Hypertension Risk in a Large Cohort of People Living With HIV After a Switch to Dolutegravir

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E.A. Laker Odongpiny[1,2], B. Otaalo[1] , J. Musaazi[1] , K.Hill[2] , E.A. Nalugga[1] , A. Ddungu[1] , N. Owarwo[1] , B. Castelnuovo[1] , D. Byonanebye[1], A. Semeere[1] , M. Kesby[2] ,M. Holden[2] , D. Sloan[2] , C. Sekaggya[1,2]

1. Infectious Diseases Institute, Kampala, Uganda, 2. University of St. Andrews, School of Medicine, Fife, United Kingdom

BACKGROUND

- Over 90% of PLWH in Low-and-Middle-Income-Countries take Dolutegravir (DTG)-based ART[1]
- Clinical trials of DTG were not mainly conducted in black Africans, but this is the main population in which the drug is used.
- Data on whether DTG use is associated with an increased risk of hypertension (HTN) are conflicting[2,3]
- It is unclear whether weight gain at a threshold of 5% or 10% increase is associated with HTN risk
- **We determined the association of switch to DTG and increased risk of HTN**

METHODS

- A before-after study among PLWH switched to DTG between 2017-2023 at the Infectious Diseases Institute, Kampala Uganda
- HTN defined as any of: 1) two consecutive systolic blood pressure (SBP) or diastolic blood pressure (DBP) readings of ≥ 140 mm Hg or ≥ 90 mm Hg respectively, 2) initiation of anti-HTN treatment, 3) documented diagnosis of HTN in the clinic database
- Incidence rates of HTN were described using Cox proportional models (24 months before DTG compared to 24 months on DTG)
- The risk of incident HTN associated with a ≥ 5% and ≥ 10% weight increase in the DTG period was reported

Switching to Dolutegravir is associated with an increased risk of hypertension

RESULTS

- The median age was 43 years (Interquartile range [IQR]: 37-49), with a median ART duration of 8.5 years (IQR: 5.9-12.4) and a median BMI of 23.7 kg/m^2 (IQR: 20.9-27.4))

Table 1. Baseline Characteristics of PLWH Included in the Study.

Characteristic	Median (IQR)/ Mean (SD)/ Freq (%)
Sex, female	2842 (61.9%)
Age at study entry (years)	[Mean (SD)] 43 (9.2)
Body mass index (kg/m^2),	[Median (IQR)] 23.7 (20.9-27.4)
ART anchor drug pre-DTG, n (%)	
Nevirapine (NVP)	1186 (24.7)
Efavirenz (EFV)	2870 (59.6)
Protease Inhibitors (PIs)	685 (14.2)
Other	71 (1,5)
Duration on ART (years)	[Median (IQR)] 8.5 (5.9-12.4)
Diabetes Mellitus, Yes	92 (1.8)

Table 2. Median Blood Pressure Changes at Key Timepoints.

	-24 months	-12 months*	0 months*	12 months £	24 months £
Median SBP	110(103-120)	110 (102-120)	113 (104-124)	118 (108-130)	119 (108-131)
Median change in SBP (overall), mmHg	N/A	0.0 (-10.0 to 9.0)	0.0 (-10.0 to 9.0)	4.0 (-5.0 to 15.0)	5.0 (-5.0 to 17.0)
Median DBP	70 (67-80)	70 (66-80)	73 (67-80)	78 (70-85)	79 (71-86)
Median change in DBP (overall), mmHg	N/A	0 (-8 to 6)	0 (-8 to 6)	4 (-3 to 12)	5 (-3 to 13)

*differences are from the baseline (at - 24 months before DTG switch)
£differences are from the baseline (at DTG switch).

Key Results:

- Median increase in SBP at 24 months: 5.0 mmHg (IQR: -5.0 to 17.0)
- Median increase in DBP at 24 months: 5.0 mmHg (IQR: -3.0 to 13.0)
- The Hazard ratio (HR) for increased risk of HTN after switch to DTG was 1.30 (CI: 1.02-1.64)

- BMI (time updated log) also associated with risk of HTN [HR 1.97 (CI: 1.27-3.05)]

In the 24 months after initiation of DTG

- A 5-<10% increase in weight is associated with HTN risk [HR 1.73 (CI: 1.30-2.32)]
- A ≥10% increase in weight is associated with HTN Risk [HR 1.96 (CI: 1.42-2.69)]

Table 3. Model Generated Relative hazards of Hypertension Risk and Associated Factors

Characteristic	Adjusted Hazard Ratio (95%CI)	P-value
DTG period		
Pre-DTG	1.00	-
DTG	1.30 (1.02-1.64)	0.032
Time updated log BMI	1.97 (1.27-3.05)	0.003
Age Category		
• 15-34	1.00	-
• 35-44	1.22 (0.87-1.70)	0.239
• 45-54	1.84 (1.33-2.55)	P<0.001
• ≥55	2.28 (1.55-3.30)	P<0.001

Variables adjusted for include duration on ART, WHO HIV stage at ART initiation, previous use of stavudine and zidovudine and diabetes mellitus.

CONCLUSIONS

- DTG use was associated with increased risk of HTN, which occurs independently of weight gain
- Age > 45 years was independently associated with increased risk of HTN
- Both a 5% and 10% change in weight were associated with increased risk of HTN
- Lifestyle modification and HTN management should be integrated in HIV programs in LMICs

ADDITIONAL KEY INFORMATION

References

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Corresponding Author; elaker@idi.co.ug

PLAIN LANGUAGE SUMMARY

People living with HIV in Uganda who switch to Dolutegravir-based regimens experience increases in both systolic and diastolic blood pressures and are at risk of hypertension.