Treatment-naive Genotype 5 or 6

Recommended Regimens by evidence level and alphabetically for:

Genotype 5 or 6, Treatment-naive Patients, with and Without Cirrhosis

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, B
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	IIa, B

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 5 and 6 infection in patients with and without cirrhosis (Feld, 2015). ASTRAL-1 included 24 genotype 5 treatment-naive subjects with and without cirrhosis, 23 of whom achieved SVR12 (96%), and 38 genotype 6 treatment-naive subjects with and without cirrhosis, all of whom achieved SVR12 (100%).

Ledipasvir/sofobuvir

Although there are limited data on patients with HCV genotype 5 infection, the in vitro activity for sofobuvir and ledipasvir is quite good with EC_{50} of 15 nM and 0.081 nM, respectively. Abergel and colleagues reported data from an open-label, single-arm study that included 41 HCV genotype 5-infected patients with an overall SVR12 rate of 95% (39/41) (Abergel, 2016). The SVR12 rate was also 95% specifically in treatment-naive patients (20/21), of whom only 3 had cirrhosis, but all of whom achieved SVR12.

Ledipasvir has in vitro activity against most HCV genotype 6 subtypes (except for 6e) (Wong, 2013); (Kohler, 2014). A small, two-center, open-label study (NCT01826981) investigated the safety and in vivo efficacy of ledipasvir/sofosbuvir for 12 weeks in treatment-naive and -experienced patients with HCV genotype 6 infection. Twenty-five patients (92% were treatment-naive) who were primarily Asian (88%) had infection from seven different subtypes (32%, 6a; 24%, 6e; 12%, 6l; 8%, 6m; 12%, 6p; 8%, 6q; 4%, 6r). Two patients (8%) had cirrhosis. The SVR12 rate was 96% (24/25), and the 1 patient who experienced relapse had discontinued therapy at week 8 because of drug use. No patient discontinued treatment owing to adverse events (Gane, 2015).

Elbasvir/grazoprevir

C-SCAPE evaluated the efficacy and safety of 12 weeks of elbasvir (50 mg)/grazoprevir (100 mg) with or without weight-based ribavirin for 12 weeks in treatment-naive, non-cirrhotic genotype 2, 4, 5, and 6 patients. Eight genotype 5 and eight genotype 6 patients were included in this trial. In patients with HCV genotype 5 infection, administration of a 12-week regimen of elbasvir (50 mg)/grazoprevir (100 mg) plus ribavirin appears to be more active (SVR 100%, 4/4) than the same regimen without ribavirin (SVR12 25%, 1/4). Administration of a 12-week regimen of elbasvir (50 mg)/grazoprevir (100 mg) ± ribavirin to non-cirrhotic, treatment-naive patients with HCV genotype 6 infection achieved an SVR12 of 75% irrespective of the addition of ribavirin (Brown, 2015).

C-EDGE evaluated 10 treatment-naive genotype 6 patients who were treated with 12 weeks of the fixed-dose combination therapy, elbasvir (50 mg)/grazoprevir (100 mg). Eight of 10 (80%) achieved SVR12 (Zeuzem, 2015f).

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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