

Comparative Analysis of the Efficacy and Safety of HIV/AIDS Treatment Strategies: A Comprehensive Review of Clinical Trial Data

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ABSTRACT

This comprehensive review and meta-analysis aimed to evaluate the comparative efficacy and safety of various antiretroviral (ARV) therapy regimens for HIV/AIDS treatment based on clinical trial data over 48 and 96 weeks. We conducted a systematic search across multiple databases, identifying 17 randomized controlled trials that met our inclusion criteria. These studies provided data on 12 different ARV regimens, focusing on integrase strand transfer inhibitor (INSTI)-based, non-nucleoside reverse transcriptase inhibitor (NNRTI)-based, and protease inhibitor (PI)-based treatments. Efficacy was measured by the percentage of participants achieving viral load suppression below 50 copies/mL, while safety was assessed through the incidence of serious adverse events. The analysis revealed significant variability in the efficacy and safety profiles of the ARV regimens studied. INSTI-based treatments, notably elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) and dolutegravir/lamivudine (DTG/3TC), demonstrated the highest levels of viral suppression, maintaining effectiveness at both the 48 and 96-week benchmarks. Notably, a weak positive correlation was identified between the efficacy of these treatments and the incidence of serious adverse events. Despite this correlation, the overall link between a regimen's efficacy and its safety was found to be weak, highlighting the critical importance of tailoring HIV treatment to the individual patient's needs and circumstances. The study underscores the importance of individualizing HIV/AIDS treatment strategies to optimize both efficacy and safety outcomes. While INSTI-based regimens show promise in terms of efficacy, the slightly increased risk of serious adverse events calls for careful consideration in treatment selection and monitoring. Future research should focus on longitudinal studies and the development of predictive models to further refine treatment strategies, helping ensure they are tailored to meet the individual needs of patients living with HIV/AIDS.

KEYWORDS HIV/AIDS, antiretroviral therapy, efficacy, safety, INSTI-based regimens

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INTRODUCTION

The global health landscape has been significantly challenged by human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS), affecting millions worldwide. Despite advancements in treatment options, primarily through antiretroviral therapy (ART), the quest for optimizing treatment strategies remains central to improving patient outcomes (1). The dynamic nature of HIV, characterized by its mutation potential, necessitates continuous evaluation of treatment efficacy and safety to adapt to changing patient needs and virus characteristics (2). Current literature provides extensive insights into individual HIV/AIDS treatment strategies but often falls short of offering a comprehensive comparative analysis. Although there have been previous systematic reviews and meta-analyses on the efficacy and safety of HIV/AIDS treatments, this report offers novel insights by comparing a broader range of regimens, including newer integrase strand transfer inhibitor (INSTI)-based therapies over extended periods of 48 and 96 weeks improving the ability of healthcare providers to make more fully informed treatment decisions and highlighting the need for a detailed comparative review of the efficacy and safety of these strategies (3).

Globally, the response to HIV/AIDS has been diverse, with significant advancements in some regions, while others continue to struggle with the epidemic. For instance, recent studies from North America and Europe have shown a promising decrease in HIV transmission rates, attributed to effective ART regimens and preventive measures such as pre-exposure prophylaxis (PrEP) (4). In contrast, Sub-Saharan Africa, despite housing approximately two-thirds of the global HIV positive population, has faced challenges in accessing these advanced treatments, leading to a slower decline in prevalence (5). In Asia, particularly in China, the approach to HIV/AIDS treatment has evolved significantly over the past decade. The Chinese government and healthcare providers have made considerable efforts to improve access to ART, resulting in improved treatment outcomes and reduced HIV transmission rates (6). However, disparities in treatment accessibility and quality

still exist, particularly in rural areas and among marginalized communities (7).

The study of ART's efficacy and safety profiles is ongoing, with newer drugs and treatment combinations continually being tested. Recent studies from 2021 to 2024 have further elucidated the benefits and drawbacks of various ART regimens. For instance, recent meta-analyses have highlighted the superior efficacy of INSTIs over other drug classes in achieving viral suppression (8), yet they have raised concerns about their long-term safety and potential side effects. Additionally, updated guidelines and studies from 2021-2024 have emphasized the need for continuous monitoring and adaptation of treatment strategies to manage emerging drug resistance (9).

Moreover, the emergence of HIV drug resistance remains a significant concern, undermining the efficacy of existing treatment strategies. Studies from both developed and developing countries have reported increasing rates of resistance to first-line ART regimens, calling for a reevaluation of current treatment protocols and the development of novel therapeutic options (10). The significance of the present study lies in its direct implications for HIV/AIDS treatment. By providing a detailed comparative analysis of various treatment regimens, this study aims to help healthcare providers make better informed decisions that could improve patient management and outcomes. Specifically, it highlights the efficacy and safety of newer INSTI-based regimens compared to traditional treatments, thereby offering valuable insights for optimizing HIV/AIDS therapy. Additionally, the study identifies gaps in current research and suggests areas for future investigation, particularly in managing drug resistance and increasing long-term treatment sustainability (11).

