No Increased Risk for Hypertension with CAB-LA Compared to TDF/FTC for HIV PrEP in HPTN 083

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BACKGROUND

Results from some trials of HIV treatment, including 2SD, D2EF, ADVANCE, and NAMSAL suggest an excess risk of hypertension (HTN) associated with integrase strand transfer inhibitors (INSTIs, and DTG in particular), independent of changes in weight or BMI; but some trials including NEAT022 and RESPOND did not when compared to PIs.

HPTN 083 randomized HIV negative MSM and transgender women (TGW) to every-8-week injectable cabotegravir (CAB) or daily oral tenofovir disoproxil fumarate-emtricitabine (TDF-FTC) for HIV PrEP. The study demonstrated superiority of the CAB arm compared to TDF-FTC for prevention of incident HIV infection. After early weight loss with TDF/FTC, annualized weight gain was similar in both arms at approximately 1 kg/year.

We performed a post-hoc analysis of HPTN 083 to compare incidence rates for HTN in the absence of HIV infection.

METHODS

Incident HTN was defined as two consecutive BP readings with systolic BP (SBP) ≥140mmHg or diastolic BP (DBP) ≥90mmHg, a new diagnosis of HTN, or initiation of new HTN medications with an HTN indication. The timing of incident HTN was measured from treatment initiation to the first HTN event, using the date of the first reading if based on two measurements.

Changes in blood pressure were analyzed over time using mixed effect linear models. The primary analysis used Cox regression to estimate the hazard ratio for HTN with CAB compared to TDF/FTC. Analyses adjusted for enrollment region and race, age, use of anti-HTN medications for other purposes, BMI at entry and % change in weight as a time-updated covariate. Sensitivity analyses censored at DSMB action and excluded participants taking anti-HTN medication for other purposes.

RESULTS

3,971 participants with a total of 10,293 person-years of follow-up were included. Participants were similar across groups, with 75% under age 30 and 4% over 45. Most were normal or underweight at study entry (Table 1). Changes in SBP and DBP over time were modest (Figure 1). BMI and SBP showed a weak correlation (rho)<0.2 across weeks.

There were 450 incident cases of HTN: 237 (12%) with CAB and 213 (11%) with TDF/FTC. Most cases (75%) were based on a grade <2 clinical diagnosis (Figure 2).

Incident-HTN was more frequent in US and African participants, older participants or those with higher BMI, and those on anti-HTN drugs for other reasons. No differences between MSM and TGW were apparent.

The hazard ratio for developing HTN was 1.11 for CAB versus TDF/FTC unadjusted (95% CI 0.92, 1.33), and 1.00 (95% 0.83, 1.21) after adjusting for race, baseline age and BMI, time-updated weight increase from baseline and baseline anti-HTN medication use for non-HTN purposes. (Figure 5). Findings were unchanged in sensitivity analyses.

CONCLUSIONS

In HPTN 083, HTN incidence was generally low in a young population. No significant statistical difference in HTN incidence was found between CAB and TDF/FTC users, over 3 years of follow-up. Risk factors for HTN included older age, baseline obesity, and weight gain over time. Absent the inflammatory milieu of HIV infection, we did not find evidence of excess risk for incident HTN in MSM and TGW.

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