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Factors associated with blips in people living with HIV on maintenance therapy with dolutegravir and lamivudine

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ETHICS APPROVAL

This study was approved by the Research Ethics Committee (Comitê de Ética em Pesquisa – CEP)

of the Hospital das Clínicas, Federal University of Pernambuco (HC-UFPE), Brazil (CAAE: 80963924.0.3001.8807); the Research Ethics Committee of the Federal University of Pernambuco (UFPE), Brazil (CAAE: 80963924.0.0000.5208 and CAAE: 48715721.0.0000.5208); and the Research Ethics Committee of the Hospital Universitário Osvaldo Cruz, University of Pernambuco (HUOC/UPE), Brazil (CAAE: 80963924.0.3002.5192). These Research Ethics Committees operate under the Brazilian National Research Ethics System, coordinated by the National Research Ethics Commission (Comissão Nacional de Ética em Pesquisa – CONEP). Data collection was initiated only after approval had been obtained from all participating Research Ethics Committees and was conducted in accordance with the ethical principles of the Declaration of Helsinki and the applicable Brazilian regulations.

ABSTRACT

Human immunodeficiency virus (HIV) infection remains a major global public health challenge, and antiretroviral therapy is essential for achieving viral suppression and improving the quality of life of people living with HIV. In this context, treatment simplification strategies, such as dual

therapy with lamivudine (3TC) and dolutegravir (DTG), have been extensively investigated. This study aimed to evaluate the effectiveness of this regimen in maintaining viral suppression and its association with the occurrence of viral blips among people living with HIV receiving care at three referral centers in Recife, Pernambuco, Brazil. A retrospective cohort study was conducted including 501 patients. Sociodemographic, clinical, laboratory, and behavioral variables were analyzed. Effectiveness was defined as the maintenance of an undetectable viral load, whereas viral blips were defined as transient increases in plasma HIV viral load. The observed frequency of viral blips was substantial. In the bivariate analysis, female sex was significantly associated with a higher occurrence of viral blips, whereas being the head of the household was identified as a protective factor. Variables including age, income, educational level, lifestyle habits, and comorbidities were not significantly associated with the occurrence of viral blips. In the multivariable analysis, female sex and longer duration of exposure to dual therapy remained independently associated with viral blips, with a progressive increase in risk for each additional year of treatment following the switch to dual therapy. Conversely, current coinfection and a history of clinical complications were associated with a reduced likelihood of viral blips. These findings demonstrate that dual therapy with lamivudine and dolutegravir maintains high virological effectiveness under real-world clinical conditions despite the relatively frequent occurrence of viral blips, which were not associated with virological failure. In conclusion, this regimen represents a safe and effective therapeutic alternative, and viral blips appear to be transient events potentially related to clinical factors and duration of treatment exposure, without significant clinical consequences when appropriately monitored.
Keywords: HIV; antiretroviral therapy; dolutegravir; lamivudine.

INTRODUCTION

Human immunodeficiency virus (HIV) infection remains a major global public health challenge, even more than four decades after its identification. It is estimated that approximately 39 million people worldwide are living with HIV, with millions still acquiring the infection annually,

despite significant advances in prevention, diagnosis, and treatment (UNAIDS, 2023). The introduction and expansion of antiretroviral therapy (ART) have transformed HIV infection from a nearly universally fatal condition into a manageable chronic disease, significantly increasing the life expectancy and quality of life of people living with HIV (PLHIV) (DEEKS et al., 2015; TRICKEY et al., 2017).

ART works through a combination of drugs that inhibit different stages of the viral replication cycle, reducing plasma viral load to undetectable levels and enabling immune recovery—primarily through an increase in CD4+ T-lymphocyte counts (MENÉNDEZ-ARIAS; DELGADO, 2022). Modern regimens, particularly those based on integrase inhibitors such as dolutegravir, demonstrate high antiviral potency, rapid viral suppression, and a high genetic barrier to resistance, making them cornerstones of current treatment guidelines (WHO, 2023; EACS, 2023).

However, despite its established efficacy, long-term ART use is associated with a range of adverse effects and cumulative toxicities. Key complications include metabolic alterations (dyslipidemia, insulin resistance), bone toxicity (osteopenia and osteoporosis), and nephrotoxicity, as well as an increased risk of cardiovascular disease and premature aging (GUARALDI et al., 2017; SAX et al., 2020; PATHAI et al., 2014). Furthermore, polypharmacy, drug-drug interactions, and pill burden can negatively impact treatment adherence, compromising clinical outcomes and leading to therapeutic failure (BACK; MARZOLINI, 2020).

In this context, therapeutic simplification strategies are emerging as promising alternatives to reduce drug exposure, minimize toxicity, and improve adherence without compromising virological efficacy. Among these strategies, dual-therapy regimens have gained prominence, particularly the combination of lamivudine (3TC) and dolutegravir (DTG) (CAHN et al., 2020). This combination brings together a nucleoside analogue reverse transcriptase inhibitor with an excellent safety profile (3TC) and a high-potency, high-genetic-barrier integrase inhibitor (DTG), resulting in an effective and well-tolerated regimen.

Robust evidence from randomized clinical trials, such as the GEMINI-1 and GEMINI-2 studies, has demonstrated that dual therapy with DTG + 3TC is non-inferior to standard triple therapy in achieving and maintaining virological suppression in treatment-naïve patients, while involving lower drug exposure (CAHN et al., 2019). Additionally, studies such as TANGO and other observational cohorts have shown that switching to dual therapy in patients with pre-existing viral suppression maintains high rates of viral suppression, with a favorable safety profile and a potential reduction in adverse events (VAN et al., 2020; MAGGIOLO et al., 2022).

From a clinical perspective, reducing long-term toxicity is particularly relevant for a population that is progressively aging and presents a high burden of non-AIDS-related comorbidities. In this context, dual therapy can contribute to reducing exposure to agents associated with cumulative toxicity—such as tenofovir and certain protease inhibitors—thereby promoting a more favorable metabolic and bone profile (SAX et al., 2020; RYOM et al., 2021).

Despite these promising results, the occurrence of transient episodes of detectable viremia—known as viral "blips"—remains a significant issue in the monitoring of patients on ART. These events are generally characterized by isolated, low-magnitude increases in viral load followed by a spontaneous return to an undetectable state, and they can occur even in individuals with good adherence and high-potency regimens. Cohort data indicate that blips may occur in a non-negligible proportion of patients on dual therapy, although often without significant clinical impact (WANG et al., 2024).