This study's comprehensive review of clinical trial data, incorporating both international and national literature, underscores the ongoing need to adapt HIV/AIDS treatment strategies in the face of evolving challenges. By comparing the efficacy and safety profiles of various treatment strategies, this research aims to provide actionable insights that can help guide policy and practice, ultimately contributing to the global effort to control and eventually eradicate HIV/AIDS.

METHODS

Search strategy

To ensure a comprehensive collection of data, an extensive literature search was conducted across multiple databases: PubMed, Embase, Cochrane Library, and Web of Science, covering publications from January 2000 to December 2022. The search strategy included both MeSH terms and free-text terms with variations and combinations of “HIV,” “AIDS,” “ART,” “clinical trial,” “treatment efficacy,” “safety,” and “outcome comparison.” The search was augmented by scrutinizing the reference lists of selected articles for additional relevant studies (12).

Inclusion and exclusion criteria

The study selection followed predefined inclusion and exclusion criteria to ensure relevance and quality. Inclusion criteria specified randomized controlled trials (RCTs) comparing different HIV/AIDS treatment strategies with outcomes related to efficacy (e.g., viral suppression, CD4⁺ cell count improvement) and safety (e.g., adverse events, drug resistance). Exclusion criteria were studies not directly comparing treatment strategies, non-randomized trials, observational studies, case reports, reviews, and studies not in English. Additionally, studies focusing on pediatric populations were excluded due to distinct treatment modalities (13).

Data extraction

Data extraction was conducted independently by two researchers using a standardized form designed for this study. This form captured comprehensive details including study identification (author, year), methodology (study design, duration, location), participants (sample size, age, baseline CD4⁺ count, HIV viral load), treatment strategies compared, outcome measures, and results. Discrepancies in data extraction were resolved through consensus or involvement of a third reviewer if necessary. This meticulous process was followed to maximize the accuracy and reliability of the data used for analysis (14).

Statistical analysis

For the statistical analysis, the study employed meta-analytic techniques using RevMan 5.4 software. The effect sizes were calculated as relative

risks (RR) for binary outcomes and mean differences (MD) for continuous outcomes, both with 95% confidence intervals (CIs). Heterogeneity among studies was assessed using the χ^2 test and I^2 statistics, categorizing heterogeneity into low ($I^2 < 25\%$), moderate ($25\% \leq I^2 < 75\%$), and high ($I^2 \geq 75\%$). Based on the heterogeneity results, a fixed-effects model was used for low heterogeneity, while a random-effects model was applied for moderate to high heterogeneity. Sensitivity analysis was conducted to explore the influence of individual studies on the overall results, and publication bias was assessed through funnel plots and Egger's test (15).

Quality assessment

The quality of included studies was rigorously assessed using the Cochrane Collaboration's tool for assessing the risk of bias in randomized trials. This assessment focused on seven domains: sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other potential sources of bias. Each domain was rated as “low risk,” “high risk,” or “unclear risk” of bias. This comprehensive evaluation informed the interpretation of the meta-analysis results, providing insights into the reliability of the findings (16).

Ethical considerations

Given the study's design as a systematic review and meta-analysis of published data, ethical approval was not required. However, all procedures were performed in accordance with relevant guidelines and regulations, including adherence to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. This adherence underscores the commitment to transparency, reproducibility, and ethical standards in conducting and reporting scientific research (17).

RESULTS

Selection and quality evaluation of studies for a systematic review on HIV antiretroviral therapy efficacy and safety

1. Literature search and study selection

A comprehensive search across multiple databases yielded 2,682 records. After removing duplicates with Zotero, 2,575 records remained.

Initial screening based on titles excluded 2,025 articles that did not meet the study's criteria. Further scrutiny of abstracts and full texts led to the exclusion of an additional 550 articles. Ultimately, 17 studies were included in this systematic review and meta-analysis, covering 12 different antiviral regimens focused on three main classes of antiretroviral (ARV) drugs: integrase strand transfer inhibitors (INSTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), and protease inhibitors (PIs) (Figure 1A). The quality of these 17 studies was rigorously assessed using the Cochrane Collaboration's tool for assessing the risk of bias in randomized trials, ensuring robust and reliable conclusions.

