BMC Infectious Diseases

https://doi.org/10.1186/s12879-026-13013-2

Article in Press

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Received: 5 December 2025

Accepted: 2 March 2026

Published online: 09 March 2026

Cite this article as: Tadenfok C., Fokam J., Semengue E.N.J. *et al.* Efficacy of dolutegravir-based therapy in achieving virological suppression in PLHIV in low- and middle-income countries: real-world evidence from a large clinical cohort in Cameroon. *BMC Infect Dis* (2026). https://doi.org/10.1186/s12879-026-13013-2

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Efficacy of Dolutegravir-Based Therapy in Achieving Virological Suppression in PLHIV in Low- and Middle-Income Countries: Real-World Evidence from a Large Clinical Cohort in Cameroon

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ABSTRACT (350/350)

BACKGROUND:

HIV treatment has significantly improved with the introduction of potent antiretroviral therapy (ART), particularly dolutegravir (DTG)-based regimens. With suboptimal adherence reported in resource-limited settings (RLS), real-word evidence on DTG-effectiveness within ART clinics is limited. This study assessed virological response, drug resistance profiling and HIV-1 diversity among ART recipients at the Yaoundé Central Hospital (YCH), Cameroon.

METHODS:

A facility-based study was conducted at YCH from May-2023 to February-2025. HIV plasma viral load (PVL) was measured by RT-PCR. Viral suppression (VS) was defined as PVL<1,000copies/mL. Genotypic resistance testing (GRT) was performed for participants with PVL≥1,000copies/mL. Drug resistance mutations (DRMs) were interpreted using Stanford HIVdb v9.8 and statistics were performed with significance at $p<0.05$.

RESULTS:

Among 6,364 participants enrolled (median-age: 50 [IQR:42–59] years; 71% women), 76% (4,811/6364) were on DTG-based regimens. Median ART-duration was 13 [IQR:9.03–17.4] years, including 3.4 [IQR:3–5] years of DTG-exposure in the DTG-based sub-group. Overall, 93.2% (5,932/6,364) participants achieved VS in 2025; 94% among DTG-based versus 91% among DTG-sparing regimens (OR=1.66; p=0.000002). Interestingly, VS was higher with age ≥50years (aOR=1.44; p<0.001), DTG-based ART (aOR=1.65; p<0.0001) and DTG-exposure ≥3.4years (aOR=1.29; p=0.044). Between 2021-2025 specifically, VS remained consistently high among participants; with those on DTG-based showing significantly higher and more durable VS compared to those on DTG-sparing therapies (relative risk of failure >1 for DTG-sparing throughout). Furthermore, from those virally unsuppressed in 2025, 9% (39/432) were lost-to-follow-up, 22% (94/432) were transfer-out to other health facilities and 65% (232/432) re-suppressed after enhanced adherence counselling; leaving us with 17 participants eligible for GRT (PVL≥1000copies/mL). GRT was successful for 70.5% (12/17) and DRMs detected in 83% (10/12), including major DRMs to protease inhibitors (17%), to nucleoside reverse transcriptase inhibitors (75%) and to non-nucleoside reverse transcriptase inhibitors (83%). CRF02_AG (75%) was the prevailing HIV-1 group M clade, followed by A3, D, and CRF18_cpx (each 8.3%).

CONCLUSION:
These real-life data reveal viral suppression rates closer to the epidemic control (95%) among DTG-based recipients, especially with older age and DTG-exposure over three years. Considering the broad HIV diversity observed, these findings are essential for modelling the long-term effectiveness of DTG in RLS and beyond.

Study registration: Register on 10/05/2023; **Ethical Clearance Number** 2023/022045/CEIRSH/ESS/BC

Keywords: Dolutegravir; HIV Epidemic Control; Low-middle income countries; Cameroon.

1. BACKGROUND

Human Immunodeficiency Virus (HIV) remains a major global public health challenge, particularly in sub-Saharan Africa, where the epidemic continues to exert substantial pressure on already fragile healthcare systems [1]. In Cameroon, HIV prevalence remains high, and a large proportion of individuals require antiretroviral therapy (ART) to achieve and maintain viral suppression [2,3]. Recent advances in ART have led to the development of more effective regimens, among which dolutegravir (DTG) has emerged as a preferred first-line option due to its high efficacy, favorable safety profile, and robust genetic barrier to resistance [2, 4]. Despite these therapeutic improvements, ongoing viral replication can select for drug-resistance mutations, contributing to the extensive genetic diversity of HIV-1 [5,6]. This diversity encompasses multiple pure subtypes and circulating recombinant forms (CRFs), which influence treatment outcomes and complicate clinical management [6,7].

The Yaoundé Central Hospital, one of the largest HIV treatment centers in Cameroon, has been at the forefront of national ART delivery, providing care to thousands of patients annually [8]. Since the adoption of the “Test and Treat’’ strategy in 2015, ART coverage has steadily increased, reaching 448,818 individuals on treatment in 2024 [9]. However, the widespread use of regimens with lower genetic barriers, coupled with variable adherence, has contributed to the emergence of antiretroviral drug resistance (HIVDR) [10]. These mutations affecting key viral enzymes such as reverse transcriptase, protease, and integrase can impair drug efficacy, drive virological failure, and accelerate disease progression if therapeutic adjustments are not implemented [11,12]. Resistance patterns vary across ART drug classes and HIV-1 subtypes, reflecting the virus’s high mutation rate, recombination frequency, and rapid replication dynamics [7,12,13]. HIV-1 genetic variability also influences viral transmissibility, pathogenicity, and susceptibility to antiretroviral drugs [5]. With growing concerns over HIVDR especially to NNRTIs many countries have transitioned from efavirenz/nevirapine-based regimens to DTG-based combinations [14]. DTG remains highly effective in both ART-naïve and treatment-experienced individuals, and its high genetic barrier minimizes the likelihood of clinically significant resistance [15,16]. As DTG continues to be scaled up in low- and middle-income countries (LMICs), it is critical to assess real-world virological outcomes, resistance patterns, and viral diversity to guide national HIV treatment strategies [15–17]. Furthermore, WHO highlights the importance of routine HIVDR surveillance both transmitted and acquired to optimize ART programming in resource-limited settings (RLS) [5,6,18,19]. Understanding local patterns of HIV-1 clades and resistance mutations remains essential for improving clinical management and informing public health policies [20,21].

The present study evaluates virological response, HIVDR profiles, and HIV-1 genetic diversity among ART recipients at the Yaoundé Central Hospital. Through analysis of viral suppression, treatment adherence, and factors associated with therapeutic outcomes, this work provides

critical real-world evidence on the effectiveness of DTG-based regimens in a resource-limited context such as Cameroon.

