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Clinical Effectiveness, Adherence, Clinical and Paraclinical Outcomes Associated with Tenofovir Alafenamide/Emtricitabine/Bictegravir (TAF/FTC/BIC) in Patients Diagnosed with Human Immunodeficiency Virus (HIV) in Colombia: A Real-Life Study

Research Question

What are the clinical effectiveness, adherence, and clinical and paraclinical outcomes associated with Tenofovir Alafenamide/Emtricitabine/Bictegravir (TAF/FTC/BIC) in patients diagnosed with HIV in a Colombian EPS?

- P (Population): Patients aged 18 years and older diagnosed with HIV.
- I (Intervention): Treatment with TAF/FTC/BIC.
- C (Comparison): N/A.
- (Outcomes): Clinical effectiveness, adherence, and clinical and paraclinical outcomes.

Summary

HIV remains one of the most serious global pandemics, affecting 38 million people, with the highest prevalence in sub-Saharan Africa. Stigma and discrimination continue to hinder diagnosis and treatment, impacting marginalized populations most significantly. In Latin America, prevalence remains stable at approximately 0.4%, though Colombia faces unique challenges, with an epidemic concentrated among men who have sex with men. Recently published high-cost data from Colombia indicate that there are currently 165,405 people living with HIV (PLHIV), with 14,670 new cases reported in 2023. Social and economic factors, along with Venezuelan migration, complicate access to treatment in Colombia.

Advances in ART have been made with the use of integrase inhibitors such as TAF/FTC/BIC, which has demonstrated effectiveness across various populations. However, real-world studies specific to Colombia are lacking. In this study, we aim to evaluate adherence, effectiveness, and clinical outcomes of TAF/FTC/BIC treatment in a cohort of 169 patients within a larger group of 15,300 HIV patients under the EPS SURA program, generating evidence that is relevant to the Colombian context.

Problem Statement and Relevance

HIV remains one of the most significant global pandemics, with approximately 38 million people living with HIV worldwide, according to medical literature. The prevalence is particularly high in sub-Saharan Africa, which accounts for 70% of infections (1-3). Additionally, HIV is a leading cause of disability-adjusted life years (DALYs), ranking as the fifth leading cause globally in 2010 (4).

Stigma and discrimination remain major barriers to the diagnosis and treatment of HIV, disproportionately affecting marginalized populations such as sex workers, people who inject drugs, men who have sex with men, and transgender individuals (5). Despite advances in treatment, HIV remains a chronic condition that requires lifelong drug therapy to suppress viral load and prevent transmission (6).

In Latin America, HIV infection is recognized as a public health issue with unique epidemiological characteristics and challenges that vary across the region. HIV prevalence is relatively stable in Latin America, averaging 0.4% in the general population, though significant differences exist both between and within countries. Brazil, Mexico, and Colombia have the highest number of cases (7,8). In the Caribbean, for example, prevalence among adults exceeds 1% in several countries, where a decrease in new infections has also been observed (8).

HIV infection in Colombia poses a significant public health challenge, as the country has the fourth highest incidence rate of HIV/AIDS in Latin America, which has been rising since the 1980s (9). The epidemic is concentrated within key populations, such as men who have sex with men, who bear a high HIV burden in the country's major cities, with prevalence ranging from 6% to 24% (10). In 2023, 14,603 new cases were reported, marking a 13.5% increase compared to 2022. Of these cases, 34% were diagnosed at the AIDS stage. This trend of rising incidence and late diagnoses has been observed since the COVID-19 pandemic, likely due to delayed healthcare access. In 2023, new diagnoses in men accounted for 83% of cases compared to women.

HIV transmission in Colombia is influenced by social and economic factors, including social inequalities and sex tourism, particularly in cities like Cartagena (11). Co-infection with the hepatitis C virus is also becoming a growing issue among people living with HIV. Of the 1,058 new cases of hepatitis C reported in Colombia in 2023, 69.47% were co-infected with HIV (12). Additionally, hepatitis C is emerging as a significant problem among people who inject drugs (13). While access to antiretroviral therapy (ART) has improved, significant barriers to early diagnosis and timely treatment remain, exacerbated by social stigma, limited access to healthcare, and the impact of large-scale migration from Venezuela. This migration has placed added pressure on the Colombian healthcare system and disrupted the continuity of care for migrants living with HIV (14,15).

Current recommendations for the initiation of antiretroviral therapy (ART) include the use of an integrase strand transfer inhibitor (INSTI), such as bictegravir or dolutegravir, in combination with a nucleoside reverse transcriptase inhibitor (NRTI). These options have proven to be effective, with a high genetic barrier and potent activity in infected patients (16,17). Bictegravir/Emtricitabine/Tenofovir Alafenamide (TAF/FTC/BIC) is a single-tablet combination therapy developed for the treatment of HIV. Its mechanism of action combines the INSTI bictegravir with the NRTIs emtricitabine and tenofovir alafenamide,

demonstrating efficacy in both treatment-naïve patients (those without prior exposure to ART) and patients previously exposed to ART (18).

