Treatment-naive Genotype 4 Without Cirrhosis

Recommended Regimens by evidence level and alphabetically for:

Genotype 4, Treatment-naive Patients, Without Cirrhosis

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) and weight-based ribavirin	12 weeks	I, A
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg)	12 weeks	IIa, B
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	IIa, B

Paritaprevir/ritonavir/ombitasvir

PEARL-I was an open-label phase IIb study that included a cohort of 86 treatment-naive patients with HCV genotype 4 infection without cirrhosis who received 12 weeks of the daily fixed-dose combination of paritaprevir/ritonavir/ombitasvir (PrO) with or without weight-based ribavirin. SVR12 rates were 100% (42/42) in the group receiving ribavirin and 90.9% (40/44) in the group not receiving ribavirin. Adverse effects were generally mild, with headache, asthenia, fatigue, and nausea most commonly reported. There were no discontinuations owing to adverse events (Hézode, 2015). The AGATE-I trial, in its first phase, randomized 120 treatment-naive and -experienced patients with genotype 4 HCV and compensated cirrhosis to receive 12 weeks or 16 weeks of paritaprevir/ritonavir/ombitasvir (PrO) plus weight-based ribavirin. The SVR12 rates in the 12-week and 16-week arms were 96% and 100%, respectively. The regimens were well tolerated (Asselah, 2015a). Similarly, the ongoing AGATE-II trial offered 100 treatment-naive and -experienced non-cirrhotic patients with genotype 4, PrO plus weight-based ribavirin for 12 weeks. The SVR12 was 94%. These data continue to support the use of PrO plus ribavirin for 12 weeks in treatment-experienced genotype 4 patients (Esmat, 2015).

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 4 infection in patients with and without cirrhosis. ASTRAL-1 included 64 genotype 4 treatment-naive subjects with and without cirrhosis, all of whom achieved SVR12 (100%) (Feld, 2015).

Elbasvir/grazoprevir

Sixty-six treatment-naive genotype 4 patients have been treated with daily elbasvir (50 mg)/grazoprevir (100 mg) for 12 weeks with (n=10) and without (n=56) weight-based ribavirin in the phase 2/3 clinical program. 9.1% (n=6) were cirrhotic and 42.4% (n=28) had HIV/HCV coinfection. Overall 97% (64/66) achieved SVR12. There was 1 treatment failure and 1 subject was lost to follow-up. The impact of ribavirin could not be assessed, however the addition of ribavirin numerically increased the SVR12 rates in treatment-experienced subjects. Baseline RASs and subgenotype did not appear to impact SVR12 rates (Asselah, 2015).

Ledipasvir/sofosbuvir

The SYNERGY trial was an open-label study evaluating 12 weeks of ledipasvir/sofosbuvir in 21 HCV genotype 4-infected 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. All of the 20 patients who completed treatment achieved an SVR12; thus, the SVR12 rate was 95% in the intention-to-treat analysis and 100% in the per-protocol analysis. Abergel and colleagues reported data from an open-label single-arm study including 22 HCV genotype 4-infected, treatment-naive patients (only 1 with cirrhosis) with an SVR12 rate of 95% (21/22) (Abergel, 2016). These two pilot studies support the use of this regimen in patients with HCV genotype 4 infection.

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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