Safety and efficacy of ravidasvir plus sofosbuvir for 12 weeks in non-cirrhotic and 24 weeks in cirrhotic patients with hepatitis C virus genotypes 1, 2, 3 and 6: the STORM-C-1 phase II/III trial stage 1 results


AIM

The STORM-C-1 trial is an open label trial aiming to assess the efficacy, safety, tolerance and pharmacokinetics of sofosbuvir plus ravidasvir (SOF-DRV) in Malaysia and Thailand, where genotypes 1 and 3 are prevalent.

METHODS

Study design

Two-stage, open-label, multicentre trial:
- 12 weeks SOF-DRV in patients with chronic HCV infection and no cirrhosis (Metavir F0 to F3)
- 24 weeks SOF-DRV in patients with compensated cirrhosis (Metavir F4 and Child Tzoro Pugh class A)
We report here the results of the stage 1 trial.

Stage 1 analysis strategy

Based on published results for other treatments, we considered that the overall SVR12 rate should be ≥85% in the ITT analysis. A sample size of 300 patients provided over 86% power to detect at least 6% improvement in the overall SVR12 rate from this pre-specified performance goal of 85% (two-sided exact binomial test, alpha=0.05).

Efficacy analysis populations

Intention to treat (ITT)

Patients who:
- Did not report active injection drug use at eligibility visit.
- Received at least one dose of a study drug.

Primary endpoint: sustained virologic response at 12 weeks post-treatment (SVR12).

RESULTS

POPULATION BASELINE CHARACTERISTICS

300 patients enrolled between October 2016 and June 2017 were included in the intention-to-treat (ITT) analysis:

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Genotype %</th>
<th>Gender</th>
<th>Race</th>
<th>Age (years)</th>
<th>F0</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>HIV co-inf</th>
<th>SBP</th>
<th>HBV co-inf</th>
<th>Cirrhosis</th>
<th>Decomp</th>
<th>Decomp cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>32 (104)</td>
<td>80</td>
<td>0</td>
<td>40-56</td>
<td>19</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>8</td>
<td>0</td>
<td>65 (25%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1b</td>
<td>9 (30)</td>
<td>0</td>
<td>100</td>
<td>30-40</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>53 (160)</td>
<td>61</td>
<td>67</td>
<td>40-56</td>
<td>4</td>
<td>13</td>
<td>27</td>
<td>9</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>32 (104)</td>
<td>0</td>
<td>0</td>
<td>18-28</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

SUSTAINED VIROLOGIC RESPONSE AT 12 WEEKS POST-TREATMENT (SVR12)

Overall SVR12 rate in ITT analysis: 97.0% (95% CI: 94.4% to 98.6%), significantly >85% (p<0.001)

PHARMACOKINETIC INTERACTIONS WITH ANTIRETROVIRALS

No clinically significant drug interactions were observed between ravidasvir and the usual HIV antiretroviral drugs (Cresssey, CRIO 2018).

CONCLUSIONS

- With 12 weeks of treatment in non-cirrhotic and 24 weeks in cirrhotic patients, sofosbuvir plus ravidasvir was highly effective, regardless of HCV genotype, HIV infection and previous interferon experience. Treatment was well tolerated in all subgroups.
- Stage 2 of this study is under preparation. Further studies are being designed to ensure good representation of all key subgroups, in particular those with genotype 6, as well as key populations (people who inject drugs, people with advanced liver disease, people co-infected with HIV).

ACKNOWLEDGEMENTS

Ministry of Health C, Ministry of Public Health Thailand, Phrao, Prasarn, Geneve University Hospital, Dr Sabine Yerly, Pr. Francesco Negro, Dr. Alexandra Colmy, Clinical Research Center Malaysia, Dr Ahlim Yusu, Medecins Sans Frontieres, STARR foundation, the patients and their care givers.

CONTACT INFORMATION

Landteux.meyer@dndi.org