820

No Increased Risk for Hypertension with CAB-LA Compared to TDF/FTC for PrEP: Results from HPTN 084

Sinead Delany-Moretlwe[1], Heather Ribaudo[2], Younjung Choi[2], Brett Hanscom[3], Nyaradzo Mgodi[4], Joseph Makhema[5], Harriet Nuwagaba-Biribonwoha[6], Scott Rose[7], Lydia Soto-Torres[8], James Rooney[9], Alex Rinehart[10], Raphael Landovitz[11], Mina Hosseinipour[12] [1]University of the Witwatersrand, Johannesburg, South Africa, [2]Harvard TH Chan School of Public Health, Boston, MA, USA, [3]Fred Hutchinson Cancer Center, Seattle, WA, USA, [4]University of Zimbabwe Clinical Trials Research Centre, Harare, Zimbabwe, [5]Botswana Harvard AIDS Institute Partnership (BHP), Gaborone, Botswana, [6]Eswatini Prevention Center, ICAP at Columbia University Mailman School of Public Health, New York, NY, USA, [7]FHI 360, Washington, DC, USA, [8]National Institute of Allergy and Infectious Diseases, Baltimore, MD, USA, [9]Gilead Sciences, Inc, Foster City, CA, USA, [10]ViiV Healthcare, Research Triangle Park, NC, USA, [11]University of California Los Angeles, Los Angeles, CA, USA, [12]University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

HPTN HIV Prevention Trials Network

BACKGROUND

Several studies, including D2EFT, ADVANCE, and NAMSAL, suggest an increased risk of hypertension (HTN) associated with the initiation of integrase strand transfer inhibitors (INSTIs) for HIV treatment, potentially mediated by weight gain. HPTN 083 found no increased risk of hypertension with CAB-LA compared to TDF/FTC for HIV PrEP in men who have sex with men (MSM) and transgender women (TGW), but little is known about cisgender women.

HPTN 084 randomized HIV-negative individuals born female aged 18-45 years in Sub-Saharan Africa to receive either every-8-week injectable cabotegravir (CAB) or daily oral tenofovir disoproxil fumarate-emtricitabine (TDF-FTC) for HIV pre-exposure prophylaxis (PrEP). The study demonstrated that both CAB and TDF-FTC were highly effective for HIV prevention in this population. A mean weight gain of approximately 2 kg/year was observed in both study arms.

We conducted a post-hoc analysis of the HPTN 084 trial to investigate whether CAB-LA was associated with an increased incidence of HTN.

METHODS

Incident HTN was defined as a new diagnosis of hypertension (systolic blood pressure [BP]≥140mmHg or diastolic BP ≥90mmHg) made during routine clinical assessments after starting study treatment or the initiation of new HTN medications after randomization through 161 weeks of follow up. Time to incident HTN was measured from the start of study treatment to the first HTN-defining event.

Of 3,224 enrolled participants, 3,071 with study drug exposure and without pre-existing HTN were included in the analysis. The primary analysis used Cox regression analysis to estimate the cause-specific hazard ratio for incident hypertension in the CAB group as compared with the TDF group with 95% confidence intervals; P-values are based on the Wald statistics. The analysis adjusted for baseline age, baseline BMI, and region. Modelling also evaluated time-updated risk factors for HTN including percentage weight change from baseline (TUWC), incident pregnancy, and contraceptive method.

Table 1: Baseline Characteristics of Analysis Population

	CAB (N=1543)	TDF (N=1528)	Total (N=3071)
Region			
East Africa	432 (28%)	422 (28%)	854 (28%)
South Africa	624 (40%)	634 (41%)	1258 (41%)
Southern Africa	487 (32%)	472 (31%)	959 (31%)
Gender Identity			
Female	1541 (100%)	1525 (100%)	3066 (100%)
Non-Female	2 (0%)	3 (0%)	5 (0%)
Age (years)			
Median (Q1, Q3)	24 (22, 29)	24 (21, 29)	24 (22, 29)
Weight (kg)			
Median (Q1, Q3)	65 (56, 78)	64 (55, 76)	65 (56, 77)
BMI (kg/m²)			
Median (Q1, Q3)	25.6 (22.3, 30.8)	25.5 (22.1, 30.1)	25.6 (22.2, 30.4)
Contraception Type			
IUD	64 (4%)	64 (4%)	128 (4%)
Implant	474 (31%)	470 (31%)	944 (31%)
DMPA	776 (50%)	748 (49%)	1524 (50%)
NET-EN	156 (10%)	179 (12%)	335 (11%)
Oral	54 (3%)	55 (4%)	109 (4%)

Hypertension incidence in this population was low, with no difference between women using CAB vs. TDF/FTC PrEP