2. METHODS

2.1 Study design and settings

This was a longitudinal study conducted from the 15/05/2023 to 28/02/2025 among ART-experienced participants followed at YCH-Cameroon from 2020 to 2025. The enrollment of participants was done at the Care Unit for People Living with HIV, located within the hospital; this is the main center hosting the largest cohort of people living with HIV nationwide. The YCH is a government institution of the Ministry of public Health, dedicated to provide high-quality medical care, promote public health in Cameroon. As a major referral hospital, it aims to offer specialized healthcare services, improve patient outcomes, and support the development of the country's healthcare system. Additionally, the hospital plays a crucial role in training healthcare professionals and conducting medical research to address public health challenges [22].

2.2 Characteristics of Participants

All participants receiving their ART at the YCH were eligible for inclusion. The enrollment of participants and data collection follow a structured process. All participants were identified through hospital registers and consultation records, ensuring that they meet the inclusion criteria (People living with HIV; of all ages; followed at the YCH; receiving ART for more than six months; with an updated medical record). Once identified, they were enrolled during hospital visits, and those who agreed to participate provided a written informed consent. Following enrolment, baseline data were collected, in the registers and soft databases. Collected data included, demographic information (such as age, gender, and residence), clinical history (such as ART initiation and regimen history), and adherence-related information.

A 5mL blood sample was then collected in an EDTA tube for plasma viral load (PVL) quantification at the hospital’s laboratory. Subsequently, participants with a PVL ≥1000 copies/mL were scheduled for enhanced adherence counseling and follow-up testing over a period of one to three months. During this follow-up, an additional blood sample was taken to assess virological response, and patients with persistent PVL≥1000 copies/mL underwent HIV genotypic resistance testing (GRT) at a reference laboratory

2.3Viral Load Measurement

Plasma Viral load (PVL) measurement at YCH was performed by using the Biocentric HIV platform, according to the manufacturer’s instructions. RNA extraction was done using the GenoXtract extraction kit form Bruker Life sciences (https://www.bruker.com/en/products-and-solutions/molecular-diagnostics/diagnostic-instruments/genoxtract.html). A protocol utilizing 250µL of plasma was employed for RNA extraction, followed by simultaneous amplification and detection using real-time polymerase chain reaction (RT-PCR). The assay's detection range spanned from >390 to <5,000,000 HIV-1 RNA copies/mL. For PVL<390 copies/ml, further confirmatory analyses were conducted in a reference laboratory with a lower limit of detection

(<40 copies/ml). Viral suppression (VS) was defined as a PVL <1,000 copies/mL, virological failure as PVL ≥1,000 copies/mL, and virological control PVL<50 copies/ml in accordance with WHO guidelines for RLS [23]. Importantly, routine clinical adherence assessment was conducted among patients experiencing virological failure and was therefore not systematically available for the entire cohort.

2.4 Genotypic Resistance Test

Genotypic resistance testing was conducted on the *pol* gene (reverse transcriptase and protease regions only) using the in-house protocol [24]. Briefly, viral RNA was extracted from 1 mL of plasma with the QIAGEN kit (cat number and manufacturer address), following the manufacturer's instructions. The target sequence was amplified through Reverse Transcription PCR with BS ("5′-GAC AGG ATT ATT TTT TAG GG-3′") and FRA S1 ("5′-TT CCC CAT ATT ACT ATG CTT-3′") primers in a 25µL reaction mixture for 40 cycles. A semi-nested PCR was then performed using BS ("5′-GAC AGG ATT ATT TTT TAG GG-3′") and TAK3 ("5'-GGC TCT TGA TAA TGA TAT TAT GT-3′") primers in a 50µL reaction mixture for 30 cycles. The PCR products were visualized using 1% agarose gel electrophoresis. Successfully amplified samples were purified and sequenced using the following primers: B ("5′-AGC AGA CCA GAG CCA ACA GC-3′"), F ("5′-CCA TCC ATT CCT GGC TTT AAT-3′"), SEQ1 ("5′-GAA TGG ATG GCC CAA AA-3′"), SEQ2 ("5′-TTG AGA TAC AAT GGA AAA GGA AGG-3′"), SEQ3 ("5′-CCC TGT GGA AAG CAC ATT GTA-3′"), SEQ4 ("5′-GCT TCC ACA GGG ATG GAA-3′"), SEQ5 ("5′-CTA TTA AGT CTT TTG ATG GGT CA-3′"), and TAK3 ("5′-CCT TGT TTC TGT ATT TCT GCT-3′"). The sequencing reaction products were purified via size-exclusion chromatography by SEPHADEX G50 resin and subsequently analyzed with a genetic analyzer (ABI 3500).

2.5 Sequence Analysis for HIVDR Profiling, Subtyping and Drug efficacy

Generated sequences were assembled and manually edited using Recall version 2.28. Drug resistance mutations (DRMs) were analyzed using the Stanford HIVdb software v9.8 (http://www.hivdb.stanford.edu, accessed on 05 Jan 2025), allowing for the identification of all resistance-associated mutations in the samples. The predictive efficacy of each antiretroviral drug was assessed based on the genotypic drug susceptibility score provided by the HIVdb algorithm (http://www.hivdb.stanford.edu, accessed on 05 Jan 2025). Resistance interpretation was based on the Stanford HIV Drug Resistance Database (HIVdb) penalty score system as follows: 0–9, susceptible; 10–14, potential low-level resistance; 15–29, low-level resistance; 30–59, intermediate resistance; ≥60, high-level resistance.

[25]. Subtyping was performed using rapid subtyping tools, including COMET, REGA, with molecular phylogeny used for subtype confirmation. Sequence alignment and cleaning were

conducted using Bio edit version 7.2, while phylogenetic tree inference was performed using the maximum likelihood method in MEGA 11.

2.6 Data collection, entry and statistical analysis

Patient information was obtained from both electronic and physical records maintained at the hospital. In particular, data on patients' past and current treatment histories were gathered. Importantly, we retrospectively assessed YCH database from 2021 to evaluate the influence ART-switch may have had on current' (2025) treatment outcomes. Data were entered and analyzed using Epi Info v7.2.2.6. Categorical variables were summarized using frequencies and percentages. To compare proportions of qualitative variables, the Chi-squared test was applied, as appropriate. All values were reported with their 95% confidence intervals, and statistical significance was set at 5% ($p<0.05$). For multivariate analysis, logistic regression was performed to adjust for potential confounders such as age, sex. Variables with a p-value < 0.2 in the bivariate analysis were included in the final model.

3. RESULTS

3.1 General Characteristics of Study Population

3.1.1 Sociodemographic characteristics

A total of 6,364 HIV-positive patients receiving antiretroviral treatment were enrolled in the study, of whom 71% (4537/6364) were women. The median age of participants was 50 [42-59] years. The majority of participants, 89% (5667/6364), resided in urban area (Table 1). In 2021, 2948 participants were under DTG-based regimens versus 4811 in 2025. Median ART-duration was 13 [IQR:9.03–17.4] years, including 3.4 [IQR:3–5] years of DTG-exposure in the DTG-based sub-group, and 13 [IQR:9.03–17.4] years of DTG-sparing in the DTG sparing subgroup. Notably, the study population counted 11 (0.17%) female sex workers (FSW); one (0.02%) homosexual man (MSM); nine (0.14%) pregnant women and 78 (1.2%) breastfeeding women. Figure1 give a breakdown of participants' enrollment and evolution in the cohort in 2025.