The regimens include INSTI-based treatments such as elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF), elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate (E/C/F/TDF), bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF), abacavir/dolutegravir/lamivudine (ABC/DTG/3TC), dolutegravir/lamivudine (DTG/3TC), dolutegravir/emtricitabine/tenofovir disoproxil fumarate (DTG/F/TDF), dolutegravir/emtricitabine/tenofovir alafenamide (DTG/F/TAF), and raltegravir/emtricitabine/tenofovir disoproxil fumarate (RAL/XTC/TDF); NNRTI-based treatments such

as efavirenz/emtricitabine/tenofovir disoproxil fumarate (EFV/F/TDF), anvinovir/ lamivudine/tenofovir disoproxil fumarate (ANV/3TC/TDF), and efavirenz/lamivudine/tenofovir disoproxil fumarate (EFV/3TC/TDF); and the PI-based treatment lopinavir/ritonavir plus lamivudine (LPV/r+3TC). Notably, efavirenz/lamivudine/tenofovir disoproxil fumarate (EFV/3TC/TDF) is the most commonly used national first-line anti-HIV treatment, with efavirenz/emtricitabine/tenofovir disoproxil fumarate (EFV/F/TDF) and anvinovir/lamivudine/tenofovir disoproxil fumarate (ANV/3TC/TDF) included to establish networked meta-bridging relationships.

Characteristics and quality assessment of included studies

The 17 included studies were all RCTs, comprising 15 studies registered internationally and 2 studies registered in China. Among these, 13 were phase III clinical trials, 3 were phase II, and one study conducted in China (ChiCTR1900024611) did not specify its phase. Quality assessment revealed varying levels of bias risk across studies, depicted in a risk of bias graph (Figure 1B), with green indicating low risk, yellow indicating medium risk, and red indicating high risk. The primary source of high risk was identified as selective reporting,

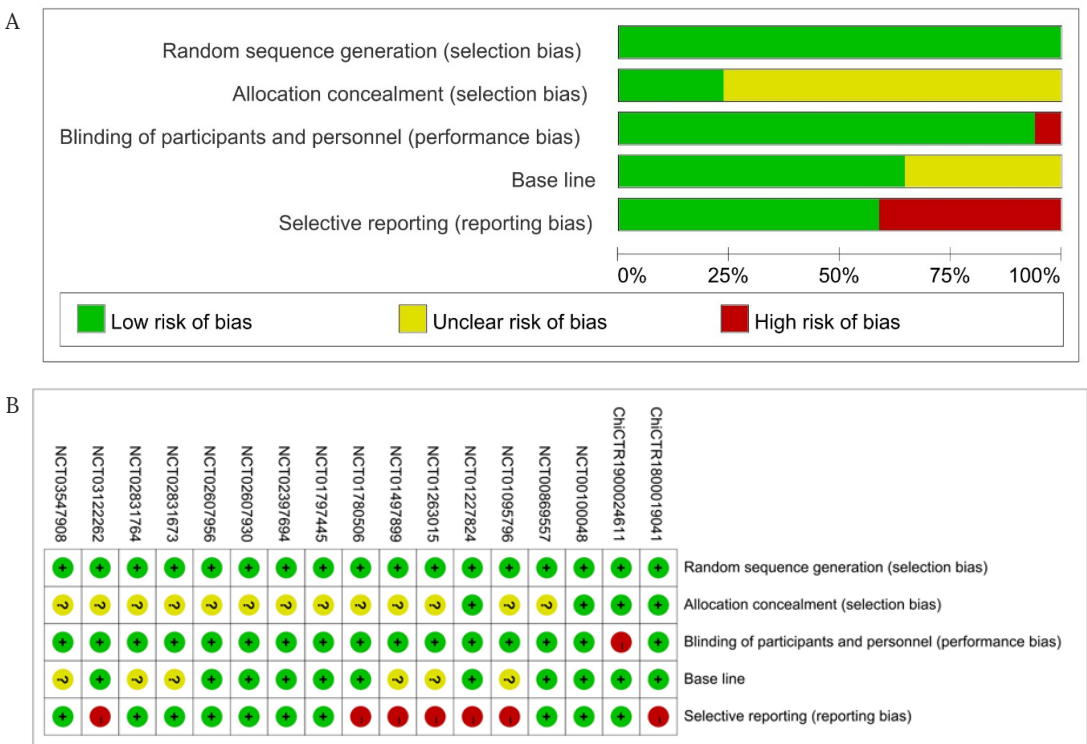


Figure 1. Risk of bias summary (A), Risk of bias assessment for individual studies (B)

given the extensive set of efficacy and safety indicators evaluated, with not all studies reporting in detail on these indicators.

