Establishment of High Rates of Functional Control and Reversal of Fibrosis Following Treatment of HBeAg Negative Chronic HBV Infection with REP 2139-Mg / REP 2165-Mg, Tenofovir Disoproxil Fumarate and Pegylated Interferon Alpha-2a

M. Bazinet1, V. Pântea2, G. Placinta3, I. Moscalu4, V. Cebotarescu5, L. Cojjuhari6, P. Jimbei7, L. Iarovoi8, V. Smesnoi9, T. Musteata10, A. Jucov11, A. Krawczyk12, A. Vaillant1

1.Replicor Inc. Montreal, Canada
2.Department of Infectious Diseases, Nicolae Testemitanu University of Medicine and Pharmacy, Chisinau, Republic of Moldova.
3. ARRINS Institute of Medical Research, Chisinau, Republic of Moldova
4. Toma Cizmar Infectious Clinic Hospital, Chisinau, Republic of Moldova
5. Universitätsklinikum Essen, Institute for Virology, Essen, Germany

INTRODUCTION

Nucleic acid polymers block the assembly and release of HBV subviral particles, allowing clearance of serum HBsAg by host immune function. Previous clinical studies have demonstrated that NAP monotherapy is associated with high rates of HBsAg reduction to < 1 IU/mL and is accompanied by HBeAg and HBsAg seroconversion, HBV DNA, HBV RNA and HBV DNA declines and HBsAg RNA clearance (in HDV co-infected patients). When used in combination with immunotherapy, control of all of the above is maintained during treatment free follow-up in the majority of patients treated.

The REP 401 protocol (ICT05657219) is a randomized, controlled trial assessing the safety and efficacy of REP 2139-Mg and REP 2165-Mg (Table 1) in combination with tenofovir disoproxil fumarate (TDF) and pegylated interferon alpha-2a (pegIFN) in patients with chronic HBV infection without HBeAg.

MATERIALS AND METHODS

REP 2139-Mg and REP 2165-Mg (magnesium chelate complex) drug products (Table 1) are optimized for subcutaneous (SC) injection and administered via intravenous infusion in the REP 401 study to assess tolerability in preparation for transition to SC in future trials.

Twenty weeks of lead-in TDF was followed by randomization (1:1) into experimental and control groups. The experimental group received 48 weeks of TDF, pegIFN (180ug SC qW) and REP 2139-Mg or REP 2165-Mg (1:1, 250 mg IV infusion qW). The control group received 24 weeks of TDF. ALT flares in all patients crossing over to 48 weeks of experimental therapy due to poor tolerability or consent withdrawal are monitored on the Abbott Architect and Realtime platforms.

DISCLOSURES

MB and AV are employees of and shareholders in Replicor Inc. All other authors have no conflicts to declare.

CONTACT

Andrew Vaillant: availlant@replicor.com

Table 1. REP 401 Study Design and Follow-up Summary

<table>
<thead>
<tr>
<th>Category</th>
<th>Baseline</th>
<th>EOT</th>
<th>FW24</th>
<th>FW48</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg (IU/mL)</td>
<td>&lt; 0.05</td>
<td>0%</td>
<td>50%</td>
<td>62%</td>
</tr>
<tr>
<td>Anti-HBs (mIU/mL)</td>
<td>0%</td>
<td>55%</td>
<td>59%</td>
<td>62%</td>
</tr>
<tr>
<td>HBV DNA (IU/mL)</td>
<td>undetectable</td>
<td>5%</td>
<td>60%</td>
<td>94%</td>
</tr>
</tbody>
</table>

CONCLUSIONS

1. REP 2139-Mg and REP 2165-Mg are equivalently well tolerated and effective in achieving high rates of HBsAg clearance/loss and seroconversion in a 48 week combination regimen with TDF and pegIFN.

2. ALT flares occur in ~ 90% of patients and are likely therapeutic in nature:
   - Self resolving
   - Otherwise asymptomatic (even in patients with advanced fibrosis)
   - Correlated with antiviral responses and establishment of functional control off therapy

3. High rates of inactive HBV (44%) and functional cure (41%) are established with accompanying normalization of liver function and apparent reversal of fibrosis.

4. 85% of patients meet the level of control associated with low risk of progression of liver disease and reduced risk of HCC.

5. Although pegIFN is well tolerated, other immunotherapies which do not negatively impact T-cell function may improve upon the functional control achievable when used in combination with REP 2139-Mg.

REFERENCES