**Lenacapavir as part of a combination regimen in treatment naïve PWH: Week 54 results**

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**Background:** Lenacapavir (LEN), an inhibitor of capsid function, is in development for treatment and prevention of HIV-1. CALIBRATE is an ongoing, open-label, phase 2 study evaluating subcutaneous (SC) and oral LEN, in combination with other antiretrovirals, in treatment-naïve people with HIV-1 (PWH). At Week 28(W28), LEN + emtricitabine/tenofovir alafenamide (F/TAF) led to high rates of virologic suppression (94%).

**Methods:** Participants were randomized (2:2:2:1) to 1 of 4 treatment groups (TG). TG1 and TG2 both received SC LEN + oral daily (QD) F/TAF for 28 weeks, after which virologically- suppressed participants continued a 2-drug maintenance regimen: SC LEN with QD TAF (TG1) or QD bictegravir (B/BIC) (TG2). TG3 received oral QD LEN + F/TAF and TG4 received oral QD B/F/TAF throughout. We report the primary endpoint at W54.

**Results:** 182 participants were randomized (n=52, 53, 52, 25 in TG1 to TG4). At W28 (as previously reported), 94%, 92%, 94%, and 100% had VL <50 copies/mL in TG1 to TG4. At W54, 90%, 85%, 83%, and 92% had VL<50 copies/mL by FDA Snapshot Among those with VL <50 copies/mL at W28 when starting the 2-drug maintenance regimen in TG1 and TG2, 94% (46/49) and 92% (45/49) had VL <50 copies/mL at W54. For participants in TG1 to TG3 (i.e. those who received LEN), CD4 count increased by a median of 219 cells/µL at W54 (vs 177 in TG4). No participant experienced a study drug-related serious adverse event (SAE). Two participants in TG2 discontinued LEN due to AEs (both Grade 1 injection site induration). Injection site reactions (ISRs) included erythema (17%), swelling (16%), and pain (15%), which were mostly mild or moderate. The most frequent non-ISR AEs were headache and nausea (13% each).

**Conclusion:** LEN, given subcutaneously or orally in combination with TAF, BIC, or F/TAF, maintained high rates of virologic suppression at one year and was well-tolerated. These results support ongoing evaluation of LEN, as both injectable and oral formulations, in combination with other antiretroviral agents for the treatment of HIV.

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