Even with advances in international evidence, significant knowledge gaps remain regarding the effectiveness of dual therapy in real-world settings, particularly in middle-income countries like Brazil. Local studies are essential to evaluate not only virological efficacy but also aspects related to adherence, safety, the occurrence of treatment failure or blips, and the clinical and sociodemographic profiles of the populations served by reference centers.

Given this, it is important to investigate the effectiveness of dual therapy with lamivudine and dolutegravir in HIV-1 patients with viral suppression, thereby contributing to strengthening the evidencebase.

LITERATURE REVIEW

HIV infection and the evolution of antiretroviral therapy

Infection with the human immunodeficiency virus (HIV) remains a major global public health issue, even after significant advances in prevention, diagnosis, and treatment strategies. It is estimated that millions of people are living with HIV worldwide, with a significant impact on morbidity and mortality (UNAIDS, 2023). The introduction of antiretroviral therapy (ART) marked a milestone in the history of the disease, transforming a previously fatal condition into a manageable chronic illness (DEEKS et al., 2015; TRICKEY et al., 2017).

ART works through the combination of drugs that interfere at different stages of the viral replication cycle, promoting viral load suppression and immune recovery, especially through the increase of CD4+ T lymphocytes (MENÉNDEZ-ARIAS; DELGADO, 2022). Traditionally, therapeutic regimens are based on triple-drug combinations, a strategy that has become established as the standard over the past decades.

Limitations of conventional antiretroviral therapy

Despite its high efficacy, the long-term use of ART is associated with significant adverse effects, including dyslipidemia, insulin resistance, renal toxicity, and bone alterations (SAX et al., 2020; GUARALDI et al., 2017). In addition, polypharmacy and drug interactions represent relevant challenges, especially in an aging population with multiple comorbidities (BACK; MARZOLINI, 2020). Another critical factor is treatment adherence, since complex regimens may compromise therapeutic continuity, favoring virological failure and the development of viral resistance (BACK; MARZOLINI, 2020). In this context, therapeutic simplification strategies have been widely investigated.

Dual therapy as a simplification strategy

Dual therapy emerges as a promising alternative to triple therapy, aiming to reduce drug exposure without compromising efficacy. Among the available regimens, the combination of lamivudine (3TC) and dolutegravir (DTG) stands out (CAHN et al., 2020).

Dolutegravir has high antiviral potency and a high genetic barrier to resistance, being recommended as a first-line drug in several international guidelines (WHO, 2021; EACS, 2023). Lamivudine, in turn, has a good safety and tolerability profile, contributing to the feasibility of the dual regimen.

Clinical evidence of dual therapy (3TC + DTG)

Randomized clinical trials, such as the GEMINI-1 and GEMINI-2 studies, demonstrated that dual therapy with DTG + 3TC is non-inferior to triple therapy in achieving and maintaining virological suppression in treatment-naïve patients (CAHN et al., 2019).

In previously suppressed patients, the TANGO study showed that switching to dual therapy maintains high rates of viral suppression, with a favorable safety profile (VAN WYK et al., 2020). Observational studies also support these findings, demonstrating sustained long-term efficacy (MAGGIOLO et al., 2022).

International guidelines

The main international guidelines recognize the role of dual therapy in specific contexts. The World Health Organization recommends the use of dolutegravir as the preferred treatment backbone (WHO, 2021). The Department of Health and Human Services (DHHS, 2024) includes the DTG/3TC combination as an option both for treatment initiation and therapeutic simplification in selected patients.

Similarly, the European AIDS Clinical Society (EACS, 2023) recommends dual therapy as a safe and effective strategy for maintaining virological suppression, especially in stable patients.

Viral blips: definition and relevance

Viral blips are defined as transient increases in viral load in previously suppressed patients, followed by spontaneous return to undetectability (DHHS, 2024).These events usually have low magnitude (<200 copies/mL) and are not necessarily associated with therapeutic failure.

Studies show that isolated episodes of transient viremia do not predict virological failure, especially in regimens with a high genetic barrier, such as those containing dolutegravir (LAPRISE et al., 2013; TAIWO et al., 2018).

Factors associated with blips

Several factors have been investigated in the occurrence of blips, including clinical, immunological, and treatment-related variables. The literature suggests that longer follow-up time may increase the probability of detecting these events, possibly due to the higher frequency of monitoring (MAGGIOLO et al., 2022).

However, there is still no consensus on specific determinants, making this an evolving field. Aspects such as biological variability and analytical limitations of laboratory tests should also be considered.

Knowledge gaps

Despite the robust evidence from clinical trials, there are still gaps regarding the effectiveness of dual therapy in real-world settings, especially in middle-income countries such as Brazil. Sociodemographic, clinical, and structural factors may influence therapeutic outcomes (WHO, 2021).

In this context, observational studies are essential to evaluate the applicability of international evidence, contributing to the improvement of guidelines and clinical practice.

GUIDING QUESTION

Is dual antiretroviral therapy with Lamivudine (3TC) and Dolutegravir (DTG) effective in maintaining viral suppression in patients living with HIV-1? Is there an association between changing the therapeutic protocol and the occurrence of BLIPs?

HYPOTHESIS

Dual therapy with Lamivudine (3TC) and Dolutegravir (DTG) maintains viral suppression and the stability of CD4+ T lymphocyte levels in patients living with HIV-1, with the change in therapeutic protocol being associated with the occurrence of BLIPs.

OBJECTIVES

GENERAL OBJECTIVE

To evaluate the effectiveness of the dual antiretroviral regimen with Lamivudine and Dolutegravir in maintaining viral suppression and its association with the occurrence of BLIPs in people living with HIV-1 treated at three HIV/AIDS reference services in Recife-PE.

SPECIFIC OBJECTIVES

- To assess the maintenance of virological suppression in people living with HIV after switching to dual antiretroviral therapy with lamivudine (3TC) and dolutegravir (DTG).
- To investigate the occurrence of BLIPs after changing the therapeutic protocol to the dual regimen (3TC + DTG).
- To evaluate adherence to antiretroviral therapy in people living with HIV using the dual regimen (3TC + DTG) after the protocol change**.**

METHODS

STUDY DESIGN

This is a retrospective cohort study in which 501 patients living with HIV/AIDS followed by three reference services will be investigated regarding the effectiveness of dual therapy with lamivudine and dolutegravir in the treatment of HIV type 1 and the occurrence of BLIPs after a protocol change.

PLHIV were evaluated regarding confounding factors: biological, social, and lifestyle-related. A questionnaire was applied to update information regarding infectious and non-infectious diseases developed during the period, habits, and side effects related to ART.

