LENACAPAVIR WITH BNABS GS-5423 AND GS-2872 DOSED EVERY 6 MONTHS IN PEOPLE WITH HIV

Authors:
Eron J[1], Little S[2], Crofoot G[3], Cook P[4], Ruane PJ[5], Jayaweera D[6], DeJesus E[7], Waldman SE[8], Mehrotra ML[9], VanderVeen L[9], Huang H[9], Collins S[9], Paul W[10]*, Baeten J[9], Caskey M[11]

[1]UNC, Chapel Hill, NC, [2]University of California, San Diego, San Diego, CA, [3]CrofootMD Clinic and Research Center, Houston, TX, [4]East Carolina University, Greenville, NC, [5]Ruane Clinical Research, Los Angeles, CA, [6]University of Miami Miller School of Medicine, Miami, FL, [7]Orlando Immunology Center, Orlando, FL, [8]University of California, Davis, Davis CA, [9]Gilead Sciences, Inc., Foster City, CA, [10] Gilead Science Pty Ltd, Melbourne. AUS, [11]Rockefeller University, New York, NY
*Listed as author for presentation purposes only with permission of all authors

Background:
Lenacapavir (LEN) is an HIV-1 capsid inhibitor and GS-5423 and GS-2872 are broadly neutralizing antibodies (bNAbs). GS-5423 targets the CD4 binding site of gp120; GS-2872 binds to the V3 loop of gp120. Both bNAbs were modified to extend their half-life to allow less frequent dosing. We conducted a phase 1b randomized trial to evaluate the safety and efficacy of LEN + GS-5423 + GS-2872 dosed every 6 months in people with HIV (PWH).

Methods:
Participants were adult PWH virologically-suppressed ≥2 years (HIV-1 RNA <50 copies/mL) on ART, sensitive to both bNAbs by HIV proviral DNA phenotype, a CD4 nadir ≥350, and CD4 count ≥500 at study entry. Participants were randomized 1:1 to two active treatment groups consisting of LEN (927mg subcutaneous + GS-5423 (30mg/kg IV) + GS-2872 (10mg/kg in Group 1 and 30mg/kg in Group 2 IV). Participants were monitored clinically with plasma HIV-1 RNA every four weeks until the primary endpoint at 26W. The primary endpoint was safety; secondary endpoints included virologic outcomes by FDA Snapshot analysis.

Results:
Of 124 screened participants, 55 were sensitive to both bNAbs, 21 were randomized, and 20 received the study regimen. There were no serious adverse events (AEs), no grade 4 or 5 AEs, and no AEs leading to study drug discontinuation.
One participant in Group 1 had a confirmed HIV RNA ≥50 copies/mL (155 copies/mL, confirmed 524 copies/mL) at 16W and resuppressed with reinitiation of baseline ART; one participant in Group 2 withdrew consent at 12W (with HIV-1 RNA <50 copies/mL). 18/20 (90%) participants had HIV-1 RNA <50 copies/mL at 26W.

Conclusion:
The combination of LEN + GS-5423 + GS-2872 was well-tolerated with high efficacy for 26W in select virologically-suppressed persons living with HIV. These results provide a

proof-of-concept that this combination may provide long-acting treatment for HIV with twice-yearly dosing.