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Prevalence of INSTI drug resistance: Population-based data from four African countries, 2019-2022

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BACKGROUND

With excellent tolerability, effectiveness and a high barrier to drug resistance (DR), integrase strand transfer inhibitors (INSTI) are widely used as the backbone of HIV treatment regimens, including for treatment-naïve people living with HIV (PWH). The second generation of INSTI, including dolutegravir (DTG), are used for treatment-naïve PWH due to their lack of drug-drug interactions, good rates of virologic suppression, tolerability, and barrier to resistance.

A 2024 World Health Organization brief on HIV DR reported on recent studies in low- and middle-income countries with INSTI DR mutation prevalence estimates ranging from 3.9% to 19.6% among PWH who have detectable viremia receiving antiretroviral therapy (ART) that include DTG.[1]

Many countries in southern and eastern Africa, including Eswatini, Mozambique, Uganda, and Zimbabwe include INSTI as first-line HIV treatment. We examined population-based INSTI DR mutation prevalence in these four high HIV burden African countries using INSTI as first-line antiretroviral (ARV) therapy.

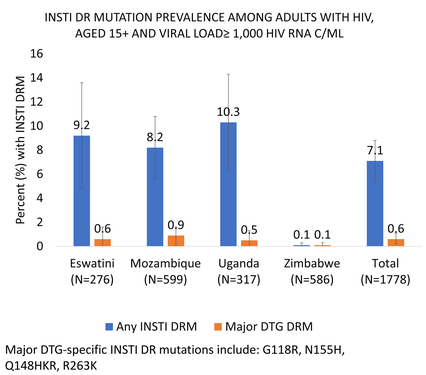
METHODS

We analyzed data from four nationally representative Population-based HIV Impact Assessments conducted between 2019-2022 in Eswatini, Mozambique, Uganda, and Zimbabwe, individually and in a pooled analysis. INSTI DR mutations were identified using Sanger-based sequencing. We assessed the prevalence of any INSTI DR mutation and of major dolutegravir (DTG) DR mutations (G118R, N155H, Q148HRK, R263K), among PWH aged ≥15 years with HIV RNA viral load (VL) ≥1,000 copies (c)/mL.

We examined the weighted prevalence of any INSTI DR mutation and major DTG-specific INSTI DR mutations. Next, we examined INSTI DR mutations among PWH with recent HIV infection based on LAg-avidity <2.0 optical density units, VL≥1000 c/mL and lack of detectable ARVs; then, among those with a long-term infection, we examined awareness of HIV diagnosis (self-report or ARV detected), and various ARV statuses. Nonoverlapping confidence intervals were used for comparisons.

Nationally representative INSTI DR mutation prevalence among people living with HIV with VL ≥ 1,000 c/ml ***was 7%*** across four countries in Africa. **Prevalence of major DTG mutations was <1%.**

Figure 1



Major DTG-specific INSTI DR mutations include: G118R, N155H, Q148HKR, R263K

Figure 2

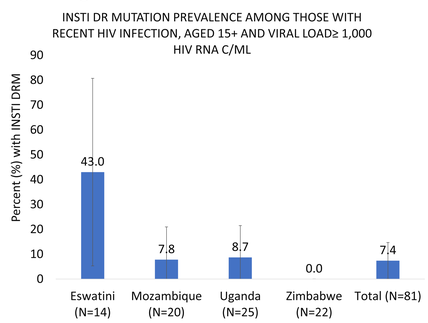


Figure 3

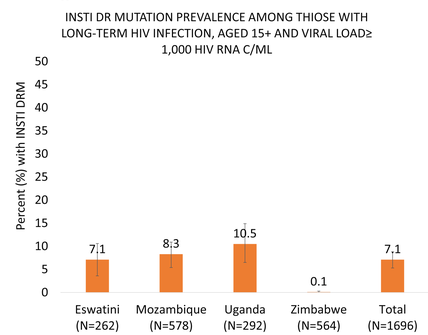


Table 1: INSTI DR MUTATION PREVALENCE AMONG THOSE WITH LONG-TERM HIV INFECTION, AGED 15+ AND VIRAL LOAD ≥ 1,000 HIV RNA C/ML

