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Research Article

Impact of First-line Antiretroviral Therapy Regimen on CD4+ T-cell Count Recovery at 12 months in HIV-infected Adults in Libreville, Gabon: A Retrospective Cohort Study

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ABSTRACT

Background: Before the introduction of dolutegravir, first-line antiretroviral therapy (ART) in sub-Saharan Africa mainly relied on non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimens. Evidence on whether regimen choice independently affects CD4+ T-cell recovery at 12 months remains limited in Central Africa. This study aimed to describe CD4+ trajectories and assess the relationship between ART regimen composition and immune reconstitution at Month 12 among HIV-infected adults in Libreville, Gabon.

Methods: We conducted a retrospective cohort study including ART-naive HIV-infected adults initiating first-line ART in a referral clinic in Libreville. Patients with a documented CD4+ count at 12 months (±3 months) were eligible. The primary outcome was CD4+ count at Month 12, analyzed as a continuous variable and dichotomized (≥500 cells/mm^3). Regimens were categorized by NRTI backbone (TDF-AZT-ABC-based) and third agent (efavirenz [EFV] or nevirapine [NVP]). Multivariate logistic regression identified factors associated with complete immune reconstitution, adjusting for baseline CD4, WHO stage, age, sex, and opportunistic infections.

Results: A total of 132 patients were included (70.5% female; median age 42 years). The most common regimen was TDF+FTC+EFV (39.4%). Median CD4+ count rose from 218 to 325 cells/mm^3 at Month 12 ($p < 0.001$). Complete immune reconstitution was achieved in 23.5% of patients. No significant differences in CD4 recovery were observed across NRTI backbones or between EFV- and NVP-based regimens. In multivariate analysis, regimen type was not associated with immune reconstitution. Only baseline CD4 <200 cells/mm^3 predicted failure to reach ≥500 cells/mm^3 (aOR = 0.13; $p = 0.017$).

Conclusions: In this pre-dolutegravir cohort, ART regimen choice did not independently influence immune recovery. Advanced immunosuppression at initiation was the main limiting factor, while possible undetected virological failure may explain CD4 decline in some patients. These findings highlight the importance of early HIV diagnosis and systematic viral load monitoring.

KEYWORDS
HIV, Antiretroviral therapy, CD4+ T-cell count, Immune reconstitution, Gabon, Sub-Saharan Africa, Efavirenz, tenofovir.

Introduction

Despite sustained global progress in the scale-up of antiretroviral therapy (ART), sub-Saharan Africa continues to bear the highest burden of HIV infection, accounting for approximately 65% of the estimated 40.8 million people living with HIV worldwide in 2024 [1]. In Gabon, an estimated 49,000 people were living with HIV in 2022, with an adult prevalence of approximately 3.4%, among the highest in Central Africa [2]. A persistent challenge in this setting is late presentation to care: patients frequently initiate ART with advanced immunosuppression, characterised by CD4+ T-cell counts below 200 cells/mm^3, which is independently associated with increased morbidity, mortality, and suboptimal immune reconstitution [3,4].

Prior to the nationwide introduction of dolutegravir (DTG) in Gabon, first-line ART regimens consisted predominantly of two nucleoside reverse transcriptase inhibitors (NRTIs) combined with a non-nucleoside reverse transcriptase inhibitor (NNRTI), in line with World Health Organization (WHO) guidelines applicable from 2010 to 2019 [5]. The most widely used regimens included tenofovir disoproxil fumarate (TDF) or zidovudine (AZT) as the NRTI backbone, partnered with lamivudine (3TC) or emtricitabine (FTC), and efavirenz (EFV) or nevirapine (NVP) as the third agent [5,6]. Abacavir (ABC)-containing regimens were used in specific clinical contexts.

CD4+ T-cell count recovery under ART is a critical marker of therapeutic success and a key determinant of clinical outcomes, particularly the risk of opportunistic infections and non-AIDS-related morbidity [7,8]. The extent of immune reconstitution at 12 months is influenced by multiple patient-level factors, including baseline CD4 count, WHO clinical stage, age, sex, and the presence of co-infections [3,9,10]. Whether the composition of the ART regimen itself specifically the NRTI backbone or the choice of NNRTI independently influences the magnitude of CD4 recovery remains a debated question. Published data from sub-Saharan Africa have yielded inconsistent results, with some studies reporting inferior immune recovery with AZT containing regimens compared to TDF-based combinations [11], whilst others found no significant difference [12].