As of January 2024, EPS SURA manages a cohort of approximately 15,300 HIV patients. The control, evaluation, and follow-up of these patients are primarily conducted by specialized healthcare institutions (IPS), with a smaller proportion monitored by affiliated IPS providers. Program indicators include treatment abandonment rates, virological success rates, virological success with ART in the last 3 months, HIV viral load, and CD4 T-lymphocyte levels in the past 6 months for patients with HIV. To assess patient adherence, regular weekly evaluations are conducted, which include laboratory monitoring and attendance at medical appointments. In cases of non-compliance, a strict follow-up plan is established by a designated physician and a pharmaceutical chemist to verify medication intake and evaluate risk factors associated with non-adherence on an individual basis. From 2020 to 2023, 169 patients within the HIV program were prescribed TAF/FTC/BIC treatment.

To date, few studies have been conducted in real-life conditions (19-22) to evaluate the effectiveness, safety, and clinical outcomes of TAF/FTC/BIC initiation, especially in patients at later stages of HIV, in everyday contexts. These outcomes are influenced by factors such as timely access to healthcare, follow-up, and proper adherence. No real-life studies have been conducted in Colombia, despite integrase inhibitors being the first-line treatment in the country and widely available as part of the mandatory health plan. Therefore, it is essential to evaluate the effectiveness, adherence, and clinical outcomes within our cohort. Generating our own data will allow us to create evidence with significant population impact.

Theoretical framework

Human Immunodeficiency Virus (HIV) is a retrovirus from the *Retroviridae* family,

specifically an enveloped positive-stranded RNA virus (5). There are two main types: HIV-1, the most common worldwide, and HIV-2, which is more prevalent in West Africa (23). The virus is transmitted through bodily fluids such as blood, semen, vaginal secretions, and breast milk. Once inside the body, HIV primarily targets CD4+ T lymphocytes of the immune system, binding to CD4 receptors and one of the chemokine co-receptors, CCR5 or CXCR4, to enter the host cell (6). This process of viral entry and replication leads to the progressive destruction of CD4+ T lymphocytes, resulting in severe immunodeficiency if not treated promptly (6,24).

The molecular structure of HIV includes several key proteins. The virus is enveloped by a lipid membrane containing envelope glycoproteins (Env), specifically gp120 and gp41, which form a functional trimer. These glycoproteins are crucial for binding and fusion with host cells. Gp120 binds to the CD4 receptor on the surface of T lymphocytes, causing conformational changes that allow it to interact with the CCR5 or CXCR4 co-receptors, facilitating viral entry (25-27).

Its genome is RNA-based and encodes 15 distinct proteins, including structural Gag proteins (MA, CA, NC, p6), Pol enzymes (protease, reverse transcriptase, integrase), and accessory and regulatory proteins such as Tat, Rev, Nef, Vif, Vpr, and Vpu (28). These proteins play critical roles in the viral life cycle, from entry to replication and assembly (26,28). While HIV-1 and HIV-2 share structural similarities, they also exhibit significant differences in their envelope glycoproteins, which influence their pathogenicity and immune response. For example, HIV-2 has lower pathogenicity and a greater capacity to induce neutralizing antibodies (29,30). These structural and functional characteristics are crucial for understanding the mechanism of infection and for developing therapeutic and prevention strategies, such as vaccines (25,26).

Pathophysiology of HIV

The pathophysiology of HIV involves a series of complex mechanisms that result in

progressive immunosuppression (31-33). The process begins with the binding of the HIV envelope glycoprotein to the CD4 receptor on the surface of CD4+ T lymphocytes and other cells, such as macrophages (31). This facilitates virus entry and replication within host cells. During primary infection, acute viremia occurs with extensive viral shedding, and the virus is sequestered in the germinal centers of lymphoid tissues (34). There is massive destruction of memory CD4+ T lymphocytes early in the infection, although this does not initially lead to overt immunodeficiency. However, over time, the regeneration of these cells proves insufficient, resulting in the failure of immune homeostasis and progression to AIDS (Acquired Immunodeficiency Syndrome) (32,33).

In addition, chronic immune activation and immune dysfunction contribute significantly to the pathogenesis of the virus. Inappropriate activation of the immune system and the elevated secretion of proinflammatory cytokines regulate HIV expression in tissues (34). Infection of progenitor cells in the bone marrow and thymus also contributes to the impaired regeneration of immunocompetent cells (34). Furthermore, HIV causes direct damage to various tissues, such as the gut, brain, and lungs, through infection and activation of mononuclear cells (24). Systemic immune response activation and the destruction of lymphoid follicle integrity are hallmark features of pathogenic infection (35).

Clinical Manifestations of HIV

The clinical manifestations of HIV are varied and affect multiple systems due to the progressive immunosuppression and chronic immune activation that characterize the infection. HIV can be divided into several clinical phases, each with distinct characteristics:

1. Acute infection: This phase occurs within the first few weeks after exposure to the virus. Symptoms may include fever, adenopathy, pharyngitis, rash, myalgias, and arthralgias. This phase resembles an acute viral syndrome and is often underdiagnosed (36,37).
2. Chronic asymptomatic phase: Many patients enter a clinical latency phase that can last for several years. During this time, the virus continues to replicate and destroy

CD4+ T cells, but patients may remain asymptomatic (36,37).

