Lenacapavir (GS-6207) Targets Multiple Stages of HIV Replication Cycle

• LEN is a novel, highly potent, long-acting, first-in-class, HIV-1 capsid inhibitor
• LEN can meet significant unmet HIV treatment and prevention needs:
  – A new mechanism of action for people with multidrug-resistant (MDR) HIV-1 who are heavily treatment-experienced (HTE) and have limited treatment options
  – Reduction of daily pill burden through less frequent dosing for treatment and prevention
  – Highly desirable in vitro profile, with picomolar antiviral activity (EC50: 50-100 pM)
  – Retains full activity against mutants resistant to nucleoside reverse-transcriptase inhibitors (NNRTIs), nonnucleoside reverse-transcriptase inhibitors (NNRTIs), integrase strand transfer inhibitors (INSTIs), protease inhibitors (PIs), and entry inhibitors
  – No observed pre-existing resistance

LEN has the potential to become an important new treatment option for individuals who have been treated with many antiretrovirals and for whom few treatment choices remain.

LEN was previously administered to 2,570 people with HIV in the CAPELLA study, and the SAFER and PARTNER trials. In this study, the safety and efficacy of LEN were assessed in two clinical settings: (1) extending the treatment options for some patients on a failing regimen (Failing regimen arm), including those with treatment-experienced (HTE) and have limited treatment options, and (2) providing an integrative treatment option for those on a functional background regimen (OBR) that was not considered to be adequate for ongoing treatment (Non-OBR arm).

Current patients in the Failing regimen arm included those on a failing regimen with known INSTI resistance and those with effi cacy among subgroups who were considered more diffi cult to treat (eg, those with high HIV-1 RNA, low CD4 count, INSTI resistance, no fully active agents in the OBR).

Results

Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Randomized Cohort (n = 53)</th>
<th>Nonrandomized OBR (n = 12)</th>
<th>P-Value (vs. Failing Regimen)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range), years</td>
<td>40 (18-67)</td>
<td>46 (23-74)</td>
<td>0.002</td>
</tr>
<tr>
<td>Sex, % female at birth</td>
<td>43</td>
<td>42</td>
<td>1.000</td>
</tr>
<tr>
<td>Race, % Black</td>
<td>46</td>
<td>38</td>
<td>0.038</td>
</tr>
<tr>
<td>HIV-1 RNA, median (range), log10 c/mL</td>
<td>6.0 (3.7-6.4)</td>
<td>6.0 (3.2-4.7)</td>
<td>0.744</td>
</tr>
<tr>
<td>CD4 count, median (range), cells/μL</td>
<td>196 (138-262)</td>
<td>180 (108-236)</td>
<td>0.094</td>
</tr>
<tr>
<td>INSTI resistance, %</td>
<td>78</td>
<td>69</td>
<td>0.042</td>
</tr>
<tr>
<td>≥ 2 INSTI agents, %</td>
<td>47</td>
<td>47</td>
<td>1.000</td>
</tr>
</tbody>
</table>

Objective

To evaluate Week 52 efficacy (assessed using U.S. Food & Drug Administration Snapshot algorithm) by subgroup analyses in a randomized cohort of PWHS by demographics, and baseline HIV-1 RNA, CD4, OBR, and INSTI resistance

Methods

Study Design

Study Design

LEN SC Q6M for 52 wkb

Conclusions

• In PWHS who were HTE with limited treatment options due to MDR, LEN in combination with an OBR led to high rates of virologic suppression
• No clinically relevant differences were seen in efficacy among subgroups who were considered more diffi cult to treat (eg, those with high HIV-1 RNA, low CD4 count, INSTI resistance, no fully active agents in the OBR, or no DTG or DRV in the OBR)
• LEN has the potential to become an important agent for PWHS who are HTE with MDR
• These data support the ongoing evaluation of LEN for treatment and prevention of HIV

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