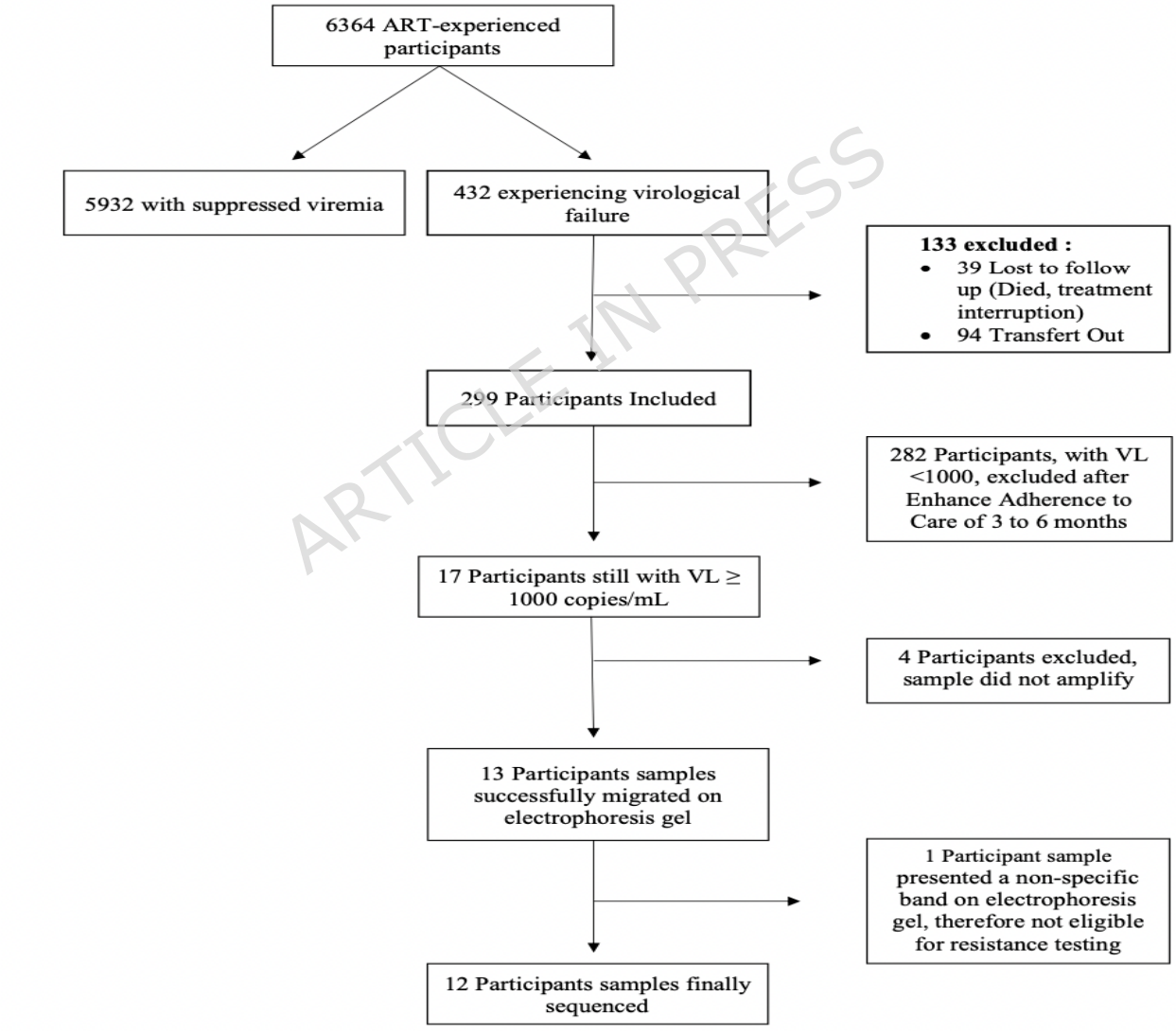

Figure 1. Flow chart of patients' enrollment and follow-up in the study population in 2025.

3.1.2 Description of ART History

In 2021, 46.3% (2948/6364) patients were on DTG-based treatment protocol such as: TDF+3TC+DTG, DRV/r+DTG+TDF+3TC, TDF+3TC+DTG+ATV/r. The rest of patients, 53.7% (3416/6364) were on non DTG-sparing regimens: TDF+3TC+EFV, TDF+FTC+ATV/r, TDF+3TC+ATV/r, TDF+3TC+LPV/r, AZT+3TC+ATV/r, AZT+3TC+LPV/r, ABC+3TC+ATV/r, ABC+3TC+EFV, ABC+3TC+LPV/r, DRV/r+TDF+3TC.

The majority of patients in 2025, 75.6% (4811/6364) were on DTG-based treatment such as: TDF+3TC+DTG, TDF+3TC+DTG + ATV/r, DRV/r + DTG + TDF/3TC, TLD+DRV+RTV and ABC+3TC+DTG. The rest of participants, 24.4% (1553/6364) were on others treatment protocol such as, ABC+3TC+ATV/r, AZT+3TC+ATV/r, DRV/r+TDF+3TC, TDF+3TC+EFV, TDF+3TC+ATV/r, TDF+FTC+EFV, See table 1 bellow.

Table 1: Baseline characteristics of study participants

Characteritics	**Overall/Average N= 6364**	**Percentages/median**
Male, n (%)	1827	28.7%
Female, n (%)	4537	71%
Age, median yrs (IQR)	48.66 ± 11.91	50 [42-59]
Age at enrollment	38.42 ± 11.13	37 [30-46]
Others socio-demographic factors		
Exclusively breastfeeding	78	1.2%
Pregnant	9	0.14%
MSM	1	0.02%
FSW	11	0.17%
DTG-based treatment	**Number**	**Proportion**
TDF+3TC+DTG	4785	75.2%
TDF+3TC+DTG + ATV/r	3	0.05%
DRV/r+DTG+TDF/3TC	11	0.17%
ABC+3TC+DTG	11	0.2%
DTG-sparing treatment	**Number**	**Proportion(%)**
ABC+3TC+ATV/r	162	2.6%
AZT+3TC+ATV/r	97	1.6%
DRV/r+TDF+3TC	1	0.02%
TDF+3TC+EFV	635	10%

TDF+3TC+ATV/r	643	10.1%
TDF+FTC+EFV	14	0.2%

3.2 Virological Response

Viral load assessment in 2021 showed that 94% (2,775/2,948) of individuals on DTG-based regimens were virologically suppressed, compared with 92.4% (3,157/3,415) among those on DTG-sparing regimens. At the 2025 assessment, the overall rate of VS was 93.2% (5,932/6,364), 94% (4,526/4,811) of participants receiving DTG-based regimens were virologically suppressed, compared with 90.5% (1,406/1,553) among those on DTG-sparing regimens (see Table 2). As regarding specific population in 2025, all FSW (11/11), MSM (1/1) and pregnant women (9/9) achieved VS whereas only 91% (71/78) of breastfeeding women achieved VS.

