



Treatment-Naive Genotype 2 With Compensated Cirrhosis

Recommended and alternative regimens listed by evidence level and alphabetically for:

Treatment-Naive Genotype 2 Patients With Compensated Cirrhosis^a

RECOMMENDED	DURATION	RATING 
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) ^b	12 weeks	I, B
ALTERNATIVE	DURATION	RATING 
Daily daclatasvir (60 mg) ^c plus sofosbuvir (400 mg)	16 to 24 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.

^c The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on [HIV/HCV coinfection](#) for patients on antiretroviral therapy.

Recommended Regimens

Sofosbuvir/Velpatasvir

The daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) for 12 weeks was approved by the FDA for the treatment of genotype 2 infection in patients without cirrhosis or with compensated cirrhosis. ASTRAL-2 compared 12 weeks of sofosbuvir/velpatasvir to 12 weeks of sofosbuvir plus ribavirin in 266 treatment-naive and -experienced patients without cirrhosis or with compensated cirrhosis. The study showed superior efficacy of sofosbuvir/velpatasvir compared to sofosbuvir plus ribavirin (SVR12 99% vs 94%); ([Foster, 2015a](#)). ASTRAL-1 also included 104 genotype 2 treatment-naive and -experienced patients without cirrhosis or with compensated cirrhosis, all of whom achieved SVR12 ([Feld, 2015](#)). Pooled analysis of all genotype 2 patients in ASTRAL-1 and ASTRAL-2 demonstrated 100% SVR12 in those with compensated cirrhosis (29/29) and 99% SVR12 in treatment-naive participants (194/195). Among patients with genotype 2 receiving sofosbuvir/velpatasvir, the presence of baseline NS5A or NS5B RASs was not associated with virologic failure ([Asselah, 2018](#)).

The POLARIS-2 phase 3 study randomized DAA-naive patients to 8 weeks of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100mg) versus 12 weeks of sofosbuvir/velpatasvir. Fifty-three patients with genotype 2 were included in the sofosbuvir/velpatasvir arm and all achieved SVR12 (100%). This study confirms the high efficacy and safety of this 12-week regimen in patients with genotype 2 infection ([Jacobson, 2017](#)).

Glecaprevir/Pibrentasvir

EXPEDITION-1 was a multicenter, open-label, single-arm, phase 3 trial that enrolled 146 treatment-naive or -experienced patients (interferon or peginterferon ± ribavirin, or sofosbuvir plus ribavirin ± peginterferon) with genotype 1, 2, 4, 5, or 6

infection and compensated cirrhosis. Participants 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. Across all genotypes, 145/146 (99%) achieved SVR12 ([Forns, 2017](#)). EXPEDITION-1 included 31 treatment-naive and -experienced persons with genotype 2 infection and compensated cirrhosis; all achieved SVR12. Baseline NS5A RASs were detected (by next-generation sequencing using a 15% detection cutoff) in 40% of 133 tested participants. Baseline NS5A RASs had no effect on SVR rates among treatment-naive and -experienced patients with genotype 2 infection.

Alternative Regimen

Daclatasvir + Sofosbuvir

Daclatasvir (60 mg) plus sofosbuvir (400 mg) for 12 weeks was approved by the FDA for the treatment of genotype 3 infection in patients without cirrhosis or with compensated cirrhosis. Although this regimen was not approved for the treatment of genotype 2 infection, daclatasvir maintains adequate activity against genotype 2 despite a 50% effective concentration (EC_{50}) that increases by several logs in the presence of the prevalent M31 substitution ([Wang, 2014](#)). In fact, daclatasvir with sofosbuvir was associated with high SVR rates in treatment-naive patients with genotype 2 infection with both 12 weeks and 24 weeks of therapy ([Wyles, 2015](#)); ([Sulkowski, 2014a](#)). It is unclear if there is a subgroup of genotype 2-infected patients who would benefit from extending treatment. For patients who require treatment but cannot tolerate sofosbuvir/velpatasvir or glecaprevir/pibrentasvir, a regimen of daclatasvir with sofosbuvir for 12 weeks is reasonable.

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Related References

Asselah T, Bourgeois S, Pianko S, et al. [Sofosbuvir/velpatasvir in patients with hepatitis C virus genotypes 1-6 and compensated cirrhosis or advanced fibrosis](#). *Liver Int*. 2018;38(3):443-450.

Feld JJ, Jacobson IM, Hézode C, et al. [Sofosbuvir and Velpatasvir for HCV Genotype 1, 2, 4, 5, and 6 Infection](#). *The New England Journal of Medicine*. 2015;373(27):2599 - 2607.

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](#). *The Lancet. Infectious Diseases*. 2017;17(10):1062-8.

Foster GR, Afdhal NH, Roberts SK. [Sofosbuvir and Velpatasvir for HCV Genotype 2 and 3 Infection](#). *N Engl J Med*. 2015;373(27):2608-17.

Jacobson IM, Lawitz E, Gane EJ, et al. [Efficacy of 8 Weeks of Sofosbuvir, Velpatasvir, and Voxilaprevir in Patients With Chronic HCV Infection: 2 Phase 3 Randomized Trials](#). *Gastroenterology*. 2017;153(1):113 - 122.

Sulkowski MS, Gardiner DF, Rodriguez-Torres M, et al. [Daclatasvir plus sofosbuvir for previously treated or untreated chronic HCV infection](#). *N Engl J Med*. 2014;370(3):211-221.

Wang C, Jia L, O'Boyle DR, et al. [Comparison of daclatasvir resistance barriers on NS5A from hepatitis C virus genotypes 1 to 6: implications for cross-genotype activity](#). *Antimicrob Agents Chemother*. 2014;58(9):5155-5163.

Wyles DL, Ruane PJ, Sulkowski MS, et al. [Daclatasvir plus sofosbuvir for HCV in patients coinfecting with HIV-1](#). *N Engl J Med*. 2015;373(8):714-725.

