Sofosbuvir Experienced, Genotype 3 Patients

Recommended Regimens by evidence level and alphabetically for:

Genotype 3, Sofosbuvir-based Treatment-experienced Patients (No Prior NS5A Treatment)

RECOMMENDED	DURATION	RATING
Deferral of treatment is recommended, pending availability of data, for patients with HCV genotype 3, in whom previous treatment with a sofosbuvir-based regimen has failed (no prior NS5A treatment), who do not have cirrhosis,‡ and do not have reasons for urgent retreatment	NA	IIb, C
Daily daclatasvir (60 mg*) plus sofosbuvir (400 mg) with weight-based ribavirin, regardless of cirrhosis status;‡ for patients who require urgent retreatment	24 weeks	IIb, C
Daily fixed-dose elbasvir (50 mg)/grazoprevir (100 mg) plus sofosbuvir (400 mg) with or without weight-based ribavirin, regardless of cirrhosis status;‡ for patients who require urgent retreatment	12 weeks to 16 weeks	IIb, C
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) plus weight-based ribavirin, regardless of cirrhosis status;‡ for patients who require urgent retreatment.	12 weeks	IIb, C

‡ For decompensated cirrhosis, please refer to the appropriate section.
* The dose of daclatasvir may need to increase or decrease when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.

Daclatasvir plus sofosbuvir

In the ALLY-3 study, 7 patients previously treated with sofosbuvir-containing regimens (with ribavirin and/or PEG-IFN) were retreated with daclatasvir plus sofosbuvir for 12 weeks. Of these patients, 5 (71%) achieved an SVR12 (Nelson, 2015). Based on these limited data, 12 weeks of daclatasvir plus sofosbuvir may be insufficient, and extending the duration to 24 weeks of therapy and adding weight-based ribavirin is recommended.

Elbasvir/grazoprevir plus sofosbuvir plus ribavirin

The C-ISLE study included two patients who had failed prior sofosbuvir plus ribavirin. Both of these patients had a SVR12 (Foster, 2016b). Despite the paucity of data, this is a logical strategy, since all three directly acting antivirals in the regimen are known to have activity against genotype 3 infection and have shown high efficacy in other treatment-experienced patients with cirrhosis. The exact duration and need for ribavirin is not clear but due to the lack of extensive data, optimization with extended therapy and the addition of weight-based ribavirin is recommended when possible.

Sofosbuvir/velpatasvir

No data are available evaluating retreatment of patients with genotype 3 infection with sofosbuvir/velpatasvir, who previously failed treated with sofosbuvir plus ribavirin with or without PEG-IFN. However, retreatment with sofosbuvir/velpatasvir plus weight-based ribavirin for 12 weeks is a logical strategy in patients who require immediate treatment due to the general lack of treatment-emergent NS5B resistance substitutions in sofosbuvir regimen failures and the high efficacy of this regimen in phase 2 trials (Pianko, 2015).

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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