3. Advanced Immunosuppression and AIDS: As the infection progresses and CD4+ T-lymphocyte counts decline, patients become increasingly susceptible to opportunistic infections and neoplasms. Common opportunistic infections include *Pneumocystis jirovecii* pneumonia, esophageal candidiasis, cytomegalovirus disease, cerebral toxoplasmosis, and pulmonary or disseminated tuberculosis, among others. The prevalence of these infections varies depending on the degree of immunosuppression and the geographical region. Some neoplasms associated with HIV include Kaposi's sarcoma, non-Hodgkin's lymphoma, and invasive cervical cancer (24,36,37).
4. Non-Infectious Manifestations: HIV is also linked to a range of non-infectious complications due to chronic immune activation and systemic inflammation. These include cardiovascular, hepatic, renal, bone, and neurological diseases. Cardiovascular disease in HIV patients may manifest as coronary artery disease, dilated cardiomyopathy, pulmonary hypertension, and endothelial dysfunction. Liver complications may involve virus-associated viral hepatitis and drug-induced hepatotoxicity, while renal dysfunction can present as HIV-associated nephropathy (37-39).
5. Hematological Manifestations: These are common and may include anemia, leukopenia, and thrombocytopenia. These conditions may result from the direct infection of hematopoietic progenitor cells, bone marrow dysfunction, and activation of the reticuloendothelial system (40).
6. Immune Reconstitution Inflammatory Syndrome (IRIS): In patients initiating ART, a paradoxical exacerbation of underlying infections may occur due to partial recovery of the immune system. IRIS can complicate clinical management and requires careful monitoring (24,41). In some cases, ART initiation should be postponed for a few weeks, especially when diagnosing opportunistic infections such as cytomegalovirus disease or meningeal cryptococcosis, to avoid exacerbation or worsening of symptoms, which can lead to considerable morbidity

and mortality.

Diagnosis of HIV

HIV diagnosis is performed using a combination of tests that detect viral RNA, p24 antigen, and HIV-specific antibodies. This approach allows for the identification of both acute and chronic infections:

1. HIV RNA: Detection of viral RNA is possible approximately 10-12 days after exposure to the virus, making this test particularly useful in the acute phase of infection, when antibodies are not yet detectable (23).
2. p24 Antigen: The p24 antigen appears in serum or plasma about 15-17 days after exposure. Detection of p24 antigen is a key feature of fourth- and fifth-generation tests, which allow for the identification of infection before antibodies develop (5,23).
3. Specific Antibodies: HIV antibodies (IgM and IgG) are detectable in serum or plasma approximately 21 days after exposure. Today, fourth-generation tests combine antibody detection with p24 antigen detection, improving sensitivity and enabling earlier detection of infection (5,42,43).

The diagnostic algorithm recommended by the CDC in the United States begins with a laboratory antigen/antibody (Ag/Ab) combination test. If this test is reactive, it is followed by an antibody differentiation test to distinguish between HIV-1 and HIV-2. If the differentiation test is negative or indeterminate, a nucleic acid amplification test is conducted to confirm acute infection (43,44). In Colombia, there is also a diagnostic algorithm that begins with a first rapid test (ELISA, chemiluminescence, or molecular test). If the first test is reactive, a second test should be performed to confirm the diagnosis. In cases of discordance, a molecular test for RNA detection or the Western Blot technique can be used (45).

HIV Treatment

It is critical that HIV treatment be initiated as early as possible (45). There is substantial

medical evidence that early initiation of ART prevents complications related to immunosuppression and reduces mortality. Treatment requires lifelong ART, which has transformed a fatal disease into a manageable chronic condition. Modern ART consists of combinations of at least three drugs from two or more different classes, providing long-lasting virologic suppression and improving clinical outcomes (46,47). Regimen selection is based on factors such as virologic efficacy, adverse effect profiles, pill burden, dosing frequency, drug-drug interactions, resistance test results, comorbidities, and cost (46).

In low- and middle-income countries, access to this therapy remains uneven due to economic constraints, inadequate health infrastructure, and social stigmatization (48,49). Despite these challenges, global efforts have enabled millions of people in these regions to access life-saving treatment (49). However, significant barriers to achieving universal coverage remain, including the need for improved early detection and timely initiation of treatment (50).

Recent innovations in ART include the development of drugs with improved safety and resistance profiles, as well as combination therapies that enhance adherence, such as single-tablet regimens and long-acting ARVs (46,47). These advances are particularly promising for improving adherence and reducing treatment burdens in low- and middle-income countries (50). Additionally, research into curative therapies, such as latency reversal agents and gene therapy, is ongoing, although their implementation faces challenges due to differences in host genetics and viral subtypes (48,51).

Bictegravir is a second-generation integrase strand transfer inhibitor (INSTI) used in HIV treatment. It is a key component of BikARVTy®, a fixed-dose regimen combining bictegravir, emtricitabine, and tenofovir alafenamide in a single daily tablet (52,53). This drug is notable for its high genetic barrier to resistance, meaning the virus is less likely to develop resistance to it compared to other INSTIs such as raltegravir and elvitegravir (54,55). It also has a limited drug-drug interaction profile, making it suitable for use in

combination with other antiretrovirals (52,56).

