151 - Efficacy and Safety of Lenacapavir, Teropavimab, and Zinlirvimab: Phase II Week 26 Primary Outcome

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Session Name
Antivirals For HIV, MPXV, and SARS-CoV-2: New Drug Strategies and Resistance

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Key Terms
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Category
General Abstract Submission

SubCategory
(G) Antiviral Therapy: Pre-Clinical Data, Randomized Trials, Efficacy, and Effectiveness Studies in HIV or SARS-CoV-2 or MPXV in Adults

Background
In a non-comparative pilot Phase 1b study (NCT04811040), the long-acting HIV-1 capsid inhibitor lenacapavir (LEN) in combination with broadly neutralizing antibodies (bNAbs) teropavimab (TAB, GS-5423) and zinlirvimab (ZAB, GS-2872) maintained virologic suppression (VS; HIV-1 RNA <50 copies/mL) for 6 months after dosing in 18/20 people with HIV-1 (PWH) highly susceptible to both bNAbs. In this Phase 2 study (NCT05729568), efficacy and safety of switching to LEN+TAB+ZAB (LTZ) every 6 months (Q6M) versus staying on stable baseline oral antiretroviral regimen (SBR) is being evaluated.

Methods
This open-label study enrolled virologically suppressed PWH (≥12 months on ART) with HIV-1 highly susceptible to both bNAbs (IC_{90} ≤2 µg/mL [Monogram PhenoSense mAb DNA assay] at screening). Participants were randomized 2:1 to switch to subcutaneous (SC) LEN 927 mg Q6M (+ oral 600 mg on Days 1+2), plus intravenous (IV) TAB 2550 mg Q6M and IV ZAB 2550 mg Q6M, or SBR. Primary endpoint was the proportion of participants with HIV-1 RNA ≥50 copies/mL at Week (W) 26 per FDA snapshot algorithm. Secondary endpoints included change from baseline in CD4 cell count at W26 and adverse events (AEs).

Conclusion
Efficacy of Q6M LTZ was similar to that of daily oral ART through W26. LTZ was well tolerated. These results demonstrate high efficacy of LTZ through W26 and support further investigation of LTZ as the first Q6M combination treatment for PWH.

Results
Fifty-three participants received LTZ and 27 SBR. Median (range) age was 51 (20–65) years, 15% were female, 36% were Black, and mean (SD) CD4 count was 749/µL (245). At W26, 1 of 53 (2%) receiving LTZ and none in the SBR arm had HIV-1 RNA ≥50 copies/mL in the analysis window; 51 (96%) and 26 (96%) remained virologically suppressed, respectively **(Table)**. One participant in each arm withdrew; both had HIV-1 RNA <50 copies/mL. CD4 count increased from baseline to W26; mean change (SD): +23/µL (143) with LTZ; +69/µL (203) with SBR. Treatment-emergent AEs (TEAEs) were observed in 45 (85%) and 17 (63%) of participants in the LTZ and SBR arms, respectively. The most common TEAEs in the LTZ arm were Grade 1 (mild) injection site reactions related to SC LEN. No infusion-related reactions to TAB or ZAB, study drug-related Grade ≥3 TEAEs, serious TEAEs, or TEAEs leading to study drug or study discontinuation occurred in the LTZ arm. One participant in the SBR arm discontinued the study due to a serious TEAE.