No study has specifically addressed this question in the Gabonese context, where epidemiological characteristics, treatment access, and patient profiles may differ substantially from better-documented settings. Generating such local evidence is essential to inform national treatment guidelines, programme design under universal Test-and-Treat (UTT) policies, and differentiated service delivery strategies [13].

The objectives of this study were: (i) to describe the evolution of CD4+ T-cell count at 12 months under first-line pre-DTG ART regimens in HIV-infected adults in Libreville, Gabon; (ii) to compare CD4+ count at Month 12 across NRTI backbone types and third-agent classes; and (iii) to identify baseline clinical and regimen-related factors independently associated with complete immune reconstitution at Month 12.

Methodology

Study design and setting

This was a retrospective cohort study based on routinely collected clinical and biological data from HIV-infected adults followed at Centre Hospitalier Universitaire de Libreville (CHUL), a reference HIV care facility in Libreville, Gabon. The study period covered patients who began antiretroviral therapy before the introduction of DTG-based regimens in Gabon, from January to December 2019.

Study population

Eligible patients were HIV-infected adults (aged ≥18 years) who were ART-naive at enrolment, initiated a first-line ART regimen, and had at least one documented CD4+ count measurement at Month 12 (defined as 9-15 months post-ART initiation). Patients on second-line regimens at the time of the 12-month evaluation.

Data collection and variables

Data were extracted from patient clinical records and laboratory registers. Sociodemographic variables included age, sex, marital status, and occupation. Clinical variables collected at ART initiation included WHO clinical stage, baseline CD4+ count (categorised as < 200, 200–499, and ≥ 500 cells/mm^3), presence and type of opportunistic infections, delay from HIV diagnosis to first clinical consultation, and cotrimoxazole prophylaxis use. Hepatitis B surface antigen (HBsAg) serology was recorded when available.

ART regimen variables included: the NRTI backbone (TDF-based, AZT-based, or ABC-based); the companion NRTI (3TC or FTC for TDF-based regimens); and the third agent (EFV, NVP, or protease inhibitor [PI]). Reasons for ART regimen changes were categorised as: drug toxicity; adherence problem; immunological failure; drug stock-out; or therapeutic simplification.

Outcome definitions

The primary outcome was the CD4+ T-cell count at Month 12 (M12), analysed both as a continuous variable and dichotomised as ≥ 500 cells/mm^3, corresponding to the WHO/NIH criterion for complete immune reconstitution [14]. Secondary outcomes included the proportion of patients achieving CD4 ≥ 200 cells/mm^3

(threshold below which prophylaxis for opportunistic infections is recommended), and the absolute CD4 gain from baseline to M12.

Statistical analysis

Continuous variables were described as medians with interquartile ranges (IQR) and compared using the Mann-Whitney U test (two groups) or the Kruskal-Wallis test (≥ 3 groups). Categorical variables were described as frequencies and proportions. Change in CD4 count from baseline to M12 was assessed using the Wilcoxon signed-rank test. Pairwise comparisons between backbone groups were performed with the Mann-Whitney U test.

Factors associated with complete immune reconstitution (CD4 ≥ 500 cells/mm³ at M12) were examined using logistic regression. Univariate analysis was performed for all variables of interest. Variables with $p < 0.20$ in univariate analysis, or with a priori clinical relevance (age, sex, baseline CD4 category, WHO stage, opportunistic infection, NRTI backbone, third agent), were entered simultaneously into the multivariate model. ART regimen variables (backbone and third agent) were included in the multivariate model regardless of their univariate p-value, given the primary research question. The PI group was excluded from regression models due to insufficient sample size. Results are expressed as adjusted odds ratios (aOR) with 95% confidence intervals (CI). The NVP group was subject to sensitivity analysis given the potential for channelling bias by indication, as less likely to present with advanced disease. A significance threshold of $p < 0.05$ was applied. All analyses were performed using Statview 5.0

Ethics approval and consent to participate

The study protocol was approved by the National Ethics Committee for Research (**Protocol N° 0027/2022/CNER/SG/P**). Research authorisations were also obtained from CHUL authorities. Oral informed consent was obtained from each participant (or guardian when applicable) after study explanations. Confidentiality was maintained by anonymising participants with identification numbers. All study participants received medical care at the IDW-CHUL.