3.2.1 Factors associated to Virological Response.

Based on bivariate analysis, gender was not found to be associated with VS in this study. On the other hand, older age ≥ 50 years, inclusion of DTG in the regimen for treatment, treatment duration on DTG were found to be associated with VS, and these were all confirmed in multivariate analysis (see tables 2 and 3).

Table 2: Evaluation of sociodemographic factors potentially associated with viral suppression

Variable	**Viral Suppression**		**Odd ratio [IC=95%] (p-Value)**
Age	**Yes**	**No**	
≥ 50	3062	176	**1.55 [1.27-1.89] (0.00001)**
<50	2870	256	
Sex			
Female	4228	309	0.99 [0.79-1.22] (0.95)
Male	1704	123	
Treatment type (In 2025)			
DTG-based	4526	285	**1.66[1.35-2.04] (0.000002)**
DTG-sparing	1704	147	
Duration on any treatment (years)			
<13	2960	254	0.725 [0.51-1.02] (0.079)
≥ 13	2972	178	
Duration on DTG-sparing treatment (years)			
<13	691	84	1.3796 [0.9791-1.9441] (0.079)
≥ 13	715	63	

Duration on DTG-based treatment (years)			
<3.4	2198	161	**1.336 [1.051-1.699]**
≥ 3.4	2328	124	**(0.0 1)**

Table 3: Adjusted Odds Ratios for Predictors of Viral Suppression

Variables		aOR (95% CI)	P-value
Age	(≥ 50 /<50)	1.44 (1.18-1.77)	**0.0004**
Gender	(Male/Female)	0.92 (0.70-1.2)	0.5235
DTG-based	(Yes/No)	1.65 (1.34-2.03)	**0.0000**
Treatment duration	(≥ 13/<13)	1.33 (1.08-1.63)	**0.0057**
Duration DTG-based **Duration DTG-sparing**	(≥ 3.4/<3.4) (≥ 13/<13)	1.29 (1.01-1.65) 1.32 (0.95-1.87)	**0.0443** 0.1132

3.2.2 Virologic outcomes over time: Comparative Suppression and failure rates for DTG-based vs DTG-sparing (2021-2025)

From our database, a total of 2,415 patients with complete virological data between 2021 and 2025 were included in this sub-analysis. In 2021, 2,373 (98%) patients achieved VS (PVL<1000 copies/mL), including 2,158 (91%) with virological control (PVL<50 copies/mL), viral suppression was 99.0% (95% CI: 98.2–99.4) among participants receiving DTG-based regimens compared with 97.6% (95% CI: 96.6–98.3) among those on DTG-sparing regimens. In 2023, suppression rates were 94.1% (95% CI: 92.7–95.3) and 93.1% (95% CI: 91.5–94.5), respectively. By 2025, viral suppression remained high at 95.3% (95% CI: 94.3–96.2) among DTG-based recipients compared with 91.2% (95% CI: 88.8–93.2) among DTG-sparing recipients (table 4).

Table 4: Viral loads dynamics among patients over time

YEAR	TOTAL PATIENTS	DTG-BASED	VS AMONG DTG-BASED (N, %)	DTG-SPARING	VS AMONG DTG-SPARING (N, %)	RELATIVE RISK OF VIROLOGICAL FAILURE AMONG DTG-SPARING REGIMENS	PERCENTAGE OF VIROLOGICAL FAILURE ATTRIBUTABLE TO DTG-SPARING REGIMENS
2021	2,415	1,156	1,144 (99%)	1,259	1,229 (97.6%)	RR_{2021}= 2.29	56.3%
2023	2,415	1,323	1,245 (94%)	1,092	1,017 (93%)	RR_{2023}=1.16	13.8%
2025	2,415	1,798	1,714 (95%)	617	563 (91%)	RR_{2025}=1.87	46.5%

Overall, viral suppression remained consistently high overtime, with DTG-based regimens demonstrating sustained higher viral suppression rates compared to DTG sparing regimens, (Figure 2). Furthermore, there was a consistent risk of virological failure associated with the uptake of DTG-sparing regimens; translating specifically that 56.3% of participants receiving DTG-sparing ART were at risk of virological failure; 13.8% in 2023 and 46.5% in 2025.

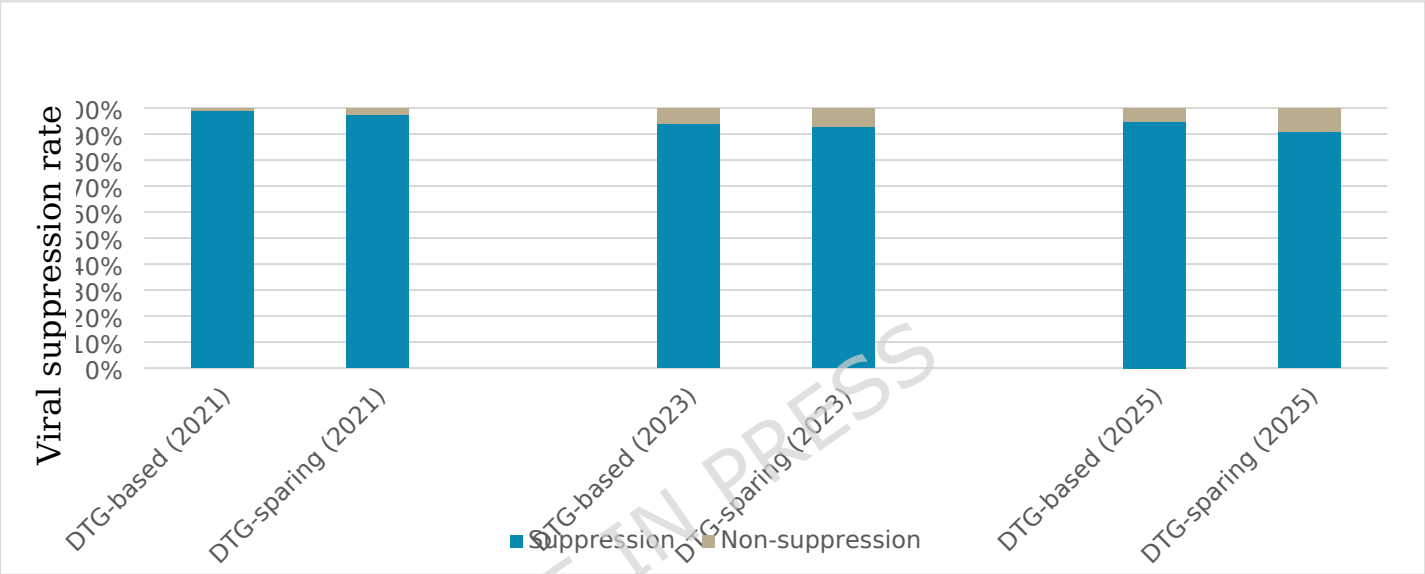

Figure 2: Evolution of virological response by regimen over time.

