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Detection of Arv-Resistant Mutants in HIV-1-Infected Individuals in a Context of Systematic Switching to an Association Based on Dolutegravir in Abidjan, Côte d'Ivoire

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Abstract

The emergence of antiretroviral resistance mutations represents a major threat to the achievement of national and global goals for the elimination of HIV-1 infection. The global strategy in 2019 in Côte d'Ivoire is a new national policy for the management of people living with HIV with the administration of dolutegravir (DTG)-based fixed-dose combination. The aim of our study was to evaluate HIV-1 resistance to antiretrovirals (ARVs) in infected adult subjects in Côte d'Ivoire in the context of a systematic switch to a DTG-based combination. Between February 2022 and October 2023, a cross-sectional survey with random sampling was conducted in 06 services caring for people living with HIV. A total of 139 participants were included in the study. Adults with a viral load ≥ 1000 copies/mL were tested for HIV-1 ARV resistance mutations. Molecular analyses were performed using protocol of ANRS-MIE (National Agency for Research on AIDS and emerging infectious diseases). The interpretation is performed by HIVGRAD (https://www.hiv-grade.de/cms/grade/). The frequencies of HIV-1 resistance to non-nucleotide reverse transcriptase inhibitors (NNRTIs), nucleotide reverse transcriptase inhibitors (NRTIs), integrase inhibitors (IINTs) and protease inhibitors (PIs) were 82%, 73%, 19% and 11% respectively. The main mutations observed in the different classes were K103N

(45%), M184V (64%), E157Q (19%) and L10V/M46I/A71V/I54V (6%) respectively. This study reveals the emergence of resistance to DTG-based fixed-dose combinations, favored by high rates of resistance to NRTIs and NNRTIs. This finding underlines the need for enhanced viral load monitoring and HIV-1 genotyping tests to guide the choice of NRTIs for combination therapy. In addition, monitoring for mutations to second-generation NRTIs is essential, given the scale-up of DTG-based regimens currently underway in Côte d'Ivoire.

Keywords

Resistant Mutants, Dolutegravir, HIV-1, Antiretrovirals, Côte d'Ivoire

1. Introduction

The advent of antiretroviral therapy (ART) has led to a 59% reduction in new human immunodeficiency virus (HIV) infections worldwide since the peak in 1995 [1]. However, the emergence of HIV-1 variants resistant to antiretrovirals (ARVs) is threatening efforts to combat the disease. Several studies have shown alarming levels of HIV-1 resistance to ARVs, particularly to the widely used non-nucleoside reverse transcriptase inhibitors (NNRTIs), mainly nevirapine and efavirenz [2].

To remedy this problem, UNAIDS has recommended triple therapy as the first-line treatment for HIV-1 in all countries, comprising two nucleoside reverse transcriptase inhibitors (NRTIs) combined with dolutegravir (DTG), a second-generation integrase inhibitor offering a greater genetic barrier to resistance.

Since March 1, 2019, Côte d'Ivoire has changed its national first-line treatment policy by systematically switching all infected people to a fixed-dose combination of ARVs based on tenofovir disoproxil (TDF), lamivudine (3TC) and dolutegravir (TLD) [3], without prior viral load testing or resistance genotyping, due to its limited capacity to monitor these biological markers, as in many resource-limited countries.

This pragmatic approach to the implementation of the new treatment regimen raises concerns in Côte d'Ivoire, as a recent study evaluated NRTI resistance in children and adults with virological failure in the context of a systematic switch to a DTG-based combination, and estimated it at 65% [4]. It is therefore likely that this approach to the transition to TLD exposes a significant number of people to the risk of ending up on ineffective functional monotherapy with DTG, and thus developing resistance to DTG.

Data on DTG resistance obtained in routine health care are scarce in Côte d'Ivoire. It is therefore necessary to monitor HIV-1 resistance patterns to ARVs in the context of routine switching to a DTG-based combination in order to optimize treatment efficacy. The aim of our study was to evaluate HIV-1 resistance to ARVs in infected adult subjects in Côte d'Ivoire, in the context of a systematic switch to a DTG-based combination.

2. Methodology

2.1. Framework of the Study

This was a prospective, descriptive and analytical study which was carried out from February 2022 to October 2023 in 02 hospital and university centers (CHU) in the city of Abidjan, namely, the Cocody CHU and the CHU de Treichville

The services selected were the infectious and tropical diseases department of the Treichville University Hospital (SMIT), the ambulatory care and advice unit of the Treichville University Hospital (USAC), the outpatient department of Cocody University Hospital, the pneumophtisiology department of Cocody University Hospital (PPH), the neurology department of Cocody University Hospital, and the care service for people living with HIV at the Pasteur Institute of Côte d'Ivoire (IPCI).

2.2. Recruitment of Study Participants

The objectives of the study and the blood collection procedures were previously explained to all participants in simple terms in order to obtain their informed consent or assent before selection.

To be eligible, participants had to be adults infected with HIV-1, followed regularly in a cohort and in virological failure (viral load ≥ 1000 copies/mL) during the last 6 months or naive to antiretroviral treatment. Sociodemographic data, viral load and treatments were collected from the medical records of study participants.