Efficacy and immune response of ARV therapies at the 48-week milestone

1. Efficacy assessment of ARV regimens at the 48-week milestone

Within the scope of our study, **Figure 2** delineates the suppression rates of viral load below 50 copies/ml at the 48-week juncture for a spectrum of ART. The data reveals a gradient of efficacy levels, with the E/C/F/TAF regimen leading the cohort, where a noteworthy 90% of patients achieved the desired viral suppression threshold. This high level of efficacy is closely followed by the DTG/3TC and DTG/F/TAF regimens, both demonstrating viral suppression in over 85% of patients. Conversely, regimens such as ANV/3TC/TDF and RAL/XTC/TDF manifest at the lower spectrum of viral suppression efficacy, with rates oscillating around the 70% mark. This disparity in efficacy not only underscores the diverse virological responses elicited by different treatment regimens but also stresses the critical need for individualized therapeutic strategies tailored to patient-specific clinical profiles.

2. Immune response delineated by CD4⁺ count changes at 48 weeks

The **Figure 3** illustrates the change in CD4⁺ cell counts at the 48-week benchmark across a spectrum of ART. The vertical dispersion of CD4⁺ cell count changes signifies the immuno-

logical response variability among the studied cohort. Each regimen presents a unique profile of immune reconstitution, with some regimens, such as E/C/F/TAF and DTG/F/TAF, demonstrating more substantial median increases indicative of a robust immunological rebound. Conversely, treatments like RAL/XTC/TDF and LPV/r+3TC exhibit relatively modest median increases, highlighting a more constrained immune restoration.

The interquartile range within each box provides insights into the homogeneity of the immune response among patients receiving the same treatment. A narrower interquartile range, as observed in the DTG/3TC regimen, suggests a more consistent response across the patient population, while wider ranges imply a greater variability in treatment outcomes.

The visualization succinctly captures the heterogeneity of immune recovery, suggesting that while some treatments elicit strong and consistent CD4⁺ count surges, others may require additional support or consideration in treatment planning. This detailed depiction of immunological outcomes is crucial for clinicians tailoring treatment strategies and contributes valuable data for longitudinal studies of ARV treatment efficacy.