3.3 HIV Drug Resistance Patterns

Among the individuals with unsuppressed PVL in 2025, 9% (39/432) were lost to follow-up, 22% (94/432) were transferred to other health facilities, and 65% (232/432) achieved viral re-suppression following enhanced adherence counseling. Consequently, 17 participants remained eligible for genotypic resistance testing (GRT) based on a persistent PVL ≥ 1000 copies/mL, of whom 70.5% (12/17) were successfully sequenced. Overall prevalence of HIVDR was at 83% (10/12). DRMs to nucleoside reverse transcriptase inhibitors (NRTIs) were found at 75% (9/12), with M184V (66.7%) as the most prevalent NRTI-DRM (see figure 3). DRM to non-nucleoside reverse transcriptase inhibitors (NNRTIs) were found at 83.3% (10/12), with K103N (41.7%) as the most prevailing NNRTI-DRM (see figure 4). DRM to Protease Inhibitors (PIs) was at 8.3% (1/12), with co-prevalence of K20T, V82L, N88S (see figure 5). Dual-class (NRTI_NNRTI) resistance was at 66.7% (8/12), and triple-class (NNRTI_NRTI_PI/r) resistance was at 16.7% (2/12).

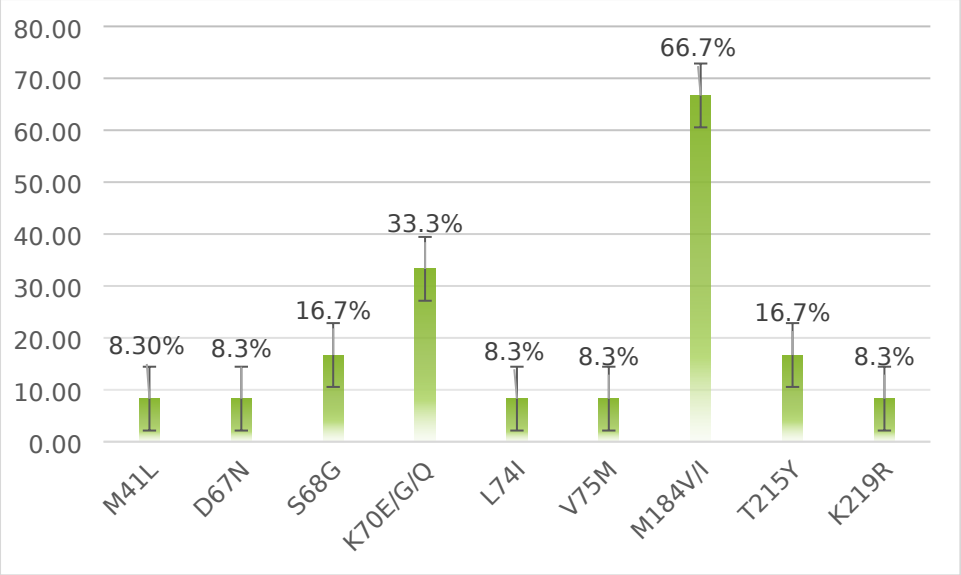

Figure 3: Distribution of major nucleoside reverse transcriptase inhibitors (NRTIs) associated mutations

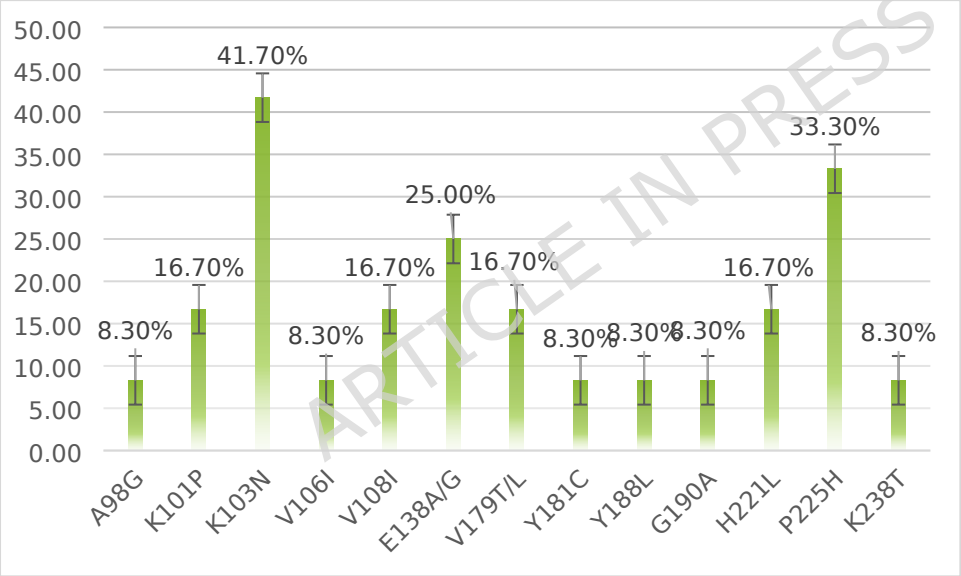

Figure 4: Distribution of major non-nucleoside reverse transcriptase inhibitors (NNRTIs) associated mutations.