Results

General Characteristics of the cohort

A total of 132 HIV-infected adults were included in the analysis. The cohort was predominantly female (n=93; 70.5%), with a median age of 42 (35-55) years. HIV-1 mono-infection accounted for 91.7% of cases. The majority of patients (59.8%) presented within one month of diagnosis, while 15.9% had a delay exceeding six months. Sociodemographic and clinical characteristics are detailed in (Table 1).

At ART initiation, 52.9% the median time to entry into care was patients with a documented WHO stage (n=121) presented with advanced HIV disease. Baseline CD4+ count was available for 114 patients (86.4%). Of these, 89.5% (n=102) had a baseline CD4 count below 500 cells/mm³. Opportunistic infections (IO) were documented in 36 (27.3%) patients, with pulmonary tuberculosis being the most frequent, followed by herpes zoster and oropharyngeal candidiasis.

Table 1: Sociodemographic, clinical and biological characteristics of HIV-infected adults at ART initiation - Libreville, Gabon (N=132).

Characteristic	N	%
Sociodemographic characteristics		
Age (years)		
< 35	33	25.0
35-44	39	29.5
45-54	32	24.2
≥ 55 y	28	21.2
Marital status		
Married / Union	64	49.2
Single	63	48.5
Widowed / Divorced	5	3.8
Occupation		
Unemployed / No occupation	87	65.9
Manual worker	38	28.8
Civil servant / Professional	7	5.3
HIV type		
HIV-1	121	91.7
HIV-1 & HIV-2	3	2.3
Delay: diagnosis to first visit (months)		
≤ 1 month	79	59.8
> 1-6 months	32	24.2
> 6 months	21	15.9
Clinical & biological characteristics at ART initiation		
Occupation		
WHO clinical stage		
Stage 1-2	57	47.1
Stage 3-4	64	52.9
Baseline CD4+ count (cells/mm³)		
< 200 cells/mm³	54	47.4
200-499 cells/mm³	48	42.1
≥ 500 cells/mm³	12	10.5
Pulmonary tuberculosis	23	17.4
Herpes zoster	13	9.8
Oropharyngeal candidiasis	3	2.3
HBsAg positive (among tested, n=61)	4	6.6
Cotrimoxazole prophylaxis initiated	67	50.8

ART regimen distribution

ART regimen data were available for 124 patients (93.9%). The TDF-based regimen was the most frequent (65.9%), followed by AZT-based (18.9%) and ABC-based (9.1%). EFV was the third agent in 80.3% of patients, while NVP was used in 10.6%. The three most commonly prescribed full regimens were TDF+FTC+EFV (39.4%), TDF+3TC+EFV (18.9%), and AZT+3TC+EFV (12.9%). Patients receiving NVP based regimens had significantly less advanced disease at baseline compared to those receiving EFV:

71.4% (n=10/14) were at WHO stage 1-2 versus 42.9% (n=42/98) of EFV-treated patients (p=0.020).

Thirty-nine patients (29.5%) had documented ART regimen changes during follow-up. The main reasons were drug toxicity (n=7; 36.8%), adherence problems (n=5; 26.3%), immunological failure (n=4; 21.1%), and drug stock-out (n=4; 21.1%). ART regimen modification was not significantly associated with CD4 count at M12 (Mann-Whitney, p=0.40).

CD4+ count at Month 12: overall evolution

The median CD4+ count increased significantly from 218 cells/mm³ (IQR 95-349) at baseline to 325 cells/mm³ (IQR 208-474) at Month 12 (Wilcoxon, p<0.001), representing a median absolute gain of 107 cells/mm³ among patients with paired measurements (n=114). At Month 12; 22.7% of patients (n=30) had CD4 counts below 200 cells/mm³, 53.8% (n=71) were in the 200-499 range, and 23.5% (n=31) achieved CD4 ≥ 500 cells/mm³, the threshold for complete immune reconstitution.

CD4+ count at Month 12 by ART regimen

No statistically significant difference in CD4 count at Month 12 was observed according to the NRTI backbone. Median CD4 counts were not significantly different according to the NRTI backbone (p=0.86). Pairwise comparisons between TDF and AZT backbones (p=0.60) and between TDF and ABC backbones (p=0.73) likewise showed no significant differences. Similarly, the proportion of patients achieving CD4 ≥ 500 cells/mm³ did not differ significantly across backbone types (23.0% TDF vs 28.0% AZT vs 25.0% ABC).

