Peginterferon/Ribavirin-Experienced, Genotype 2 Patients Without Cirrhosis

Recommended and alternative regimens listed by evidence level and alphabetically for:

Peginterferon/Ribavirin-Experienced, Genotype 2 Patients Without Cirrhosis

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[a]	8 weeks	I, A
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
ALTERNATIVE	**DURATION**	**RATING**
Daily daclatasvir (60 mg)[b] plus sofosbuvir (400 mg)	12 weeks	IIa, B

[a] This is a 3-tablet coformulation. Please refer to the prescribing information.
[b] The dose of daclatasvir may need to be increased or decreased 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.

Recommended Regimens

Glecaprevir/Pibrentasvir

The SURVEYOR-II, part 4 trial was a single-arm study of the daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) administered as three 100 mg/40 mg fixed-dose combination pills for 8 weeks in patients with genotype 2, 4, 5, or 6 infection without cirrhosis who were treatment-naive or -experienced (interferon or peginterferon ± ribavirin, or sofosbuvir plus ribavirin ± peginterferon) (Asselah, 2018b). One hundred forty-five genotype 2-infected patients were enrolled with a 98% SVR12. Two patients experienced relapse; both were treatment experienced.

Sofosbuvir/Velpatasvir

In the randomized, open-label ASTRAL-2 study, genotype 2-infected patients were treated with 12 weeks of the daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) or sofosbuvir plus ribavirin (Foster, 2015a). Of the 266 participants, a minority (15%) had a history of previous peginterferon/ribavirin treatment failure and a similar proportion (14%) had compensated cirrhosis. Overall, the combination of sofosbuvir/velpatasvir yielded a statistically significant superior SVR12 rate of 99% vs 94% for sofosbuvir plus ribavirin. The only treatment failure in the sofosbuvir/velpatasvir arm was a patient who withdrew from the study after a single day due to side effects (anxiety). In contrast, there were 6 virologic failures in the sofosbuvir plus ribavirin arm. Fatigue and anemia were more commonly reported in patients receiving sofosbuvir plus ribavirin.

The phase 3 POLARIS-2 study randomized patients to 8 weeks of the fixed-dose combination of sofosbuvir/velpatasvir/voxilaprevir versus 12 weeks of sofosbuvir/velpatasvir. Fifty-three genotype 2-infected patients were in the sofosbuvir/velpatasvir arm and all achieved SVR (100%, 53/53) (Jacobson, 2017). This study confirms the high efficacy and safety of this 12-week regimen in patients with genotype 2 infection, including those with a past peginterferon/ribavirin treatment failure and patients with compensated cirrhosis.

Alternative Regimen

Daclatasvir + Sofosbuvir

Daclatasvir (60 mg) plus sofosbuvir (400 mg) for 12 weeks to 24 weeks has been shown to have efficacy in genotype 2 infection. However, available data in patients previously treated with peginterferon/ribavirin are very limited (Wyles, 2015); (Sulkowski, 2014a). For patients who require treatment and are unable to access sofosbuvir/velpatasvir, treatment with daclatasvir/sofosbuvir for 12 weeks is an alternative regimen with consideration of extension of therapy to 24 weeks in more difficult-to-treat patients, such as those with cirrhosis.

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Related References

Asselah T, Kowdley KV, Zadeikis N, et al. Efficacy of glecaprevir/pibrentasvir for 8 or 12 weeks in patients with hepatitis C virus genotype 2, 4, 5, or 6 infection without cirrhosis. *Clin Gastroenterol Hepatol*. 2018;16(3):417-426.

Foster GR, Afdhal NH, Roberts SK. Sofosbuvir and Velpatasvir for HCV Genotype 2 and 3 Infection. *N Engl J Med.* 2015;373(27):2608-17.

Jacobson IM, Lawitz E, Gane EJ, et al. Efficacy of 8 Weeks of Sofosbuvir, Velpatasvir, and Voxilaprevir in Patients With Chronic HCV Infection: 2 Phase 3 Randomized Trials. *Gastroenterology*. 2017;153(1):113 - 122.

Sulkowski MS, Gardiner DF, Rodriguez-Torres M, et al. Daclatasvir plus sofosbuvir for previously treated or untreated chronic HCV infection. *N Engl J Med*. 2014;370(3):211-221.

Wyles DL, Ruane PJ, Sulkowski MS, et al. Daclatasvir plus sofosbuvir for HCV in patients coinfected with HIV-1. *N Engl J Med*. 2015;373(8):714-725.