In phase 3 clinical trials, the bictegravir/emtricitabine/tenofovir alafenamide regimen has been shown to be non-inferior to dolutegravir-based regimens in both treatment-naïve and treatment-experienced patients, achieving effective virologic suppression without the emergence of resistance (53,57,58). Additionally, it is well tolerated and does not require prior HLA-B*5701 testing, which facilitates its rapid initiation in HIV treatment (53,57).

The most common adverse effects reported in clinical trials include diarrhea, nausea, and headache, with an incidence of at least 5% in treated subjects (59). Other less frequent adverse effects (≥2%) include fatigue, abnormal dreams, dizziness, insomnia, and abdominal distension (59). Regarding laboratory abnormalities, increases in serum creatinine, which stabilized throughout treatment, and increases in total bilirubin, mainly grade 1 and 2, were observed. Most adverse events were grade 1, and discontinuations due to adverse events were uncommon (59). Psychiatric events, such as suicidal ideation and depression, have also been reported, particularly in subjects with a history of psychiatric conditions. In subjects with end-stage renal disease, serious adverse events such as pneumonia and fluid overload were observed (59).

Objectives

General Objective: To estimate the clinical effectiveness and safety of HIV-positive patients on TAF/FTC/BIC treatment within an EPS in Colombia.

Specific Objectives:

- To characterize the sociodemographic and clinical profile of patients with HIV who initiate antiretroviral therapy with TAF/FTC/BIC.
- To identify the proportion of patients who have been on different pretreatment regimens before initiating TAF/FTC/BIC therapy.
- To assess the proportion of patients achieving virologic suppression at weeks 24

and 48 following the initiation of TAF/FTC/BIC therapy.

- To determine the proportion of patients with effective access to TAF/FTC/BIC therapy.
- To describe the impact of TAF/FTC/BIC treatment on CD4+ T-lymphocyte count, renal function, and lipid profile at weeks 24 and 48 after starting therapy.
- To determine the proportion of patients with a rapid onset of TAF/FTC/BIC therapy.
- To characterize the proportion of treatment-related adverse events at weeks 24 and 48 after initiating TAF/FTC/BIC therapy.
- To identify the proportion of patients meeting the criteria for adherence to TAF/FTC/BIC therapy.

Methodology

Study Design

This is an observational, retrospective cohort study that will include adult patients who received treatment with TAF/FTC/BIC between January 2020 and December 2023. The study will include both treatment-naïve patients and those who have been previously exposed to other treatments. The index date will correspond to the initiation date of the drug, at which point baseline demographic and clinical characteristics will be recorded.

Data Collection Plan/Source Documents

SURA is one of Colombia's leading insurers and has an integrated network of care centers. The clinical and administrative records of all its affiliates are stored in a centralized digital information system, which includes both structured and unstructured data. Data collection will be conducted through a retrospective review of electronic medical records, using a pre-designed Excel database (with an institutional Office license). This database will include the variables defined in the project. The study will utilize secondary data collected from the electronic records generated for each patient during the provision of health services. The conversion of unstructured data into structured

data during the execution of the protocol will be done solely through automated/algorithmic methods on a computer. To ensure consistency and standardization, the template will be parameterized with predefined answers or options for each variable. These will be defined based on medical experience, the availability of information, and in accordance with the protocol's guidelines.

All data will undergo a cleaning process, evaluating four key aspects: consistency, completeness, validity, and uniformity. Consistency is checked to ensure that the data are coherent and that harmonized codes and labels are used. Completeness ensures that the data are fully filled out and ready for use. Validity verifies that the data meet the required standards and fall within the established range. Uniformity ensures that the data are not duplicated and cannot be confused with other entries.

Subsequently, all relevant information will be extracted, creating a copy of the original record, which will be sent to the requester in tabular format (Microsoft Excel). The principal investigator or their delegate will import the Excel file into RStudio and Jamovi. Unstructured data will be obtained through a manual search of the patients' medical records, ensuring that the information is accurate, authentic, attributable, complete, consistent, legible, timely, and durable. These will be manually recorded in a flat file (Microsoft Access) and subsequently transferred to RStudio and Jamovi for analysis.

The following ICD-10 codes are considered key data for searching patient medical records:

- B200: HIV disease resulting in mycobacterial infection.
- B201: HIV disease resulting in other bacterial infections.
- B202: HIV disease resulting in cytomegalovirus disease.
- B203: HIV disease resulting in other viral infections.
- B204: HIV disease resulting in candidiasis.
- B205: HIV disease resulting in other mycoses.

