VIR-2218 and VIR-3434 with or without Pegylated Interferon Alfa-2a for the Treatment of Chronic HBV Infection: End of Treatment (EOT) Results After 24 Weeks of Therapy (MARCH Study Part B)

Edward Gane, Kosh Agarwal, Wayne Bai, Alina Jucov, Tien-Huey Lim, Young-Suk Lim, Anca Streinu-Cercel, Grace Wong, Ruveena Bhavani Rajaram, Ki Tae Yoon, Shenghua Mao, Li Wang, Andrea L. Cathcart, Rachel Wong, Michael Chattergoon, Andre Arizpe, Daniel Cloutier, Carey Hwang, Man-Fung Yuen

Background: There is an unmet need for a well-tolerated curative regimen for chronic hepatitis B virus (HBV) infection, which is associated with significant morbidity and mortality. VIR-2218 is an investigational small interfering ribonucleic acid (siRNA) targeting the HBx region of the HBV genome, and VIR-3434 is an investigational engineered human monoclonal antibody targeting the antigenic loop of HBsAg. We previously reported that 24 weeks of VIR-2218 + PEG-IFNα achieved HBsAg loss in 5.6% of participants at EOT. Part B of the ongoing phase 2 open-label MARCH study is evaluating the safety, tolerability, and antiviral activity of 24- and 48-week regimens of VIR-2218 and VIR-3434 with or without PEG-IFNα for the treatment of chronic HBV infection. Here, we report data through EOT for the 24-week cohorts.

Methods: Eligible participants were adults with chronic HBV infection and any baseline HBsAg level who were on continuous NRTI therapy for ≥2 months. This preliminary analysis reflects on treatment data from cohorts evaluating VIR-2218 + VIR-3434 for 20 weeks or VIR-2218 + VIR-3434 + PEG-IFNα for 24 weeks. VIR-2218, VIR-3434, and PEG-IFNα are administered SC at 200 mg every 4 weeks (Q4W), 300 mg Q4W, and 180 µg weekly, respectively. Participants are followed for ≥48 weeks post-EOT. Primary endpoints are the proportion of participants with TEAEs, SAEs, and HBsAg loss (<0.05 IU/mL) at EOT and at 24 weeks post-EOT.

Results: A total of 41 participants were enrolled across VIR-2218 + VIR-3434 (n=20) and VIR-2218 + VIR-3434 + PEG-IFNα (n=21); 65.9% were HBeAg-negative. The proportions of participants achieving HBsAg loss or HBsAg <10 IU/mL at EOT are presented in the Figure. Grade 3 or 4 TEAEs were reported in no subjects in the VIR-2218 + VIR-3434 cohort and 6/21 subjects in the VIR-2218 + VIR-3434 + PEG-IFNα cohort (all were deemed related to PEG-IFNα). One of these 6 participants in the VIR-2218 + VIR-3434 + PEG-IFNα cohort also experienced 2 PEG-IFNα-related SAEs.

Conclusion: When administered for 20-24 weeks, VIR-2218 + VIR-3434, with and without PEG-IFNα, achieved similar HBsAg loss rates of 14.3% and 15% of participants at EOT, approximately 3 times higher than the rate previously observed for 24 weeks of VIR-2218 + PEG-IFNα. This supports an additive effect of VIR-3434. No new safety concerns were identified for the combination with PEG-IFNα. Additional cohorts evaluating 48 weeks of treatment are ongoing.
Figure: HBsAg Distribution at Baseline and End of Treatment by Cohort

<table>
<thead>
<tr>
<th></th>
<th>VIR-2218 + VIR-3434</th>
<th>VIR-2218 + VIR-3434 + PEG-IFNα</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>20 Weeks</td>
<td>24 Weeks</td>
</tr>
<tr>
<td>n</td>
<td>20</td>
<td>21</td>
</tr>
<tr>
<td><strong>Baseline</strong></td>
<td>95%</td>
<td>85.7%</td>
</tr>
<tr>
<td><strong>EOT</strong></td>
<td>55.5%</td>
<td>66.7%</td>
</tr>
</tbody>
</table>

- **HBsAg value**
  - < 0.05 IU/mL (LLOQ)
  - 0.05 – < 10 IU/mL
  - 10 – < 100 IU/mL
  - ≥ 100 IU/mL
  - Missing

**Legend:**
- Dark blue: < 0.05 IU/mL (LLOQ)
- Light blue: 0.05 – < 10 IU/mL
- Gray: 10 – < 100 IU/mL
- Light gray: ≥ 100 IU/mL
- White: Missing