Peginterferon/Ribavirin-Experienced, Genotype 2 Patients With Compensated Cirrhosis

Recommended regimens listed by evidence level and alphabetically for:

<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)</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)</td>
<td>12 weeks</td>
<td>I, B</td>
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**Sofosbuvir/Velpatasvir**

In the randomized, open-label ASTRAL-2 study, genotype 2 patients were treated with 12 weeks of the daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) or sofosbuvir plus ribavirin (Foster, 2015a). Of the 266 participants, a minority (15%) had a history of previous peginterferon/ribavirin treatment failure and a similar proportion (14%) had compensated cirrhosis. Overall, the combination of sofosbuvir/velpatasvir yielded a statistically significant superior SVR12 of 99% vs 94% for sofosbuvir plus ribavirin. The only treatment failure in the sofosbuvir/velpatasvir arm was a patient who withdrew from the study after a single day due to side effects (anxiety). In contrast, there were 6 virologic failures in the sofosbuvir plus ribavirin arm. Fatigue and anemia were more commonly reported in patients receiving sofosbuvir plus ribavirin.

The phase 3 POLARIS-2 study randomized patients to 8 weeks of sofosbuvir/velpatasvir/voxilaprevir or 12 weeks of sofosbuvir/velpatasvir. Fifty-three genotype 2 patients were included in the sofosbuvir/velpatasvir arm and all achieved SVR (100%, 53/53) (Jacobson, 2017). This study confirms the high efficacy and safety of this 12-week regimen in patients with genotype 2, including those with a past peginterferon/ribavirin treatment failure and patients with compensated cirrhosis.

Considering the high SVR12 and fewer side effects with sofosbuvir/velpatasvir, regimens with peginterferon and/or ribavirin are no longer recommended for genotype 2.

**Glecaprevir/Pibrentasvir**

The phase 3, single arm, open-label EXPEDITION-1 study investigated the safety and efficacy of a 12-week course of the daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) administered as three 100 mg/40 mg fixed-dose combination pills in patients with genotype 1, 2, 4, 5, or 6 and compensated cirrhosis (Forns, 2017). 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. The SVR12 in the genotype 2
patients was 100% (31/31). Overall, 91% percent (133/146) of patients had a Child-Pugh score of 5, and 9% (13/146) had a Child-Pugh score of 6. Twenty percent of patients had a platelet count <100 x 10^9/L and all but 1 participant had a normal albumin level. In this patient population with compensated cirrhosis, the regimen was safe and well tolerated. There were 11 serious adverse events; none were DAA-related and no adverse events led to discontinuation of the study drugs. This is a safe and highly efficacious 12-week regimen in patients with well-compensated cirrhosis.

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**Related References**