2.3. Ethical Consideration

The national ethics committee for life sciences and health (CNESVS) gave ethical consent for this study to be carried out (Reference number: 197-20/MSHP/CNESVS-kp). All participants provided written informed consent and assent before being recruited into the study.

2.4. Collection and Preprocessing of Study Samples

Venous blood was collected in 03 tubes containing ethylene diamine tetra acetic acid (EDTA) at a rate of 6ml per tube and sent to the molecular biology platform of the Pasteur Institute of Adiopodoumé, Côte d'Ivoire, for analyzes. The blood was centrifuged at 2200 rpm for 10 minutes to obtain plasma, of which 05 aliquots were stored at −80˚C.

2.5. Genotyping HIV-1 Drug Resistance Mutations

HIV-1 genotyping was performed using the reference technique of the AC43 HIV-1 resistance study group of ANRS-MIE (http://www.hivfrenchresistance.org).

2.5.1. Viral Extraction

Viral RNA was extracted using the QIAamp Viral RNA Mini Kit (Qiagen, Germany) according to the manufacturer's recommendations.

2.5.2. RT-PCR

Amplification of the HIV-1 pol (reverse transcriptase, protease and integrase) gene regions of interest was performed using the Eppendorf thermal cycler (VAPO Protect). The SuperScript III One-Step RT-PCR System with Platinum-Taq DNA kit (Invitrogen) was used for the first PCR according to the manufacturer's recommendations.

Briefly, a 50 uL reaction containing, 25 uL of Master mix (2X), 20 uL RNA, 0.5 nM each primer for RT-PCR, 1 uL Platinum Taq-RT Superscript III and 20 uL extracted RNA.

Primer pairs used were MJ3/MJ4, 5'PROT1/3'PROT1 and INPS1/INPR8 for reverse transcriptase, protease and integrase respectively (Table 1).

Thermal amplification conditions for the RT-PCR were 55˚C for 30 min (Activation), 94˚C for 2 min (Denaturation) and 94˚C for 30 s, 55˚C for 30 s, 68˚C for 1 min 30 s for 45 cycles and a final extension at 68 ◦C for 5 min.

2.5.3. Nested-PCR

Nested-PCR was performed using the FIREPol Master (SOLIS BIODYNE) according to the manufacturer's recommendations.

Primers pairs used were A35, NE135, INPS3, INPR9, 5'PROT2, 3'PROT2 for reverse transcriptase, integrase and protease respectively (Table 1). The nested PCR is a 50 uL reaction containing 10 uL of FIREPol Master Mix 5×, 10 uL amplicons (PCR products), 0.5 nM each primer, 10 uL Buffer 10× and nuclease free water.

For Nested-PCR, the thermal conditions for amplification were 95˚C for 5 min (Denaturation) and 95˚C for 30 s, 61˚C for 60 s, 72˚C for 4 min for 45 cycles and a final extension at 72˚C for 10 min.

Table 1. PCR and sequencing Primers (https://hivfrenchresistance.org/protocols/).

Name	Sequences (5'-3')	Target
MJ3	AGT AGG ACC TAC ACC TGT CA	Reverse Transcriptase
MJ4	CTG TTA GTG CTT TGG TTC CTC T	
A35	TTG GTT GCA CTT TAA ATT TTC CCA TTA GTC CTA TT	
NE135	CCT ACT AAC TTC TGT ATG TCA TTG ACA GTC CAG CT	
5'PROT1	TAA TTT TTT AGG GAA GAT CTG GCC TTC C	Protease
3'PROT1	GCA AAT ACT GGA GTA TTG TAT GGA TTT TCA GG	
5'PROT2	TCA GAG CAG ACC AGA GCC AAC AGC CCC A	
3'PROT2	AAT GCT TTT ATT TTT TCT TCT GTC AAT GGC	
INPS3	GAA GCC ATG CAT GGA CAA G	Integrase
INPR9	ATC CTC ATC CTG TCT ACT TGC C	
INPS1	TAG TAG CCA GCT GTG ATA AAT GTC	
INPR8	TTC CAT GTT CTA ATC CTC ATC CTG	

2.5.4. Purification and Sequencing

ChargeSwitch-ProPCR Cleanup Kit (Invitrogen) was used to purify positive amplicons on agarose gel (1%) according to the manufacturer's recommendations. The BigDye Terminator v3.1 kit (Applied biosystems) was used for the sequencing reaction according to the manufacturer's recommendations. An ethanolic purification process with Agencourt CleanSEQ (BECKMAN) was used for purification of sequence reaction products in accordance with the manufacturer's recommendations. The Analyser 3500 XL genetic analyzer (Applied biosystems) was used to sequence the genes of interest.

2.6. Data Processing and Statistical Analysis

Sequence analysis for the determination of viral genetic mutations and was performed using HIVGRAD viral genotyping software (https://www.hiv-grade.de/cms/grade/) using the ANRS-MIE algorithm (ANRS-AC43: resistance group genotype interpretation). Microsoft Excel 2013 was used for data processing and SPSS Statistics 17.0.1 for statistical analyses.