Comparison of EFV and NVP-based regimens showed a higher median CD4 count in the NVP group (382 vs 320 cells/mm³), but this difference did not reach statistical significance (p=0.52), above. Among patients receiving TDF as the backbone, the choice of NRTI (FTC vs 3TC) had no significant impact on CD4 count at M12 (296 vs 356 cells/mm³, p=0.58) (Table 2).

Factors associated with complete immune reconstitution

In univariate analysis, advanced WHO stage 3-4 (OR=0.20, 95% CI [0.08-0.50], p<0.001) and baseline CD4 count below 200 cells/mm³ (OR=0.15; 95% CI [0.05-0.46], p<0.001) were significantly associated with failure to achieve CD4 ≥ 500 cells/mm³ at Month 12. Neither backbone type, third agent, sex, nor age was significantly associated with the outcome in univariate analysis.

In multivariate logistic regression, after simultaneous adjustment for all covariates including ART regimen variables, baseline CD4 count below 200 cells/mm³ remained the sole independently significant predictor of failure to achieve complete immune reconstitution (p=0.017) (Table 3). Neither the NRTI backbone (AZT vs TDF; ABC vs TDF) nor the third agent (NVP vs EFV: aOR=1.36; p=0.659) was independently associated with immune reconstitution at M12 after adjustment (Table 3). Advanced WHO stage and opportunistic infection at entry did not reach significance in the multivariate model, likely because their effect was substantially captured by the baseline CD4 variable. Full results are presented in (Table 3).

Table 2: CD4+T-cell count at Month 12 according to first-line ART regimen composition bivariate analysis.

ART Regimen / Component	N	CD4+ at M12 Median [IQR] (cells/mm³)	CD4+ ≤ 500 at M12 N (%)	*P* value
All patients	132	325 [208–474]	31 (23.5)	
NRTI backbone (reference: TDF-based)				
TDF-based (tenofovir)	87	298 [209-467]	20 (23.0)	-
AZT-based (zidovudine)	27	375 [203-519]	7 (28.0)	0.60
ABC-based (abacavir)	12	332 [217-399]	3 (25.0)	0.73
Overall (Kruskal–Wallis)				0.86
Third agent (reference: EFV)				0.52
EFV (efavirenz)	106	320 [210-456]	24 (22.6)	-
NVP (nevirapine)	14	382 [184-630]	5 (35.7)	-
PI (protease inhibitor)	3	9 [6-48]	0 (0)	-
TDF backbone: companion NRTI				0.58
TDF + FTC (emtricitabine)	53	296 [209-460]	12 (22.6)	-
TDF + 3TC (lamivudine)	33	356 [208-479]	8 (24.2)	-
Five most frequently prescribed full regimens				
TDF + FTC + EFV	52	296 [213-460]	12 (23.1)	-
TDF + 3TC+ EFV	25	356 [208-479]	8 (32.0)	-
AZT + 3TC + EFV	17	371 [240-572]	5 (29.4)	-
ABC + 3TC + EFV	12	332 [210-375]	2 (20.0)	-
TDF + 3TC + NVP	5	356 [140-660]	2 (28.6)	-

Table 3: Factors associated with complete immune reconstitution (CD4 ≥ 500 cells/mm³) at Month 12 - multivariate logistic regression (N=132).

Variables	aOR	95%	P. value
Patient demographics			
Age (per 1-year increment)	1.01	[0.98-1.05]	0.444
Male sex (vs female)	1.01	[0.30-2.47]	0.778
Advanced WHO stage 3-4	0.75	[0.19-2.94]	0.674
Baseline CD4 < 200 cells/mm³	0.13	[0.03-0.70]	0.017
Baseline CD4 200-499 cells/mm³	0.44	[0.14-1.38]	0.160
Opportunistic infection at entry	0.63	[0.19-2.02]	0.434
ART regimen variables (reference: TDF-based backbone + EFV)			
AZT-based backbone (vs TDF)	0.96	[0.30-3.02]	0.943
ABC-based backbone (vs TDF)	0.86	[0.14-5.20]	0.872
NVP as 3rd agent (vs EFV)	1.36	[0.35-5.32]	0.659

Discussion

To our knowledge, this is the first study to evaluate the relationship between first-line ART regimen composition and CD4+ T-cell count recovery at 12 months in HIV-infected adults in Gabon. Our principal finding is that the choice of NRTI backbone or NNRTI third agent was not independently associated with the magnitude or completeness of immune reconstitution at M12. Across all regimen comparisons TDF vs AZT vs ABC backbone, EFV vs NVP, and FTC vs 3TC as companion NRTI CD4 counts at Month 12 did not differ significantly. Instead, baseline CD4+ count below 200 cells/mm³ at ART initiation emerged as the sole significant independent predictor of failure to achieve complete immune reconstitution.

