## Treatment-Naive Genotype 2 With Compensated Cirrhosis

### 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 3 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. 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**