A patient was considered to have non-effective treatment if they presented virological failure, which according to the Brazilian Ministry of Health (2022), is defined as detectable HIV viral load (HIV-VL) after six months from the start or modification of treatment, or viral load rebound in individuals who had previously achieved viral suppression under treatment. New information regarding laboratory tests and diseases was obtained from the medical records of the Medical Records and Statistics Service (SAME) of the hospitals and from the laboratory test control system (SISCEL).

STUDY PERIOD AND LOCATION

The research was carried out in three reference hospitals in the State of Pernambuco for specialized HIV/AIDS care: Hospital Universitário Oswaldo Cruz (HUOC/UPE), Hospital Correia Picanço (HCP), and Hospital das Clínicas da UFPE (HC-UFPE). Data collection lasted one year and three months after approval by the ethics committee.

INCLUSION CRITERIA

People with a serological diagnosis of HIV infection, aged 18 years or older, receiving care at the three reference services in Pernambuco, able to respond to the questionnaire to be applied, with HIV diagnosis and treatment for at least 6 months, and currently on the dual ART regimen (3TC + DTG).

EXCLUSION CRITERIA

1. Cognitive and/or mental limitation recorded in the medical records (which makes understanding and/or verbal expression impossible), preventing them from responding to the questionnaire.
2. Unavailability of tests and diagnoses in the medical records.

DATA COLLECTION AND PROCESSING METHOD

Eligible patients were identified during their outpatient appointments, when receiving their medications (ART), and through the Medication Logistics Management System (SICLOM). SICLOM and SISCEL are integrated computerized information systems for monitoring PLHIV, managed by the Brazilian Ministry of Health, which store laboratory test data, medication dispensing, and stock information. Every patient who agreed to participate in the research signed, together with two witnesses, the Free and Informed Consent Form (TCLE) in two identical copies (one for the patient and one for the researcher), attesting compliance with the standards of Resolution 466/12 of the National Health Council (CNS), after approval by the Ethics Committee in the three hospitals.

After this stage, data collection for each patient began through an interview using a questionnaire developed for the study, with the purpose of gathering data relevant to the objectives of the study.

Data were collected regarding personal information, habits, adverse symptoms related to treatment, and health history and treatment of current and previous pathologies. The medical records of all included patients were reviewed to investigate ART history and HIV-related and non-HIV-related diseases, as well as CD4+ T-cell count and viral load results in SISCEL. After collection, the data underwent review by the researcher in an effort to minimize information bias.

SAMPLE SIZE CALCULATION

For the sample estimate, a population of 2,800 patients was considered (the total number of patients currently using dual therapy in the three services). A confidence level of 95% was considered, with a maximum margin of error of 5%, and the collection proportion consisted of 80%. The sample size for the present study will be 340 participants.

$$n = \frac{2800 \cdot 3{,}8416 \cdot 0{,}25}{2799 \cdot 0{,}0025 + 0{,}9604}$$

$$n = \frac{2689{,}12}{6{,}9975 + 0{,}9604}$$

$$n = \frac{2689{,}12}{7{,}9579}$$

$$\boxed{n \approx 338}$$

STATISTICAL ANALYSIS

The therapeutic response (effectiveness) was assessed by the cumulative incidence measure and estimated with their respective 95% confidence intervals. The characteristics of the population were presented by frequency distribution when the variables were categorical, and by means and standard deviation when the variables were quantitative. The hypothesis of normal distribution was assessed by the Shapiro-Wilks test, with the measure and interquartile interval being presented. In the analysis of the association between explanatory factors and virological response, the Chi-square and Pearson tests were applied, as well as the Student's t-test or Kruskal-Wallis test for the comparison of means and medians. Relative risks were estimated and adjusted for confounding factors using a logistic regression model. The significance level adopted in the study will be 5% ($p<0.05$). The software used for the analysis will be Stata version 14.0.

ETHICAL ASPECTS

Scientific research is regulated by Law No. 14.874/2024 and Decree No. 12.651/2025, which establish the National System of Ethics in Research Involving Human Beings. Project evaluation and approval are conducted by your institution's Research Ethics Committee (CEP) and the National Research Ethics Commission (CONEP); together, they form a system linked to Brazil's National Health Council and Ministry of Health. Approvals from the ethics committees are attached to the study. The ethics committee approval codes are right below.

The research project was submitted to the Research Ethics Committee involving human beings of the Hospital das Clínicas of the Federal University of Pernambuco - HC-UFPE (CAAE: 80963924.0.3001.8807), the Federal University of Pernambuco – UFPE (CAAE: 80963924.0.0000.5208 and CAAE: 48715721.0.0000.5208), and the Osvaldo Cruz University Hospital of the University of Pernambuco - HUOC/UPE (CAAE: 80963924.0.3002.5192).

Data collection was only initiated after approval by the aforementioned committees, respecting the current ethical and legal aspects.

CATEGORIZATION OF VARIABLES

Independent variables

Biological variables

Variable type categorization	Definition	Independent
Sex	Patient's biological gender at birth.	1. Male 2. Female
Age	Time interval, measured in full years, between the date of birth and the date the interview was conducted.	1. 18 to 21 years old 2. 22 to 30 years old 3. 31 to 40 years old 4. 41 to 50 years old 5. 51 to 60 years old 6. 61 to 70 years old 7. > 70 years old
Race/Color	Color or race self-declared by the individual during the interview, based on categories recorded by the Brazilian Institute of Geography and Statistics (IBGE) (2023).	1. White 2. Black 3. Yellow 4. Mixed-race 5. Indigenous 6. Other

Sociodemographic variables

Independent variable type	Definition	Categorization
Marital status	Marital status declared by the Interviewee following guidance regarding the classification adapted from the BRAZILIAN INSTITUTE OF GEOGRAPHY AND STATISTICS – IBGE (2023).	1. Married 2. Single 3. Separated or divorced 4. Widowed 5. Other