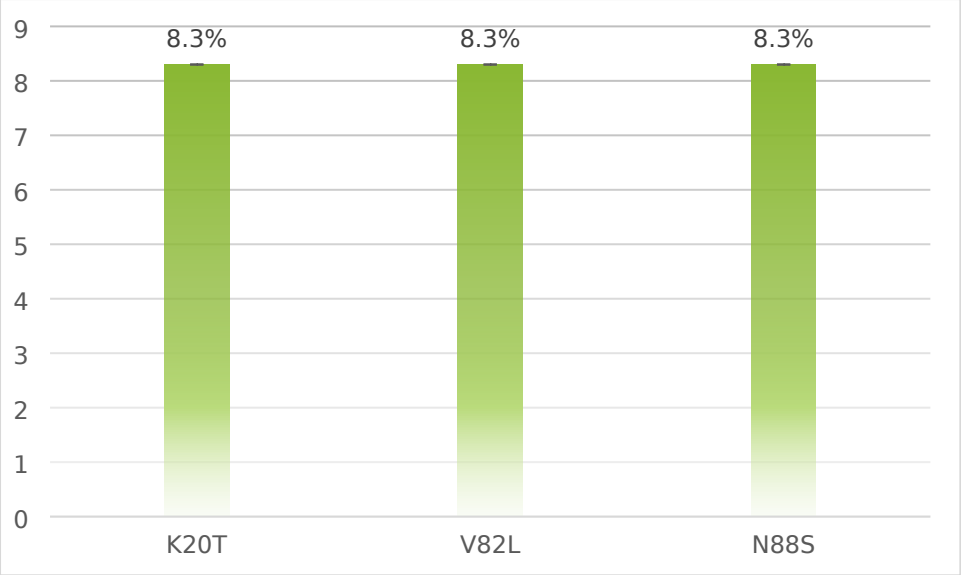

Figure 5: Distribution of major Protease Inhibitors (PIs) associated mutations

3.4 Potentially Active Drugs

Stanford HIVdb resistance scores showed distinct patterns across antiretroviral classes, with drug-specific variability in resistance levels. Among NRTIs, lamivudine (3TC) and emtricitabine (FTC) consistently exhibited high-level resistance, with scores ranging from 60 to 70, while tenofovir (TDF) remained largely susceptible or only mildly affected, with scores spanning from −10 and 5 (susceptible) to 15 (low-level resistance**)** and up to 50 (intermediate resistance). Zidovudine (AZT) was predominantly susceptible with scores of −10, although isolated profiles showed intermediate resistance (score 50) and high-level resistance (score 105). Abacavir (ABC) demonstrated heterogeneous resistance patterns, with scores ranging from 5 (susceptible) to 15 (low-level resistance), 30–40 (intermediate resistance), and up to 75 (high-level resistance).

Among NNRTIs, efavirenz (EFV) showed scores between 30 and 45 (intermediate resistance) and 75 to 130 (high-level resistance), while nevirapine (NVP) displayed scores from 45 (intermediate resistance) to 60–140 (high-level resistance), indicating extensive cross-resistance within first-generation NNRTIs. Doravirine (DOR) exhibited a wide distribution of scores, including 0 (susceptible), 10 (potential low-level resistance), 15 (low-level resistance), 30–45 (intermediate resistance), and 85 (high-level resistance). Similarly, rilpivirine (RPV) scores ranged from 0–5 (susceptible) to 20 (low-level resistance), 30–45 (intermediate resistance), and 60–85 (high-level resistance), whereas etravirine (ETR) showed scores of 0 (susceptible), 10 (potential low-level resistance), 20 (low-level resistance), 30 (intermediate resistance), and 60 (high-level resistance), suggesting variable residual activity across newer NNRTIs.

Regarding protease inhibitors, darunavir/ritonavir (DRV/r) remained fully susceptible with a score of −5, while atazanavir/ritonavir (ATV/r) showed high-level resistance with a score of 75 in one participant. Overall, these score distributions indicate widespread high-level resistance

to 3TC, FTC, EFV, and NVP, contrasted with preserved or partial activity of TDF, AZT, selected second-generation NNRTIs, and boosted darunavir.

Drug resistance profiles showed heterogeneous activity among NRTIs, with preserved susceptibility to TDF and AZT in most cases, whereas high-level resistance to 3TC was frequent. NNRTIs exhibited substantial resistance, particularly to EFV and NVP, while DOR, ETR and RPV retained variable residual activity. In contrast, protease inhibitors remained largely effective, with DRV/r fully active across all samples and high activity maintained for ATV/r and LPV/r (Fig. 6).

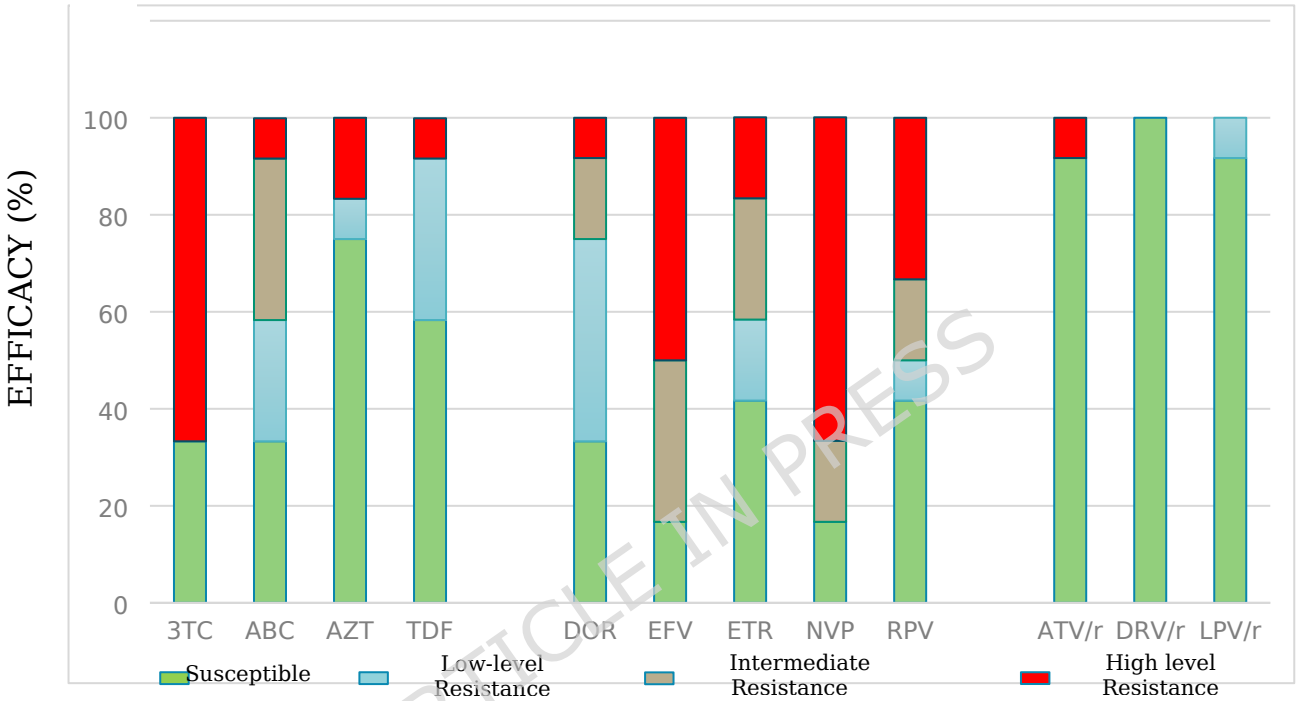

Figure 6: Potentially active drugs

3.5 Genetic Diversity

Phylogenetic analysis of the sequences confirmed that all patients were infected with type 1 viruses, specifically belonging to group M. A total of 4 viral strains were identified, including subtypes A3 (8,3%; 1/12), D (8,3%; 1/12) and recombinant forms CRF18_cpx (8,3%; 1/12) and prevailing CRF02_AG (75%; 9/12) see figure 7.

