Peginterferon/Ribavirin-Experienced, Genotype 5 or 6 Patients With or Without Compensated Cirrhosis

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

Peginterferon/Ribavirin-Experienced, Genotype 5 or 6 Patients With or Without Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[b] for patients without cirrhosis	8 weeks	IIa, B
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[b] for patients with compensated cirrhosis	12 weeks	I, B
Daily fixed-dose combination ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	IIa, B
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	IIa, B

[a] For decompensated cirrhosis, please refer to the appropriate section.
[b] This is a 3-tablet coformulation. Please refer to the prescribing information.

Recommended Regimens

Glecaprevir/Pibrentasvir

A combined analysis 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 or 12 weeks among 1,904 patients participating in phase 2 and phase 3 clinical trials included 30 patients with genotype 5 infection and 41 with genotype 6 infection (Puoti, 2017). Approximately 21% to 26% of patients in the overall study had a prior interferon-based treatment failure (DAA failure was excluded); no patients had cirrhosis. SVR among treatment-naive or -experienced, genotype 5-infected participants was 100% (2/2) for those receiving 8 weeks of glecaprevir/pibrentasvir and 100% (28/28) for those receiving 12 weeks of glecaprevir/pibrentasvir. SVR rates among treatment-naive or -experienced, genotype 6-infected participants were 90% (9/10) for those receiving 8 weeks of glecaprevir/pibrentasvir and 100% (31/31) among those receiving 12 weeks of glecaprevir/pibrentasvir. The single treatment failure in the 8-week group was a nonvirologic failure.

Ledipasvir/Sofosbuvir

Ledipasvir has in vitro activity against most genotype 6 subtypes, except 6e (Wong, 2013); (Kohler, 2014). A small, 2-center, open-label study (NCT01826981) investigated the safety and efficacy of a 12-week course of the daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) in treatment-naive or -experienced patients with genotype 6

infection. Twenty-five patients (92% treatment naive) who were primarily of Asian descent (88%) were infected with different genotype 6 subtypes (n=8 6a; n=6 6e; n=3 6l; n=2 6m; n=3 6p; n=2 6q; n=1 6r). Two patients (8%) had compensated cirrhosis. The SVR12 rate was 96% (24/25). The single patient who experienced relapse had discontinued therapy at week 8 because of drug use. No patient discontinued treatment owing to adverse events (Gane, 2015).

Similarly, 41 patients with genotype 5 infection were treated with 12 weeks of ledipasvir/sofosbuvir. The group included both treatment-naive and -experienced patients, with and without cirrhosis. The SVR was 93% (38/41) (Abergel, 2016).

Sofosbuvir/Velpatasvir

Velpatasvir has in vitro activity against genotypes 5 and 6. The ASTRAL-1 study included 35 patients with genotype 5 infection and 41 patients with genotype 6 infection. Among those participants, only 11 and 3, respectively, were treatment experienced (Feld, 2015). All genotype 5 and 6, treatment-experienced patients treated with 12 weeks of sofosbuvir (400 mg)/velpatasvir (100 mg) achieved SVR12.

Last update: September 21, 2017

Related References

Abergel A, Asselah T, Metivier S, Loustaud-Ratti V. Ledipasvir-sofosbuvir in patients with hepatitis C virus genotype 5 infection: an open-label, multicentre, single-arm, phase 2 study. *Lancet Infect Dis.* 2016;16(4):459-464.

Feld JJ, Jacobson IM, Hézode C, et al. Sofosbuvir and Velpatasvir for HCV Genotype 1, 2, 4, 5, and 6 Infection. *The New England Journal of Medicine*. 2015;373(27):2599 - 2607.

Gane EJ, Hyland RH, An D, et al. Efficacy of ledipasvir and sofosbuvir, with or without ribavirin, for 12 weeks in patients with HCV genotype 3 or 6 infection. *Gastroenterology*. 2015;149(6):1454-1461.

Kohler JJ, Nettles JH, Amblard F, et al. Approaches to hepatitis C treatment and cure using NS5A inhibitors. *Infect Drug Resist*. 2014;7:41-56.

Puoti M, Foster G, Wang S. High SVR rates with eight and twelve weeks of pangenotypic glecaprevir/pibrentasvir: integrated efficacy and safety analysis of genotype 1–6 patients without cirrhosis [Abstract LB-15]. In: *52nd Annual Meeting of the European Association for the Study of the Liver (EASL)*. 52nd Annual Meeting of the European Association for the Study of the Liver (EASL).; 2017.

Wong KA, Worth A, Martin R, et al. Characterization of Hepatitis C virus resistance from a multiple-dose clinical trial of the novel NS5A inhibitor GS-5885. *Antimicrob Agents Chemother*. 2013;57(12):6333-6340.

Wong RJ, et al. Community-based real-world treatment outcomes of Sofosbuvir/ledipasvir in Asians with chronic hepatitis C virus genotype 6 in the US. *J Viral Hepatitis*. 2017;24:17-21.