PEG-IFN/Ribavirin Experienced, Genotype 3 Patients Without Cirrhosis

Recommended Regimens by evidence level and alphabetically for:

Genotype 3, PEG-IFN/Ribavirin Treatment-experienced Patients, Without Cirrhosis

RECOMMENDED	DURATION	RATING
Daily daclatasvir (60 mg*) plus sofosbuvir (400 mg)¶	12 weeks	I, A
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)¶	12 weeks	I, A

* 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.
¶ RAS testing for Y93H is recommended for cirrhotic patients and ribavirin should be included in regimen if present.

Daclatasvir plus sofosbuvir

In the ALLY-3 study, treatment-experienced patients without cirrhosis did well with an SVR12 rate of 94% (32/34) (Nelson, 2015).

Sofosbuvir/velpatasvir

The phase III ASTRAL-3 study evaluated the fixed-dose combination of sofosbuvir/velpatasvir for 12 weeks without ribavirin in 277 genotype 3-infected patients, including 71 with prior treatment experience and 80 with cirrhosis (Foster, 2015a). Despite a high combined SVR12 rate of 95% (264/277), both prior treatment (90% SVR) and cirrhosis (91% SVR) had a moderate negative impact on treatment responses. The addition of ribavirin did appear to increase SVR12 rates in a phase II study of treatment-experienced genotype 3 patients treated for 12 weeks with 25 or 100 mg of velpatasvir combined with sofosbuvir (Pianko, 2015).

Baseline NS5A substitutions in genotype 3 also impact DAA treatment response, with the Y93H substitution being the most challenging. In the ALLY-3 study the Y93H was detected in 13 (9%) of patients with an SVR12 of 54% (7/13); including a 67% SVR12 in patients without cirrhosis. In the ASTRAL-3 study the Y93H was detected in 25 (9%) of patients with an SVR12 rate of 84% (21/25). Given that cirrhotic patients in whom prior treatment with PEG-IFN/ribavirin has failed are already recommended to have ribavirin added with or without extension of therapy depending on the specific regimen, baseline testing for NS5A RASs in genotype 3 would only impact treatment approaches for patients in whom prior treatment with PEG-IFN/ribavirin has failed without cirrhosis. Pending additional data, baseline NS5A RAS testing is recommended in all treatment-experienced genotype 3 patients without cirrhosis. If the Y93H substitution is identified, weight-based ribavirin should be added to the treatment course.

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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