3. Results

3.1. Characteristics of Study Participants

A total of 139 people were recruited, including 92 women and 47 men, with an average age of 44 for the study population. 36 people, or 24%, were without ARVs, and 103 participants, or 76%, were on ARV therapy. Of these, 48% were on dolutegravir-based triple therapy. The average duration of ARV treatment was 5 years. The median viral load was 4.8 with an Intervale of 3 to 8 (**Table 2**).

3.2. Results of Molecular Analysis

We genotyped 139 HIV-1-infected samples for mutations in the reverse transcriptase, protease and integrase genes. Of the 139 samples analyzed, 52% (73/139) were successfully amplified and sequenced.

Biostatistical analyses were carried out on 15% (11/73) of the reverse transcriptase sequences, 88% (64/73) of the protease sequences and 22% (16/73) of the integrase sequences.

3.3. Frequency of HIV-1 Resistance to Different ARV Classes

The frequency of HIV-1 resistance to NRTIs was 73% (8/11). Resistance to 3TC, FTC and ISL was observed in 64% (7/11) of participants. Resistance to ABC was also observed at a frequency of 36% (4/11), and to AZT and TDF/TAF at a frequency of 27% (3/11) (**Figure 1**).

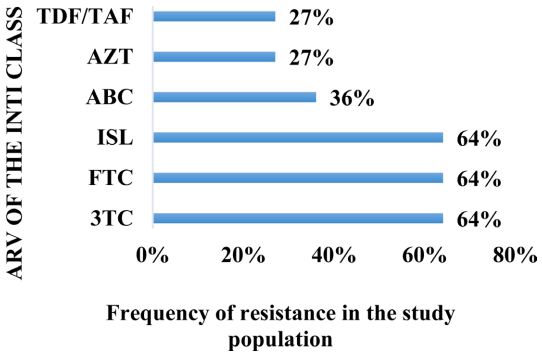
NNRTI resistance was observed in 82% (9/11) of people living with HIV-1. The frequency of resistance to EFV and NVP was 73% (8/11). The frequencies of resistance to DOR, RPV and ETR were 36% (4/11), 27% (3/11) and 9% (1/11) respectively (**Figure 2**). The frequency of resistance to PIs was 11% (7/64). It was

9% (6/64) for LPV and ATV/r and 6% (4/64) for DRV_QD. There was 0% resistance to DRV (Figure 3). The frequency of IINT resistance was 19% (3/16). HIV-1 resistance to EVG and RAL was 19% (3/16). Participants were resistant to BIC, CAB and DTG at a frequency of 6% (1/16). Resistance to DTG_BID was 0% (0/16) (Figure 4).

Table 2. Social, demographic, biological and therapeutic characteristics of study participants.

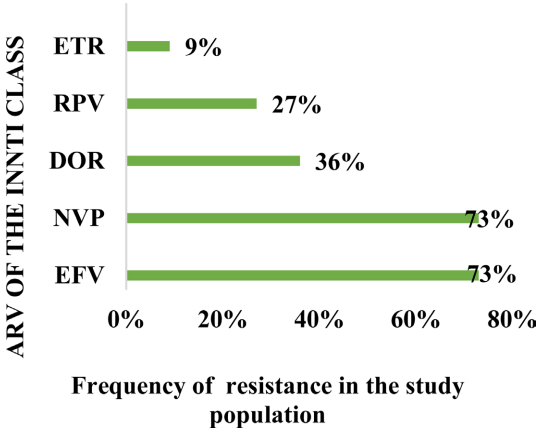
Sex at birth (n: 139)	
Men, n (%)	47 (34)
Women, n (%)	92 (66)
Age (years) Average (Range)	
Study population	44 (17 - 77)
Men	46 (17 - 70)
Women	43 (18 - 77)
Therapeutic status n (%)	
Naive	36 (24)
On ARV treatment	103 (76)
Viral load (Log10 copies/mL) Median (Interval)	4.8 (3 - 8)
Duration of treatment (years) Mean (Interval)	5 (1 - 19)
Therapeutic lines	
ARV-naive subjects	36 (26)
ARV regimen	103 (74)
TDF-3TC-DTG/AZT-3TC-DTG /TDF-3TC-DTG-DRV/r	50 (48)
TDF-3TC-EFV	15 (15)
TDF-3TC-LPV/r	3 (3)
TDF-3TC-ATV/r	3 (3)
TDF-3TC-DRV/r	1 (1)
TDF-3TC-DRV-RAL/r	1 (1)
AZT-3TC-LPV/r	11 (11)
AZT-3TC-ATV/r	9 (9)
AZT-3TC-EFV	1 (1)
ABC-3TC-ATV/r	4 (4)
ABC-3TC-EFV	2 (2)
ABC-3TC-LPV/r	3 (3)

3TC: lamivudine; AZT: zidovudine; ABC: abacavir, TDF: tenofovir disoproxil fumarate; ATV/r: Atazanavir/ritonavir; LPV/R: Lopinavir/ritonavir; DRV/r: Darunavir/ritonavir; EFV: Efavirence; DTG: Dolutegravir. *: First detection of HIV, without treatment.