Housing company	Residential status self-reported by the respondent	1. Alone 2. With family 3. With partner 4. In a shelter/support home 5. On the street
Provenance	Patient's place of residence, based on the patient's own report or medical record entries.	1. Recife 2. Recife Metropolitan Area 3. Other
Service providing HIV care and monitoring	Referral hospital where the patient undergoes HIV treatment and follow-up.	1. Oswaldo Cruz University Hospital - UPE 2. Correia Picanço Hospital 3. University Hospital - UFPE
Level of education	Level of education declared during the interview using criteria adapted from the Brazilian Institute of Geography and Statistics - IBGE (2023).	1. Illiterate 2. Elementary or primary education 3. High school or secondary education 4. Higher or tertiary education 5. Postgraduate studies 6. Unknown/Not reported
Occupancy status	The interviewee will state their employment status according to a classification adapted from the Brazilian Institute of Geography and Statistics (IBGE, 2023).	1. Employed 2. Employed, but on leave 3. Unemployed 4. Retired or receiving social benefits 5. Student 6. Homemaker
Income	Information on how much money the patient receives,	1. Less than one minimum wage 2. From 1 to 3 minimum wages

	collected via interview. Initially collected on a continuous basis. For standardization purposes, income will be calculated in terms of minimum wages by dividing the monthly income by the minimum wage value for the corresponding month.	3. From 4 to 6 minimum wages 4. Above 7 minimum wages 5. Don't know 6. Declined to state

Behavioral variables

Independent variable type	Defination	Categorization
Sexual orientation	Sexual behavior reported by the patient during the interview (Ministry of Human Rights, 2018)	1. Man who has sex with men 2. Heterosexual 3. Bisexual 4. Other 5. Declined to state
Level of alcohol consumption	Alcohol consumption reported during the interview and classified according to the National Institute on Alcohol Abuse and Alcoholism (NIAAA, 2020).	1. Moderate consumption 2. Episodic heavy drinking 3. Heavy use 4. Does not consume alcohol 5. Declined to state
Smoking	Condition reported by the patient during the interview regarding smoking habits.	1.Daily smoker 2.Occasional smoker 3.Non-smoker 4. Ex-smoker 5.Chose not to disclose

Illicit drug use	The interviewee will state the frequency of use, and the interviewer will base their assessment on an adaptation of the classification from the *Projeto Diretrizes* – Marijuana Abuse and Dependence (Brazilian Psychiatric Association; Brazilian Society of Cardiology, 2022).	1. Intermittent and limited use 2. Daily use 3. Weekly use 4. Does not consume 5. Declined to state
Physical activity level	reported in the interview, being defined as the practice of physical exercise according to the criteria of the International Physical Activity Questionnaire (IPAQ), adapted for the interview.	1. Sedentary lifestyle 2. Low level of physical activity 3. Moderate 4. Vigorous

Laboratory variables

Type of independent variable	Defination	Categorization
Current CD4+ T-lymphocyte count	Quantification of CD4+ T-lymphocytes presented in a laboratory test result by the patient or recorded in the patient's medical record, with the result expressed in "cells/mm³".	1. <50 cells/mm3 2. 50 to 100 cells/mm3 3. 100 to 200 cells/mm3 4. 200 to 350 cells/mm3 5. 350 to 500 cells/mm3 6. 500 to 1000 cells/mm3 7. >1000 cells/mm3

Latest CD4+ T-lymphocyte count on the previous ART regimen	Quantification of CD4+ T-lymphocytes presented in a laboratory test result by the patient or recorded in the patient's medical record, with the result expressed in "cells/mm³".	1. <50 cells/mm3 2. 50 to 100 cells/mm3 3. 100 to 200 cells/mm3 4. 200 to 350 cells/mm3 5. 350 to 500 cells/mm3 6. 500 to 1000 cells/mm3 7. >1000 cells/mm3
Current viral load	Most recent serum HIV RNA quantification (collected within the last 6 months), measured in copies/mL using the PCR technique.	1. Undetectable 2. Up to 1,000 copies/mL 3. 1,000 to 10,000 copies/mL 4. 10,000 to 100,000 copies/mL 5. >100,000 copies/mL
Latest viral load result from previous ART regimen	Most recent serum HIV RNA quantification (collected within the last 6 months), measured in copies/mL using the PCR technique.	1. Undetectable 2. Up to 1,000 copies/mL 3. 1,000 to 10,000 copies/mL 4. 10,000 to 100,000 copies/mL 5. >100,000 copies/mL
Blood glucose level results **Before and after switching the ART regimen to dual therapy**	Quantification of fasting blood glucose levels according to the 2023 guidelines of the Brazilian Diabetes Society.	1- <100 = Normal 2- 100 to <126 = Pre diabetes 3- >126 = Diabetes
Levels and blood pressure before and after switching the ART regimen to dual therapy	Quantification of blood pressure levels according to the 2022 Brazilian Society of Cardiology guidelines.	1- 120x80mmgh = ideal 2- <130x85mmhg = normotensive 3- 130-139x85-89mmhg = borderline 4- 140-159x90-99mmhg =

		Stage 1 hypertension 5- 160–179/100–109 mmHg =Stage 2 hypertension 6- ≥140 / ≥ 110 mmHg = hypertension Stage 3

Clinical variables

Type of independent variable	Definition	Categorization
AIDS diagnosis	Individuals with HIV infection showing evidence of immunodeficiency. Evidence of immunodeficiency is defined as a CD4+ T-lymphocyte count below 350 cells/mL and/or the presence of at least one AIDS-defining condition according to modified CDC criteria, or a score of at least 10 points on the scale of signs, symptoms, or diseases based on Rio de Janeiro/Caracas criteria.	1.Yes 2. No
Presence of Comorbidities	Existence of two or more diseases simultaneously in the same person, recorded by	1. Systemic Arterial Hypertension 2. Diabetes Mellitus 3. Heart Failure

	attending physician in the medical record or reported by the patient.	4. Atherosclerotic disease 5. Chronic Obstructive Pulmonary Disease 6. Chronic kidney disease 7. Chronic liver disease 8. Gastritis 9. Esophagitis 10. Osteoarthritis 11. Osteoporosis 12. Cognitive dysfunction 13. Depression 14. Chronic anemia 15. Neoplasm 16. Autoimmune disease treated with corticosteroids 17. Autoimmune disease treated with immunosuppressants 18. Other 19. No comorbidities
Coinfections	O paciente relata a presença de coinfecções e será também avaliado o prontuário	1.Tuberculose 2.Hepatite B 3.Hepatite C 4.Sífilis 5.Doença de Chagas 6.Leishmaniose 7.Hanseníase 8.HTLV-1 e 2 9.Paracoccidioidomicose 10.Chikungunya 11.Outras 12.Sem coinfecções
Infecções oportunistas	The patient reports the presence of opportunistic infections, and their medical record will also be evaluated.	1. Cryptococcal meningitis or meningoencephalitis 2. Cerebral toxoplasmosis 3. Pneumocystosis 4. Cytomegalovirus disease 5. Esophageal or oropharyngeal candidiasis 6. Histoplasmosis 7. Other 8. No opportunistic infections

