Background

- DCV + ASV was evaluated in a global phase 3 study in patients with GT 1b who were treatment-naive, non-responders to peg-IFN/RBV, or peg-IFN/RBV ineligible/intolerant.
- Daclatasvir (DCV) - Patient, pangenotypic NS5A inhibitor
- Once daily with low potential for drug-drug interactions
- Safe and well tolerated in > 5000 patients treated
- Asunaprevir (ASV) - H53 protease inhibitor
- Clinical data in GT 1 and 4
- Generally well tolerated in > 2000 patients treated

Primary efficacy and safety results (including data on resistance) from this study were presented at EASL 2014.

Efficacy and safety results in patients with and without cirrhosis are presented here.

Methods

Study Design

This global phase 3 study evaluated DCV (60 mg tablet once daily) combined with ASV (100 mg softgel capsule twice daily) in patients with GT 1b:

- Treatment-naive
- Non-responders to peg-IFN/RBV (null or partial response)
- Peg-IFN/RBV ineligible/intolerant (treatment-naive or -experienced)
- Compensated advanced fibrosis/cirrhosis (F3/F4) with thrombocytopenia (screening platelet counts < 90 x 10^9/L) and/or history of thrombocytopenia on peg-IFN/RBV

Patient Eligibility Criteria

- Patients: men and women aged ≥ 18 years
- Treatment-naive
- Prior peg-IFN/RBV non-responders (null or partial response)
- Peg-IFN/RBV ineligible/intolerant (treatment-naive or -experienced)
- Compensated advanced fibrosis/cirrhosis (F3/F4) with thrombocytopenia (screening platelet counts < 90 x 10^9/L) and/or history of thrombocytopenia on peg-IFN/RBV

Primary endpoint: proportion of DCV + ASV-treated patients with SVR24
- Efficacy and safety with DCV + ASV were assessed in patients with and without cirrhosis
- Presence of cirrhosis assessed by liver biopsy or transient elastography (FibroScan; ≥ 14.6 kPa)

*Includes 2 patients inadvertently assigned. Instead of randomization, to DCV + ASV: patients were excluded from efficacy analysis but both-achieved SVR24.
Results

Demographics & Baseline Disease Characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cirrhotic (N = 223)</th>
<th>Non-cirrhotic (N = 523)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median years</td>
<td>59</td>
<td>56</td>
</tr>
<tr>
<td>Race, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>153 (48)</td>
<td>384 (68)</td>
</tr>
<tr>
<td>Black</td>
<td>8 (4)</td>
<td>14 (6)</td>
</tr>
<tr>
<td>Asian</td>
<td>60 (27)</td>
<td>126 (24)</td>
</tr>
<tr>
<td>Other*</td>
<td>2 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>HCV RNA, log IU/mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 800,000 log IU/mL</td>
<td>48 (23)</td>
<td>106 (20)</td>
</tr>
<tr>
<td>≥ 800,000 log IU/mL</td>
<td>175 (78)</td>
<td>418 (80)</td>
</tr>
<tr>
<td>IL28B genotype, % CC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CC</td>
<td>65 (33)</td>
<td>132 (20)</td>
</tr>
<tr>
<td>Non-CC</td>
<td>152 (67)</td>
<td>211 (36)</td>
</tr>
<tr>
<td>Prior treatment experience, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonresponder</td>
<td>49 (23)</td>
<td>258 (49)</td>
</tr>
<tr>
<td>Responder</td>
<td>63 (28)</td>
<td>143 (27)</td>
</tr>
<tr>
<td>Ineligible/intolerant</td>
<td>111 (50)</td>
<td>124 (22)</td>
</tr>
</tbody>
</table>

*Includes North African, Caribbean Indian, Chinese, Korean, Southeast Asian/Pacific Islander, and Other ethnicity.

Virologic Response by Cirrhosis Status

- SVR12 was achieved in a similar proportion of cirrhotic and non-cirrhotic patients
- When patients with missing SVR12 data were counted as treatment failures, rates were identical except for treatment-naive non-cirrhotic patients (88%) and ineligible/intolerant cirrhotic patients (79%)
- 49% of cirrhotic patients and 76% of non-cirrhotic patients completed DCV + ASV treatment

Virologic Response in Cirrhotics & Non-Cirrhotics by Patient Subgroup

- Patients with cirrhosis achieved high SVR12 rates across all subgroups
- Among ineligible/intolerant patients, SVR12 rate was slightly lower in those with advanced fibrosis/cirrhosis with thrombocytopenia (71%) versus depression (82%) and anemia/neutropenia (91%)

Virologic Response by Baseline Platelet Count

- In the subgroup with advanced fibrosis/cirrhosis with thrombocytopenia, SVR12 rates were lower in patients with baseline platelet counts < 90 versus ≥ 90 × 10^9 cells/L

- Similar results seen in the overall patient population

Primary Endpoint: Virologic Response SVR12

- SVR12 rates documented on or after post-treatment Week 12
  - Treatment-naive: 91%
  - Non-responders: 82%
  - Ineligible/intolerant: 83%

Virologic Response bySignup
Cirrhotic and non-cirrhotic patients had similar virologic responses based on baseline factors. DCV + ASV was well tolerated. No clinically meaningful differences between cirrhotic and non-cirrhotic patients were observed in treatment safety and tolerability parameters. Similar proportions of cirrhotic and non-cirrhotic patients achieved SVR12, regardless of cirrhosis severity. DCV + ASV was generally well tolerated, with no clinically meaningful differences observed between cirrhotic and non-cirrhotic patients. DCV + ASV is being further evaluated in all eligible/intolerant groups in multiple patient populations of high unmet need.

**Patients Without SVR12 by Cirrhosis Status**

<table>
<thead>
<tr>
<th>Patients, n (%)</th>
<th>Cirrhotics (N = 206)</th>
<th>Non-cirrhotics (N = 438)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirrhosis (%)</td>
<td>20 (10)</td>
<td>42 (10)</td>
</tr>
<tr>
<td>Posttreatment failures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Virologic breakthrough</td>
<td>16 (8)</td>
<td>29 (7)</td>
</tr>
<tr>
<td>Detectable or missing RNA at end of treatment</td>
<td>8 (4)</td>
<td>8 (2)</td>
</tr>
<tr>
<td>Relapse or missing RNA at posttreatment Week 12*</td>
<td>8 (5)</td>
<td>16 (4)</td>
</tr>
</tbody>
</table>

*Data on an intention-to-treat basis. 1

**Virologic Response in Cirrhotics by Baseline Factors**

**Conclusions**

- In this global, phase 3 study with a high proportion of cirrhotic patients (≈30%), all-oral DCV + ASV achieved high SVR12 rates (documented on or after post-treatment Week 12).
- SVR12 achieved in 84% and 85% of cirrhotic and non-cirrhotic GT 1b patients, respectively.
- In cirrhotic patients, SVR12 rates were 91% in treatment-naive, 87% in non-responder, and 81% in PIF-eligible/intolerant groups.
- DCV + ASV was generally well tolerated.
- No clinically meaningful differences between cirrhotic and non-cirrhotic patients in safety parameters.
- DCV is being further evaluated in all-oral combination regimens in multiple patient populations of high unmet need.

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