NS5A Inhibitor DAA-Experienced Genotype 1 Patients

**Recommended and alternative regimens for:**

**NS5A Inhibitor DAA-Experienced, Genotype 1 Patients With or Without Compensated Cirrhosis**

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>DURATION</th>
<th>RATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100mg)</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>ALTERNATIVE</th>
<th>DURATION</th>
<th>RATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) except NS3/4 protease inhibitor inclusive DAA combination regimens</td>
<td>16 weeks</td>
<td>IIa, B</td>
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</tbody>
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**Recommended Regimen**

**Sofosbuvir/Velpatasvir/Voxilaprevir**

The placebo-controlled, phase 3 POLARIS-1 trial evaluated a 12-week course of the daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100mg) in patients with a prior NS5A inhibitor-containing DAA regimen. The majority (61%) experienced a failure with a combination regimen of an NS5B inhibitor plus an NS5A inhibitor, such as sofosbuvir/ledipasvir ([Bourliere, 2017](#)). The overall SVR12 rate was 97% (146/150) in genotype 1-infected patients. SVR12 rates were 96% (97/101) for participants with genotype 1a infection and 100% (45/45) for those with genotype 1b infection. A single genotype 1-infected patient experienced relapse; this individual had subtype 1a infection and cirrhosis. Baseline RASs and the presence of cirrhosis were not significant predictors of virologic failure in genotype 1 infection. Serious adverse events were similar between the placebo and treatment arms; only 1 patient discontinued therapy due to an adverse event. Headache, diarrhea, and nausea were more common in those patients receiving sofosbuvir/velpatasvir/voxilaprevir compared to placebo.

**Alternative Regimen**

**Glecaprevir/Pibrentasvir**

In parts 1 and 2 of the MAGELLAN-1 trial, 42 genotype 1-infected patients had previously been treated with either an NS5A inhibitor or an NS3/4A protease inhibitor ([Poordad, 2017](#); [Poordad, 2017b](#)). Twenty-four percent of these patients had cirrhosis and 79% were genotype 1a infected. Patients who were previously treated with an NS5A inhibitor (ledipasvir or daclatasvir) and not concomitantly treated with a NS3/4A protease inhibitor were retreated 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 16 weeks. Among these patients, 94% (16/17) achieved SVR 12. The single patient who did not respond to therapy had an on-treatment virologic failure. Due to the 16-week duration of therapy and limited supporting data, this is recommended as an alternative regimen.

**Last update:** September 21, 2017

**Related References**

