H-02

# Rising Dolutegravir Resistance in Tanzania: A Concern for the ART Programme

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## 1. BACKGROUND

- Dolutegravir (DTG) remains the cornerstone of 1st line ART in SSA, yet resistance is increasingly reported, ranging from 3.9% to 19.6%.
- In 2020, DTG resistance was reported in 5.8% of PLHIV with high viraemia in Tanzania
- Therefore, five years later, we assessed patterns of acquired drug resistance in Tanzania using a WHO-recommended laboratory-based survey method.

## 2. METHODS

- A cross-sectional study was conducted in 12 HIV viral load testing laboratories and 2 referral laboratories in Tanzania.
- The study was conducted for 3 months.
- A total of 220 remnant plasma samples with HIV viral load ≥1000 copies/mL were analysed.
- HIV genes **(reverse transcriptase, protease, and integrase)** were amplified by PCR and directly sequenced.

**Sampling**
- Randomisation-1: Selection of 50 eligible samples per HVL testing lab, then shipped to MUHAS
- Randomisation-2: Sample size per Probability Proportional to Size (PPS)

**Lab Analysis**
- RNA extraction- PureLink ™ Viral RNA/DNA Mini Kit

**Lab Analysis**
- Nested PCR & Sanger sequencing (ABI 3500)-Applied Biosystem ™ HIV-1 Genotyping kit with Integrase (ThermoFisher)

**Data Analysis**
- Seqscape software and the Stanford HIVDB program

### Table 1: Distribution of participants' demographic and clinical characteristics (N=189)

| Characteristics | Number | Percent (%) |
|---|---|---|
| **Sex** | | |
| Female | 122 | 64.6 |
| Male | 67 | 35.4 |
| **Age** | | |
| Children | 17 | 9.0 |
| Adults | 172 | 91.0 |
| **Age mean ± SD (years)** | | |
| Children | 9 ± 4.2 | |
| Adults | 40 ±13 | |
| **Viral load (copies/mL)** | | |
| Median | 63,200 | |
| IQR | 19,060 – 210,421 | |
| **Duration on ART (months)** | | |
| 6 | 6 | 3.2 |
| 12 | 20 | 10.6 |
| 24 | 14 | 7.4 |
| 36 | 22 | 11.6 |
| >48 | 127 | 67.2 |
| **Current ART regimen** | | |
| DTG-based | 171 | 90.5 |
| PI-based | 13 | 6.9 |
| NNRTI-based | 5 | 2.6 |

***Key Findings:***

**- DTG resistance in Tanzania has increased by more than 2-fold (from 5.8% to 17.8%) in PLHIV with high viremia in a span of 5 years.**

**- Protease inhibitors remain susceptible and suitable for PLHIV with INSTI resistance in Tanzania.**

## 3. RESULTS

### 1: HIV-1 subtypes distribution in Tanzania

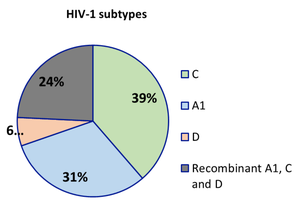



**Figure 1: HIV subtype distribution in Tanzania.**
This figure shows the HIV subtypes co-circulating in Tanzania (n = 116).

### 2: Prevalence estimates of acquired HIV-1 DRMs in Tanzania

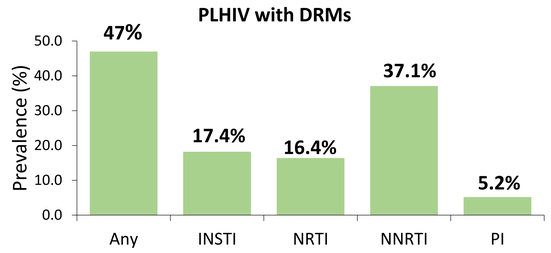



**Figure 2: Prevalence estimates of acquired HIV-1 DRM in Tanzania.**
This figure illustrate frequency of PLHIV with acquired HIV DRMs to NNRTI, NRTI, PI and INSTI ART drug classes as detected in remnant plasma samples integrase (IN) sequences (n = 132) and protease reverse transcriptase (PPRT) (n = 116).