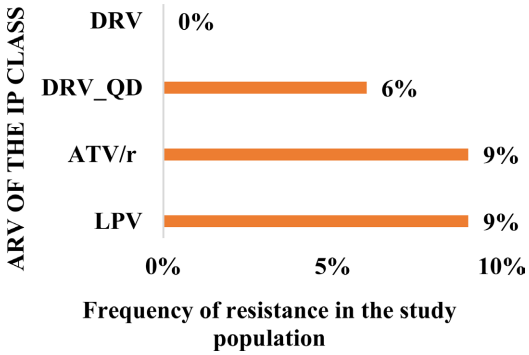
TDF: tenofovir disoproxil fumarate, TAF: tenofovir alafenamide; AZT: zidovudine; ABC: abacavir; ISL: Islatravir FTC: emtricitabine; 3TC: lamivudine.

Figure 1. Frequency of NRTI resistance in the study population.



ETR: Etravirine; RPV: Rilvipirine; DOR: Doravirine; NVP: Nevirapine EFV: Efavirence.

Figure 2. Frequency of NNRTI resistance in the study population.

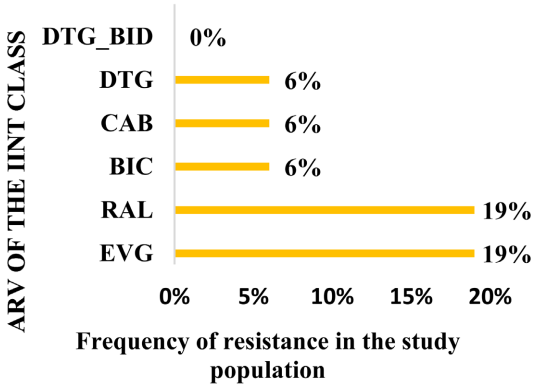


DRV: Darunavir; DRV_QD: Darunavir (Double dose) ATV/r: Atazanavir/ritonavir; LPV: Lopinavir.

Figure 3. Frequency of NNRTI resistance in the study population.

3.4. Distribution of Resistance Mutations in Reverse Transcriptase, Protease and Integrase Genes

Analysis of the 11 reverse transcriptase sequences identified 25 substitutions, 84% (21/25) of which were major NRTI mutations and 16% (4/25) minor mutations.



DTG_BID: Dolutegravir double dose; DTG: Dolutegravir; CAB: Cabotegravir; BIC: Bictegravir; RAL: Raltegravir; EVG: Elvitegravir.

Figure 4. Frequency of PI resistance in the study population.

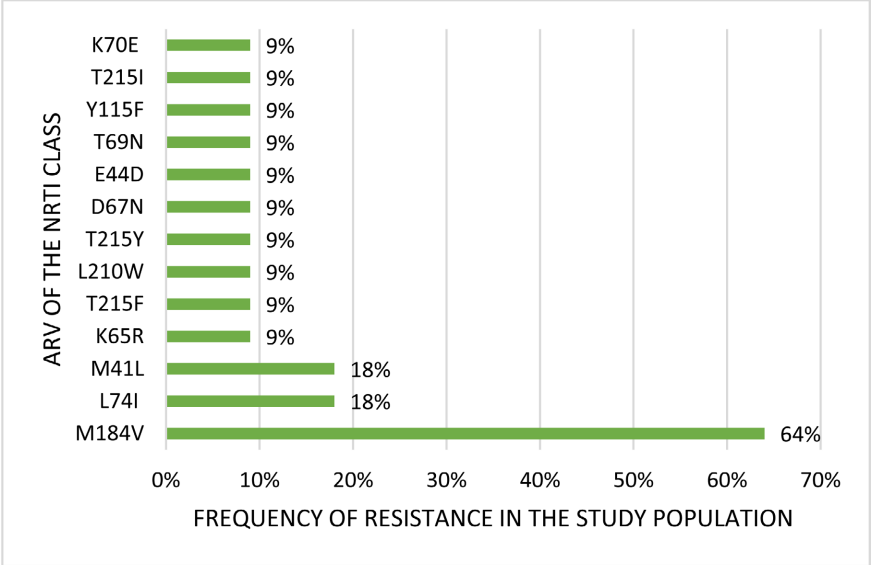


Figure 5. Major mutations in HIV-1 resistance to NRTIs and their frequency of occurrence in the study population.

The most frequently observed major mutation in HIV-1 resistance to NRTIs was the substitution of a methionine at position 184 by a valine (M184V), with a frequency of occurrence of 64% (7/11). The minor mutation frequently associated with NRTI resistance was the substitution of Aspartic Acid at position 67 by Asparagine (D67N), with a frequency of 18% (2/11) (Figure 5).

Analysis of the 11 reverse transcriptase sequences identified 23 substitutions, of which 65% (15/23) were major HIV-1 NNRTI mutations and 35% (8/23) were minor mutations.