Long-term efficacy and immune response of ARV therapy over 96 weeks

1. Longitudinal efficacy of ARV treatments in maintaining viral suppression

The longitudinal study of ART revealed varied

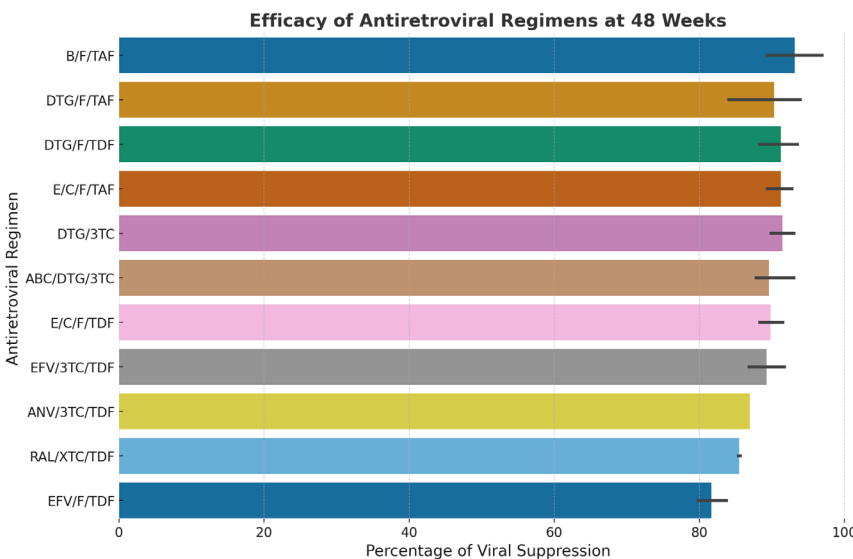


Figure 2. 48-Week viral suppression rates among antiretroviral therapy regimens

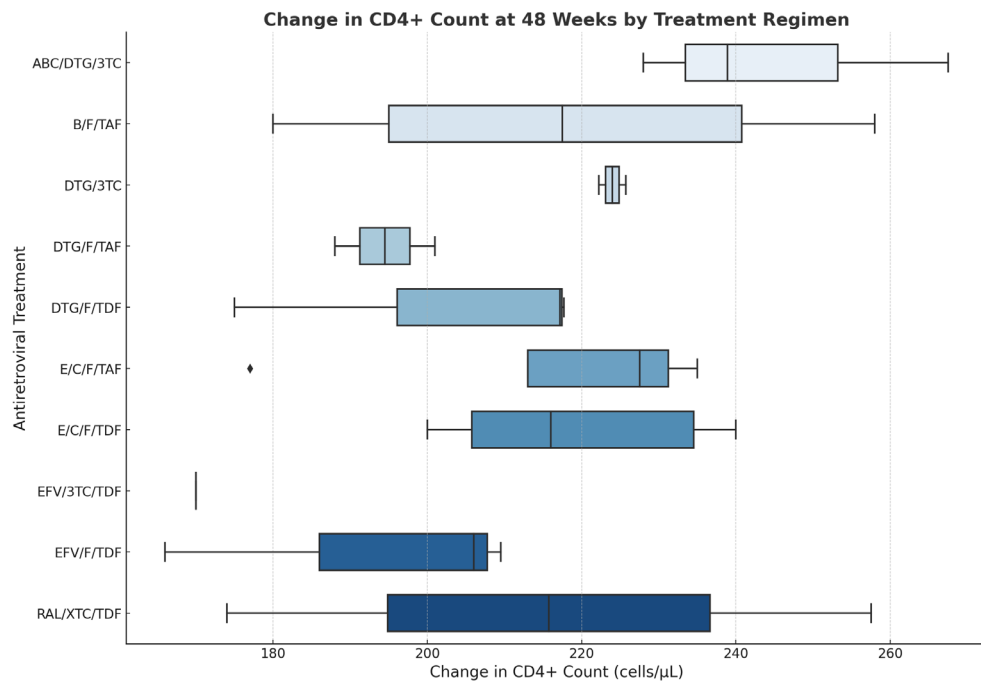


Figure 3. Change in CD4⁺ count at 48 weeks across different antiretroviral treatment regimens

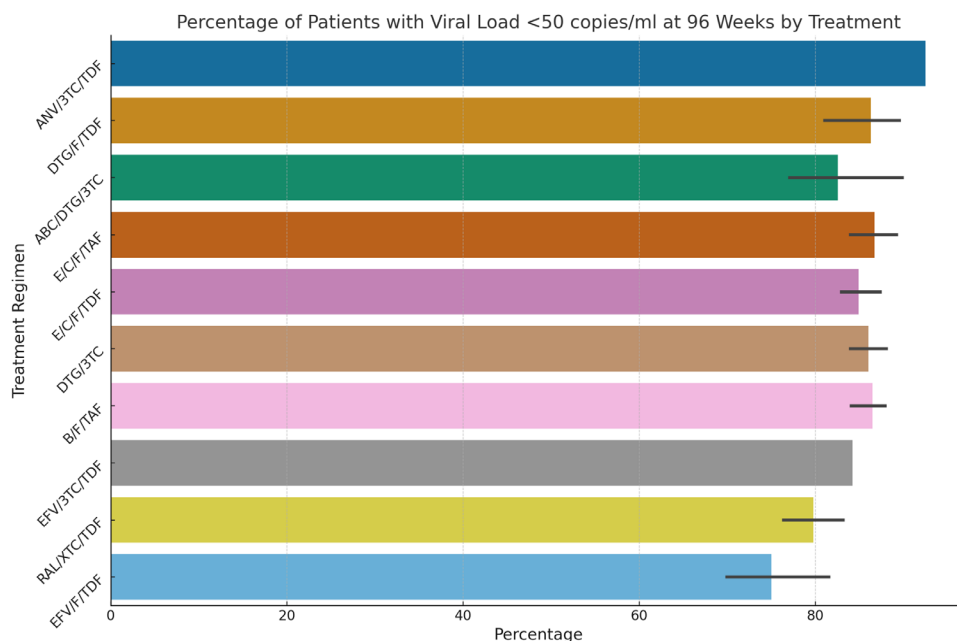


Figure 4. Comparative analysis of 96-week viral suppression rates by antiretroviral regimen

success rates in achieving viral loads of less than 50 copies/mL at the 96-week milestone. **Figure 4** and **Table 1** present these rates across different treatment regimens, showing a gradient of efficacy. The E/C/F/TAF regimen had the highest efficacy with 84% suppression, followed by ABC/DTG/3TC at 82%. At the lower end, EFV/3TC/TDF had a suppression rate of 65%. These results indicate significant variability in long-term efficacy among different treatment regimens. E/C/F/TAF emerges as the most effective regimen,

with the majority of patients achieving the desired viral suppression. ABC/DTG/3TC also shows a high rate of suppression, suggesting strong long-term control of the viral load. In contrast, regimens like EFV/3TC/TDF have a significantly lower proportion of patients attaining similar levels of suppression. This highlights the importance of selecting treatments that offer not just immediate viral suppression but also maintain that suppression over extended periods. A chi-square test confirmed significant differences in

