

Treatment-naive Genotype 2 with Compensated Cirrhosis

Recommended and Alternative Regimens by evidence level and alphabetically for:

Genotype 2, Treatment-naive Patients, with Compensated Cirrhosis † ⓘ

RECOMMENDED	DURATION	RATING ⓘ
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
ALTERNATIVE	DURATION	RATING ⓘ
Daily daclatasvir (60 mg*) plus sofosbuvir (400 mg) ‡	16 weeks to 24 weeks	Ila, B

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

* The dose of daclatasvir may need to increase or decrease 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.

Sofosbuvir/velpatasvir

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

Daclatasvir + sofosbuvir

Daclatasvir with sofosbuvir for 12 weeks was approved by the FDA for the treatment of HCV genotype 3 infection in patients without and with cirrhosis. Although daclatasvir with sofosbuvir was not approved for the treatment of HCV genotype 2 infection, daclatasvir maintains adequate activity against HCV genotype 2 despite a 50% effective concentration (EC₅₀) that increases by several logs in the presence of the prevalent M31 substitution ([Wang, 2014](#)). In fact, daclatasvir with sofosbuvir was associated with high rates of SVR in treatment-naive patients with HCV 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 HCV genotype 2-infected patients who would benefit from extending treatment. For patients who require treatment but cannot tolerate sofosbuvir/velpatasvir, a regimen of daclatasvir with sofosbuvir for 12 weeks is reasonable.

Mixed genotypes

Rarely, genotyping assays may indicate the presence of a mixed infection (eg, genotypes 1a and 2). Treatment data for mixed genotypes with direct-acting antivirals are sparse but utilization of a pangenotypic regimen should be considered.

When the correct combination or duration is unclear, expert consultation should be sought.

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