The major NNRTI resistance mutation frequently observed was the substitution of a Lysine at position 103 by an Asparagine (K103N), with a frequency of 45% (5/11).

Minor mutations frequently associated with HIV-1 resistance to NNRTIs were the substitution of a Valine in position 90 by an Isoleucine (V90I) and the subs-

titution of an Alanine in position 98 by a Glycine (A98G), with a frequency of 18% (2/11) for each mutation (Figure 6).

Analysis of the 64 HIV-1 protease sequences identified 56 substitutions, of which 80% (45/56) were major mutations and 20% (11/56) minor mutations.

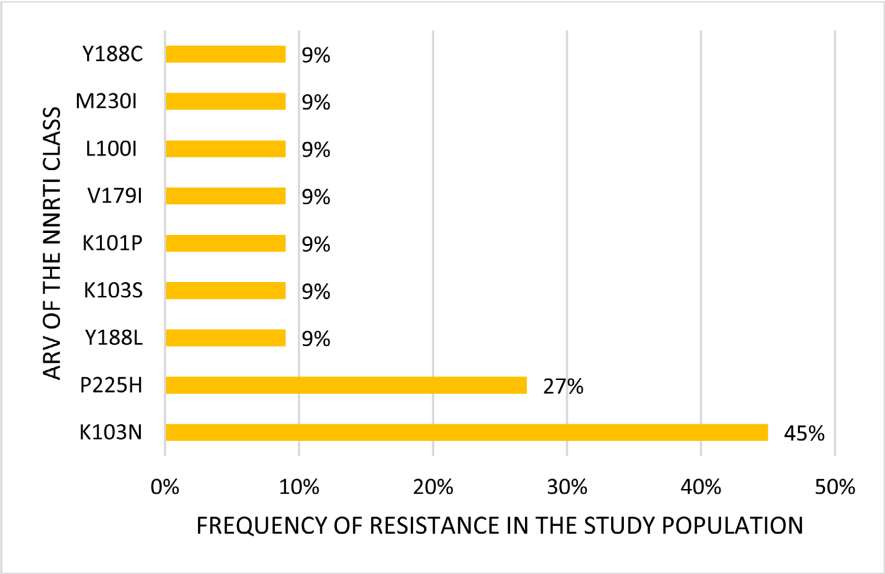


Figure 6. Major mutations in HIV-1 resistance to NNRTIs and their frequency of occurrence in the population studied.

04 major mutations were frequently observed, each conferring 6% (4/64) resistance to PIs: these were the substitution of a Leucine in position 10 by a Valine (L10V), the substitution of a Methionine in position 46 by an Isoleucine (M46I), the substitution of an Alanine in position 71 by a Valine (A71V) and the substitution of an Isoleucine in position 54 by a Valine (I54V). The minor mutation frequently associated with PI resistance was the substitution of an Isoleucine at position 84 by a Valine (I84V) (Figure 7).

Analysis of the 16 integrase sequences identified 15 substitutions, of which 40% (6/15) were major mutations and 60% (9/15) minor mutations.

The most frequently observed major mutation conferring IINT resistance was the substitution of glutamic acid at position 157 by glutamine (E157Q), with a frequency of 19% (3/16). The minor mutation frequently associated with IINT resistance was the substitution of leucine at position 74 by isoleucine (L74I), with a frequency of 25% (4/16) (Figure 8).

4. Discussion

Our study evaluated HIV-1 resistance to ARVs in infected adults in Côte d'Ivoire in the context of a systematic switch to a dolutegravir-based combination. The NNRTI resistance rate was 82%. This rate is lower than that of Kouamou and colleagues, who conducted a study in Zimbabwe in 2019 on resistance to ARVs after optimising treatment regimens with dolutegravir and found a prevalence of

