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

0789

Raphael J. Landovitz[1], Heather J. Ribaudo[2], Younjung Choi[2], Kari Chansky[3], Zoe Wang[3], Mina Hosseinipour[4], Sinead Delany-Moretlwe[5], Lydia Soto-Torres[6], Sheryl Zwerski[6], Marybeth McCauley[7], James F. Rooney[8], Alex R. Rinehart[9], Beatriz Grinsztejn[10]

[1]University of California Los Angeles, Los Angeles, CA, USA, [2]Harvard TH Chan School of Public Health, Boston, MA, USA, [3]Fred Hutchinson Cancer Center, Seattle, WA, USA, [4]University of North Carolina at Chapel Hill, Chapel Hill, NC, USA, [5]University of the Witwatersrand, Johannesburg, South Africa, [6]National Institute of Allergy and Infectious Diseases, Baltimore, MD, USA, [7]FHI 360, Washington, DC, USA, [8]Gilead Sciences, Inc, Foster City, CA, USA, [9]ViiV Healthcare, Research Triangle Park, NC, USA, [10]Oswaldo Cruz Foundation - Fiocruz, Rio de Janeiro, Brazil

BACKGROUND

Results from some trials of HIV treatment, including 2SD, D2EFT, ADVANCE, and NAMSAL suggest an excess risk of hypertension (HTN) associated with integrase strand transfer inhibitors (INSTIs, and DTG in particular, and when compared to NNRTIs 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.

Table 1: Baseline Characteristics of Analysis Population

	CAB (n=1993)	TDF/FTC (n=1978)	Total (n=3971)
REGION			
United States	702 (35%)	675 (34%)	1377 (35%)
Latin America (LA)	873 (44%)	884 (45%)	1757 (44%)
Asia (AS)	360 (18%)	354 (18%)	714 (18%)
Africa (AF)	58 (3%)	65 (3%)	123 (3%)
GENDER IDENTITY			
Male	1728 (87%)	1694 (86%)	3422 (86%)
AGE (YEARS)			
Median (Q1, Q3)	26 (22, 30)	26 (22, 31)	26 (22, 31)
WEIGHT (KG)			
Median (Q1, Q3)	71.7 (63.0, 83.0)	71.3 (62.5, 82.5)	71.5 (62.8, 82.7)
BMI (KG/M²)			
Median (Q1, Q3)	24.0 (21.5, 27.4)	24.0 (21.5, 27.1)	24.0 (21.5, 27.2)
OTHER USE OF ANTI-HTNs			
Yes	35 (2%)	53 (2%)	88 (2%)

