PEG-IFN/Ribavirin Experienced, Genotype 4 Patients with Compensated Cirrhosis

Recommended and Alternative Regimens by evidence level and alphabetically for:

Genotype 4, PEG-IFN/Ribavirin Treatment-experienced 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); for patients who experienced virologic relapse after prior PEG-IFN/ribavirin therapy	12 weeks	IIa, B
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) and weight-based ribavirin; for genotype 4 patients with prior on-treatment virologic failure (failure to suppress or breakthrough) while on PEG-IFN/ribavirin	16 weeks	IIa, B
Daily ledipasvir (90 mg)/sofosbuvir (400 mg) and weight-based ribavirin; for patients who are eligible for ribavirin.	12 weeks	IIa, B
ALTERNATIVE	**DURATION**	**RATING**
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	24 weeks	IIa, 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

The AGATE-I trial 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). 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, reported recently, 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, 2015a).

Ledipasvir/sofosbuvir

In the SYNERGY trial, 20 patients with HCV genotype 4 infection were treated with ledipasvir/sofosbuvir for 12 weeks. Of these patients, 40% were treatment-experienced and 40% had advanced fibrosis. Preliminary data demonstrate efficacy, with 95% achieving SVR12 based on an intention-to-treat analysis (Kohli, 2015).

Sofosbuvir/velpatasvir

Velpatasvir is also active in vitro against genotype 4 and the combination of sofosbuvir/velpatasvir for 12 weeks was evaluated in 116 genotype 4-infected patients included in the ASTRAL-1 study (Feld, 2015). 100% SVR12 was achieved, including 52 treatment-experienced patients.

Elbasvir/grazoprevir

An integrated analysis of all phase 2/3 elbasvir/grazoprevir studies demonstrated efficacy of this regimen for both treatment-naive (n=66) and -experienced (n=37) patients with genotype 4 HCV infection (Asselah, 2015). The overall SVR12 rate among treatment-experienced genotype 4-infected patients was 87% (32/37) with numerical response differences based on prior interferon treatment response (relapse vs on-treatment viral failure) and elbasvir/grazoprevir duration (12 vs 16 weeks) and/or ribavirin usage (no ribavirin vs ribavirin). Numbers within any specific subgroup are too small to make definitive recommendation; however, trends emerged that were used to guide the current recommendations pending additional data. No treatment failures were seen in patients who relapsed after prior PEG-IFN/ribavirin therapy, regardless of elbasvir/grazoprevir treatment duration or ribavirin usage. In contrast, response rates were numerically lower in patients with prior on-treatment virologic failure in the non-ribavirin-containing arms (12 weeks: 78%, 16 weeks: 60%) compared to ribavirin-containing treatment (12 weeks + ribavirin: 91%, 16 weeks + ribavirin: 100%). Given the lack of sufficient numbers to differentiate response between 12 weeks with ribavirin and 16 weeks with ribavirin, the use of 16 weeks plus ribavirin in genotype 4-infected patients with prior on-treatment virologic failure represents the most conservative approach.

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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