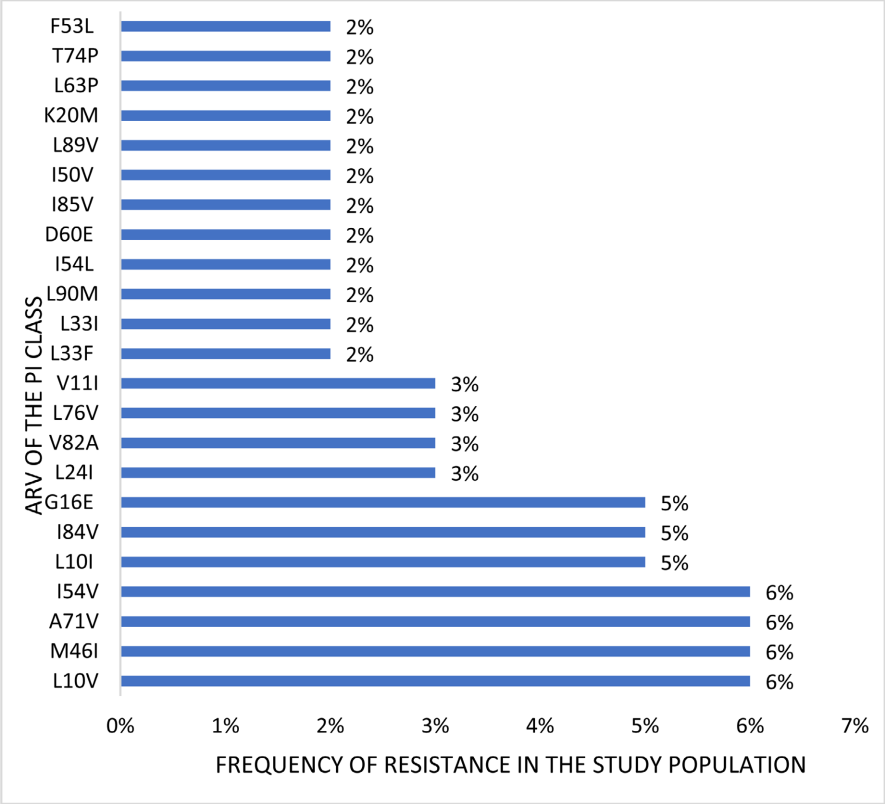


Figure 7. Major mutations in HIV-1 resistance to PIs and their frequency of occurrence in the study population.

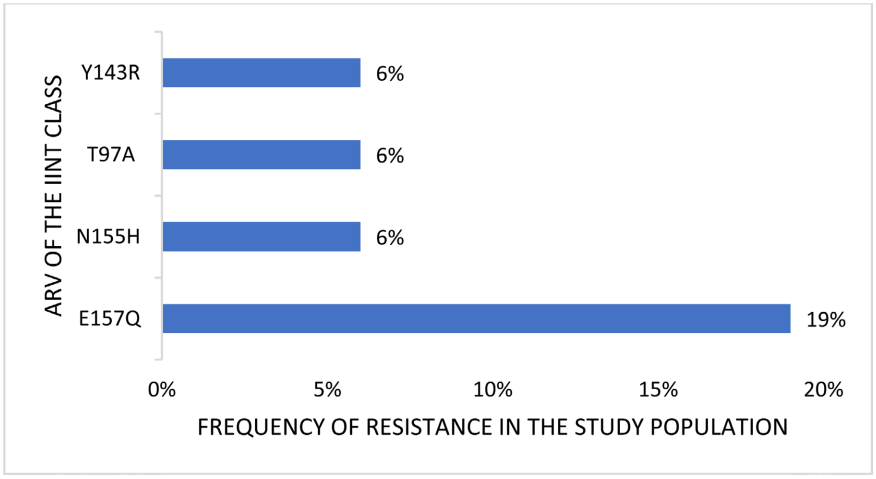


Figure 8. Major mutations in HIV-1 resistance to IINTs and their frequencies of occurrence in the population studied.

85%. The difference observed could be explained by the large size of the Kouamou sample [5]. Other studies carried out in Gabon in 2022 by Bivigou-Mboumba and colleagues [6] and in Ghana in 2023 by Appah and colleagues [7] revealed lower prevalences of 71.7% and 12% respectively; the high rate of HIV-1 resistance to NNRTIs observed in our study is probably due to the prolonged exposure of our participants to this class of ARVs before switching to TLD. The median duration

of antiretroviral treatment (interquartile range) was 5 (1 - 19) years.

The most frequently observed NNRTI resistance mutation was K103N with a frequency of 45%. This prevalence is lower than that obtained by Bivigou-Mboumba, who obtained a frequency of 68.9% [6]. These high prevalences of this resistance mutation could explain the high resistance of HIV-1 to NNRTIs [8].

The NRTI resistance rate was 73%. This rate is lower than that of Fily and colleagues in 2018 in Uganda, who found a prevalence of 82.8%. The difference observed could be explained by the fact that participants in Fily's study were mainly patients who had failed second-line treatment and had therefore been exposed to NRTIs for a long time [9]. However, other studies have shown lower prevalences of HIV-1 resistance to NRTIs. In Côte d'Ivoire, Dechi and colleagues conducted a study in 2022 on HIV-1 resistance to nucleoside reverse transcriptase inhibitors in children and adults in the context of a systematic switch to a dolutegravir-based combination, and found a rate of 65% [4]; the study by Salou and colleagues in Togo in 2020 revealed an NRTI resistance rate of 2.2%; the difference observed could be explained by the accumulation of mutations predicting resistance to NRTIs in many of Salou's viral strains [10].

The most frequently observed NRTI resistance mutations were M184V, L74I and M41L. These mutations were identified by Maena and colleagues in their study of the determinants of viral load non-reduction in adolescents in Mbale district, eastern Uganda [11], and by Koay and colleagues in their study of HIV drug resistance in children and adolescents [12]. The high prevalence of HIV-1 resistance mutations to NRTIs could explain the virological failures of PLHIV-1 on regimens consisting of 2 NRTIs + 1 NNRTI, and would probably be responsible for the functional monotherapy of dolutegravir-based regimens.

