Integrase strand transfer inhibitor resistance mutations in HIV patients on ARV treatment in Rwanda, 2022-2023, A CADRE preliminary analysis.

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Ntawunga I, L,[1] Remera E,[1] Mupenzi V,[2] Kayitesi C,[1] Umwanankandi F,[1] Gatete G,[1] Mujawamariya G[1], Nirere JD,[1] Gashegu M[1], Rwibasira N, G[1]. Rwanda Biomedical Centre/Ministry of Health

BACKGROUND

In this study, we investigated integrase strand transfer inhibitor drug resistance mutations (INSTI-DRMs) in HIV patients on ARV treatment in Rwanda.

METHODS

A longitudinal cross-sectional survey utilizing remnant samples routinely collected for viral loads from 208 adults was conducted and cryopreserved at the sixteen (16) regional laboratories supporting viral load testing in Rwanda. Resistance levels were assessed based on the presence of specific drug resistance mutations (DRMs) in the HIV integrase gene. Each mutation was assigned a penalty score for individual drugs. The total score for a particular drug was obtained by summing the penalty scores of all relevant mutations detected in the viral sequence. This total score was then used to estimate the level of resistance, classified as susceptible, low-level, or intermediate resistance. These categories corresponded to drug resistance scores of 30 to 59, while high-level resistance was associated with a score of 60 or greater, as per the Stanford HIV Drug Resistance guidelines.

Most participants can still be effectively treated with dolutegravir (DTG), as drug resistance changes are rare. In some cases, with mutations (Q148H and N155H), they may slightly alter the virus enzyme, reducing drug binding.

RESULTS

Based on the Cyclic Acquired Drug Resistance (CADRE) survey data collected, INSTI results were available for 208 adult participants tested between August 2022 and December 2023. The average age was 40.1 years, and the majority (58.2%) of participants were females. The estimated INSTI-DRMs for Bictegravir (BIC), Cabotegravir (CAB), Elvitegravir (EVG), and Raltegravir (RAL) ranged between 2.4% high-level to 9.1% any-level and 2.4% high-level to 6.2% any-level of resistance for INSTI Dolutegravir (DTG). INSTI-DRMs were detected in 83 (14%) individuals; 11 (5.3%) had more than one INSTI-DR mutation. Most participants (n=195, 93.8%) were susceptible to dolutegravir; three (1.4%) had potential low, two (1.0%) low, three (1.4%) intermediate, and five (2.4%) high-level dolutegravir resistance. In Rwanda, the 'major' INSTI-resistance mutations T66AIK, E92QV, G118R, F121Y, E138AT, G140ACS, Y143CHR, S147G, Q148HKR, or N155HS were rarely selected. The 'accessory' INSTI-DRMs included H51Y, L68IV, KL74ILM, T97TA, E138AK, G140ACS, G149A, S153F, E157EQ, G163AGKR, and R263K. In INSTI-treated patients, G118R was the most common major mutation selected.

	Integrase strand transfer inhibitor									
Resistance	**INSTI_BIC**	**%**	**CAB**	**%**	**DTG**	**%**	**EVG**	**%**	**RAL**	**%**
High-level	**5**	**2.4**	**7**	**3.4**	**5**	**2.4**	**7**	**3.4**	**5**	**2.4**
Intermediate	**3**	**1.4**	**2**	**1.0**	**3**	**1.4**	**3**	**1.4**	**4**	**1.9**
Low-level	**0**	**0.0**	**1**	**0.5**	**0**	**0.0**	**1**	**0.5**	**2**	**1.0**
No data	**2**	**1.0**	**2**	**1.0**	**2**	**1.0**	**2**	**1.0**	**2**	**1.0**
Potential low-level	**2**	**1.0**	**2**	**1.0**	**3**	**1.4**	**6**	**2.9**	**6**	**2.9**
Susceptible	**196**	**94.2**	**194**	**93.3**	**195**	**93.8**	**189**	**90.9**	**189**	**90.9**

CONCLUSIONS

Most participants are still susceptible to DTG, and the major INSTI-DRM mutations were rarely selected. Q148H and N155H mutations are thought to trigger conformational changes within the catalytic pocket that result in lower binding affinity of INSTIs to IN.

ADDITIONAL KEY INFORMATION

Additional Resources

1. Rwanda National HIV Treatment Guidelines
2. WHO recommendations on dolutegravir-based regimens
3. Relevant peer-reviewed publications on INSTI resistance trends

Corresponding Author
Dr. Laurence I, NTAWUNGA
Ministry of Health
Rwanda Biomedical Centre/HDPC
Email: research.laurence@gmail.com
Country: Rwanda

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PLAIN LANGUAGE SUMMARY

Most participants can still be successfully treated with dolutegravir (DTG). It's reassuring to know that significant drug resistance changes are quite rare. In the small number of cases where some mutations like Q148H and N155H appeared, they might slightly alter the shape of the virus enzyme, which could make the drug bind a bit less effectively.