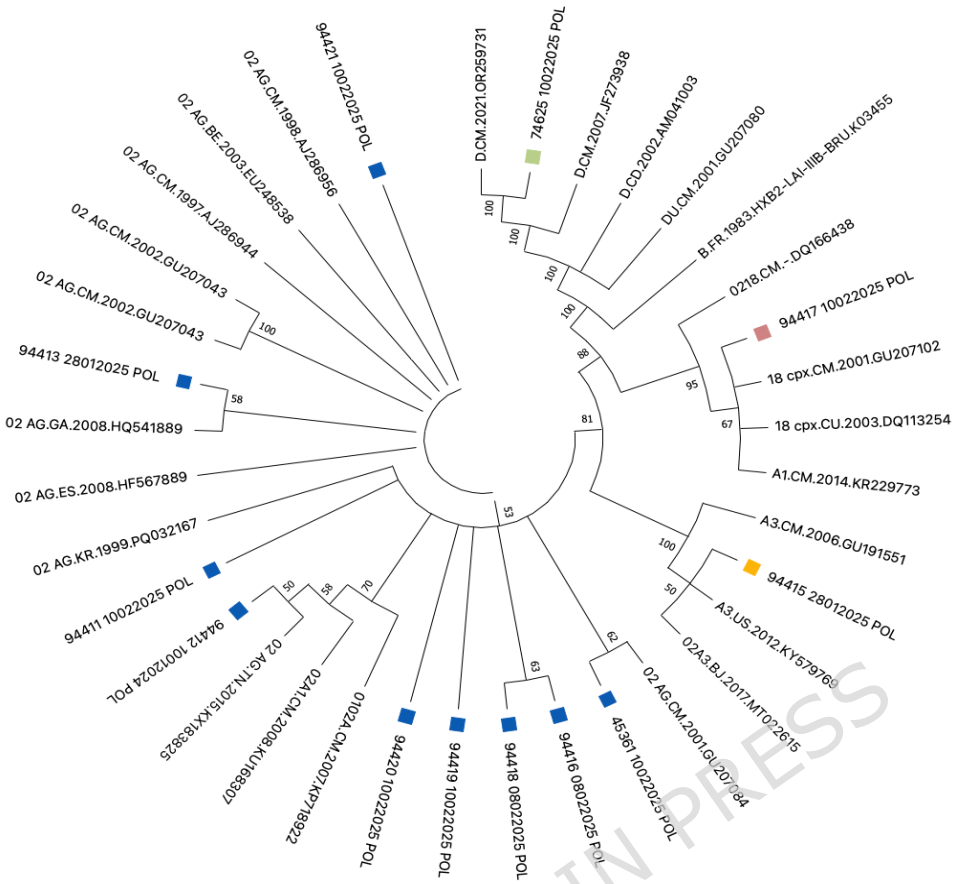

Figure 7: Phylogenetic tree of HIV-1 sequences from ART individuals.

The evolutionary history was reconstructed using the Maximum Likelihood method with the Tamura-Nei model. The initial tree(s) for the heuristic search were automatically generated using the Neighbor-Join and BioNJ algorithms, based on a pairwise distance matrix estimated with the Tamura-Nei model. The topology with the highest log-likelihood value was then selected. ****CRF =** Circulating Recombinant Forms.* ****cpx =** complex recombinant forms.*

Table 4 below presents the different subtypes found for each of our sequences as well as participant VL. We can notice a predominance of the CRF02_AG subtype at (75%; 9/12). The highest VL was with CRF02_AG (4,000,483 copies/mL).

Table 4: Integrated Virological and Genotypic Data by Participant: Treatment History, Viral Load, Drug Resistance Mutations, and HIV-1 Subtypes

ID	ART regimen	VL (copies/mL)	Resistance associated mutations			HIV Subtype
			Protease	Reverse transcriptase mutations		
				NRTIs	NNRTIs	
94413	TDF/3TC/DTG	67422	None	K70Q, M184I	K103N, P225H	CRF02_AG
95415	TDF/3TC/DTG	53141	None	S68G, K70Q, M184V	K103N, V108I, E138G, V179L, H221Y, K238T	A3
94416	TDF/3TC/ATV/r	4000483	None	M184V	K101P, K103N, V179T	CRF02_AG
94418	TDF/3TC/EFV	991668	None	M184V	K101P, K103N	CRF02_AG
45361	TDF/3TC/ATV/r	1889	None	S68G, L74I, M184V, T215V	A98G, V106I, Y188L	CRF02_AG
94411	TDF/3TC/DTG	63094	None	None	None	CRF02_AG
94412	TDF/3TC/ATV/r	67115	None	None	Y181C	CRF02_AG
74625	TDF/3TC/ATV/r	129037	V82L, N88S, K20T	M41L, D67N, K70G, V75M, M184V, T215Y	E138A, G190A	D
94417	TDF/3TC/DTG	50267	None	K70E, M184V	K103N, V108I, H221Y, P225H	CRF18_cpx
94419	TDF/3TC/ATV/r	166013	L23I	K219R	P225H	CRF02_AG
94420	TDF/3TC/DTG	854785	None	None	None	CRF02_AG
94421	TDF/3TC/ATV/r	23858	None	M184V	P225H	CRF02_AG

4. DISCUSSION

The use of real-world data offers key advantages over controlled clinical trials, including broader patient representation, faster and more cost-effective data acquisition, and the capacity to assess long-term outcomes features particularly valuable in LMIC. Our study, conducted in the largest ART cohort in Cameroon [21]**,** provides an updated and comprehensive snapshot of virological response, HIV-1 diversity, and resistance patterns in clinical routine settings. A predominant proportion of participants (71%) were women, reflecting the gender distribution typically observed in the Cameroonian context [26,27]**.** The wide age range (14–103 years) aligns with national reports and suggest a mature epidemic in which individuals are surviving longer on ART [27]**.**

More than 93.2% of participants achieved viral suppression, demonstrating strong overall treatment effectiveness, albeit slightly below the global 95% UNAIDS' target. As expected, patients on DTG-based regimens
showed statistically higher viral suppression rates compared with those on DTG-sparing regimens, consistent with national guidelines and emerging evidence supporting DTG scale-up [28,14]**.** However, given the observational and cross-sectional nature of this analysis, these differences should be interpreted as associations rather than evidence of superiority. Importantly, older age (≥50 years) was associated with better virological response, echoing prior findings that adolescents and young adults frequently experience poorer outcomes due to adherence challenges, psychosocial barriers, and delayed linkage to care [29–31,32]**.** Furthermore, a sub-analysis of 2415 participants followed from 2021-2025 at this same facility reveals high levels of viral suppression were observed in this sub-cohort over time with higher relative risk of virological failure observed among those on DTG-sparing regimens compared to those on DTG-based regimens. It is worth noting that this potential superiority effect of DTG-based regimens was conserved despite the fact that majority of participants in the DTG-sparing sub-group were switched to DTG-based regimens along the line; suggesting that these later participants should have been under sub-optimal regimens before the switch and/or are probably at risk of acquired resistance to DTG in the nearer future [33]. Despite the overall viral suppression rate of 93.2% in 2025, 94% of participants on DTG-based regimens achieved viral suppression, further supporting the effectiveness of DTG and its high genetic barrier in routine care [2,9,15,34,35]. Conversely, other studies reported strong association between virological failure and a longer exposure on suboptimal regimens [9,33,34]; and this discrepancy may be explained in the present cohort by the gradual expansion to DTG-based regimens, suggesting DTG's potency might have mitigated the limitations of earlier regimens (providing that they remained strictly adherent to this later prescription). These findings therefore advocate for the continuous scale-up of DTG-based regimens in LMIC for achieving UNAIDS' third-95 target and further HIV epidemic control.