- B206: HIV disease resulting in *Pneumocystis carinii* pneumonia.
- B207: HIV disease resulting in multiple infections.
- B208: HIV disease resulting in other infectious or parasitic diseases.
- B209: HIV disease resulting in unspecified infectious or parasitic disease.
- B210: HIV disease resulting in Kaposi's sarcoma.
- B211: HIV disease resulting in Burkitt's lymphoma.
- B212: HIV disease resulting in other types of non-Hodgkin's lymphoma.
- B213: HIV disease resulting in other malignant tumors of lymphoid, hematopoietic, and related tissues.
- B217: HIV disease resulting in multiple malignant tumors.
- B218: HIV disease resulting in other malignant tumors.
- B219: HIV disease resulting in unspecified malignant tumors.
- B220: HIV disease resulting in encephalopathy.
- B221: HIV disease resulting in lymphoid interstitial pneumonitis.
- B222: HIV disease resulting in cachectic syndrome.
- B227: HIV disease resulting in multiple illnesses classified elsewhere.
- B230: Acute HIV infection syndrome.
- B231: HIV disease resulting in generalized lymphadenopathy (persistent).
- B232: HIV disease resulting in immunologic and hematologic abnormalities, not elsewhere classified.
- B238: HIV disease resulting in other specified conditions.
- B24X: Human immunodeficiency virus (HIV) disease, not otherwise specified.
- F024: Dementia in human immunodeficiency virus (HIV) disease (B22.0†).
- Z21X: Asymptomatic human immunodeficiency virus (HIV) infection status.

All information on the variables of interest will be extracted from the clinical records. The process of data collection and form completion will be carried out by personnel from the Clinical Research Unit, following training to ensure standardized data capture. Quality

control of the data will be performed, including the review of codes, missing data, and any incorrect or improperly transcribed characters, according to the variable, by the researchers before the dataset is purified for analysis.

Study Population

All patients who meet the defined selection criteria within the established time frame for the search will be included:

- Inclusion Criteria:
  - Male or female patients aged 18 years or older.
  - Individuals with a confirmed HIV diagnosis.
  - Individuals enrolled in EPS SURA during the study period.
  - Patients receiving treatment with the TAF/FTC/BIC regimen.
- Exclusion Criteria:
  - Patients with a concurrent diagnosis of tuberculosis.
  - Pregnant patients during the study period.
  - Patients with virologic failure.
  - Patients who started treatment with TAF/FTC/BIC but changed providers or discontinued treatment before completing six months of therapy.

Variables

Variable Name	Definition	Nature	Measuring Level
Primary diagnosis of HIV	Patient with primary ICD-10 diagnosis of: B200, B201, B202, B203, B204, B205, B206, B207, B208, B209, B210, B211, B212, B213, B217, B218, B219, B220, B221, B222, B227, B230, B231, B232, B238, B24X, F024 or Z21X	Qualitative	Text
Diagnosis date	Date of first confirmed repeat HIV diagnosis recorded in the medical record	Quantitative, continuous	dd/mm/yyyy
Date of birth	Patient's date of birth	Quantitative, continuous	dd/mm/yyyy
Sex	Sex defined by patient's medical history	Qualitative	0: Female; 1: Male.
Race	Race defined by patient's medical history	Qualitative	Texto

Type of insurance	Insurance from the health system to whom the patient is covered.	Qualitative	0: Public 1: Private
Residence department	Department of Colombia where the patient lives	Qualitative	Text
AHT	Patient with hypertension marked in electronic medical record	Qualitative	0: No 1: Yes
Diabetes Mellitus	Patient with diabetes marked in electronic medical record	Qualitative	0: No 1: Yes
Chronic kidney disease	Patient with chronic kidney disease marked in electronic medical record	Qualitative	0: No 1: Yes
Hepatitis B co-infection	Patient with repeated confirmed ICD-10 diagnosis of B181 Chronic type B viral hepatitis, no delta agent from the date of HIV diagnosis to the end of follow-up.	Qualitative	0: No 1: Yes
Hepatitis C co-infection	Patient with repeated confirmed ICD-10 diagnosis of B182 Chronic viral hepatitis type C from the date of HIV diagnosis to the end of follow-up.	Qualitative	0: No 1: Yes
Major depressive disorder	Patient with confirmed ICD-10 repeat diagnoses: F320, F321, F322, F323, F328, F329, F330, F331, F332, F333, F334, F338, F339, F340, F341, F348, F349, F380, F381, F388 or F39X from the date of HIV diagnosis to the end of follow-up	Qualitative	0: No 1: Yes
Start date TAF/FTC/BIC	Medication start date TAF/FTC/BIC	Quantitative, continuous	dd/mm/yyyy
End date TAF/FTC/BIC	Medication end date TAF/FTC/BIC	Quantitative, continuous	dd/mm/yyyy
NAIVE for TAF/FTC/BIC	Patient whose first HIV treatment is TAF/FTC/BIC	Qualitative	0: No 1: Yes
ARVT scheme prior to TAF/FTC/BIC	Name of ARVT scheme immediately preceding TAF/FTC/BIC used for HIV treatment	Qualitative	Text
HIV viral load at baseline	The patient has HIV viral load results at baseline (+ or - 4 weeks) of TAF/FTC/BIC therapy.	Qualitative	0: No 1: Yes
BHIV viral load at baseline value	HIV viral load value at baseline (+ or - 4 weeks) of TAF/FTC/BIC therapy	Quantitative, continuous	1, 1.5, 1.8, 2,… n
HIV viral load at week 24	The patient has HIV viral load results at week 24 (+ or - 2 weeks) of TAF/FTC/BIC therapy.	Qualitative	0: No 1: Yes
HIV viral load value at week 24	HIV viral load value at week 24 (+ or - 2 weeks) of TAF/FTC/BIC therapy	Quantitative, continuous	1, 1.5, 1.8, 2,… n
HIV viral load at week 48	The patient has HIV viral load results at week 48 (+ or - 2 weeks) of TAF/FTC/BIC therapy.	Qualitative	0: No 1: Yes
HIV viral load value at week 48	HIV viral load value at week 48 (+ or - 2 weeks) of TAF/FTC/BIC therapy	Quantitative, continuous	1, 1.5, 1.8, 2,… n
CD4 Lymphocyte count at baseline	The patient has CD4 Lymphocyte count results at baseline (+ or - 4 weeks) of TAF/FTC/BIC therapy.	Qualitative	0: No 1: Yes
CD4 Lymphocyte count at baseline value	CD4 Lymphocyte count value at baseline (+ or - 4 weeks) of therapy with TAF/FTC/BIC	Cuantitativa, continua	1, 1.5, 1.8, 2,… n