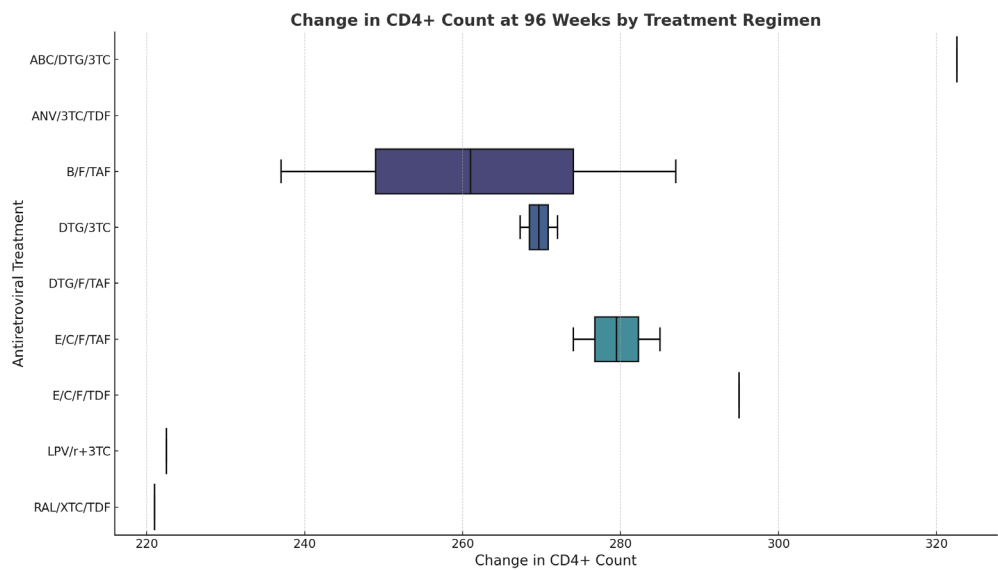


Figure 5. Distribution of CD4⁺ count changes at 96 weeks across antiretroviral treatment regimens

Table 1. Baseline and changes in CD4⁺ cell counts at 48 and 96 weeks in hiv treatment

	Baseline average CD4 ⁺ , cells/mL (SD)	Change in CD4 ⁺ at 48 weeks	Change in CD4 ⁺ at 96 weeks
Mean	399.10	221.86	267.67
Median	394.00	227.85	272.00
Std_dev	53.72	27.86	31.15

Decimal digits for mean, median, and standard deviation have been standardized for consistency to facilitate comparison

suppression rates among the treatment groups ($\chi^2=119.02$, $p < 0.001$). The design of the visualization provides an at-a-glance comparison of each treatment’s effectiveness throughout the study, offering a clear view of the enduring nature of these therapies. These findings are pivotal in understanding treatment sustainability and will help inform future therapeutic directions and patient care optimization.

2. Immune response variability in HIV treatment efficacy at 96 weeks

Our analysis extends to the exploration of immune response through changes in CD4⁺ counts, observed at the 96-week milestone across various ARV treatment regimens. Figure 5 and Table 1 delineate the distribution of CD4⁺ count changes, highlighting the variability and central tendencies within each treatment category. Notably, the regimen E/C/F/TAF showcases a broad distribution of immune responses, with a median increase significantly above other regimens, indicative of its potent efficacy in enhancing immune

recovery. Conversely, treatments like EFV/3TC/TDF exhibit a more constrained range of CD4⁺ count changes, reflecting a more uniform but modest immune response.

The stratified analysis underscores the disparities in immune recovery potential across treatment regimens, with some demonstrating pronounced increases in CD4⁺ counts, suggestive of superior immune system restoration capabilities. This variability accentuates the critical need for personalized treatment strategies, leveraging detailed insights into both virological suppression and immune system recovery to optimize therapeutic outcomes.

This comprehensive visualization of CD4⁺ count changes serves as a pivotal tool for clinicians and researchers, providing a granular view of the treatment regimens’ impact on immune restoration. The analysis underscores the heterogeneity in treatment responses, emphasizing the importance of considering both virological and immunological parameters in the assessment of ART efficacy.

Comparative long-term efficacy of pre-LPV/r+3TC ARV regimens

Our longitudinal analysis of ART efficacies within the pre-LPV/r+3TC cohort reveals significant variances in patient outcomes over 48 and 96 weeks. The synthesized data, as depicted in the **Figure 6**, demonstrates a range of viral suppression rates, with certain regimens maintaining higher efficacy over time. For instance, the E/C/F/TAF regimen showed an initial suppression rate near 90% at 48 weeks, with a marginal decline to 84% by 96 weeks, suggesting sustained efficacy. In parallel, the E/C/F/TDF regimen exhibited a similar pattern of a slight decrease in suppression from 89% to 82% across the same timepoints. These trends indicate that both regimens possess robust long-term suppressive capabilities. Other treatments, such as B/F/TAF and DTG/3TC, however, experienced a more pronounced decline in suppression rates, which could signal the need for regimen adjustments or closer monitoring. This data informs clinical decisions by highlighting the need for personalized treatment strategies, particularly in cases where long-term viral suppression is a crucial factor in patient care. The analysis underscores the diversity of responses to ARV treatments and the importance of tailoring HIV management to maintain suppression and improve overall patient health outcomes.

