Sofosbuvir plus Ribavirin, with or Without PEG-IFN, Experienced Genotype 1 Patients with or Without Cirrhosis

Recommended Regimen for:

Genotype 1 (regardless of subtype), Sofosbuvir Plus Ribavirin with or Without PEG-IFN Treatment-experienced Patients, Without Cirrhosis

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) with weight-based ribavirin	12 weeks	IIa, B

Recommended Regimen for:

Genotype 1 (regardless of subtype), Sofosbuvir Plus Ribavirin with or Without PEG-IFN Treatment-experienced Patients, with Compensated Cirrhosis‡

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) with weight-based ribavirin	24 weeks	IIa, B

‡ For decompensated cirrhosis, please refer to the appropriate section.

To date, clinical experience and trial data on the retreatment of sofosbuvir-experienced patients are very limited. However, retreatment after a sofosbuvir-containing treatment failure with a second course of treatment using sofosbuvir plus new agents, or retreatment with the same sofosbuvir-based regimen for a longer duration, have been reported.

Retreatment with ledipasvir/sofosbuvir in subjects with HCV genotype 1 infection, with or without cirrhosis, in whom a sofosbuvir-containing regimen failed has been evaluated in two small pilot studies utilizing ledipasvir/sofosbuvir for 12 weeks. With prior failures of 24 weeks of sofosbuvir plus ribavirin, high SVR rates were noted when patients were retreated with ledipasvir/sofosbuvir for 12 weeks (Osinusi, 2014). Ledipasvir/sofosbuvir plus ribavirin has also been evaluated in subjects in whom prior treatment with sofosbuvir plus PEG-IFN/ribavirin or sofosbuvir and ribavirin failed. In this study of 51 patients, retreatment with ledipasvir/sofosbuvir plus ribavirin for 12 weeks led to SVR12 in 100% of 50 patients with HCV genotype 1 infection; 1 virologic failure was observed in a patient determined to have HCV genotype 3 infection prior to retreatment (Wyles, 2015b). There are exceedingly limited data on the retreatment of such patients with cirrhosis. However, a post-hoc analysis of 352 previously treated patients with cirrhosis (240 of whom had prior protease inhibitor-based treatment failures) who were retreated with 12 weeks or 24 weeks of ledipasvir/sofosbuvir with or without ribavirin found that SVR12 was achieved in 95% to 98% (Reddy, 2015). Thus, for previously treated HCV genotype 1-infected patients with compensated cirrhosis, retreatment with 24 weeks of ledipasvir/sofosbuvir plus ribavirin is recommended.

There are no published data on retreatment of sofosbuvir-containing treatment failures with non-sofosbuvir based DAA

regimens. In theory the lack of cross resistance between SOF and all other currently available DAAs suggests that such regimens may be efficacious in retreatment settings. However, given the lack of available data recommendations cannot be made. If use of non-sofosbuvir-based DAA regimens is being considered, those patients should be treated in line with the recommendations for pegylated interferon-experienced patients according to genotype subtype and cirrhosis status.

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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