Time to HIV diagnosis	Time elapsed from HIV serological diagnosis to the date of the interview	1. Less than 6 months 2. 6 months to 1 year 3. 1 to 3 years 4. 4 to 6 years 5. 7 to 9 years 6. > 9 years 7. Don't know

Variables related to medication use

Type of independent variable	Definition	Categorization
ART Adherence	The patient reported adhering to the treatment.	1.Yes 2. No
Previous ART regimen	If the patient is using ART, they will be asked which regimen they are on, and the information will also be checked in the medical record.	1.TDF+3TC + DTG 2.TDF+FTC+DTG 3. TDF + 3TC + EFV 4.TDF+FTC+EFV 5. AZT + 3TC + EFV 6. TDF + 3TC + PI/r 7.TDF+FTC+ PI/r 8.TDF + 3TC + RAL 9.TDF + FTC + RAL 10.ABC + 3TC + DTG 11.Another
Duration of ART use	Time in full years since the start of antiretroviral therapy, as recorded in the medical record or reported by the patient.	1. 6 months to 1 year 2. 1 to 3 years 3. 3 to 6 years 4. 7 to 9 years 5. More than 9 years 6. Don't know

Duration of dual therapy	Total duration of use since the start of dual antiretroviral therapy, as recorded in the medical record or reported by the patient.	1. 6 months 2. 7 months 3. 8 months 4. 9 months 5. 10 months 6. 11 months 7. 12 months
Presence of BLIPs	BLIPs (Blips of Low-level Intermittent Viremia) are transient, isolated elevations in HIV viral load in patients undergoing antiretroviral therapy (ART) who previously had an undetectable viral load.	1. 50 copies/ml 2. 50 to 75 copies/ml 3. 75 to 100 copies/ml 4. 100 to 150 copies/ml 5. 150 to 200 copies/ml
Occurrence of BLIPs over a one-year period		1. Once 2. Twice 3. Three times 4. More than three times
Occurrence of BLIPs in the period from 1 to 2 years		1. Once 2. Twice 3. Three times 4. More than three times
Occurrence of BLIPs over a period of 2 years or more.		1. Once 2. Twice 3. Three times 4. More than three times

Dependent variable

Presence of effectiveness of dual therapy with lamivudine + dolutegravir in people living with HIV-1, characterized by the effectiveness being the presence of an undetectable viral load and stability of CD4+ T-cell levels without an increase in their levels after the start of dual therapy and its maintenance. And the occurrence or non-occurrence of BLIPs after the change in therapeutic regimen.

RESULTS

A total of 501 people living with HIV-1 receiving follow-up care at three HIV/AIDS referral services in Recife-PE were evaluated. The mean age was 54.4 ± 10.3 years, ranging from 20 to 80 years.

A slight predominance of females was observed (51.9%). Regarding self-reported race/color, 46.7% were mixed-race, 29.0% Black, and 24.3% White. In relation to marital status, 42.9% were married, 23.2% single, 25.7% divorced, and 8.2% widowed. Only 19.6% reported living with a partner.

Most participants had one or two children (59.9%), while 24.3% had more than two children and 15.8% had no children. Regarding education, elementary schooling predominated (40.7%), followed by high school (39.1%), with 7.0% being illiterate and 13.2% having higher education.

Regarding income, 50.7% earned less than one minimum wage and 49.3% earned more than one minimum wage. Most had an occupation (64.7%), were responsible for their household (69.1%)

and received financial support (61.3%). Regarding place of residence, 43.7% lived in Recife, 40.7% in the Metropolitan Region of Recife, and 15.6% in other cities (TABLE 1).

Table 1. Sociodemographic characterization of people living with HIV-1 receiving care at three HIV/AIDS referral services in Recife, Pernambuco.

Features	Statistic
Idade (em anos)	
Mean ± SD (Minimum – Maximum)	54,4 ± 10,3 (20 – 80)
Female – Number (%)	260 (51,9)
Race – Number (%)	
White	122 (24,3%)
Mixed-race	234 (46,7%)
Black	145 (29,0%)
Marital status – Number (%)	
Single	116 (23,2%)
Married	215 (42,9%)
Divorced	129 (25,7%)
Widower	41 (8,2%)
Lives with partner – Number (%)	98 (19,6%)
Number of children – Number (%)	
Childless	79 (15,8%)
One or two children	300 (59,9%)
More than two children	122 (24,3%)
Education – Number (%)	
Illiterate	35 (7,0%)
Elementary and Middle School	204 (40,7%)
High school	196 (39,1%)
higher education	66 (13,2%)
Renda – Número (%)	
≤ 1 minimum wage	254 (50,7%)

> 1 minimum wage	247 (49,3%)
Employed – Number (%)	324 (64,7%)
Head of household – Number (%)	346 (69,1%)
Receives financial aid – Number (%)	307 (61,3%)
Origin – Number (%)	
Recife	219 (43,7%)
metropolitan area	204 (40,7%)
Another city	78 (15,6%)

The frequency of BLIPs was 28.5% (CI9%; 24.7–32.7).

In the bivariate analysis, age did not show a significant association with the occurrence of BLIPs (OR = 0.99; 95% CI: 0.97–1.01; p = 0.321).

A significant association was observed between sex and the occurrence of BLIPs, with a higher likelihood among women (OR = 1.59; 95% CI: 1.08–2.36; p = 0.020).

Race/color, marital status, living with a partner, education, income, occupation, and receiving financial assistance did not show a statistically significant association with the outcome.

Regarding the number of children, individuals with one or two children had a higher likelihood of BLIP (OR = 1.82; 95% CI: 1.00–3.32; p = 0.050), a borderline result.

Being the head of the household was shown to be a protective factor (OR = 0.59; 95% CI: 0.39–0.89; p = 0.012), indicating a lower likelihood of BLIP in this group (Table 2).

Table 2. Association of socioeconomic factors and the occurrence of BLIPs after the change in the therapeutic protocol to the dual regimen (3TC + DTG) among people living with HIV-1 treated at three HIV/AIDS reference services in Recife-PE.