	Eswatini	Mozambique	Uganda	Zimbabwe	Total
	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)
Presence of a detectable ARV					
Detectable	3/22 (13.9)	10/59 (17.8)	4/45 (7.2)	0/175 (0.0)	17/301 (7.9)
Not detectable	18/240 (6.6)	36/519 (7.3)	28/247 (11.1)	1/388 (0.1)	83/1394 (6.9)
HIV diagnosis and treatment status[1]					
Unaware of HIV status	10/122 (7.5)	26/412 (7.0)	15/174 (8.3)	0/285 (0.0)	51/993 (6.2)
Aware of HIV status and not on ART	6/59 (8.1)	6/42 (15.4)	7/41 (19.0)	1/62 (0.9)	20/204 (12.7)
Aware of HIV status and on ART	5/81 (5.6)	14/121 (10.4)	10/76 (11.7)	0/217 (0.0)	29/495 (7.6)
ART status[2]					
Current ART use	5/81 (5.6)	14/121 (10.4)	10/76 (11.7)	0/217 (0.0)	29/495 (7.6)
Prior ART use	0/14 (0.0)	2/24 (4.2)	4/18 (24.3)	0/24 (0.0)	6/80 (9.0)
ART naive	16/167 (8.5)	30/430 (7.9)	18/197 (9.0)	1/323 (0.2)	65/1117 (6.9)

[1]Awareness of HIV-positive status and treatment status were based upon self-report or having detectable ARVs.

[2]Current ART use is based on self-report or having detectable ARV(s). Prior ART use is based upon self-report. ART naïve participants reported never taking ART or were unaware of their HIV-positive status and had no detectable ARV in their blood.

Note: The numerators/denominators are the unweighted counts and the percents are weighted. For estimates with denominators <25, the point estimates may not be reliable.

RESULTS

Among 9,361 people with HIV, 1,778 (26.8%) had a VL ≥1,000 c/mL and INSTI DR mutation results, and 81 (5.4%) had a recent HIV infection. See Figures 1, 2, and 3 for INSTI DR mutation and prevalence of major DTG mutations, INSTI DR mutation among those with recent HIV infection, and INSTI DR mutation among those with long-term HIV infection, respectively.

Among PWH with long-term infection and detectable ARVs, the prevalence of INSTI DR mutations was 7.9% overall (range: 0.0%-17.8%) (Table 1). Among those with long-term infection, aware of their HIV status and not on ART, INSTI DR mutations ranged from 0.9% in Zimbabwe to 19.0% in Uganda (12.7% overall). Among PWH with long-term infections, aware of their HIV diagnosis and on treatment, INSTI DR mutations ranged from 0.0% in Zimbabwe to 11.7% in Uganda (7.6%, overall). Among those with long-term infections who reported prior ARV use, INSTI DR mutations ranged from 0.0% in Zimbabwe to 24.3% in Uganda (9.0%, overall). Among PWH with long-term infections who were ARV-naïve, INSTI DR mutations ranged from 0.2% in Zimbabwe to 9.0% in Uganda (6.9%, overall).

CONCLUSIONS

Nationally representative data from four African countries demonstrated that overall INSTI DR mutation prevalence among PWH with VL ≥1000 c/mL was 7%. The prevalence of INSTI DR mutation among PWH with a VL ≥1000 c/mL was higher in Eswatini, Mozambique, and Uganda and lower in Zimbabwe. This is likely due to the timing of initial INSTI rollout in Zimbabwe and the timing of the survey. The prevalence of major DTG mutations was <1%. Wide ranging INSTI DR mutation prevalence may reflect differences in HIV subtype or access to and usage patterns of INSTI ARVs. Given the important role of INSTI for treatment and prevention of HIV, ongoing monitoring of clinical and population-based data for INSTI DR mutations is critically important.

INSIDA 2020 Inquérito Nacional sobre o Impacto do HIV e SIDA em Moçambique
SHIMS3 2020 Eswatini Population-based HIV Impact Assessment
UPHIA 2020 Uganda Population-based HIV Impact Assessment
ZIMPHIA 2020 Zimbabwe Population-based HIV Impact Assessment

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