The rate of resistance to PI was 11%. This rate is lower than those of Oluniyi and colleagues in 2022 in Nigeria [13] and Musengimana and colleagues in 2022 in Rwanda [14], who found prevalences of 6.1% and 3.5% respectively. HIV-1 resistance rates to PIs are generally low because PIs are mainly used in patients who have failed first-line treatment; they are therefore more robust to resistance. Major mutations were frequently observed, each conferring 6% (4/64) of PI resistance: these were L10V, M46I, A71V and I54V.

The percentage of participants with at least one IINT resistance mutation was 19% (3/16). This rate is higher than that of Bwire in 2023, whose study aimed to detect dolutegravir resistance and associated mutations in Tanzanian adults living with HIV-1 in Dar es Salaam. The investigators found that 10.08% of PLWH-1 had major IINT resistance mutations [15]. This difference could be related to the use of different lists of resistance mutations, as we take into account some integrase gene mutations that may be considered as polymorphisms by other interpretation algorithms.

The frequency of resistance to BIC, CAB and DTG was 6% for each molecule, and 19% for EVG and RAL. Anne-Geneviève Marcelin and colleagues also found that the frequency of resistance to 2nd-generation IINTs was lower than that of 1st-generation IINTs in their study of integrase inhibitor resistance in ARV-naive

and ARV-treated patients [16].

The E157Q mutation was at the origin of resistance to first-generation IINT and could not be the sole cause of resistance to second-generation IINT [16]. The resistance pathways identified in the present study for second-generation IINT were associated with the E157Q, N155H, T97A, Y143R and L74I mutations. These results corroborate those of Marcelin and colleagues, who also found E157Q, N155H, T97A and L74I mutations in cases of resistance to second-generation IINT. No resistance to DTG_BID has been reported, as confirmed by several studies showing that twice-daily dolutegravir-based regimens give better results than once-daily dolutegravir-based regimens [17] [18].

5. Conclusions

This study revealed HIV-1 resistance mutations in all ARV classes tested, with high rates of resistance to NRTIs, which could explain functional monotherapy in cases of virological failure of dolutegravir-based treatments. In fact, a low prevalence of PLWH-1 had resistance mutations to 2nd-generation integrase inhibitors, including dolutegravir, proving the high genetic barrier to resistance of this class of ARVs.

Routine switching to TLD may therefore put the new therapeutic regimen at risk when NRTI resistance mutations go undiagnosed. Despite its efficacy, the emergence of resistance to dolutegravir means that efforts to monitor viral load and sequencing of strains before treatment, to guide the choice of NRTIs. In addition, monitoring of resistance mutations to identified 2nd-generation INTIs is essential, as the introduction and intensification of dolutegravir-based regimens is underway in Côte d'Ivoire.

6. Limits

The sequencing method used in this work to determine HIV-1 ARV resistance mutations is the Sanger method. Although this is a reference method, the results of this research would have provided more information if new-generation sequencing methods had been used.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] ONUSIDA (2023) Fiche d'information. Dernières statistiques sur l'état de l'épidémie

de sida. https://www.unaids.org/fr/resources/fact-sheet

[2] WHO (2021) HIV Drug Resistance Report. https://www.who.int/publications-detail-redirect/9789240038608

[3] WHO (2016) World Health Organization: Consolidated guidelines. Genève. https://scholar.google.com/scholar_lookup?title=Consolidated+guidelines+on+the+use+of+antiretroviral+drugs+for+treating+and+preventing+HIV+infection.+Recommendations+for+a+public+health+approach+-+Second+edition.+2nd+ed&publication_year=2018&

[4] Dechi, J.J.R., Toni, T.D., Cisse-Camara, M., Philippe, N.J.L., Ake, A.J.A., Siransy, K.L., *et al.* (2022) Nucleoside Reverse Transcriptase Inhibitors Resistance in Children and Adults with Virological Failure in a Context of Systematic Switching to a Dolutegravir-Based Combination. *Biochemistry and Molecular Biology*, **7**, 70-74.

[5] Kouamou, V., Manasa, J., Katzenstein, D., McGregor, A.M., Ndhlovu, C.E. and Makadzange, A.T. (2019) Drug Resistance and Optimizing Dolutegravir Regimens for Adolescents and Young Adults Failing Antiretroviral Therapy. *AIDS*, **33**, 1729-1737. https://doi.org/10.1097/QAD.0000000000002284

[6] Bivigou-Mboumba, B., Iroungou, B.A., Moussavou-Boundzanga, P., Mangouka, L.G., Akombi, F.L., Bouassa-Bouassa, A., Francois-Souquière, S. and Nzenze, J.R. (2022) HIV Genetic Diversity, Virological Failure, and Drug Resistance in Libreville, Capital of Gabon, before a Total Dolutegravir-Based Regimen Transition. *World Journal of AIDS*, **12**, 156-168. https://doi.org/10.4236/wja.2022.123012

[7] Appah, A., Beelen, C.J., Kirkby, D., Dong, W., Shahid, A., Foley, B., Mensah, M., Ganu, V., Puplampu, P., Amoah, L.E., *et al.* (2023) Molecular Epidemiology of HIV-1 in Ghana: Subtype Distribution, Drug Resistance and Coreceptor Usage. *Viruses*, **15**, 128. https://doi.org/10.3390/v15010128