Adverse event profiles and their correlation in ARV treatment efficacy

1. Assessment of adverse event profiles in ARV regimen efficacy

The comprehensive evaluation of adverse event profiles among various ARV regimens conducted over pivotal timepoints of 48 and 96 weeks elucidated a landscape marked by variability in patient safety outcomes. **Figures 7 and 8** distinctly convey the incidence rates for five essential safety indicators, namely, any adverse events, drug-related adverse events, serious adverse events, adverse events leading to discontinuation, and overall discontinuation rates, each stratified by treatment regimen to underscore contrasts and facilitate nuanced analysis.

For instance, the treatment regimen E/C/F/TAF was observed to maintain a relatively higher incidence of Any Adverse Events consistently across both timepoints, raising considerations for its long-term tolerability. Meanwhile, the DTG/3TC regimen demonstrated a substantially lower frequency of Serious Adverse Events, signifying a safety profile that might be deemed more favorable in clinical practice. Notably, the rates of discontinuation due to adverse events presented considerable variability, underscoring the diverse tolerability across regimens, which becomes a pivotal factor in personalized treatment planning.

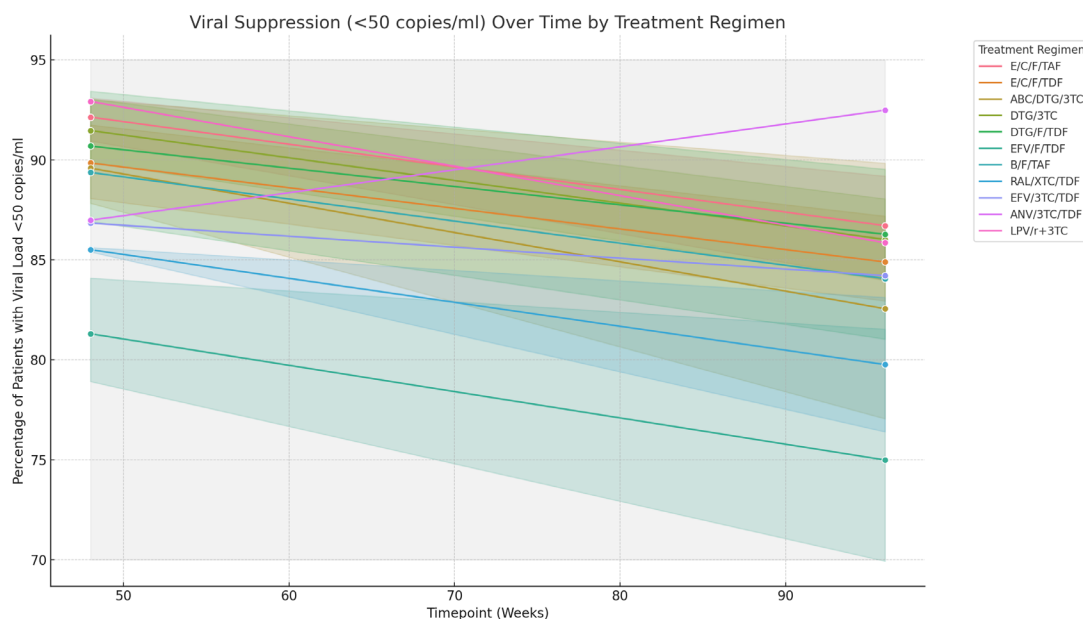


Figure 6. Comparative analysis of viral load suppression across antiretroviral regimens over 48 and 96 weeks

