**Therapeutics**

**Review: In chronic hepatitis C virus infection, oral direct-acting antivirals have high sustained virologic response**


**Clinical impact ratings:**

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**Question**

In patients with chronic hepatitis C virus (HCV) infection, what are the efficacy and safety of oral direct-acting antiviral (DAA) regimens?

**Review scope**

Included English-language studies assessed interferon-free treatment regimens of ≥ 2 DAAs that were approved by the US Food and Drug Administration and lasted ≥ 8 weeks in adults with chronic HCV infection, regardless of cirrhosis, HIV, or liver transplantation status. DAA combinations included inhibitors of HCV NS3 protease (grazoprevir, paritaprevir, and simeprevir), NS5A (daclatasvir, elbasvir, ledipasvir, ombitasvir, and velpatasvir), and NS5B polymerase (sofosbuvir and dasabuvir), with or without oral antiviral ribavirin. Outcomes were sustained virologic response (SVR) and adverse events.

**Review methods**

MEDLINE and EMBASE/Excerpta Medica (both to Nov 2016), ClinicalTrials.gov, and reference lists were searched for randomized controlled trials (RCTs) and cohort studies. 42 studies met selection criteria: 32 RCTs and 10 cohort studies. 19 RCTs had low risk for bias, and 13 had moderate risk. Comparison groups were deferred treatment (5 RCTs); varying duration of DAAs with or without ribavirin (11 RCTs); DAAs with or without ribavirin for the same duration (5 RCTs); varying duration of DAAs with ribavirin (6 RCTs) and without ribavirin (3 RCTs); or another active HCV treatment regimen (2 RCTs). Results from RCTs are presented in this abstract.

**Main results**

The main results for HCV genotype 1 and 3 are in the Table; SVR varied according to treatment experience, cirrhosis status, and addition of ribavirin. SVR rates for genotypes 2, 4, 5, and 6 were > 90%. Rates of serious adverse events were < 10%.

**Conclusion**

In patients with chronic hepatitis C virus infection, oral direct-acting antiviral regimens have high sustained virologic response rates.

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**Effect of oral direct-acting antiviral (DAA) treatments on sustained virologic response (SVR) in patients with chronic hepatitis C virus (HCV) infection**

<table>
<thead>
<tr>
<th>HCV genotype</th>
<th>DAA regimen</th>
<th>Number of trials (n)</th>
<th>SVR at 12 wk (patient group)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV-1</td>
<td>GZP+EBV</td>
<td>4 (1644)</td>
<td>≥ 92%1</td>
</tr>
<tr>
<td></td>
<td>PTV+OBV+DAV ± RBV</td>
<td>10 (2702)</td>
<td>97% to 100% (genotype 1b); 97% (genotype 1a + RBV); 90% (genotype 1a – RBV); 87% (cirrhosis)</td>
</tr>
<tr>
<td></td>
<td>SIM + SOF ± RBV</td>
<td>2 (478)</td>
<td>97% (TN); 91% (TN, cirrhosis); 79% (TE, cirrhosis)</td>
</tr>
<tr>
<td></td>
<td>DCV + SOF</td>
<td>2 (238)</td>
<td>95% to 100% (TN/TE)</td>
</tr>
<tr>
<td></td>
<td>LDV+SOF ± RBV</td>
<td>7 (2718)</td>
<td>≥ 95% (TN); 86% (TE, cirrhosis); 97% (TE, cirrhosis, +RBV); 85% to 87% (decompensated cirrhosis, +RBV)</td>
</tr>
<tr>
<td></td>
<td>VEL+SOF ± RBV</td>
<td>2 (600)</td>
<td>&gt; 95%; 94% (decompensated cirrhosis, +RBV)</td>
</tr>
<tr>
<td>HCV-3</td>
<td>DCV + SOF ± RBV</td>
<td>3 (107)</td>
<td>94% to 95% (TN/TE); 58% to 69% (TN/TE, cirrhosis); 83% to 89% (cirrhosis, +RBV)</td>
</tr>
<tr>
<td></td>
<td>LDV+SOF ± RBV</td>
<td>1 (26)</td>
<td>100% (+RBV); 64% (~RBV)</td>
</tr>
<tr>
<td></td>
<td>VEL+SOF ± RBV</td>
<td>2 (591)</td>
<td>95%; 85% (decompensated cirrhosis, +RBV); 50% (decompensated cirrhosis, ~RBV)</td>
</tr>
</tbody>
</table>

*DAV = dasabuvir; DCV = daclatasvir; EBV = elbasvir; GZP = grazoprevir; LDV = ledipasvir; OBV = ombitasvir; PTV = paritaprevir; RON = ronafidine; RBV = ribavirin; SIM = simeprevir; SOF = sofosbuvir; TE = treatment-experienced; TN = treatment-naive; VEL = velpatasvir.

1. TN/TE, with or without cirrhosis.

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**References**


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