


Treatment-Naive Genotype 2 With Compensated Cirrhosis

Recommended and alternative regimens listed by pangenotypic, 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 | 8 weeks | I, B |

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

^b Dosing is 3 coformulated tablets (glecaprevir [100 mg]/pibrentasvir [40 mg]) taken once daily. Please refer to the prescribing information.

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-naïve 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-naïve 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-naïve 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-naïve 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](#)). A real-world, pooled analysis of 12 cohort studies demonstrated an SVR of 98.5% (266/270) among adults with genotype 2 infection and compensated cirrhosis who were treated with 12 weeks of sofosbuvir/velpatasvir ([Mangia, 2020](#)).

Glecaprevir/Pibrentasvir

EXPEDITION-1 was a multicenter, open-label, single-arm, phase 3 trial that enrolled 146 treatment-naïve 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-naïve 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-naïve and -experienced patients with genotype 2 infection.

EXPEDITION-8 evaluated glecaprevir/pibrentasvir for a reduced duration of 8 weeks in 280 treatment-naïve patients with compensated cirrhosis and genotype 1, 2 (n=26), 4, 5 or 6 infection. Patients with a prior history of decompensation, hepatocellular carcinoma, and HIV or HBV coinfection were excluded from this study. SVR12 was 99% with no virologic failures ([Brown, 2018](#)). Real-world data support the use of 8 weeks in cirrhotic patients ([Flamm, 2020](#)).

Last update: October 24, 2022

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.

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Feld JJ, Jacobson IM, Hézode C, et al. [Sofosbuvir and velpatasvir for HCV genotype 1, 2, 4, 5, and 6 infection](#). *N Engl J Med.* 2015;373(27):2599-2607.

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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.

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Mangia A, Milligan S, Khalili M, et al. [Global real-world evidence of sofosbuvir/velpatasvir as simple, effective HCV treatment: analysis of 5552 patients from 12 cohorts](#). *Liver Int.* 2020;40(8):1841-1852.