Treatment-experienced Genotype 5 or 6

Few data are available to help guide decision making for patients infected with HCV genotype 5 or 6. Thus, for those patients for whom immediate treatment is required, the following recommendations have been drawn from available data.

Recommended Regimens by evidence level and alphabetically for:

Genotype 5 or 6, PEG-IFN/Ribavirin Treatment-experienced Patients, with or Without Cirrhosis

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	IIa, B
Daily fixed-dose combination ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	IIa, C

In the phase III NEUTRINO trial (Lawitz, 2013a), treatment-naive patients with HCV genotypes 1 (n=291), 4 (n=28), 5 (n=1), and 6 (n=6) were treated with sofosbuvir (400 mg daily) plus PEG-IFN (2a 180 µg weekly) and weight-based ribavirin (1000 mg [<75 kg] to 1200 mg [≥75 kg]) for 12 weeks. All six patients with HCV genotype 6 and the one patient with HCV genotype 5 achieved SVR12. The adverse event profile in these patients and in the larger study population was similar to that seen with PEG-IFN/ribavirin therapy.

Ledipasvir has in vitro activity against most HCV genotype 6 subtypes (exception 6e) (Wong, 2013); (Kohler, 2014). A small, two-center, open-label study (NCT01826981) investigated the safety and in vivo efficacy of ledipasvir/sofosbuvir for 12 weeks in treatment-naive and -experienced patients with HCV genotype 6 infection. Twenty-five patients (92% treatment-naive) who were primarily of Asian descent (88%) were infected with different subtypes of HCV genotype 6 (32%, 6a; 24%, 6e; 12%, 6l; 8%, 6m; 12%, 6p; 8%, 6q; 4%, 6r). Two patients (8%) had cirrhosis. The SVR12 rate was 96% (24/25). The 1 patient who experienced relapse had discontinued therapy at week 8 because of drug use. No patient discontinued treatment owing to adverse events.

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

Because of their limited activity against HCV genotypes 5 and 6 in vitro and in vivo, neither boceprevir nor telaprevir should be used as therapy for patients with HCV genotype 5 or 6 infection.

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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