CD4 Lymphocyte count at week 24	The patient has CD4 Lymphocyte count results at week 24 (+ or - 2 weeks) of TAF/FTC/BIC therapy.	Qualitative	0: No 1: Yes
CD4 Lymphocyte count value at week 24	CD4 Lymphocyte count value at week 24 (+ or - 2 weeks) of therapy with TAF/FTC/BIC	Quantitative, continuous	1, 1.5, 1.8, 2,… n
CD4 Lymphocyte count at week 48	The patient has CD4 Lymphocyte count results at week 48 (+ or - 2 weeks) of TAF/FTC/BIC therapy.	Qualitative	0: No 1: Yes
CD4 Lymphocyte count value at week 48	CD4 Lymphocyte count value at week 48 (+ or - 2 weeks) of therapy with TAF/FTC/BIC	Quantitative, continuous	1, 1.5, 1.8, 2,… n
HDL at baseline	The patient has high-density lipoprotein results at baseline (+ or - 4 weeks) of TAF/FTC/BIC therapy	Qualitative	0: No 1: Yes
HDL value at baseline	High-density lipoprotein value at baseline (+ or - 4 weeks) of TAF/FTC/BIC therapy	Quantitative, continuous	1, 1.5, 1.8, 2,… n
HDL at week 24	The patient has high-density lipoprotein results at week 24 (+ or - 2 weeks) of TAF/FTC/BIC therapy.	Qualitative	0: No 1: Yes
HDL value at week 24	High-density lipoprotein value at week 24 (+ or - 2 weeks) of TAF/FTC/BIC therapy	Quantitative, continuous	1, 1.5, 1.8, 2,… n
HDL at week 48	The patient has high-density lipoprotein results at week 48 (+ or - 2 weeks) of TAF/FTC/BIC therapy.	Qualitative	0: No 1: Yes
HDL value at week 48	High-density lipoprotein value at week 48 (+ or - 2 weeks) of TAF/FTC/BIC therapy	Quantitative, continuous	1, 1.5, 1.8, 2,… n
LDL at baseline	The patient has low-density lipoprotein results at baseline (+ or - 4 weeks) of TAF/FTC/BIC therapy.	Qualitative	0: No 1: Yes
LDL value at baseline	Low-density lipoprotein value at baseline (+ or - 4 weeks) of TAF/FTC/BIC therapy	Quantitative, continuous	1, 1.5, 1.8, 2,… n
LDL at week 24	The patient has low-density lipoprotein HDL results at week 24 (+ or - 2 weeks) of TAF/FTC/BIC therapy.	Qualitative	0: No 1: Yes
LDL value at week 24	Low-density lipoprotein HDL value at week 24 (+ or - 2 weeks) of TAF/FTC/BIC therapy	Quantitative, continuous	1, 1.5, 1.8, 2,… n
LDL at week 48	The patient has low-density lipoprotein results at week 48 (+ or - 2 weeks) of TAF/FTC/BIC therapy.	Qualitative	0: No 1: Yes
LDL value at week 48	Low-density lipoprotein value at week 48 (+ or - 2 weeks) of TAF/FTC/BIC therapy	Quantitative, continuous	1, 1.5, 1.8, 2,… n
AST at baseline	The patient has aspartate aminotransferase results at baseline (+ or - 4 weeks) of TAF/FTC/BIC therapy.	Qualitative	0: No 1: Yes
AST at baseline value	Aspartate aminotransferase value at baseline (+ or - 4 weeks) of TAF/FTC/BIC therapy	Quantitative, continuous	1, 1.5, 1.8, 2,… n
AST at week 24	The patient has aspartate aminotransferase results at week 24 (+ or - 2 weeks) of TAF/FTC/BIC therapy.	Qualitative	0: No 1: Yes
AST value at week 24	Aspartate aminotransferase value at week 24 (+ or - 2 weeks) of TAF/FTC/BIC therapy	Quantitative, continuous	1, 1.5, 1.8, 2,… n

