**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).

**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.
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

Abergel A, Metivier S, Samuel D, et al. 
Ledipasvir plus sofosbuvir for 12 weeks in patients with hepatitis C genotype 4 infection. 

Asselah T, Reesink H, Gerstoft J, et al. 
Efficacy of elbasvir and grazoprevir in participants with hepatitis C virus genotype 4 infection: a pooled analysis. 
Liver Int. 2018;38(9):1583-1591.

Preliminary efficacy and safety of 8-week glecaprevir/pibrentasvir in patients with HCV genotype 1-6 infection and compensated cirrhosis: the EXPEDITION-8 study [Abstract LB-7]. 
The Liver Meeting. 2018.

Sofosbuvir and velpatasvir for HCV genotype 1, 2, 4, 5, and 6 infection. 

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. 

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. 

Ledipasvir and sofosbuvir for hepatitis C genotype 4: a proof-of-concept, single-centre, open-label phase 2a cohort study. 