As concerns HIVDR, DRMs observed among unsuppressed participants revealed notable patterns. The M184I/V mutation identified in 66.7% is commonly selected under lamivudine or emtricitabine pressure [26,35,36]**,** conferring high-level resistance but paradoxically increasing susceptibility to AZT and TDF [36]**.** TAMs (e.g., T215V, M41L, D67N) also appeared, reflecting selective pressure from thymidine analogues [36–39]**.** NNRTI mutations were dominated by K103N and P225H (each 25%), which drive high-level resistance to efavirenz and nevirapine [37,38, 40,41]**.** Accessory mutations such as E138A and K101P further compromised susceptibility to second-generation NNRTIs [16,42]**.** Less frequent mutations (G190A, Y181C, V108I, etc.) contributed additional resistance heterogeneity [36,43,44]**.** PI-associated mutations, although rare, were detected and warrant monitoring, particularly in the context of regimen switches. These findings emphasize the clinical relevance of resistance testing, especially in the presence of virological failure, to avoid suboptimal treatment choices and to ensure optimal regimen selection.

In this limited subset of samples successfully genotyped (n=17), CRF02_AG was the predominant strain (75%), a finding consistent with its longstanding predominance in Cameroon and much of West/Central Africa [14,25,45-48]. Subtypes A3, D, and CRF18_cpx were also detected. These observations align with Cameroon’s known status as an epicenter of HIV-1 genetic heterogeneity [46, 47,49]. Although limited, these findings highlight the continued relevance of monitoring circulating clades to inform treatment strategies in the region.

5. STUDY LIMITATIONS

Key populations such as MSM, FSWs, and adolescents were underrepresented, potentially limiting the generalizability of findings to these subgroups. The reliance on hospital records may have introduced missing data or misclassification biases.

A key limitation of this study is the absence of integrase (INSTI) sequencing, which precluded the assessment of resistance mutations associated with dolutegravir exposure and limited comprehensive interpretation of resistance patterns among individuals receiving DTG-based regimens.

Although conducted in a single urban referral center, the Yaoundé Central Hospital receives patients from diverse regions across the country, supporting reasonable national applicability of these findings. The small sample size of genotyped samples (n=17) limits the ability to comprehensively assess viral diversity within the entire cohort, although the findings are consistent with Cameroon’s known status as an epicenter of HIV-1 genetic heterogeneity. Future research should focus on conducting larger-scale, prospective studies with more genotyped samples to comprehensively assess HIV-1 viral diversity and its implications for treatment strategies in Cameroon".

6. CONCLUSIONS

This study provides comprehensive insight into virological outcomes and treatment patterns under real-world conditions, in the largest cohort of HIV-positive individuals receiving ART in Cameroon during the DTG scale-up era. The findings highlight a high rate of viral suppression, mostly favored by old-age (which goes along with increased adherence) and exposure to DTG-based regimens. While these results are reassuring concerning the successful transition strategy to DTG-based in the country, it is also of paramount importance to highlight that ongoing surveillance, expanded access to resistance testing, and continuous efforts to improve access to DTG—particularly in underserved or high-risk populations—remain essential for achieving national and global HIV control targets.

7. DECLARATIONS

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Following the ethical principles of the Helsinki Declaration, ethical clearance was obtained from the Institutional Ethics Committee for Research on Human Health, N**2023/022045/CEIRSH/ESS/BC.** Authorizations from host structures involved in the study were obtained before the beginning of the study. A written informed consent was obtained from each participant before enrollment. The various exams were free-of charge to the participants, and the results were given to the physicians to optimize the treatment. We used a specific identifier, to insured confidentiality; and data were protected by using a password on computers and phones.

AVAILABILITY OF DATA AND MATERIALS: All sequences generated in the current study have been submitted to Genbank under the accession numbers: PX625282-PX625293.

COMPETING INTEREST: The authors declare no competing interests.

FUNDING: Authors did not receive funding for this study.

AUTHORS' CONTRIBUTIONS: CT, JF, ENJS designed the study and wrote the original manuscript under the senior guidance of CN. LM, JN, PN have conducted the enrolment and counseling of participants. SO collected and sent samples for viral load and resistance test, CT and SO performed viral load tests, GAB, SD, AND, DT, ACK, BY and CCA, performed resistance tests and interpreted data with support from JF. DTAN, TTA, LF, AK, AF performed data abstraction. CT wrote the first manuscript draft and ELE, RAA, HH, AZKB, MV and AJ, provided extensive edits to all manuscript drafts. NN, CFP, CK and CN provided critical scientific input on the manuscript.

ACKNOWLEDGEMENTS: We thank the Yaoundé Central Hospital participants and staff, and the CIRCB for making this study possible.

8. LIST OF ABBREVIATIONS

ADR: Acquired Drug Resistance; **AIDS:** Acquired Immune Deficiency Syndrome; **ART:** Antiretroviral Therapy; **ARV:** Antiretroviral; **ATV/r:** Atazanavir boosted by ritonavir; **COP22:** Cameroon Operation Plan 2022; **CIRCB:** Chantal BIYA International Reference Center for Research on HIV / AIDS Prevention and Management; ; **CD4:** Cluster of Differentiation 4; **CRF:** Circulating Recombinant Forms; **DRMs:** Drug Resistance Mutations; **DTG:** Dolutegravir; **EAC:** Enhanced Adherence Council; **EFV:** Efavirenz; **EDTA:** Ethylenediaminetetraacetic acid; **HIV:** Human Immunodeficiency Virus; **HIVDR:** HIV Drug Resistance; **IQR:** Interquartile range; **LMICs:** Low and middle-income countries ; **NNRTI:** Non-Nucleoside Reverse Transcriptase Inhibitors ; **NRTIs:** Nucleoside Reverse Transcriptase Inhibitors; **PCR:** Polymerase chain reaction; **PDR**: Pre-treatement Drug Resistance; **PI:** Protease Inhibitors; **PLHIV:** People Living with HIV; **PrEP:** Pre-Exposure Prophylaxis; **RNA:** Ribonucleic Acid; **RT-PCR:** Real-Time Polymerase Chain Reaction; **SSA:** Sub-Saharan Africa; **UNAIDS:** United Nation program of HIV/AIDS; **PVL:** Plasma Viral Load; **WHO**: World Health Organization; **FSW:** Female Sex Worker; **MSM:** Men who have sex with Men.

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