AST at week 48	The patient has aspartate aminotransferase results at week 48 (+ or - 2 weeks) of TAF/FTC/BIC therapy.	Qualitative	0: No 1: Yes
AST value at week 48	Aspartate aminotransferase value at week 48 (+ or - 2 weeks) of TAF/FTC/BIC therapy	Quantitative, continuous	1, 1.5, 1.8, 2,… n
ALT at baseline	The patient has alanine aminotransferase results at baseline (+ or - 4 weeks) of TAF/FTC/BIC therapy.	Qualitative	0: No 1: Yes
ALT value at baseline	Alanine aminotransferase value at baseline (+ or - 4 weeks) of TAF/FTC/BIC therapy	Quantitative, continuous	1, 1.5, 1.8, 2,… n
ALT week at 24	The patient has alanine aminotransferase results at week 24 (+ or - 2 weeks) of TAF/FTC/BIC therapy.	Qualitative	0: No 1: Yes
ALT value week at 24	Alanine aminotransferase level at week 24 (+ or – 2 weeks) of TAF/FTC/BIC therapy	Quantitative, continuous	1, 1.5, 1.8, 2,… n
ALT week at 48	The patient has alanine aminotransferase results at week 48 (+ or - 2 weeks) of therapy with TAF/FTC/BIC.	Qualitative	0: No 1: Yes
ALT value at week 48	Alanine aminotransferase value at week 48 (+ or - 2 weeks) of therapy with TAF/FTC/BIC.	Quantitative, continuous	1, 1.5, 1.8, 2,… n
Total bilirubin at baseline	The patient has total bilirubin results at baseline (+ or - 4 weeks) of therapy with TAF/FTC/BIC.	Qualitative	0: No 1: Yes
Total bilirubin value at baseline	Total bilirubin value at baseline (+ or - 4 weeks) of therapy with TAF/FTC/BIC.	Quantitative, continuous	1, 1.5, 1.8, 2,… n
Total bilirubin at week 24	The patient has total bilirubin results at week 24 (+ or - 2 weeks) of therapy with TAF/FTC/BIC.	Qualitative	0: No 1: Yes
Total bilirubin value at at week 24	Total bilirubin value at week 24 (+ or - 2 weeks) of therapy with TAF/FTC/BIC.	Quantitative, continuous	1, 1.5, 1.8, 2,… n
Total bilirubin at week 48	The patient has total bilirubin results at week 48 (+ or – 2 weeks) of TAF/FTC/BIC therapy	Qualitative	0: No 1: Yes
Total bilirubin value at week 48	Total bilirubin value at week 48 (+ or – 2 weeks) of TAF/FTC/BIC therapy	Quantitative, continuous	1, 1.5, 1.8, 2,… n
Serum creatinine at baseline	The patient has baseline serum creatinine results (+ or – 4 weeks) of TAF/FTC/BIC therapy	Qualitative	0: No 1: Yes
Serum creatinine value at baseline	Baseline serum creatinine value (+ or – 4 weeks) of TAF/FTC/BIC therapy	Quantitative, continuous	1, 1.5, 1.8, 2,… n
Serum creatinine at week 24	The patient has serum creatinine results at week 24 (+ or – 2 weeks) of TAF/FTC/BIC therapy	Qualitative	0: No 1: Yes
Serum creatinine value at week 24	Serum creatinine value at week 24 (+ or – 2 weeks) of TAF/FTC/BIC therapy	Quantitative, continuous	1, 1.5, 1.8, 2,… n
Serum creatinine at week 48	The patient has serum creatinine results at week 48 (+ or – 2 weeks) of TAF/FTC/BIC therapy	Qualitative	0: No 1: Yes
Serum creatinine value at week 48	Serum creatinine value at week 48 (+ or – 2 weeks) of TAF/FTC/BIC therapy	Quantitative, continuous	1, 1.5, 1.8, 2,… n

Glomerular filtration rate at baseline	The patient has the estimated glomerular filtration rate (eGFR) by CKD-EPI at baseline (+ or - 4 weeks) of TAF/FTC/BIC therapy	Qualitative	0: No 1: Yes
Value of glomerular filtration rate at baseline	Value of estimated glomerular filtration rate (eGFR) calculated by CKD-EPI at baseline (+ or - 4 weeks) of TAF/FTC/BIC therapy	Quantitative, continuous	1, 1.5, 1.8, 2,… n
Glomerular filtration rate at week 24	The patient has an estimated glomerular filtration rate (eGFR) calculated by CKD-EPI at week 24 (+ or - 2 weeks) of TAF/FTC/BIC therapy	Qualitative	0: No 1: Yes
Glomerular filtration rate value at week 24	Value of estimated glomerular filtration rate (eGFR) calculated by CKD-EPI at week 24 (+ or - 2 weeks) of TAF/FTC/BIC therapy	Quantitative, continuous	1, 1.5, 1.8, 2,… n
Glomerular filtration rate at week 48	The patient has the estimated glomerular filtration rate (eGFR) calculated by CKD-EPI at week 48 (+ or - 2 weeks) of TAF/FTC/BIC therapy	Qualitative	0: No 1: Yes
Glomerular filtration rate value at week 48	Value of estimated glomerular filtration rate (eGFR) calculated by CKD-EPI at week 48 (+ or - 2 weeks) of TAF/FTC/BIC therapy	Quantitative, continuous	1, 1.5, 1.8, 2,… n
Number of medication claims	Number of TAF/FTC/BIC medication claims during the 48-week follow-up	Quantitative, discrete	1, 2, 3,… n
Headache emergency	The patient visited the emergency department during the period of TAF/FTC/BIC use for ICD-10 codes G444 and/or G448	Qualitative	0: No 1: Yes
Diarrhea emergency	The patient visited the emergency department during the period of TAF/FTC/BIC use for ICD-10 code A09X: Diarrhea and gastroenteritis of presumed infectious origin	Qualitative	0: No 1: Yes
Nausea and vomiting emergency	The patient visited the emergency department during the period of TAF/FTC/BIC use for ICD-10 code R11X: Nausea and vomiting	Qualitative	0: No 1: Yes
Termination of health insurance coverage	The patient terminated their health insurance with EPS SURA.	Qualitative	0: No 1: Yes
Date of termination of insurance coverage	Date of termination of health insurance with EPS SURA	Quantitative, continuous	dd/mm/yyyy
Death	The patient passed away after the index date	Qualitative	0: No 1: Yes
Date of death	Date of patient's death	Quantitative, continuous	dd/mm/yyyy

