Treatment-naive Genotype 2 Without Cirrhosis

Recommended and Alternative Regimens by evidence level and alphabetically for:

Genotype 2, Treatment-naive Patients, Without 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)	12 weeks	IIa, B

* 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 (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 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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