Figure 1: BMI Change Over Time

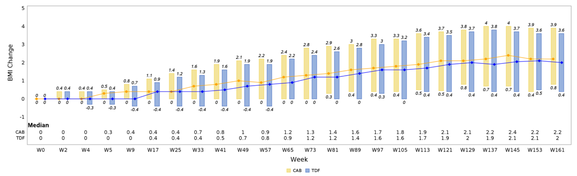


Figure 2: Percent Weight Gain from Baseline Over Time

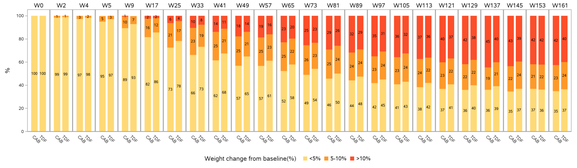


Figure 3: Cumulative Incidence of First Hypertension Event

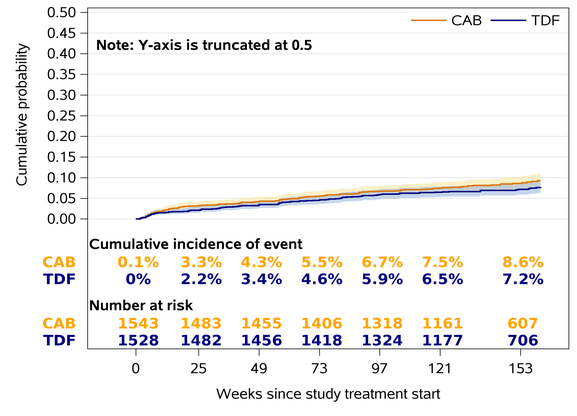


Figure 4: Cumulative Incidence of First Hypertension Event by Baseline BMI

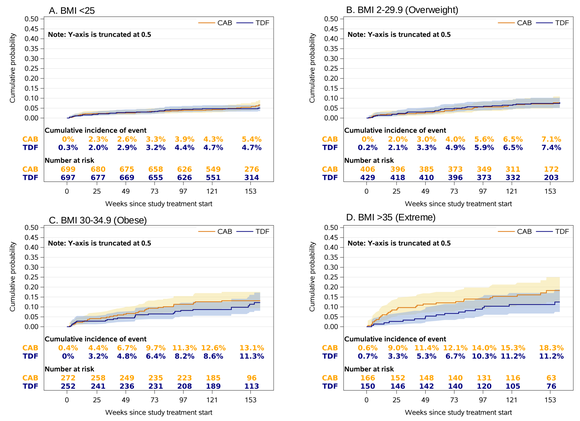
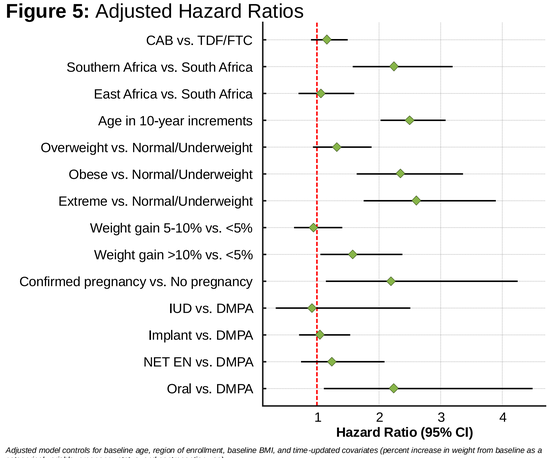


Figure 5: Adjusted Hazard Ratios



Adjusted model controls for baseline age, region of enrollment, baseline BMI, and time-updated covariates (percent increase in weight from baseline as a categorical variable, pregnancy status, and contraception use).

RESULTS

The baseline characteristics of participants were balanced between the CAB and TDF groups, with 51% aged 18–24 years and 55% with a BMI ≥ 25 kg/m2. Among the 4% of participants with pre-existing hypertension, a greater proportion were from the Southern African region, particularly Zimbabwe (50% vs. 23% without hypertension), they were older on average (33 years vs. 26 years), and had higher BMI levels, with 73% classified as overweight or obese compared to 55% of those without hypertension.

Over the study period, both groups showed increases in BMI, with median increases of 2.2 kg/m² (CAB) and 2.1 kg/m² (TDF) by week 153. More than 63% of participants in both groups gained over 5% of their baseline weight, with lower baseline BMI associated with higher relative weight gains.

Over 8252 person-years of follow up, 234 (8%) had incident HTN (127/1543 CAB, 107/1528 TDF/FTC). Cumulative HTN incidence over 3 years was 8.6% for CAB and 7.2% for TDF/FTC. In unadjusted analyses, incident HTN was higher with CAB compared to TDF/FTC use (HR 1.20, 95% CI 0.93-1.55, p=0.16) and largely unchanged (HR 1.17, 95% CI 0.91-1.50, p=0.26) after adjustment for enrolment region, age, and baseline BMI.

The hazard for HTN was increased with >10% weight gain (HR 1.58, 95% CI 1.05-2.38), pregnancy (HR 2.20, 95% CI 1.14-4.25), enrolment from the southern Africa region (Botswana, Eswatini, Zimbabwe) (HR 2.24, 95% CI 1.58-3.19), pre-existing obesity (HR 2.35, 95% CI 1.63-3.36), and older age (HR per 10 years 2.50, 95% CI 2.03-3.08).

CONCLUSIONS

In HPTN 084, HTN incidence in this population without HIV was low. Observed HTN incidence was higher in the CAB compared to TDF/FTC group, this was not statistically significant and was not apparent after adjustment for key risk factors. Higher age, obesity, excessive weight gain, and incident pregnancy appear to be more important drivers of incident HTN in this population.

HPTN 084 Long-acting Injectable For the Epidemic

ACKNOWLEDGMENTS

We thank Ryan Koffron for his assistance with this presentation. We acknowledge the HPTN 084 participants, their communities and the study staff; HPTN Leadership and Operations Center (FHI360); HPTN Laboratory Center (Johns Hopkins); HPTN Statistical and Data Management Center, Fred Hutchison Cancer Research Center; ViiV Healthcare and the Bill & Melinda Gates Foundation for financial support to the trial; and ViiV Healthcare and Gilead Sciences for pharmaceutical support. The study was sponsored by the Division of AIDS at the US National Institute of Allergy and Infectious disease (NIAID)

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 (HPTN Leadership and Operations Center), UM1AI068617 (HPTN Statistical and Data Management Center), and UM1AI068613 (HPTN Laboratory Center).

Presented at the
Conference on Retroviruses
and Opportunistic Infections
San Francisco, California
March 9 – 12 2025