Long-Acting Lenacapavir in People With Multidrug-Resistant HIV-1: Week 52 Results

Onyema Ogbuagu,1 Sorana Segal-Maurer,2 Cynthia Brinson,3 Ploschan Chetchotisakd,4 Kenneth Lichterstein,5 Joseph McGowan,4 Andrew A. Wiznia,1 Kimberly Workowski,4 Hui Wang,5 Nicolas Margot,6 Hasidas Dvoyr-Sobol,7 Martin S. Rhee,8 Jared M. Baeten,9 Jean-Michel Molina10

1 Takeda University, Tuscaloosa, AL; 2 New York Presbyterian Queens, NY; 3 Tulane New Orleans Research, New Orleans, LA; 4 Margaret Holmes Rainey, Atlanta, GA; 5 Kaiser Permanente Health Research, Seattle, WA; 6 Bristol-Myers Squibb, Cambridge, MA; 7 Korea University, Daejeon, Daejeon, South Korea; 8 University of Colorado, Denver, CO; 9 Vital Health Sciences, Inc., Framingham, MA; 10 Saint-Louis University, Paris, France

Introduction

Lenacapavir (LEN; GS-6207) Targets Multiple Stages of HIV Replication Cycle1

- LEN is a novel, highly potent, long-acting, first-in-class, HIV-1 capsid inhibitor
- LEN can meet significant unmet medical needs
  - A new mechanism of action for heavily treatment-experienced (HTE) people with multidrug-resistant (MDR) HIV-1 and complex treatment regimens
  - Reduction of daily pill burden through less frequent dosing for treatment and prevention
  - LEN achieved its primary endpoint as a functional monotherapy when added to a failing regimen8
- LEN is a novel, highly potent, long-acting, first-in-class, HIV-1 capsid inhibitor

Week 26 efficacy was summarized only for the randomized cohort (n=36), as most participants in the nonrandomized cohort have not yet reached Week 52
- Safety was summarized for both the randomized and nonrandomized cohorts (N=72)

Methods

Study Design

- To evaluate the safety and efficacy (using the FDA Snapshot algorithm) of LEN in people with MDR HIV-1
- Previously in the CAPELLA Study (NCT04150068) in HTE people with MDR HIV-1:
  - LEN was well tolerated, with only 1 ISR leading to discontinuation
  - LEN led to clinically meaningful increases in CD4 counts at Week 52

Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Randomized Cohort (n=36)</th>
<th>Nonrandomized Cohort (n=24)</th>
<th>Combined Cohort (n=60)</th>
<th>Total Cohort (n=72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>49.4 (10.6)</td>
<td>50.5 (9.1)</td>
<td>50.0 (9.9)</td>
<td>50.0 (9.9)</td>
</tr>
<tr>
<td>Race, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>94</td>
<td>84</td>
<td>90</td>
<td>88</td>
</tr>
<tr>
<td>Hispanic/Latinx</td>
<td>6</td>
<td>16</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td>Sex, % female at birth</td>
<td>33.3</td>
<td>45.8</td>
<td>37.0</td>
<td>41.7</td>
</tr>
<tr>
<td>HIV-1 RNA ≥400 c/mL</td>
<td>77.8</td>
<td>83.3</td>
<td>80.0</td>
<td>80.0</td>
</tr>
<tr>
<td>CD4 count, median (range), cells/μL</td>
<td>195 (3–1296)</td>
<td>172 (16–827)</td>
<td>183 (3–1296)</td>
<td>183 (3–1296)</td>
</tr>
<tr>
<td>No. of fully active agents in OBR, %</td>
<td>38</td>
<td>36</td>
<td>37</td>
<td>37</td>
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<tr>
<td>Known resistance to ≥2 drugs in class, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NRTI</td>
<td>99</td>
<td>97</td>
<td>98</td>
<td>98</td>
</tr>
<tr>
<td>PI</td>
<td>83</td>
<td>80</td>
<td>81</td>
<td>81</td>
</tr>
<tr>
<td>NNRTI–</td>
<td>100</td>
<td>99</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

Emergent LEN Resistance* | 4 (11) | 3 (12) | 3.5 (11) | 3.5 (11) |

Oblique resistance to NNRTI (p<0.001)²

No serious AEs were related to study drug
- Mostly Grade 1 or 2 ISRs
- No Grade 4 ISRs, but 2 participants had Grade 3: 1 participant with swelling and erythema, which resolved in 4 and 8 d, respectively, and 1 participant with pain, which resolved in 1 d
- All nodules were Grade 1, except in 1 participant who had 2 AES of Grade 2 nodules, each after the 2nd and 3rd injections (both resolved after 3 d)
- 1 participant discontinued study drug at Week 52 due to an ISR (nodule; Grade 1)

Grade 1 or 2 Laboratory Abnormalities

- None of the Grade 3 or 4 laboratory abnormalities were clinically relevant
- None of the Grade 3 or 4 hematologic abnormalities were clinically relevant
- None of the Grade 3 or 4 liver abnormalities were clinically relevant

Conclusions

- In HTE PWH with limited treatment options due to MDR:
  - LEN in combination with an OBR led to high rates of virologic suppression at Week 52 (83%)
  - LEN led to clinically meaningful increases in CD4 counts at Week 52
  - LEN was well tolerated, with only 1 ISR leading to discontinuation
- These data support the ongoing evaluation of LEN for treatment and prevention of HIV-1 infection

- In HTE people with MDR HIV
  - In treatment-naïve and -experienced PWH in combination with other agents
  - In people who could benefit from pre-exposure prophylaxis

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