Figure 1. BP Changes over Time

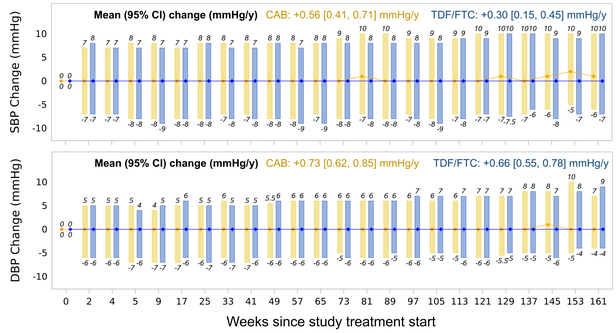


Figure 2. Cumulative Incidence of First HTN Event

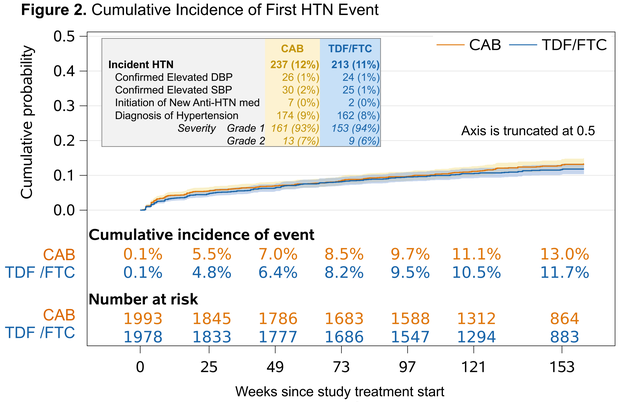


Figure 3. Cumulative Incidence Of First HTN Event By Region

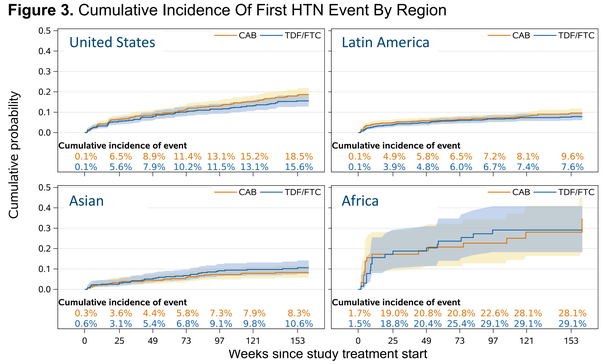


Figure 4. Cumulative Incidence of First HTN Event by COHORT

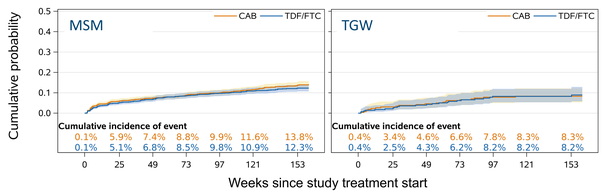
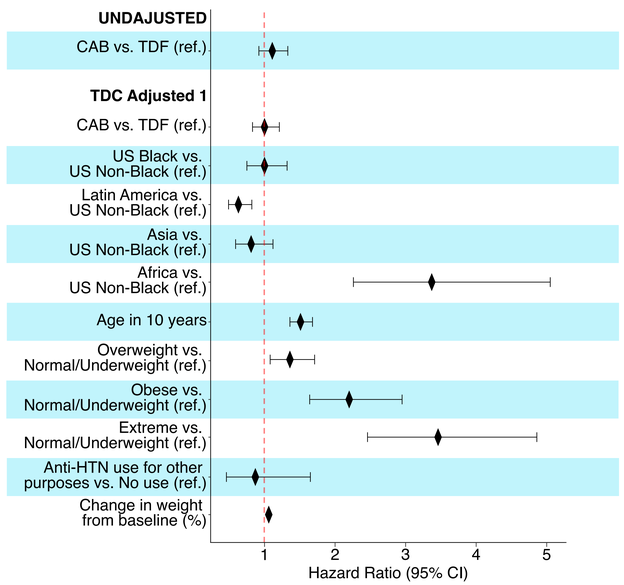


Figure 5. Proportional Hazard Ratios



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 all 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.

ACKNOWLEDGEMENTS

Funding: U.S. National Institute of Allergy and Infectious Diseases (NIAID), National Institute of Mental Health (NIMH), National Institute on Drug Abuse (NIDA), and the National Institute of Child Health and Human Development (NICHD) all components of the U.S. National Institutes of Health (NIH), Additional funding from ViiV Healthcare. **Pharmaceutical Support:** ViiV Healthcare, Gilead Sciences, Inc. **Special Thanks:** HPTN 083 Study Team, Community Program Managers, Community Educators & Recruiters, CAB Members, Our 43 Sites in 7 countries, and our Study Participants

For more information, visit **hptn.org** and follow us:

@HIVptn

Overall support for the HIV Prevention Trials Network (HPTN) is provided by the National Institute of Allergy and Infectious Diseases (NIAID), Office of the Director (OD), National Institutes of Health (NIH), National Institute on Drug Abuse (NIDA), the National Institute of Mental Health (NIMH), and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) under Award Numbers UM1AI068619-15 (HPTN Leadership and Operations Center), UM1AI068617-15 (HPTN Statistical and Data Management Center), and UM1AI068613-15 (HPTN Laboratory Center).

Presented at the Conference on Retroviruses and Opportunistic Infections
Denver, Colorado
March 3 – 6 2024