# LENACAPAVIR PLUS bNAbs FOR PEOPLE WITH HIV AND SENSITIVITY TO EITHER TEROPAVIMAB OR ZINLIRVIMAB

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**Background**:
Lenacapavir (LEN) is a long-acting capsid inhibitor approved for treatment of HIV-1 infection in adults with multidrug resistance. Teropavimab (TAB) & zinlirvimab (ZAB) are long-acting broadly neutralizing antibodies (bNAbs), targeting the CD4-binding site & V3 loop of gp120. In a phase 1b study, LEN+TAB+ZAB maintained virologic suppression (VS) for 6 months (26W) in 18/20 participants with high-level sensitivity to both bNAbs. We evaluated safety & efficacy of LEN+TAB+ZAB in participants who met viral sensitivity criteria to either TAB or ZAB.

**Methods:**
Virologically suppressed adults on antiretroviral therapy (ART; HIV-1 RNA <50 copies/mL for ≥18 months), with high-level sensitivity to TAB or ZAB but not both by HIV proviral DNA phenotype, a CD4 nadir of ≥350 cells/μL, & CD4 ≥500 cells/μL at baseline were randomized 1:1 to one of two active treatment groups: LEN (927 mg subcutaneously) + TAB (30 mg/kg intravenously [IV]) + ZAB (Group 1, 10 mg/kg IV, n=5; Group 2, 30 mg/kg IV, n=6). The primary endpoint was incidence of treatment-emergent serious adverse events at 26W; secondary endpoints included virologic outcomes (VS or ≥50 copies/mL) at 26W by FDA Snapshot analysis.

**Results:**
Eleven participants were randomized & treated. No adverse events led to study drug discontinuation. Safety outcomes were similar between groups. At 26W, 8/10 participants maintained VS (Group 1, 2/4; Group 2, 6/6). Of the two participants in Group 1 who had virologic rebound, one had sensitivity to TAB & was diagnosed with acute COVID-19 at the time of rebound, & one had sensitivity to ZAB & rebounded at 26W; both had HIV RNA <100 copies/mL.

**Conclusions:**
LEN+TAB+ZAB was well-tolerated, with a favorable safety profile. All participants in Group 2 maintained VS for 26W, which suggests that more inclusive sensitivity criteria

may be appropriate for treatment studies of LEN+TAB+ZAB when higher bNAb levels are maintained.

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