VIROLOGIC FAILURE AFTER ROUTINE SWITCHING TO DOLUTEGRAVIR-BASED ART

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BACKGROUND

- Since 2019, WHO recommends dolutegravir (DTG) as the third drug in first-line antiretroviral therapy (ART) for people living with HIV (PLWH)[1].
- There are concerns that PLWH who switch from a NNRTI-based to a DTG-based regimen with HIV viremia (and possibly NRTI resistance mutations) could develop DTG resistance and virologic failure (VF).

METHODS

Aim: To compare the risk of virologic failure (VF; VL≥400 copies/ml) one year after switch from NNRTI- to DTG-based ART between participants with and without viremia at time of switch (baseline).

Participants: Adult PLWH recruited at time of routine switch to DTG-based first-line ART in two ART programs in Malawi (Lighthouse Trust, Lilongwe) and Zambia (Centre for Infectious Disease Research in Zambia), with different switching policies [2,3]

ART program	Switching to DTG *	Enrolment period
Malawi (Lighthouse)	Irrespective of VL	2019-2020
Zambia (CIDRZ)	Only if last VL<1000 c/mL	2020-2021

* Switching to DTG followed national guidelines for the clinical management of HIV. [2,3] Baseline VL results from this study were not used for patients' clinical management.

VL measurements: VL was considered available at baseline if taken within -90 to +7 days around time of switch, and VL was available at 1 year if taken within -90 to +90 days around 365 days after time of switch.

Analysis: We calculated relative risk (RR) of VF at 1 year by VF status at time of switch, and by country.

RESULTS

- Malawi: 1121/1388 (81%) participants had a VL available at 1 year and were included in the analysis. Among those, 1114/1121 (99%) were women, the median age was 35.5 (IQR 30-40) years, and the median time on ART was 6 (IQR 3.8-8.9) years. Among PLWH with baseline VL≥400 c/ml, median VL was 8'590 (IQR 1'290-52'600) c/ml (Figure). The overall proportion with VF at one year was 3.7% (42/1121).

PLWH switching to DTG-based ART with HIV viremia have higher risk of virologic failure at 1 year, especially when switched irrespectively of previous viral load.

- Zambia: 1321/1411 (93%) participants had a VL measurement available at one year, of whom 1102/1321 (83%) were women, the median age was 40 (IQR 33-45) years, and the median time on ART was 5.8 (IQR 3.3-8.4) years. Among those with baseline VL≥400 c/ml, the median VL was 1'160 (IQR 606-11'300) c/ml (see Figure with box plots). The overall proportion with VF at one year was 1.9% (25/1321).

Figure: Viral load (c/ml) at time of switch among PLWH with baseline VL≥400 c/ml, by country.

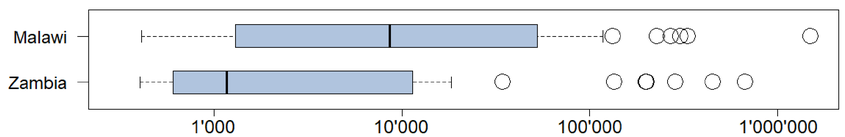

Table: Virologic outcomes of PLWH at 1 year after routine switch to DTG-based first-line ART.

	VL available at 1Y		VL missing at 1Y[b]	
	VL < 400 copies/ml N	VL ≥ 400 copies/ml N (%)[a]	N (%)[b]	Total N
Malawi				1388
VL < 400 at BL	1036	29 (2.7%)	247 (18.8%)	1312
VL ≥ 400 at BL	43	13 (23.2%)	20 (26.3%)	76
RR (95% CI)	**8.6 (4.7 to 15.5)**			
P	<0.0001			
Zambia				1411
VL < 400 at BL	1258	24 (1.9%)	87 (6.4%)	1369
VL ≥ 400 at BL	38	1 (2.6%)	3 (7.1%)	42
RR (95% CI)	**1.4 (0.19 to 9.9)**			
P	0.75			

VL, viral load; BL, baseline; 1Y, 1-year follow-up; RR, relative risk; CI, confidence interval; P, P-value
a; denominator is the number of patients with VL measurement at 1Y.
b; denominator is the number of patients with VL measurement at BL (Total N).

- Proportion of PLWH with VF at 1 year was higher in patients with than in those without VF at the time of switch, with RR=8.6 (95% CI 4.7 to 15.5) in Malawi and RR=1.4 (95% CI 0.2 to 9.9) in Zambia (Table).

CONCLUSIONS

- This unique longitudinal study of two ART programs with different criteria for switching to DTG-based ART allowed us to examine the importance of only switching those who had been virologically suppressed prior to switch.
- Virologic failure one year after switch from NNRTI- to DTG-based ART was overall infrequent, but the risk was higher in those with viremia at switch.
- The Malawi data indicates that PLWH switching to DTG with unsuppressed VL have a substantially higher risk of VF at 1 year than PLWH with suppressed VL at time of switch.
- The Zambian policy of only switching patients who were virologically suppressed at the last routine VL appears to have reduced this risk.

REFERENCES

1. *World Health Organization. Update of Recommendations on First- and Second-Line Antiretroviral Regimens. World Health Organization; 2019*
2. *Malawi Ministry of Health and Population. Clinical Management of HIV in Children and Adults: Malawi Integrated Guidelines. Malawi Ministry of Health and Population; 2018*
3. *Zambia consolidated guidelines for treatment and prevention of HIV infection. Republic of Zambia, Ministry of Health; 2018*

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