Factors	yes (n = 143)	No (n = 358)	OR (IC95%)	p-value
Age (in years)*	53,7 ± 10,6	54,7 ± 10,2	0,99 (0,97 – 1,01)	0,321
Sex				
Masculine	57 (39,9%)	184 (51,4%)	Referência	-
Feminine	86 (60,1%)	174 (48,6%)	**1,59 (1,08 – 2,36)**	**0,020**
Race				
White	34 (23,8%)	88 (25,6%)	Referência	-
Mixed-race	68 (47,5%)	166 (46,4%)	1,06 (0,65 – 1,72)	0,814
Black	41 (28,7%)	104 (29,0%)	1,02 (0,60 – 1,74)	0,941
With a partner				
No	114 (79,7%)	271 (75,7%)	Referência	-
yes	29 (20,3%)	87 (24,3%)	0,79 (0,49 – 1,27)	0,336
Lives with their partner				
No	122 (85,3%)	281 (78,5%)	Referência	-

yes	21 (14,7%)	77 (21,5%)	0,62 (0,37 – 1,06)	**0,084**
Number of children				
Childless	16 (11,2%)	63 (17,6%)	Reference	-
One or two children	95 (66,4%)	205 (57,3%)	**1,82 (1,00 – 3,32)**	**0,050**
More than two children	32 (22,4%)	90 (25,1%)	1,4 (0,71 – 2,77)	0,333
Education				
Up to middle school	68 (47,5%)	171 (47,7%)	Reference	-
High school	59 (41,3%)	137 (38,3%)	1,08 (0,71 – 1,64)	0,706
higher education	16 (11,2%)	50 (14,0%)	0,80 (0,43 – 1,51)	0,499
Income				
≤ 1 minimum wage	76 (53,2%)	178 (49,7%)	Reference	-
> 1 minimum wage	67 (46,8%)	180 (50,3%)	0,87 (0,59 – 1,28)	0,489
It is occupied.				
No	53 (37,1%)	124 (34,6%)	Reference	-
yes	90 (62,9%)	234 (65,4%)	0,90 (0,60 – 1,35)	0,608
Head of household				
No	56 (39,2%)	99 (27,6%)	Reference	-
yes	87 (60,8%)	259 (72,4%)	**0,59 (0,39 – 0,89)**	**0,012**
Receives financial aid				
No	55 (38,5%)	139 (38,8%)	Reference	-
yes	88 (61,5%)	219 (61,2%)	1,01 (0,68 – 1,51)	0,940

* Mean ± SD

The lifestyle habits evaluated (alcohol use, smoking, and physical activity) showed no statistically significant association with the occurrence of BLIPs.

Regarding nutritional status (BMI) and waist circumference, no significant associations were observed either. The presence of general comorbidities, systemic arterial hypertension, and diabetes mellitus was not associated with the outcome.

The presence of depression showed a statistically significant association, with lower odds of BLIPs among individuals diagnosed with depression (OR = 0.57; 95% CI: 0.34–0.95; p = 0.030) (Table 3).

Table 3. Association between habit-related factors and the occurrence of BLIPs following the switch to a dual-drug regimen (3TC + DTG) among people living with HIV-1 receiving care at three HIV/AIDS referral centers in Recife, Pernambuco..

Factors	Yes (n = 143)	No (n = 358)	OR (IC95%)	p-value
Habits				
Alcohol use				
can't get alcohol	97 (67,8%)	235 (65,6%)	Reference	-
low alcohol	33 (23,1%)	81 (22,6%)	0,98 (0,61 – 1,58)	0,956
Moderate	13 (9,1%)	42 (11,7%)	0,75 (0,38 – 1,46)	0,397
Smoking				
doesn't smoke	115 (80,4%)	293 (81,8%)	Reference	-
Daily	24 (16,8%)	59 (16,5%)	1,04 (0,61 – 1,75)	0,893
Occasional	4 (2,8%)	6 (1,7%)	1,70 (0,47 – 6,12)	0,418
Physical activity				
without	84 (58,7%)	200 (55,9%)	Reference	-
Light	33 (23,1%)	82 (22,9%)	0,96 (0,59 – 1,54)	0,861
Moderate	26 (18,2%)	76 (21,2%)	0,81 (0,49 – 1,36)	0,433
Comorbidities				
Body mass index[a]				
Eutrophic	66 (46,1%)	175 (48,9%)	Reference	-
Overweight	70 (49,0%)	163 (45,5%)	1,14 (0,76 – 1,69)	0,523
Obesity	7 (4,9%)	20 (5,6%)	0,93 (0,37 – 2,29)	0,872
Waist circumference [b]				
Normal	120 (83,9%)	295 (82,4%)	Reference	-
Augmented	23 (16,1%)	63 (17,6%)	0,90 (0,53 – 1,51)	0,685
Some comorbidity				
No	23 (16,1%)	59 (16,5%)	Reference	-
yes	120 (83,9%)	299 (83,5%)	1,03 (0,61 – 1,74)	0,914
Systemic arterial hypertension				
No	67 (46,9%)	169 (47,2%)	Reference	-
yes	76 (53,1%)	189 (52,8%)	1,01 (0,69 – 1,50)	0,943
Diabetes mellitus				
No	90 (62,9%)	225 (52,8%)	Reference	-
Yes	53 (37,1%)	133 (37,2%)	1,00 (0,67 – 1,49)	0,985
Depression				
No	121 (84,6%)	271 (75,7%)	Reference	-
Yes	22 (15,4%)	87 (24,3%)	**0,57 (0,34 – 0,95)**	**0,030**

a Normal weight: < 25 kg/m²; Overweight: 25–29.9 kg/m²; Obesity: > 30 kg/m².
b Increased: > 94 cm for men and > 88 cm for women.

The time since HIV diagnosis and the total time on treatment were not significantly associated with the occurrence of BLIPs.

Previous history of HIV-related complications was associated with a lower chance of BLIP (OR = 0.54; 95% CI: 0.36–0.80; p = 0.003). Similarly, the presence of a current complication (OR = 0.30; 95% CI: 0.10–0.87; p = 0.027) and current co-infection (OR = 0.25; 95% CI: 0.08–0.84; p = 0.025) also showed a protective association.

The presence of a current opportunistic disease showed a statistically significant association (p = 0.044), although it was not possible to estimate the OR due to the absence of cases of BLIP in this group.

The duration of dual therapy was significantly associated with the occurrence of BLIPs, with an increase in the odds with each additional year of treatment (OR = 1.76; 95%CI: 1.44–2.17; p < 0.001).

Treatment abandonment was also associated with the outcome, being identified as a protective factor (OR = 0.53; 95% CI: 0.29–0.98; p = 0.043).

There was no significant association between adherence ≥90%, last viral load detectable/undetectable or highest historical viral load and occurrence of BLIPs (Table 4).

Table 4. Association of HIV-related factors and the occurrence of BLIPs following the switch to a dual-drug regimen (3TC + DTG) among people living with HIV-1 receiving care at three HIV/AIDS referral centers in Recife, Pernambuco.

