Trends in HIV viral non-suppression and drug resistance among PWID on dolutegravir ART in Kenya

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BACKGROUND

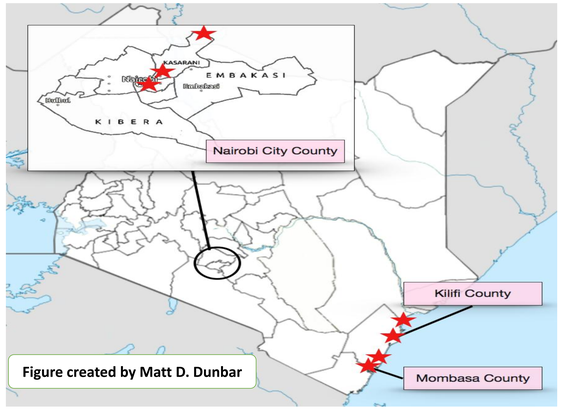
- Use of newer integrase strand transfer inhibitors (INSTI) in first-line HIV treatment regimens is a global standard recommended by WHO[1], including tenofovir (TDF) + lamivudine (3TC) + dolutegravir (DTG) (TLD).
- Little research has been done on viral suppression among people who inject drugs (PWID) on DTG-based regimens in sub-Saharan Africa[2].

Goal

- To conduct a longitudinal study to monitor **trends of viremia** and assess **drug resistance patterns** of DTG-containing regimens among PWID in Kenya over time and evaluate the demographic factors associated with viral non-suppression.

METHODS

- Prospective cohort enrolled using a convenience sampling method.
- Participants were adults 18 years and above who had injected drugs during the 1 year prior to enrollment.
- Recruited from 8 drop-in centers and methadone clinics in Nairobi and the coastal region of Kenya.
- Data analyses used Kaplan-Meier estimators and Cox regression models to ascertain factors associated with time from viral suppression to first non-suppression (VL>200).
- Plasma RNA from participants with viremia was genotyped for resistance using the Stanford HIV database algorithm using a laboratory-developed assay for the PacBio sequencing platform. HIV viral load assay using real-time polymerase chain reaction (RT-PCR) conducted by Abbott



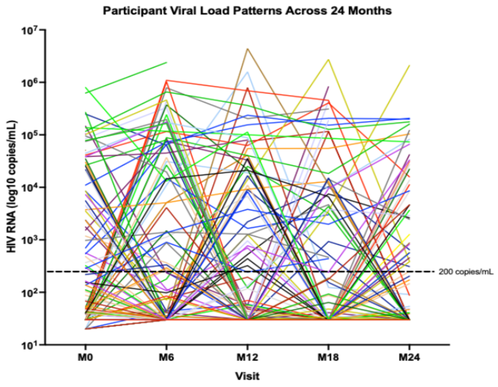
RESULTS

- Among 250 participants, 125 were on methadone; 70% were male, with a median age of 39 years. Over two years, participants' HIV viral suppression patterns were classified as: Always suppressed, intermittently suppressed, and always non-suppressed (viremic) **(Table 1).**
- Genotyping was successful in 99% of viremic samples. NNRTI resistance was common (30–45%), but major resistance to DTG-based drugs was rare: tenofovir resistance (4%), lamivudine (8%), and minority DTG resistance variants (2%) like S153F and Q148K **(Table 2).**

Table 1.

Prevalence of Viremia & Virologic Patterns Over Time

- At each visit, ~15-20% of participants were unsuppressed (>200 c/mL)
- The participants who had viremia differed over time (i.e., had "intermittent viremia)



	M0 n/250 (%)	M6 n/231 (%)	M12 n/223 (%)	M18 n/217 (%)	M24 n/205 (%)
Suppressed (<200 c/mL)	203 (81%)	185 (80%)	183 (82%)	184 (85%)	166 (81%)
Viremic (>=200 c/mL)	47 (19%)	46 (20%)	40 (18%)	33 (15%)	39 (19%)
No Data	-	19	27	33	45

While most participants on a DTG regimen achieved viral suppression and drug resistance was rare over time, ongoing efforts are needed for the 1 in 5 participants with viral non- suppression to meet 95-95-95 goals.

Table 2.

Prevalence of HIVDR at Viremia

- All viremic specimens were genotyped & analyzed for mutations to DTG/TDF/3TC

	Month 0	Month 6	Month 12	Month 18	Month 24
# with Viremia (>200 c/mL)	N=47	N=46	N=40	N=33	N=39
# with Genotyping Data	N=46	N=46	N=40	N=32	N=38
Wild-type	28/46 (61%)	28/46 (61%)	25/40 (63%)	18/32 (56%)	23/38 (61%)
Any DRM	18/46 (39%)	18/46 (39%)	15/40 (37%)	14/32 (44%)	17/38 (39%)
TDF/3TC DR	5	4	4	2*	4
DTG DR	0	0	0	2	0
DTG Accessory DRM	13	14	11	11	14

*≥1 participant overlapped with another category

- Excluded PI and NNRTI resistance from summary; however, NNRTI resistance was most common (>25%)
- Major TDF/3TC and/or DTG mutations were not commonly detected (5-10%); DTG accessory DRM were common
- Only two participants had "major" DTG resistance detected, both at M18 at 1% frequency (Q148K & S153F)
- Only three specimens did not amplify for either PacBio or Sanger sequencing

- **Fig A, B, C, D.** The Kaplan-Meier curves show the probability of becoming viremic over time for those on TLD among PWID enrolled at various Kenya sites **(A)** Overall and stratified by **(B)** Sex **(C)** Living condition **(D)** Methadone participation. X-axis: time (days); Y-axis: survival rate (%)
- **Association:** In the univariate Cox regression model, time to viremia was somewhat more rapid for males (HR=1.51, 95% CI: 0.69-3.31, p=0.29), singles/not married (HR=1.09, 95% CI: 0.45-2.65, p=0.85), and was significantly more rapid for those living in an improvised shelter (HR=4.36, 95% CI: 1.52-12.53**, p=0.006**)

Fig A.

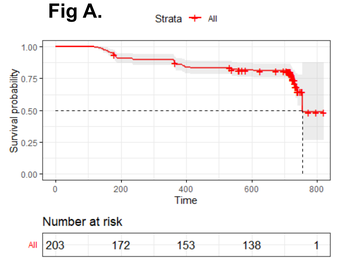


Fig B.

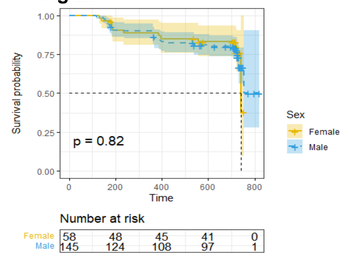


Fig C.

Fig D.

CONCLUSIONS

This longitudinal study among PWID living with HIV in Kenya shows that more than 1 in 3 participants on DTG-containing regimens had viral non-suppression at least intermittently. Resistance to DTG-containing therapy was rare across two years of follow-up.

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