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## BACKGROUND

- HIV pre-exposure prophylaxis (PrEP) is highly effective for HIV prevention.
- The oral PrEP formulation of tenofovir disoproxil fumarate-emtricitabine (TDF-FTC) is highly effective for HIV prevention, but its efficacy may be limited by incomplete adherence.
- In addition, TDF-FTC may impact bone mineral density (BMD), raising safety concerns for long-term usage.
- In HPTN 083, long-acting cabotegravir (CAB-LA) was found to be superior to TDF-FTC for HIV prevention.
- However, the relative bone safety of these regimens is unknown.

## METHODS

- HPTN 083 is a randomized (1:1), double-blind, double-dummy, noninferiority trial comparing CAB-LA (600 mg, given intramuscularly every 8 weeks) to daily oral TDF-FTC for the prevention of HIV infection in at-risk cisgender men who have sex with men (MSM) and in at-risk transgender women who have sex with men.
- A Bone Substudy was conducted at 19 sites
- BMD was measured at the lumbar spine (LS), femoral neck, and total hip by dual-energy x-ray absorptiometry (DXA) at baseline, 57 weeks, and 105 weeks.
- Scans were analyzed centrally (Tufts University, Medford, MA).
- Percentage BMD change at each anatomic site was compared between the two randomized arms by two-sample, independent t-tests in those who received at least 10 ten bi-monthly injections over 18 months from enrollment (i.e., as treated population). Models were adjusted for age and race given demographic differences in randomized groups.

In cisgender men and transgender women initiating HIV PrEP, CAB-LA was associated with BMD gain, whereas TDF-FTC led to BMD loss over 2 years. Especially for individuals with low BMD or other fracture risk factors, CAB-LA PrEP may be an important strategy to preserve bone health.

## RESULTS

Table 1. Baseline Characteristics

	TDF/FTC (N=122)	CAB-LA (N=132)
Median (Q1, Q3) or %		
Age (years)	29.0 (23.0, 41.0)	26.0 (22.0, 31.0)
Race		
ASIAN	15%	9%
BLACK	25%	36%
OTHER	13%	7%
WHITE	47%	48%
Transgender Women	8%	11%

- Young population with most at the age of peak BMD
- 8% were 50 years old or older

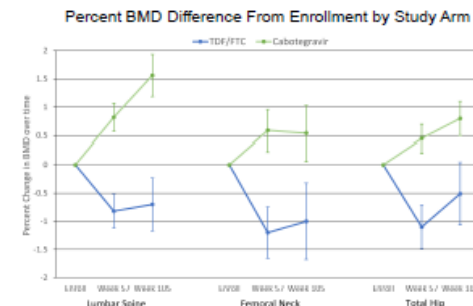
Table 2. Bone Mineral Density Z-scores at Baseline

	TDF/FTC (N=122)	CAB-LA (N=132)
Mean Z-score (SD)		
Lumbar Spine	-0.44 (1.2)	-0.59 (1.4)
Femoral Neck	-0.23 (1.0)	-0.21 (1.1)
Total Hip	-0.26 (1.0)	-0.28 (1.0)
Low BMD** %	14.8%	16.2%

\*Z-score is number of standard deviations from the average BMD in age-, race-matched population

\*\*Z-score  $\leq -2.0$  at either lumbar spine, femoral neck, total hip

- At baseline, BMD was 0.2-0.6 SD lower than a age-, sex-, race-matched reference population (i.e Z-scores -0.2 to -0.6)
- 15% had low BMD (Z-score  $\leq -2.0$  at either lumbar spine, femoral neck, total hip)



- BMD decreased in the TDF-FTC arm by 0.5-1.0%
- BMD increased in CAB-LA arm 0.5-1.5%
- After adjusting for age and race, BMD measures were significantly higher at follow-up visits among participants receiving CAB-LA compared to those receiving TDF/FTC (Z-score difference 0.09-0.20 at Week 105)

## CONCLUSIONS

- Among cisgender men MSM and transgender women, HIV PrEP with CAB-LA was associated with increases in BMD, whereas TDF-FTC led to decreases in BMD.
- As observed in other PrEP studies, this population had lower BMD than the reference population (NHANES), with ~15% having low BMD.
- 8% of the study population were 50 years or older
- Given the relationship between low BMD and subsequent fracture, persons at higher risk of fracture because of older age, lower BMD, or other osteoporosis risk factors, who are interested in PrEP may consider CAB-LA to maintain bone health.
- Longer-term follow-up will be required to evaluate the clinical significance of these findings.