Non-NS5A Inhibitor, Sofosbuvir-Containing Regimen-Experienced, Genotype 1 Patients With Compensated Cirrhosis

Recommended regimens listed by evidence level and alphabetically for:

**Non-NS5A Inhibitor, Sofosbuvir-Containing Regimen-Experienced, Genotype 1 Patients With Compensated Cirrhosis**

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>DURATION</th>
<th>RATING</th>
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<tbody>
<tr>
<td>Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg) for genotype 1a patients</td>
<td>12 weeks</td>
<td>I, A</td>
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<tr>
<td>Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg), regardless of subtype</td>
<td>12 weeks</td>
<td>IIa, B</td>
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<tr>
<td>Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) for genotype 1b patients</td>
<td>12 weeks</td>
<td>IIa, B</td>
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*For decompensated cirrhosis, please refer to the appropriate section.

**Sofosbuvir/Velpatasvir/Voxilaprevir**

The phase 3, open-label, randomized clinical trial POLARIS-4 compared a 12-week course of the daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100mg) to 12 weeks of sofosbuvir/velpatasvir in non-NS5A inhibitor DAA-experienced patients (Bourliere, 2017). Overall, 69% of patients were previously exposed to sofosbuvir plus ribavirin ± peginterferon, and 11% were exposed to sofosbuvir plus simeprevir. Cirrhosis was common, 46% in both study arms. SVR12 rates for patients with genotype 1 were 97% (76/78) for sofosbuvir/velpatasvir/voxilaprevir and 90% (60/66) for sofosbuvir/velpatasvir. Only sofosbuvir/velpatasvir/voxilaprevir met the prespecified efficacy (SVR12) threshold of 85%. The vast majority of patients had experienced prior treatment failure with a sofosbuvir plus simeprevir regimen. Overall, there was 1 relapse in the sofosbuvir/velpatasvir/voxilaprevir arm compared to 15 virologic failures (14 relapses, 1 virologic breakthrough) in the sofosbuvir/velpatasvir group. The single patient who experienced relapse in the sofosbuvir/velpatasvir/voxilaprevir arm did not have treatment-emergent RASs; 9 of the patients with relapse in the sofosbuvir/velpatasvir arm developed NS5A treatment-emergent RASs. This study supports sofosbuvir/velpatasvir/voxilaprevir as a recommended regimen for the treatment of patients with a history of treatment failure with a sofosbuvir-containing DAA regimen, regardless of the presence of cirrhosis.
**Glecaprevir/Pibrentasvir**

In the EXPEDITION-1 study, 146 patients with genotype 1, 2, 4, 5, or 6 and compensated cirrhosis were treated with the daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) administered as three 100 mg/40 mg fixed-dose combination pills for 12 weeks (Forns, 2017). Of these patients, 25 patients were previously treated with interferon or peginterferon ± ribavirin and 11 were previously treated with sofosbuvir and ribavirin ± peginterferon. Overall, 99% (145/146) of patients achieved SVR12. The single patient who did not respond to therapy had genotype 1a and relapsed at post-treatment week 8. None of the patients enrolled in the EXPEDITION-1 trial were previously treated with simeprevir plus sofosbuvir. However, 12 weeks of glecaprevir/pibrentasvir was evaluated in patients with NS3/4A treatment failure in the MAGELLAN-1 trial, which included simeprevir plus sofosbuvir treatment failures (Poordad, 2017); (Poordad, 2017b).

**Sofosbuvir/Velpatasvir**

As described in the discussion of sofosbuvir/velpatasvir/voxilaprevir, the POLARIS-4 trial included a 12-week arm of the daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) in non-NS5A inhibitor DAA-experienced patients (Bourliere, 2017). While only sofosbuvir/velpatasvir/voxilaprevir met the overall prespecified efficacy (SVR12) threshold of 85%, this was primarily driven by treatment failure in patients with genotype 1a or 3. Forty-four patients with genotype 1a, 22 with genotype 1b, 33 with genotype 2, and 52 with genotype 3 were included in the sofosbuvir/velpatasvir arm. Overall, there were 15 virologic failures (14 relapses); 5 were in genotype 1a patients and 8 were in those with genotype, and most of these patients had cirrhosis. One genotype 1b patient and a single genotype 2 patient also experienced treatment failure. Although this study was not powered to assess differences in efficacy by genotype/subtype, the SVR12 rates in genotype 1b patients were 95% and 96% for sofosbuvir/velpatasvir and sofosbuvir/velpatasvir/voxilaprevir, respectively. There were fewer genotype 1b patients who had specifically experienced a prior non-NS5A inhibitor sofosbuvir-containing regimen failure (n=12), and no virologic failures.

**Related References**