These findings are consistent with a growing body of evidence from sub-Saharan Africa. Lawn et al. demonstrated in a South African cohort that baseline CD4 count was the strongest predictor of CD4 recovery at 48 weeks, regardless of the ART regimen [3]. Kufa et al., in a national South African analysis of over 800,000 patients, confirmed that the rate of CD4 recovery was rapid in the first months of ART and stabilised around 12 months, with the baseline count being the primary determinant [9]. Fiseha et al. similarly found, in an Ethiopian cohort, that older age, male sex, and lower baseline CD4 count were the dominant predictors of suboptimal recovery, with no independent effect of regimen type [14,15].

Regarding the NRTI backbone, a collaborative analysis of southern African cohorts by Wandeler et al. reported that AZT-containing regimens impaired immunological recovery compared to other backbones [11], a finding not replicated in our data. The absence of a significant backbone effect in our cohort may reflect the relatively small sample sizes per backbone group, the heterogeneity of baseline CD4 counts across groups, and possible residual confounding, although our multivariate model explicitly adjusted for baseline immunological status.

The nominally higher CD4 count at M12 in NVP-treated patients (382 vs 320 cells/mm³) warrants careful interpretation. We documented a significant imbalance in baseline disease severity between NVP and EFV groups, with 71.4% of NVP patients at WHO stage 1-2 versus 42.9% of EFV patients. This pattern is consistent with channelling bias by indication: NVP was preferentially prescribed to patients with less advanced disease or to women of childbearing potential in whom EFV was contraindicated during early pregnancy [5]. After adjustment for baseline CD4 count in both the linear and logistic regression models, this apparent NVP advantage was substantially attenuated and did not reach statistical significance. This finding underscores the importance of confounder control when interpreting regimen comparisons in real-world observational data.

A critical public health implication of our findings is the paramount importance of early HIV diagnosis and timely ART initiation. In our cohort, 47.4% of patients with a documented baseline CD4 count presented with values below 200 cells/mm³, and 52.9% were at WHO stage 3 or 4 a pattern of late presentation that is well-documented in Central Africa [16] and is a major driver of suboptimal immune reconstitution. Under universal Test-and-Treat policies now in effect in Gabon, the objective of initiating ART before the CD4 count falls below 200 cells/mm³ takes on even greater programmatic urgency. Our data provide local evidence that achieving this goal would be the single most impactful intervention to improve 12-month immunological outcomes - irrespective of the ART regimen prescribed. This message is directly relevant to the design of differentiated service delivery strategies under the current DTG era, where the molecular and immunological landscape has evolved but the fundamental relationship between entry CD4 count and immune recovery trajectory remains operative [17].

The present study also documents ART regimen change patterns in a real-world Gabonese context. Drug toxicity (36.8% of documented changes) and adherence problems (26.3%) were the leading reasons for regimen modification, consistent with patterns reported across the region [18]. The occurrence of drug stock-outs as a cause of regimen change in 21.1% of cases reflects an important programmatic vulnerability specific to low- and middle-income country settings that can compromise treatment continuity and long-term immunological outcomes [19].

The finding that ART regimen composition does not independently predict immune reconstitution at Month 12 may reflect two complementary mechanisms that our data allow us to partially disentangle. The dominant explanation is the severity and duration of immunological damage accumulated before ART initiation. In our cohort, 47.4% of patients presented with a baseline CD4+ count below 200 cells/mm³, and 52.9% were at WHO clinical stage 3 or 4. Among the 30 patients who remained below 200 cells/mm³ at Month 12, 80% had already been below this threshold at ART initiation. Advanced HIV disease is associated with lymphoid tissue fibrosis, thymic dysfunction, and haematopoietic progenitor senescence, all of which structurally limit the capacity for immune reconstitution within 12 months of ART initiation irrespective of

the regimen prescribed [3,8,9]. Under these conditions, the choice between TDF- or AZT-based backbone, or between EFV and NVP, becomes a secondary determinant that is statistically overwhelmed by the immunological deficit at entry. This interpretation is fully consistent with the finding in our multivariate model that baseline CD4 count below 200 cells/mm³ was the sole significant independent predictor (aOR=0.13, p=0.017), whilst all ART regimen variables had odds ratios close to unity.

