Treatment-Naive Genotype 4 With Compensated Cirrhosis

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

Treatment-Naive Genotype 4 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[c]	I, B
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg)	12 weeks	IIa, B
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	IIa, 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.
[c] For HIV/HCV-coinfected patients, a treatment duration of 12 weeks is recommended.

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 4 infection in patients with or without cirrhosis. ASTRAL-1 included 64 genotype 4-infected, treatment-naive patients without cirrhosis or with compensated cirrhosis, all of whom achieved SVR12 (100%) (Feld, 2015).

The POLARIS-2 phase 3 study randomized DAA-naive patients (19% with compensated cirrhosis, overall) to 8 weeks of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg) or 12 weeks of sofosbuvir/velpatasvir. Of 57 patients with genotype 4 in the sofosbuvir/velpatasvir arm, 98% achieved SVR and 1 patient experienced relapse (Jacobson, 2017). A real-world, pooled analysis of 12 cohort studies demonstrated an SVR of 100% (38/38) among adults with genotype 4 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-naive or -experienced (interferon or peginterferon ± ribavirin, or sofosbuvir plus ribavirin ± peginterferon) patients with genotype 1, 2, 4, 5, or 6 infection and compensated cirrhosis. Patients received 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, 99% (145/146) achieved SVR12 (Forns, 2017). EXPEDITION-1 included 16 treatment-naive and -experienced genotype 4-infected participants with compensated cirrhosis. All 16 patients 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 SVR12 rates among treatment-naive and -experienced participants with genotype 4. Based on this study, a 12-week course of glecaprevir/pibrentasvir is recommended for genotype 4-infected, treatment-naive patients with compensated cirrhosis.

EXPEDITION-8 evaluated 8 weeks of glecaprevir/pibrentasvir among 280 treatment-naive patients with compensated cirrhosis and genotype 1, 2, 4 (n=13), 5, or 6 infection. SVR12 was 99% with no virologic failures (Brown, 2018). Patients with a prior history of decompensation, hepatocellular carcinoma, and HIV or HBV coinfection were excluded from the study.

Elbasvir/Grazoprevir

In an integrated analysis of phase 2/3 trials, 15 treatment-naive patients with genotype 4 infection and cirrhosis were treated with 12 weeks of elbasvir/grazoprevir with or without ribavirin, resulting in an SVR of 96% (Asselah, 2018c).

Ledipasvir/Sofosbuvir

The SYNERGY trial was an open-label study evaluating 12 weeks of ledipasvir (90 mg)/sofosbuvir (400 mg) in 21 genotype 4 patients, of whom 60% were treatment naive and 43% had advanced fibrosis (Metavir stage F3 or F4) (Kohli, 2015). One patient took the first dose and then withdrew consent. The 20 patients who completed treatment all achieved SVR12; thus, the SVR12 was 95% in the intention-to-treat analysis and 100% in the per-protocol analysis. Another open-label, single-arm study evaluating 12 weeks of ledipasvir/sofosbuvir that included 22 genotype 4, treatment-naive patients (one with cirrhosis) reported an SVR12 of 95% (21/22) in this patient population (Abergel, 2016).

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Related References

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