[8] Clutter, D.S., Jordan, M.R., Bertagnolio, S. and Shafer, R.W. (2016) HIV-1 Drug Resistance and Resistance Testing. *Infection, Genetics and Evolution*, **46**, 292-307. https://doi.org/10.1016/j.meegid.2016.08.031

[9] Fily, F., Ayikobua, E., Ssemwanga, D., Nicholas, S., Kaleebu, P., Delaugerre, C., Pasquier, E., Amoros Quiles, I., Balkan, S. and Schramm, B. (2018) HIV-1 Drug Resistance Testing at Second-Line Regimen Failure in Arua, Uganda: Avoiding Unnecessary Switch to an Empiric Third-Line. *Tropical Medicine & International Health*, **23**, 1075-1083. https://doi.org/10.1111/tmi.13131

[10] Salou, M., Butel, C., Comlan, A.S., Konou, A.A., Tegueni, K., Ehlan, A., Lack, F., Dossim, S., Ayouba, A., Delaporte, E., Dagnra, A.Y. and Peeters, M. (2020) Challenges of Scale-Up to Dolutegravir-Based Regimens in Sub-Saharan Africa. *AIDS*, **34**, 783-787. https://doi.org/10.1097/QAD.0000000000002470

[11] Maena, J., Banke-Thomas, A., Mukiza, N., Kuteesa, C.N., Kakumba, R.M., Kataike, H., *et al.* (2021) Determinants of Viral Load Non-Suppression among Adolescents in Mbale District, Eastern Rural Uganda. *AIDS Research and Therapy*, **18**, Article No. 91. https://doi.org/10.1186/s12981-021-00408-1

[12] Koay, W.L.A., Kose-Otieno, J. and Rakhmanina, N. (2021) HIV Drug Resistance in Children and Adolescents: Always a Challenge? *Current Epidemiology Reports*, **8**, 97-107. https://doi.org/10.1007/s40471-021-00268-3

[13] Oluniyi, P.E., Ajogbasile, F.V., Zhou, S., Fred-Akintunwa, I., Polyak, C.S., Ake, J.A., Tovanabutra, S., Iroezindu, M., Rolland, M. and Happi, C.T. (2022) HIV-1 Drug Resistance and Genetic Diversity in a Cohort of People with HIV-1 in Nigeria. *AIDS*, **36**, 137-146. https://doi.org/10.1097/QAD.0000000000003098

[14] Musengimana, G., Tuyishime, E., Kiromera, A., Malamba, S.S., Mulindabigwi, A.,

Habimana, M.R., Baribwira, C., Ribakare, M., Habimana, S.D., DeVos, J., Mwesigwa, R.C.N., Kayirangwa, E., Semuhore, J.M., Rwibasira, G.N., Suthar, A.B. and Remera, E. (2022) Acquired HIV Drug Resistance among Adults Living with HIV Receiving First-Line Antiretroviral Therapy in Rwanda: A Cross-Sectional Nationally Representative Survey. *Antiviral Therapy*, **27**. https://doi.org/10.1177/13596535221102690

[15] Bwire, G.M., Aiko, B.G., Mosha, I.H., Kilapilo, M.S., Mangara, A., Kazonda, P., *et al.* (2023) High Viral Suppression and Detection of Dolutegravir-Resistance Associated Mutations in Treatment-Experienced Tanzanian Adults Living with HIV-1 in Dar es Salaam. *Scientific Reports*, **13**, Article No. 20493. https://doi.org/10.1038/s41598-023-47795-1

[16] Marcelin, A.G., Grude, M., Charpentier, C., Bellecave, P., Le Guen, L., Pallier, C., *et al.* (2019) Resistance to Integrase Inhibitors: A National Study in HIV-1-Infected Treatment-Naive and -Experienced Patients. *Journal of Antimicrobial Chemotherapy*, **74**, 1368-1375. https://doi.org/10.1093/jac/dkz021

[17] Hocqueloux, L., Raffi, F., Prazuck, T., Bernard, L., Sunder, S., Esnault, J.L., *et al.* (2019) Dolutegravir Monotherapy versus Dolutegravir/Abacavir/Lamivudine for Virologically Suppressed People Living with Chronic Human Immunodeficiency Virus Infection: The Randomized Noninferiority MONotherapy of TiviCAY Trial. *Clinical Infectious Diseases*, **69**, 1498-1505. https://doi.org/10.1093/cid/ciy1132

[18] Blanco, J.L., Rojas, J., Paredes, R., Negredo, E., Mallolas, J., Casadella, M., *et al.* (2018) Dolutegravir-Based Maintenance Monotherapy versus Dual Therapy with Lamivudine: A Planned 24 Weeks Analysis of the DOLAM Randomized Clinical Trial. *Journal of Antimicrobial Chemotherapy*, **73**, 1965-1971. https://doi.org/10.1093/jac/dky093