Sample Size

No sampling will be conducted, as data from the entire population (census) that meets the eligibility criteria for this study will be used.

Statistical Analysis

The database created in Access will be transferred to RStudio and Jamovi for the corresponding descriptive analysis.

Characterization of the Sociodemographic and Clinical Profile

Absolute and relative frequencies will be calculated for categorical variables. For numerical variables, normality will be assessed using the Shapiro-Wilk test. Variables with a p-value greater than 0.05 will be considered to follow a normal distribution and will be represented by means and standard deviations. For variables that do not follow a normal distribution, medians and interquartile ranges will be used.

Proportion of Pretreatment Regimens

The proportion of patients who have received different combinations of ART prior to starting TAF/FTC/BIC will be calculated. Frequency tables will be used to display the proportion of each pretreatment regimen, supplemented by bar charts reflecting the frequencies of the most common treatments.

Virologic Suppression at 24 and 48 Weeks

Virologic suppression is defined as a viral load of <50 copies/mL at weeks 24 and 48 of treatment. The proportion of patients achieving this threshold will be calculated at both time points, and the results will be compared between weeks 24 and 48 using McNemar's test for related samples.

Effective Access to Treatment

Effective treatment is defined as the initiation of therapy within a reasonable time after prescription. The time between prescription and the initiation of treatment will be calculated (mean or median, depending on the normality test), and patients will be classified into two categories: those who initiate treatment effectively (within a short period, generally defined as initiation within 7-14 days of HIV diagnosis) and

those who experience delays.

Paraclinical Results: CD4 T-Lymphocytes, Renal Function, and Lipid Profile

To describe changes in clinical markers at weeks 24 and 48, the summary measure (mean or median, depending on the normality test) of baseline values will be compared with the values of these biomarkers at the two time points. Paired-samples t-tests or Wilcoxon tests will be used if the data distribution is non-normal.

Rapid Onset of Therapy

The frequency of patients meeting this criterion will be calculated, and the characteristics of those with rapid onset versus those without will be compared using the chi-square test.

Treatment-Related Adverse Events

Treatment-related adverse events at weeks 24 and 48 will be characterized and classified according to type and severity. The proportion of patients experiencing these events will be calculated and compared between the two time points. Contingency tables and chi-square tests will be used to analyze the relationship between adverse events and other clinical and sociodemographic variables.

Adherence to Treatment

Adherence will be measured using pharmacy claims information with the Proportion of Days Covered (PDC). PDC calculates the proportion of days the patient has access to the medication over a specified period (64,65). In this study, patients with a PDC of 80% or higher will be considered to have adequate adherence. However, studies have shown that even lower adherence levels can still result in a high rate of viral suppression.

Biases

The following biases are considered potential risks in this study:

- Information Bias: This refers to errors introduced during the measurement of exposure, events, and other variables in the study population, which, if present, may lead to erroneous conclusions regarding the hypothesis being investigated. In this study, data obtained from secondary sources such as medical records may not fully or accurately capture the information of interest. To control for this bias, a random review of at least 10% of the clinical histories will be conducted, and the information recorded in the database will be cross-referenced with that found in the clinical records.
- Loss to Follow-up Bias: Loss of participants throughout the study may introduce bias, as the selection of participants is not random.

Statement on the Application of Ethical Principles in Research

In accordance with Resolution 8430 of 1993, this study is classified as risk-free: it involves retrospective documentary research techniques and methods, with no intervention or intentional modification of the biological, physiological, psychological, or social variables of individuals. The study will be conducted through the review of medical records and will be submitted for approval to the SURA Ethics Committee.

The use of medical records will be in compliance with Resolution 1995 of 1999, ensuring data protection and confidentiality of the information collected. Furthermore, a confidentiality agreement has been signed for academic projects, establishing compliance with legal provisions. This agreement confirms that access to personal data and confidential information from medical records will be provided, data which are considered sensitive under the "habeas data" law. The dissemination of this information could affect the privacy of the data owner. Therefore, all provisions outlined in this document will be strictly adhered to.

Timeline

Activity/Month	1	2	3	4	5	6
Phase 1: Research protocol writing	■					
Phase 2: Submission to IRB		■				
Phase 3: Execution (analysis and structuring of results and discussion)			■	■		
Phase 4: Technical report writing and closing to IRB					■	
Phase 5: Writing of publication-type manuscript and submission to journal and conference						■

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