A secondary, numerically smaller but clinically important phenomenon is suggested by our data: a signal consistent with treatment failure in a subset of patients. Among the 114 patients with paired CD4 measurements, 32 (28.1%) experienced a negative CD4 gain at Month 12 that is, their CD4+ count was lower at M12 than at ART initiation. Critically, the median baseline CD4 count in this group was 446 cells/mm³, indicating that these patients did not belong to the late-presenter category. A decline in CD4 count despite ART in patients with a preserved initial immune status is a recognised pattern of immunological failure, which may be driven by virological failure, acquired drug resistance, poor adherence, or intercurrent co-infections [8,20]. In our cohort, direct evidence for treatment failure was limited by the absence of systematic viral load monitoring, but corroborating signals were present: one patient had documented FTC resistance on genotyping; four patients changed regimen for immunological failure; five patients had documented adherence problems; and four regimen changes were attributable to drug stock-outs a recognised driver of treatment interruption and subsequent resistance emergence [19]. Furthermore, five patients had a baseline CD4+ count above 200 cells/mm³ but fell below this threshold at Month 12, with a median CD4 decline of 233 cells/mm³, a pattern most consistent with treatment failure rather than insufficient reconstitution. Whilst the overall proportion of patients with probable treatment failure remains modest in absolute terms, these data underscore the importance of systematic virological monitoring under the universal Test-and-Treat paradigm, and provide a programmatic rationale for the transition to dolutegravir-based regimens, whose higher genetic barrier to resistance substantially reduces the risk of immunological failure driven by acquired drug resistance [17].

This study has several limitations that deserve explicit acknowledgment. First, its retrospective design relies on routinely collected clinical data, with inherent risks of incomplete records, particularly for baseline CD4 count (missing in 13.6%) and WHO clinical stage (missing in 8.3%). Second, and most critically, plasma viral load was not systematically available for all patients across the study period. This is the principal analytical limitation: without paired virological data at Month 12, it is impossible to formally distinguish immunological non-response in the context of virological suppression (true immune reconstitution failure) from immunological failure driven by inadequate viral suppression or acquired drug resistance. This distinction is directly relevant to the 28.1% of patients who experienced a negative CD4 gain at Month 12, and to the five patients with baseline CD4 above 200 cells/mm3 who fell below this threshold by M12 (median decline of 233 cells/mm3). Both groups may include patients with undetected virological failure or acquired resistance a hypothesis that our data raise but cannot confirm. Third, the NVP group (n=14) and PI group (n=3) were underpowered for meaningful comparison. Fourth, data on adherence, body mass index, haemoglobin, and nutritional status were insufficiently captured for systematic inclusion in regression models. Fifth, the multi-period design introduces temporal heterogeneity in treatment practices and monitoring standards. Despite these limitations, this study provides the first locally generated evidence on the regimen–immune recovery relationship in the pre-DTG era in Gabon, and the signals identified generate testable hypotheses for prospective studies integrating systematic viral load monitoring.

Conclusion

In this retrospective cohort of HIV-infected adults initiating first-line ART in Libreville, Gabon, the composition of the pre-dolutegravir ART regimen whether defined by NRTI backbone or NNRTI third agent was not independently associated with CD4+ T-cell count recovery at 12 months. Our data suggest that this finding reflects two distinct mechanisms. The dominant mechanism is the structural immunological damage accumulated prior to ART initiation: 47.4% of patients presented with a baseline CD4 count below 200 cells/mm³, and in this group the regimen cannot repair, within 12 months, the lymphoid tissue injury caused by years of uncontrolled viraemia. The secondary mechanism is a signal of probable treatment failure evidenced by a negative CD4 gain in 28.1% of paired patients, five cases of CD4 decline despite an initially preserved immune status, and directly documented resistance and immunological failure in a small subset a signal that systematic viral load monitoring would be needed to fully characterise. Together, these findings support two complementary programmatic priorities for Gabon and comparable settings in Central Africa: first, universal early ART initiation before CD4 count falls below 200 cells/mm³, which is the single most impactful lever for improving immunological outcomes; and second, the systematic integration of viral load monitoring under Test-and-Treat policies, to detect occult virological failure and guide timely regimen optimisation. The transition to dolutegravir-based first-line regimens, with their higher genetic barrier to resistance, further addresses this second priority.

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