The ASPIRE Trial: TMC435 in treatment-experienced patients with genotype 1 HCV infection who have failed previous PegIFN/RBV who treatment: Week 24 interim analysis

Stefan Ziemek,1 Graham R Foster,2 Michael W Fried,3 Christophe Hezode,2 Gideon M Hirschfield,1 Igor Nikitin,4 Fred Poodard,6 Oliver Lenz,5 Monika Peeters,5 Vanitha Sekar,5 Goeede De Smidt6

1. U. K. Geisinger University Hospital, Franklin, Germany; 2. Queen Mary University of London, London, United Kingdom; 3. University of North Carolina at Chapel Hill, North Carolina, USA; 4. Hospital Henri Mondor, Université Paris Est Créteil, France; 5. Toronto Western Hospital Liver Centre, Toronto, Canada; 6. Russian State Medical University, Moscow, Russia; 7. Cincinnati Sinai Medical Center, Las Vegas, USA; 8. TIBET-IV/BAVA, Miechelin, Belgium; 9. TIBET-IV, Yardley, PA, USA

INTRODUCTION

TMC435 is an investigational new oral, selective and specific in vitro inhibitor of HCV NS5A, a viral non-structural protein involved in viral protein translation in the host liver. TMC435 is given orally with PegIFN/RBV, and has an excellent safety profile in healthy volunteers and in patients infected with HCV. The ASPIRE trial is the first in-vivo evaluation of TMC435 in a Phase II placebo-controlled trial in patients with prior treatment failure (described here). The ASPIRE trial is the first in-vivo evaluation of TMC435 in a Phase II placebo-controlled trial in patients with prior treatment failure (described here).

METHODS

Study Design
The study is a multicenter, randomized, double-blind, placebo-controlled, 3-arm study (2:2:1 ratio) comparing TMC435 with PegIFN/RBV vs. PegIFN/RBV alone or placebo + PegIFN/RBV in treatment-experienced patients (≥ 2 prior treatment courses, or ≥ 1 prior documented course of therapy in the prior 5 years, ≥ 3 months after the previous treatment) with genotype 1 infection who had relapsed, partial or null response or viral breakthrough. TMC435 was given at a fixed 150 mg once-daily dose in combination with PegIFN/RBV. TMC435 or placebo were added after 12 weeks of treatment with PegIFN/RBV in a 2:2:1 ratio: placebo in combination with PegIFN/RBV. TMC435, TMC100 mg or TMC150 mg + PegIFN/RBV. A total of 65 patients were randomized to each treatment arm. Prior to starting TMC435, all patients were seen in a withdrawal period that included a liver biopsy to evaluate fibrosis. The ASPIRE study design.

Efficacy

The ASPIRE Trial: TMC435 in treatment-experienced patients with genotype 1 HCV infection

In the ASPIRE Study, 1,500 mg of TMC435 was given for 24 weeks in addition to PegIFN/RBV for 48 weeks. The ASPIRE study design.

Safety

The ASPIRE Study: TMC435 in treatment-experienced patients with genotype 1 HCV infection

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Patient Demographics

Baseline demographics and characteristics were well balanced between treatment arms. The ASPIRE study design.

RESULTS

Patient Disposition

A total of 193 patients were randomized, of whom 1,500 mg of TMC435 was given for 24 weeks in addition to PegIFN/RBV in a 2:2:1 ratio: placebo in combination with PegIFN/RBV. TMC435, TMC100 mg or TMC150 mg + PegIFN/RBV. A total of 65 patients were randomized to each treatment arm. Prior to starting TMC435, all patients were seen in a withdrawal period that included a liver biopsy to evaluate fibrosis. The ASPIRE study design.

Observed Virologic Response

At Week 4, 12, and 24, significantly higher virologic response rates were observed with TMC435 compared with PegIFN/RBV monotherapy. The ASPIRE study design.

TABLE 1: Baseline demographics and characteristics at treatment arm

<table>
<thead>
<tr>
<th>Treatment Arm</th>
<th>Age (years), Median [IQR]</th>
<th>Sex, Male (%)</th>
<th>BMI (kg/m²), Median [IQR]</th>
<th>HCV Infection Duration (years), Median [IQR]</th>
<th>Baseline HCV RNA (IU/mL), Median [IQR]</th>
</tr>
</thead>
<tbody>
<tr>
<td>PegIFN/RBV</td>
<td>56.0 [52.0-60.0]</td>
<td>58.0</td>
<td>27.8 [24.0-31.0]</td>
<td>8.0 [5.0-10.0]</td>
<td>8.0 [5.0-10.0]</td>
</tr>
<tr>
<td>TMC100 mg</td>
<td>57.0 [53.0-62.0]</td>
<td>56.0</td>
<td>28.0 [24.0-31.0]</td>
<td>8.0 [5.0-10.0]</td>
<td>8.0 [5.0-10.0]</td>
</tr>
<tr>
<td>TMC150 mg</td>
<td>55.0 [52.0-60.0]</td>
<td>54.0</td>
<td>27.0 [24.0-30.0]</td>
<td>8.0 [5.0-10.0]</td>
<td>8.0 [5.0-10.0]</td>
</tr>
<tr>
<td>Placebo + PR</td>
<td>57.0 [53.0-60.0]</td>
<td>58.0</td>
<td>28.0 [24.0-31.0]</td>
<td>8.0 [5.0-10.0]</td>
<td>8.0 [5.0-10.0]</td>
</tr>
</tbody>
</table>

*Data available for patients who consented to DNA research only.

REFERENCES