### 3. Patterns of NRTI, NNRTI and PI DRMs Detected from Remnant Plasma

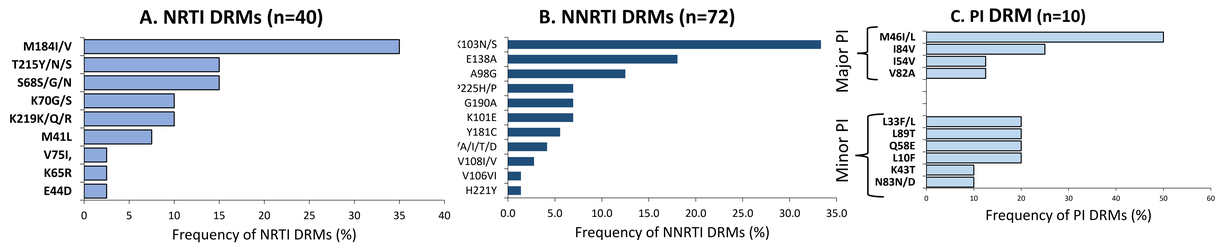



**Figure 3: Patterns of NRTI, NNRTI and PI DRMs detected from remnant plasma.**
The figure indicates the patterns and frequencies of [A.] NRTI (n=40), [B.]NNRTI (n=72) and [C.]PI major and minor (n=10) DRMs detected in remnant plasma samples from PLHIV in Tanzania

### 4. INSTI Drug Resistance Mutations

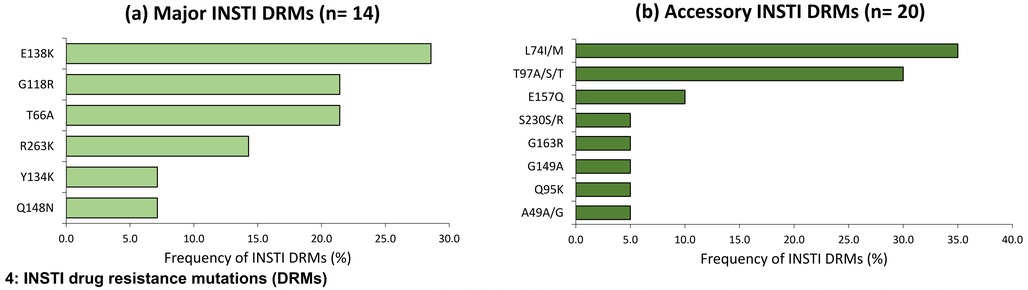



**Figure 4: INSTI drug resistance mutations (DRMs)**
This figure depicts the prevalence of major INSTI [a.] and accessory INSTI DRMs [b ] as detected in remnant plasma samples from PLHIV in Tanzania

### 5. Genotypic Prediction of INSTI, PI, NNRTI and NRTI drugs among PLHIV with INSTI Drug Resistance Mutations

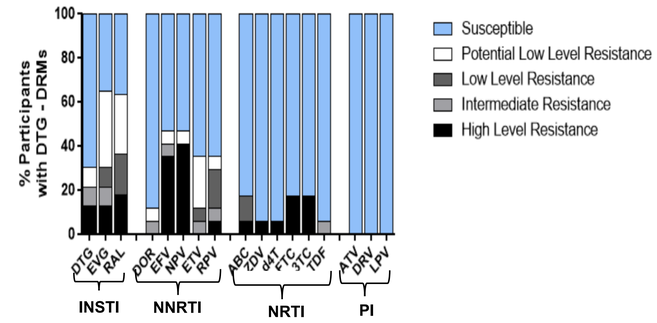



**Figure 5: Genotypic prediction of INSTI, NNRTI, NRTI, PI drugs**
The figures depict the susceptibility predictions of INSTI, NNRTI, NRTI and PI drugs in PLHIV in Tanzania. The figures depict the susceptibility predictions of INSTI, NNRTI, NRTI and PI drugs *Key:* ABC, abacavir; ATV, atazanavir; d4T, stavudine; ddI, didanosine; DOR, doravirine; DRV, darunavir; DTG, do- lutegravir; EFV, efavirenz; ETV, etravirine; EVG, elvitegravir; FTC, emtricitabine; LPV, lopinavir; NVP, nevirapine; RAL, raltegravir; RPV, rilpivirine; TDF, tenofovir disoproxil fumarate; ZDV, zidovudine; 3TC, lamivudine.

## 4. CONCLUSIONS

Our findings highlight the imminent danger to ART programs due to increased resistance to DTG, which is an important 1st line ART for the treatment of HIV infections in Tanzania and other similar settings.

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## PLAIN LANGUAGE SUMMARY

Rising DTG resistance puts Africa's ART success at risk, underscoring the urgent need to identify and curb the drivers of this resistance before treatment options are further compromised in Tanzania and across sub-Saharan Africa.