LENACAPAVIR EFFICACY IN CAPELLA PATIENTS WITH NO FULLY ACTIVE AGENTS IN OPTIMIZED BACKGROUND REGIMEN

Authors:
Ogbuagu O[1], Ratanasuwan W[2], Avihingsanon A[3], Chetchotisakd P[4], Wiznia A[5], Workowski K[6], Hung CC[7], Brunetta J[8], Trottier B[9], Rassool M[10], Wang H[11], Margot N[11], Dvory-Sobol H[11], Johnson K[12]*, Rhee MS[11], Segal-Maurer S[13]

[1]Yale School of Medicine, New Haven, Connecticut; [2]Siriraj Hospital Mahidol University, Bangkok, Thailand; [3]HIV-NAT, Thai Red Cross AIDS Research Centre, Bangkok, Thailand; [4]Khon Kaen University, Khon Kaen, Thailand; [5]Jacobi Medical Center, Albert Einstein College of Medicine, Bronx, New York, NY, USA; [6]Emory University, Department of Medicine, Atlanta, GA, USA; [7]National Taiwan University Hospital, Taipei, Taiwan; [8]Maple Leaf Medical Clinic, Toronto, ON, Canada; [9]Clinique de Medecine Urbaine du Quartier Latin, Montréal, Québec, Canada; [10]University of Witwatersrand, Clinical HIV Research Unit, Johannesburg, South Africa; [11]Gilead Sciences, Foster City, California; [12]Gilead Sciences Pty Ltd, Melbourne, AUS. [13]Division of Infectious Diseases, New York–Presbyterian Queens, Flushing, New York
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Background:
Lenacapavir (LEN), a long-acting HIV-1 capsid inhibitor, is approved for the treatment of heavily treatment-experienced (HTE) people with HIV (PWH) with multidrug resistance (MDR) in combination with other antiretrovirals (ARVs). LEN is highly potent with no overlapping resistance with other ARVs. In CAPELLA, LEN in combination with an optimized background regimen (OBR) led to high virologic suppression: 78% (n=56/72; week [W] 52). We assessed LEN efficacy in participants whose OBR had no fully active ARVs.

Methods:
The Phase 2/3 CAPELLA study enrolled HTE PWH with MDR. Eligible participants had resistance to ≥2 ARVs in ≥3 of the 4 main ARV classes (NRTI, NNRTI, PI, INSTI). After oral loading, SC LEN was administered every 6 months.. OBR overall susceptibility score was the sum of susceptibility scores for each OBR ARV; 0 (no susceptibility), 0.5 (partial susceptibility) and 1 (full susceptibility). Efficacy data (HIV-1 RNA copies/mL; FDA Snapshot algorithm) were assessed at W26, 52, and 104. LEN and OBR ARV resistance analyses were done at virologic failure (virologic rebound ≥50 copies/mL or <1 $\log_{10}$ decline vs baseline).

Results:
Of the 72 participants, 12(17%) had no fully active ARVs in their OBR; 6/12 and 1/12 had 1 or 2 partially active (score 0.5 each) ARVs. Median (range) number of OBR ARVs was 4 (2–6).. 8 participants had HIV-1 RNA <50 copies/mL at W26, 52, and 104, including 1 with LEN-resistance (R; M66I) at W10 and an OBR change at W25. 1 participant with missing W104 data was suppressed at a later visit; 1 participant not suppressed at W26 developed LEN-R (M66I) but was suppressed at W52 and 104 (OBR changed at W25); and 2 participants had HIV-1 RNA≥50 copies/mL throughout, but with a stable, low-level viral load

Conclusions:
In HTE PWH with MDR on an OBR with no fully active ARVs, LEN led to sustained virologic suppression over 104 weeks for most participants. LEN is an important option for treating HTE PWH with MDR.

Disclosure of Interest Statement:
this research was funded by Gilead Sciences