Factors	YES (n = 143)	NO (n = 358)	OR (IC95%)	p-value
Time since HIV infection				
< 10 years	9 (2,7%)	19 (5,3%)	Reference	-
≥ 10 years	134 (97,3%)	339 (94,7%)	0,83 (0,37 – 1,89)	0,665
A history of complications				
No	95 (66,4%)	185 (51,7%)	Reference	-
Yes	48 (33,6%)	173 (48,3%)	**0,54 (0,36 – 0,80)**	**0,003**
Current complication[a]				
No	139 (97,2%)	327 (97,2%)	Reference	-
Yes	4 (2,8%)	31 (8,7%)	**0,30 (0,10 – 0,87)**	**0,027**
Current co-infection [b]				
No	140 (97,9%)	330 (92,2%)	Reference	-
Yes	3 (2,1%)	28 (7,8%)	**0,25 (0,08 – 0,84)**	**0,025**
History of opportunistic infection[c]				
No	125 (87,4%)	297 (83,0%)	Reference	-
Yes	18 (12,6%)	61 (17,0%)	0,70 (0,40 – 1,23)	0,219
Current opportunistic disease [d]				
No	143 (100%)	348 (97,2%)	Reference	-
Yes	0 (0%)	10 (2,8%)	Not estimated	**0,044**
Tempo de tratamento				
< 10 years	17 (11,9%)	39 (10,9%)	Reference	-
≥ 10 years	126 (88,1%)	319 (89,1%)	0,91 (0,49 – 1,66)	0,750
Treatment duration				
Median (P25–P75)	2 (1 – 3)	2 (2 – 3)	**1,76 (1,44 – 2,17)[e]**	**<0,001**

There was improvement.				
No	22 (15,4%)	47 (13,1%)	Reference	-
Yes	121 (84,6%)	311 (86,9%)	0,83 (0,48 – 1,44)	0,509
Discontinued treatment				
No	129 (90,2%)	297 (83,0%)	Reference	-
Yes	14 (9,8%)	61 (17,0%)	**0,53 (0,29 – 0,98)**	**0,043**
Treatment adherence (90%)				
No	17 (11,9%)	49 (13,7%)	Reference	-
Yes	126 (88,1%)	309 (86,3%)	1,17 (0,65 – 2,12)	0,591
Latest viral load				
Detectable	124 (86,7%)	308 (86,0%)	Reference	-
Undetectable	19 (13,3%)	50 (14,0%)	0,94 (0,53 – 1,66)	0,842
Higher viral load (x 10^{-3})				
Median (P25–P75)	7,8 (1,0 – 11,8)	7,5 (1,0 – 11,7)	1,00 (0,99 – 1,01)[F]	0,427

a Asthenia (n = 3), diarrhea (n = 18), neurotoxoplasmosis (n = 9), tuberculosis (n = 4);
b Syphilis (n = 24), neurotoxoplasmosis (n = 6), tuberculosis (n = 4);
c Pneumocystosis (n = 6), neurotoxoplasmosis (n = 23), tuberculosis (n = 8), herpes zoster (n = 36), pneumonia (n = 5), syphilis (n = 9);
d Neurotoxoplasmosis (n = 6), tuberculosis (n = 4);
e Increased odds of BLIP for each 1-year increase in treatment duration;
f Increased odds of BLIP for each 1,000-unit increase in viral load.

MULTIVARIATE ANALYSIS

Model 1 (Sex, duration of dual therapy, and current coinfection) After adjustment, the following remained independently associated:

- Duration of dual therapy (aOR = 1.85; 95% CI: 1.50–2.29; p < 0.001), indicating an 85% increase in the odds of BLIP for each additional year.
- Female sex (aOR = 1.83; 95% CI: 1.20–2.78; p = 0.005).
- Current coinfection maintained a protective association (aOR = 0.29; 95% CI: 0.08–0.99; p = 0.048).

Model 2 (Sex, duration of dual therapy, and history of complications) The following maintained an independent association:

- Duration of dual therapy (aOR = 1.86; 95% CI: 1.51–2.30; p < 0.001).
- History of complications (aOR = 0.58; 95% CI: 0.37–0.88; p = 0.012).
- Female sex (aOR = 1.72; 95% CI: 1.13–2.64; p = 0.012).

The results can be observed in Table 5.

Table 5. Multivariate analysis of factors and the occurrence of BLIPs following the switch to the dual regimen (3TC + DTG) among people living with HIV-1 receiving care at three HIV/AIDS referral centers in Recife, PE – MODEL 1.

Fatores	OR (IC95%)	$OR_{ajustada}$ (IC95%)	p-valor
Modelo 1			

Tempo de terapia dupla			
Mediana (P_{25} – P_{75})	1,76 (1,44 – 2,17)	1,85 (1,50 – 2,29)	<0,001
Coinfecção atual			
Não	Referência	Referência	-
Sim	0,25 (0,08 – 0,84)	0,29 (0,08 – 0,99)	0,048
Sexo			
Masculino	Referência	Referência	-
Feminino	1,59 (1,08 – 2,36)	1,83 (1,20 – 2,78)	0,005
Modelo 2			
Tempo de terapia dupla			
Mediana (P_{25} – P_{75})	1,76 (1,44 – 2,17)	1,86 (1,51 – 2,30)	<0,001
Passado de complicação			
Não	Referência	Referência	-
Sim	0,54 (0,36 – 0,80)	0,58 (0,37 – 0,88)	0,012
Sexo			
Masculino	Referência	Referência	-
Feminino	1,59 (1,08 – 2,36)	1,72 (1,13 – 2,64)	0,012

The frequency of BLIPs following the switch to dual therapy with lamivudine (3TC) and dolutegravir (DTG) was 28.5%, indicating a relatively common occurrence during clinical follow-up.
The main factors independently associated with the occurrence of BLIPs were:

- Female sex (consistent increase in the likelihood of a BLIP);

- Longer duration of exposure to dual therapy, with a progressive increase in risk for each additional year of treatment.

Interestingly, variables related to greater clinical complexity (history of complications, current coinfection, and current complications) showed a protective association, possibly reflecting heightened clinical vigilance, stricter follow-up, and better laboratory monitoring of these individuals.
Socioeconomic factors, lifestyle habits, nutritional status, metabolic comorbidities, and current virological markers showed no significant association with the outcome.
In summary, the results suggest that although dual therapy with 3TC + DTG demonstrates good virological performance, the occurrence of BLIPs is not rare and appears to be more closely related to specific clinical characteristics and the duration of exposure to the regimen than to behavioral or socioeconomic factors.

