Introduction

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

LEN is a long-acting, first-in-class inhibitor of HIV-1 capsid protein

- Can be administered subcutaneously (2 x 1.5 mL [927 mg] in abdomen Q6M)
- Approved by the European Commission for the treatment of HIV-1 infection, in combination with other antiretrovirals (ARVs), in adults with multidrug resistance for whom it is otherwise not possible to construct a suppressive antiviral regimen
- Development as a long-acting agent for treatment and prevention of HIV
- In people with HIV (PWH) who are heavily treatment experienced or treatment naive, LEN in combination with other ARVs was well tolerated and led to high rates of virologic suppression through 1 year

LEN-related injection-site reactions (ISRs) were previously characterized

Objective

- To characterize adverse events (AEs) other than ISRs in participants who received ≥1 dose of oral or SC LEN in clinical studies in PWH who were heavily treatment experienced (CAPELLA [ClinicalTrials.gov NCT04150088]) or treatment naive (CALIBRATE [NCT04143594])

Methods

Study Designs

- Key eligibility criteria:
  - ≥ 18 years of age
  - HIV RNA ≥ 400 c/mL or ≥ 200 c/mL (functional treatment-naive) at baseline
  - ARV naïve or treatment-experienced
  - ≤ 2 fully active agents from 4 main ARV classes

Safety Summary

- All AEs are presented by treatment group
- AEs related to study drug
- Serious AEs
- AE leading to discontinuation
- Death

Exposure to LEN

<table>
<thead>
<tr>
<th>CAPELLA n = 72</th>
<th>CALIBRATE n = 157</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure, median, wk</td>
<td>54</td>
</tr>
<tr>
<td>Q1, Q3</td>
<td>44, 72</td>
</tr>
<tr>
<td>Min, Max</td>
<td>13, 92</td>
</tr>
</tbody>
</table>

Results

Baseline Characteristics

<table>
<thead>
<tr>
<th>CAPELLA n = 72</th>
<th>CALIBRATE n = 157</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range), years</td>
<td>52 (23-78)</td>
</tr>
<tr>
<td>Sex, % female at birth</td>
<td>25</td>
</tr>
<tr>
<td>Race, % Black</td>
<td>38</td>
</tr>
<tr>
<td>Ethnicity, % Hispanic/Latin</td>
<td>21</td>
</tr>
<tr>
<td>Weight, median, kg</td>
<td>70.5 (41.4-126)</td>
</tr>
<tr>
<td>Body mass index, median (range), kg/m²</td>
<td>25.0 (14.9-42.6)</td>
</tr>
<tr>
<td>HIV-1 RNA, median (range), log₁₀ c/mL</td>
<td>4.5 (3.5-7)</td>
</tr>
<tr>
<td>&gt; 100,000 c/mL, %</td>
<td>19</td>
</tr>
<tr>
<td>CD4 count, median (range), cells/μL</td>
<td>150 (3-1236)</td>
</tr>
<tr>
<td>&lt; 200 cells/μL, %</td>
<td>64</td>
</tr>
</tbody>
</table>

Conclusions

- Among a range of PWH using oral and/or SC LEN, LEN was well tolerated with no non-ISR AEs related to LEN leading to discontinuation
- The most common non-ISR AEs in participants who received SC LEN were nausea, diarrhea, and headache

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CAPELLA CALIBRATE LEN

In CAPELLA, gastrointestinal AEs were similar in the SC LEN vs oral LEN groups

There were no SAEs related to study drug

Most non-ISR AEs were Grade 1 or 2 and resolved during ongoing treatment with LEN

No participant discontinued LEN due to a non-ISR AE