

Treatment-naive Genotype 4 with Compensated Cirrhosis

Recommended Regimens by evidence level and alphabetically for:

Genotype 4, Treatment-naive Patients, with Compensated 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	Ila, B
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	Ila, B

[†] Please see statement on FDA [warning](#) regarding the use of PrOD or PrO in patients with cirrhosis.

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

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%. Additionally, AGATE-II randomized 60 treatment-naive and -experienced genotype 4-infected patients with compensated cirrhosis to receive either 12 or 24 weeks of PrO plus weight-based ribavirin. The SVR12 rate from the 12-week arm was 97%. These data continue to support the use of PrO plus ribavirin for 12 weeks in treatment-experienced genotype 4 patients, including those with cirrhosis ([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.

Last update: April 12, 2017