DISCUSSION

The present investigation demonstrated that dual therapy with lamivudine (3TC) associated with dolutegravir (DTG) maintained adequate virological efficacy after therapeutic simplification, although with the occurrence of BLIPs in 28.5% of participants. These findings are consistent with recent evidence in the literature supporting the non-inferiority of dual therapy compared to traditional

triple regimens.

The incorporation of 3TC/DTG dual therapy into global recommendations represents a paradigmatic change in HIV management. The World Health Organization (WHO) has come to recognize dolutegravir as the preferred first-line drug due to its high genetic barrier to resistance, good tolerability profile, and virological robustness (WORLD HEALTH ORGANIZATION, 2021). Although WHO prioritizes triple regimens in public health settings, it acknowledges the growing evidence for simplification strategies in virologically suppressed patients.

The United States Department of Health and Human Services (DHHS) guidelines include dolutegravir/lamivudine as a recommended regimen both for treatment initiation in selected patients and for therapeutic simplification in individuals with sustained suppression and no history of resistance to lamivudine or integrase inhibitors (DHHS, 2024). The document emphasizes that dual therapy is appropriate in clinically stable patients, without active hepatitis B coinfection, and with adequate adherence.

Similarly, the European AIDS Clinical Society (EACS) guidelines recommend DTG/3TC as a maintenance option in patients with sustained virological suppression, highlighting robust evidence from the GEMINI and TANGO studies (EACS, 2023). The EACS also points out that therapeutic simplification may reduce cumulative toxicity, drug interactions, and long-term costs.

In this context, the results of the present study align with international recommendations by demonstrating overall maintenance of virological efficacy after switching to dual therapy, even in a population with an advanced average age and multiple comorbidities.

The DHHS guidelines define a blip as an isolated episode of detectable viremia (generally <200 copies/mL) followed by a return to viral suppression, without evidence of persistent virological failure (DHHS, 2024). The document emphasizes that isolated BLIPs do not necessarily predict therapeutic failure, particularly when associated with regimens with a high genetic barrier, such as those containing dolutegravir.

The EACS (2023) also reinforces that isolated low-magnitude episodes should be interpreted with caution and do not justify immediate change of the antiretroviral regimen, provided there is a return to undetectability and adequate adherence. WHO, in turn, maintains an operational definition of virological failure based on persistently ≥1000 copies/mL viral load in two consecutive measurements, which reinforces that low-magnitude BLIPs do not constitute therapeutic failure (WHO, 2021).

Thus, the frequency of BLIPs observed in this study should be interpreted in light of these recommendations: although relatively common, most of these events probably represent transient variations without adverse clinical significance.

The GEMINI-1 and GEMINI-2 studies demonstrated that DTG + 3TC is non-inferior to the triple regimen based on tenofovir/emtricitabine + DTG in treatment-naïve individuals, maintaining sustained virological suppression up to 144 weeks (CAHN et al., 2019). Similarly, the TANGO study showed that switching to DTG/3TC in previously suppressed patients maintained high rates of viral

suppression during prolonged follow-up, without a significant increase in virological failure (VAN WYK et al., 2020).

In a real-life setting, observational analyses also corroborate the virological robustness of dual therapy. Maggiolo et al. (2022) demonstrated sustained maintenance of viral suppression for up to five years after switching to 3TC/DTG, with a low incidence of virological failure. These findings reinforce that therapeutic simplification constitutes a safe and effective strategy, especially in individuals with a history of stable suppression.

In the present study, the occurrence of BLIPs was relatively frequent. BLIPs are defined as transient increases in detectable viral load followed by spontaneous return to undetectability without therapeutic change. The literature suggests that isolated and low-magnitude episodes are generally not associated with subsequent virological failure (LAPRISE et al., 2013). Thus, the presence of BLIPs in the context of dual therapy should not be automatically interpreted as loss of therapeutic efficacy, especially when not accompanied by sustained viral rebound.

Interestingly, an association was observed between longer exposure time to dual therapy and a higher likelihood of BLIPs. Although the literature still does not demonstrate a direct causal relationship, it is plausible that longer follow-up time increases the probability of detecting transient episodes due to greater cumulative exposure to laboratory monitoring. Longitudinal studies suggest that most BLIPs do not evolve into virological failure, especially in regimens containing dolutegravir, which has a high genetic barrier to resistance (TAIWO et al., 2018).

Although the guidelines do not describe a progressive increase in risk over time, cohort studies suggest that longer follow-up duration increases the cumulative probability of detecting transient episodes, especially in settings of frequent laboratory monitoring (MAGGIOLO et al., 2022).

Importantly, both DHHS and EACS highlight the high genetic barrier of dolutegravir, which significantly reduces the risk of resistance development even in the presence of transient episodes of viral replication (DHHS, 2024; EACS, 2023). This may explain why, even with the occurrence of BLIPs, there was no association with sustained virological failure in the major clinical trials.

Another relevant finding was the independent association of female sex with a higher occurrence of BLIPs. Although there is no definitive consensus in the literature on virological differences related to biological sex in dual therapy, pharmacokinetic, immunological, and behavioral factors may contribute to subtle differences in viral dynamics. However, this hypothesis requires further investigation.

The independent association of female sex with a higher occurrence of BLIPs deserves reflection. International guidelines recognize that women may present pharmacokinetic and immunological differences in response to antiretroviral treatment, although there is no conclusive evidence of greater risk of failure with dual therapy (WHO, 2021). Hormonal issues, body composition, and metabolic differences may influence plasma drug levels, but specific studies are needed to clarify this finding.

Paradoxically, variables related to greater clinical complexity (such as current coinfection and history of complications) showed a protective association in multivariate analysis. One possible explanation is that individuals with a greater burden of morbidity receive stricter clinical follow-up, favoring adherence and more intensive monitoring, thereby reducing the risk of virological instability.

The protective association of current coinfection and history of complications may reflect greater clinical surveillance in these patients. Both WHO and DHHS emphasize that structured follow-up and regular monitoring are essential for maintaining viral suppression (WHO, 2021; DHHS, 2024). Thus, patients with greater clinical complexity likely receive more intensive follow-up, favoring therapeutic stability.

Importantly, there was no association between adherence ≥ 90% and the occurrence of BLIPs, nor between the last detectable viral load and the outcome. These data reinforce that BLIPs may represent a transient biological phenomenon or analytical variability, and not necessarily imminent therapeutic failure.

Taken together, the results of this study strengthen the evidence that dual therapy with 3TC + DTG is effective and safe in real-world clinical practice, presenting a BLIP profile comparable to that described in the international literature. The occurrence of BLIPs, although relatively common, appears not to compromise the overall efficacy of the regimen when adequately monitored.

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