genotype 1a infection, 22 with genotype 1b infection, 33 with genotype 2 infection, and 52 with genotype 3 infection were included in the sofosbuvir/velpatasvir arm. Overall, there were 15 virologic failures (14 relapses); 5 were in genotype 1a-infected patients and 8 were in those with genotype 3 infection, and most of these patients had cirrhosis. One genotype 1b-infected patient and a single genotype 2-infected patient also experienced treatment failure. Although this study was not powered to assess differences in efficacy by genotype/subtype, the SVR12 rates in genotype 1b-infected patients were 95% and 96% for sofosbuvir/velpatasvir and sofosbuvir/velpatasvir/voxilaprevir, respectively. There were fewer genotype 1b-infected patients who had specifically experienced a prior non-NS5A inhibitor sofosbuvir-containing regimen failure (n=12), and no virologic failures.

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Related References

Bourliere M, Gordon SC, Flamm SL, et al. [Sofosbuvir, velpatasvir, and voxilaprevir for previously treated HCV infection](#). *N Engl J Med*. 2017;376(22):2134-2146.

Forns X, Lee SS, Valdes J, et al. [Glecaprevir plus pibrentasvir for chronic hepatitis C virus genotype 1, 2, 4, 5, or 6 infection in adults with compensated cirrhosis \(EXPEDITION-1\): a single-arm, open-label, multicentre phase 3 trial](#). *Lancet Infect Dis*. 2017;17(10):1062-1068.

Poordad F, Felizarta F, Asatryan A, et al. [Glecaprevir and pibrentasvir for 12 weeks for hepatitis C virus genotype 1 infection and prior direct-acting antiviral treatment](#). *Hepatology (Baltimore, Md.)*. 2017;66(2):389 - 397.

Poordad F, Pol S, Asatryan A, et al. [MAGELLAN-1, Part 2: Glecaprevir and Pibrentasvir for 12 or 16 Weeks in Patients with Chronic HCV Genotype 1 or 4 and Prior Direct-Acting Antiviral Treatment Failure](#). *Gastroenterology*. 2017;152(5):S1057.