DAA-Experienced (Including NS5A Inhibitors Except Glecaprevir/Pibrentasvir Failures), Genotype 2 Patients, With or Without Compensated Cirrhosis

(For glecaprevir/pibrentasvir treatment failures, please see that topic.)

Recommended regimens listed by evidence level for:

**Sofosbuvir + Ribavirin-Experienced, Genotype 2 Patients, With or Without Compensated Cirrhosis**

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
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</tr>
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<tbody>
<tr>
<td>Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)</td>
<td>12 weeks</td>
<td>I, B</td>
</tr>
<tr>
<td>Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)</td>
<td>12 weeks</td>
<td>IIb, B</td>
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</tbody>
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* For decompensated cirrhosis, please refer to the appropriate section.

Dosing is 3 coformulated tablets (glecaprevir [100 mg]/pibrentasvir [40 mg]) taken once daily. Please refer to the prescribing information.

Recommended regimen for:

**Sofosbuvir + NS5A Inhibitor-Experienced (Excluding Glecaprevir/Pibrentasvir Failures), Genotype 2 Patients, With or Without Compensated Cirrhosis**

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<td>Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg)</td>
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**Sofosbuvir/Velpatasvir**

The phase 3, open-label, randomized clinical trial POLARIS-4 compared a 12-week course of sofosbuvir/velpatasvir/voxilaprevir to 12 weeks of the daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) 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. Among patients with genotype 2, 97% (32/33) who received 12 weeks of sofosbuvir/velpatasvir achieved SVR12. Overall for the study, the sofosbuvir/velpatasvir arm did not meet the prespecified performance goal of >
85% efficacy (prespecified p value 0.025). However, this was primarily driven by treatment failure in patients with genotype 3 or 1a. The single genotype 2 patient who experienced virologic failure in the sofosbuvir/velpatasvir arm had virologic breakthrough rather than relapse and was the only patient with an NS5B RAS at any time point. The S292T substitution emerged at the time of virologic failure. Diarrhea and nausea were more commonly reported in the sofosbuvir/velpatasvir/voxilaprevir group.

**Glecaprevir/Pibrentasvir**

The phase 3, randomized, double-blind, placebo-controlled ENDURANCE-2 study enrolled treatment-naive or -experienced (interferon or peginterferon ± ribavirin, or sofosbuvir plus ribavirin ± peginterferon) noncirrhotic genotype 2 patients. Participants were treated with 12 weeks of the daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) administered as three 100 mg/40 mg fixed-dose combination pills or placebo (Asselah, 2018b). Among 202 patients in the glecaprevir/pibrentasvir arm, 30% (61/202) were treatment experienced, of whom 6 had previously received sofosbuvir plus ribavirin ± peginterferon. The overall SVR12 in the intention-to-treat analysis was 99%, and SVR12 was achieved in all 6 patients with a prior sofosbuvir-based treatment failure. The most common adverse events in the glecaprevir/pibrentasvir arm were headache and fatigue.

The phase 3, single arm, open-label EXPEDITION-1 study investigated the safety and efficacy of a 12-week course of glecaprevir/pibrentasvir in patients with genotype 1, 2, 4, 5, or 6 and compensated cirrhosis. Treatment-naive and -experienced patients (interferon or peginterferon ± ribavirin, or sofosbuvir plus ribavirin ± peginterferon) were included in the trial. Overall, only 25% (n=36) of patients were treatment experienced, 11 of which had a history of sofosbuvir failure (although it is unclear how many of these patients had genotype 2). The SVR12 in the genotype 2 patients was 100% (31/31) (Forns, 2017).

No sofosbuvir treatment failures were included in the SURVEYOR study, which investigated 8 weeks of therapy in noncirrhotic patients with genotype 2. Thus, this regimen cannot be recommended in this patient population until supported by clinical data (Poordad, 2017).

**Sofosbuvir/Velpatasvir/Voxilaprevir**

POLARIS-1 evaluated 12 weeks of sofosbuvir/velpatasvir/voxilaprevir compared to placebo among patients with all genotypes who were previously treated with an NS5A inhibitor-containing regimen (including daclatasvir and velpatasvir but not glecaprevir). There were 5 genotype 2 patients and all achieved SVR12 (Bourliere, 2017).

**Last update:** November 6, 2019

**Related References**


