Higher risks of hypertension from use of TAF/FTC/DTG vs TDF/3TC/DTG in the VISEND trial

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Authors: Lloyd Mulenga[1,2,3,7,8], Sombo Fwoloshi[1,2,3], Aggrey Mweemba[3], Danielle Engamba[1,2], Nyima Mbewe[1,2], Alepali Kumar[1], Suwilanji Sivile[1,2,3], Mpanji Siwingwa[1,2], Davies Kampamba[1,3], Melody Mutinta[1], Kaitlyn McCann[5], Lameck Chirwa[1,2], William C.Wester[4,5] ,Andrew Hill The VISEND Study Team. *Affiliations*: [1]University Teaching Hospital, Adult Infectious Diseases Center, Lusaka, Zambia, [2]University of Zambia, School of Medicine, Division of Infectious Diseases, Internal Medicine, Lusaka, Zambia, [3]Ministry of Health, Ndeke House, Lusaka, Zambia [4] Levy Mwanawasa University Teaching Hospital [5]Imperial College London, Faculty of Medicine, London, UK, [6] Liverpool University, Department of Translational Medicine, Liverpool, UK, [7]Vanderbilt University Medical Center (VUMC), Department of Medicine, Division of Infectious Diseases, Nashville, TN, USA, [8]Vanderbilt Institute for Global Health (VIGH), Nashville, TN, USA.

BACKGROUND

Hypertension is a leading cause of death in sub-Saharan Africa. In the general population, risks of hypertension rise with increasing age and body weight. Many African HIV treatment programs do not include funding for treatment of hypertension.

Use of tenofovir alafenamide (TAF) and dolutegravir (DTG) have been associated with higher risks of hypertension in some randomized trials and cohort studies, but other studies have not shown these associations.

The VISEND study was conducted in Zambia to evaluate the safety and efficacy of second-line treatment, after NNRTI failure.

METHODS

The VISEND study recruited adults previously taking NNRTI based treatment. People with HIV-1 RNA <1,000 c/mL at screening (Arm A) were randomized to TDF/3TC/DTG or TAF/FTC/DTG. People with HIV-1 RNA>1,000 c/mL (Arm B) were randomized to TDF/3TC/DTG, TAF/FTC/DTG, ZDV/3TC+LPV/r or ZDV/3TC+ATV/r. Blood pressure was evaluated at study Weeks 24, 48, 96 and 144. The risk of Grade 1 hypertension (SBP/DBP >140/90 mmHg) was compared between the TDF/3TC/DTG and TAF/FTC/DTG arms, and by use of DTG vs PI/r, using Cochrane Mantel-Haenszel tests.

In VISEND, risks of treatment-emergent hypertension were significantly higher for DTG versus PI-based treatment

RESULTS

At Week 24, there were no significant differences in Grade 1 HTN between treatment groups within either Arm A or Arm B. The prevalence of hypertension increased over time in all treatment groups. By Week 144, the percentage with Grade 1 hypertension was significantly higher for people taking TAF/FTC/DTG, compared with TDF/FTC/DTG (p=0.02, stratified by Arm). In Arm B, by Week 144 there were significantly more people in the TDF/3TC/DTG and TAF/FTC/DTG arms with Grade 1 HTN (173/343, 50%) compared with the ZDV/3TC/LPV/r or ZDV/3TC/ATV/r arms (76/258, 27%) (p<0.001). Across Arms A and B, Rises in mean BMI were significantly higher for people taking TAF/FTC/DTG versus TDF/3TC/DTG (p<0.001). In Arm B, rises in BMI were significantly greater in the TAF/FTC/DTG or TDF/3TC/DTG groups, versus the ZDV/3TC+LPV/r or ZDV/3TC/ATV/r groups (p<0.001). **However there was imbalanced randomisation over time in both Arm A and B. These results need to be interpreted with caution.**

CONCLUSIONS

In the VISEND trial, risks of treatment-emergent hypertension were significantly higher for DTG than PI based ART.

Treatment arms showing the larger rises in BMI showed higher risks of hypertension.

The imbalanced randomisation means that these results need to be treated with caution.

Table 1: VISEND hypertension and BMI

	Arm A, TLD	Arm A, TAFED	Arm B, TLD	ARM B, TAFED	Arm B, ZDV/3TC+LPVr	Arm B, ZDV
Sex, female	134/207 (65%)	114/200 (57%)	110/189 (58%)	128/199 (64%)	103/148 (70%)	102/181 (56
Age, mean (SD)	44 (10)	44 (9)	38 (10)	39 (11)	38 (10)	38 (10)
Baseline BMI, mean (SD)	23.8 (5.5)	23.4 (5.0)	21.7 (4.9)	21.3 (4.5)	22.3 (4.6)	22.4 (4.4)
Mean BMI change to Week 144 (SD)	+1.15 (4.5)	+1.55 (2.7)	+1.80 (3.0)	+2.29 (3.1)	+1.38 (3.3)	+1.64 (2.9)
G1 HTN Week 24	80/207 (39%)	81/199 (41%)	58/189 (31%)	61/198 (31%)	47/147 (32%)	58/181 (32
G1 HTN Week 144	109/188 (58%)	122/178 (69%)	83/175 (47%)	90/168 (54%)	35/113 (31%)	41/145 (28