Viremia and drug resistance over 2 years after routine switching to dolutegravir-based first-line ART

676

Veronika Whitesell Skrivankova[1], Jacqueline Huwa[2], Guy Muula[3], Geldert D Chiwaya[2], Esau Banda[3], Shameem Buleya[2], Belinda Chihota[3], Joseph Chintedza[2], Carolyn Bolton[3], Thokozani Kalua[4], Roger Kouyos[5], Gilles Wandeler[6], Matthias Egger[7], **Richard J Lessells**[8]

[1]Institute of Social and Preventive Medicine, Bern, Switzerland [2]Lighthouse Trust, Lilongwe, Malawi [3]Centre for Infectious Disease Research in Zambia, Lusaka, Zambia [4]Center for International Health, Education and Biosecurity (Ciheb) at UMB, Lilongwe, Malawi [5]University Hospital Zurich, Zurich, Switzerland [6]University Hospital of Bern, Bern, Switzerland [7]University of Bern, Bern, Switzerland [8]KwaZulu-Natal Research Innovation and Sequencing Platform (KRISP), University of KwaZulu-Natal, Durban, South Africa

BACKGROUND

Since 2019, several million people living with HIV (PWH) have switched from non-nucleoside reverse-transcriptase inhibitor (NNRTI)-based antiretroviral therapy (ART) regimens to dolutegravir (DTG)-based ART

Policies and practices around viral load (VL) testing before switching differed between countries

We assessed the risk of viremia (VL >400 copies/mL) in Malawi, where switching was irrespective of viral load, and in Zambia, where switching depended on a viral load <1000 copies/mL.

METHODS

Design: Observational cohort study

Setting: Malawi (Lighthouse Trust, Lilongwe; switch irrespective of VL) and Zambia (Centre for Infectious Disease Research in Zambia; switch if VL<1000 copies/mL within the past year)

Participants: Adult PWH (≥18 years) enrolled at the time of routine switching from NNRTI-based regimen to DTG-based regimen

Follow-up and outcome ascertainment: Participants followed for up to two years, with viral load measurement at 1 year and 2 years post-switch. Sanger sequencing of HIV-1 *pol* (PR-RT and IN) for all samples with VL ≥1000 copies/mL

Analysis: Comparison of the risk of viremia (≥400 copies/mL) at 1 and 2 years by viral load at switch and between countries using logistic regression adjusted for age and sex

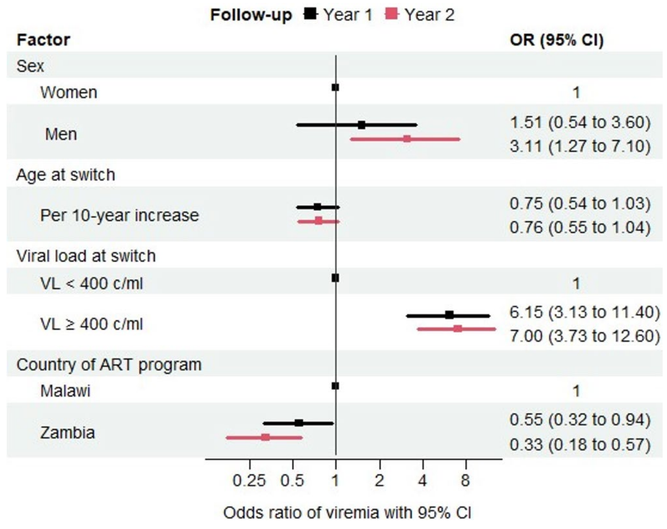
Frequency of integrase drug resistance mutations (DRMs) post-switch amongst participants with VL >1000 copies/mL.

RESULTS

- Overall, 1422/1458 (97.5%) in Malawi and 1410/1417 (99.5%) in Zambia had a VL measurement at switch and were eligible for this analysis

Switching only PWH with evidence of virologic suppression to DTG-based ART may reduce the risk of viremia and the potential for drug resistance

- Most participants were female (99.1% Malawi, 83.0% Zambia), median time on ART was about 6 years
- Most participants switched to TDF/3TC/DTG [TLD] (99.6% Malawi, 85.8% Zambia); the remaining 14.2% in Zambia switched to TAF/FTC/DTG
- Viral load measurement at 2 years for 1140/1422 (80.2%) in Malawi and 1248/1410 (88.5%) in Zambia



- 5.4% of participants viremic at switch in Malawi (5.4%), compared to 3.0% in Zambia (P=0.001).
- At 2 years, corresponding percentages were 4.7% and 1.8% (P<0.0001).
- Viremia at switch was associated with viremia at 1 year and 2 years (**Figure**)
- Viremia at 1 year and 2 years were less likely in Zambia than in Malawi (**Figure**)

Figure Odds ratios of viremia at 1 year (black) and 2 years (red) after routine switching to DTG-based first-line ART.
Results from multivariable logistic regression models

- HIV-1 pol sequencing was successful for 79/112 plasma samples with VL >1000 copies/mL from 104 participants
- Five participants (6.9%) had drug resistance mutations in the integrase gene (four from Malawi, one from Zambia).
- Two had major mutations (**Table**)

Table Cases with major INSTI DRMs at two years

Subtype (Country)	Viral load (copies/mL)			INSTI DRMs	NRTI DRMs
	Switch	1Y	2Y		
C (Malawi)	15 240	218	34 084	**T66A**, **G118R**, **E138K**, E157Q	D67N, K70R, M184V, K219Q
C (Zambia)	<50	812 791	1486	**G118R**, **E138K**	No RT sequence

CONCLUSIONS

- Most people switching to DTG-based ART maintained virological suppression at two years post-switch
- INSTI drug resistance was rare at two years post-switch suggesting most cases of viremia may have been linked to challenges with adherence
- The policy in Zambia of requiring recent VL<1000 copies/mL before switch may have reduced the incidence of viremia during follow-up and may prevent drug resistance
- Overall, the findings support the widespread transition to DTG-based ART. Continued monitoring of virological outcomes and drug resistance in this population is important to ensure the long-term effectiveness of this strategy

ACKNOWLEDGEMENTS

The research reported here was supported by the National Institute of Allergy and Infectious Diseases (R01AI152772) and the Swiss National Science Foundation (32FP30_207285, 324730_207957)

AUTHOR CONTACTS

lessellsr@ukzn.ac.za / veronika.skrivankova@ispm.unibe.ch / matthias.egger@unibe.ch