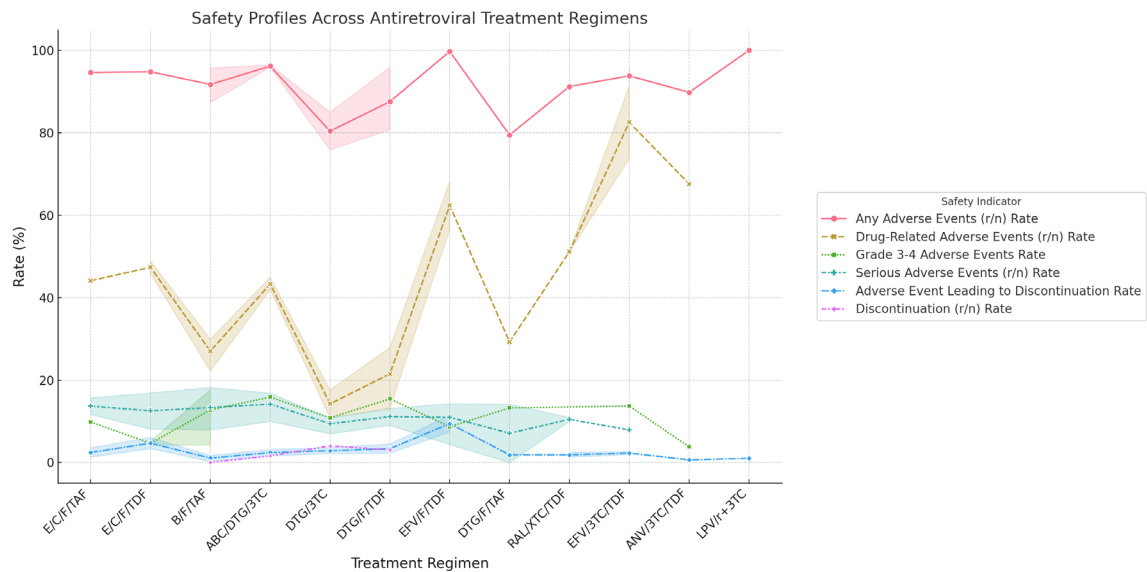


Figure 7. Comparative safety profile of antiretroviral regimens over time

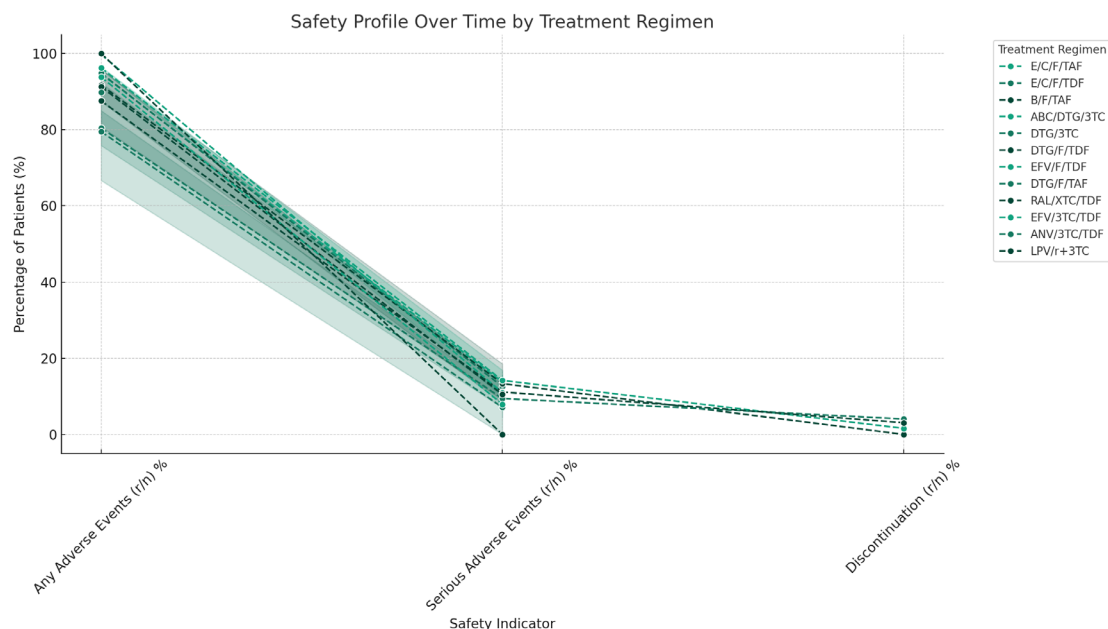


Figure 8. Comparative safety profile of antiretroviral regimens over time

The data, thus, reflect the multifaceted nature of safety profiles, advocating for the customization of therapeutic strategies that prioritize patient well-being alongside treatment efficacy. The insights derived from this analysis accentuate the imperative of ongoing safety monitoring, aiming to refine treatment paradigms and bolster the quality of care in the continuum of HIV/AIDS management, ultimately enhancing patient health outcomes and quality of life.

2. Interrelation of adverse event incidences in ARV treatments

In assessing the safety profile of ART, our analysis has identified a moderate positive correlation

between the incidence rates of any adverse events and serious adverse events. Figure 9 illustrates this relationship, with each point representing the paired incidence rates for a given treatment regimen. The average rate of any adverse event stands at approximately 90.18%, indicative of the commonality of adverse effects in treatment. In comparison, the average rate for serious adverse events is significantly lower at around 10.51%, reflecting their less frequent occurrence.

The correlation coefficient of roughly 0.47 suggests that while there is a tendency for regimens with higher overall adverse events to also have higher rates of serious adverse events, this

Correlation Between Any Adverse Events and Serious Adverse Events in Antiretroviral Therapy

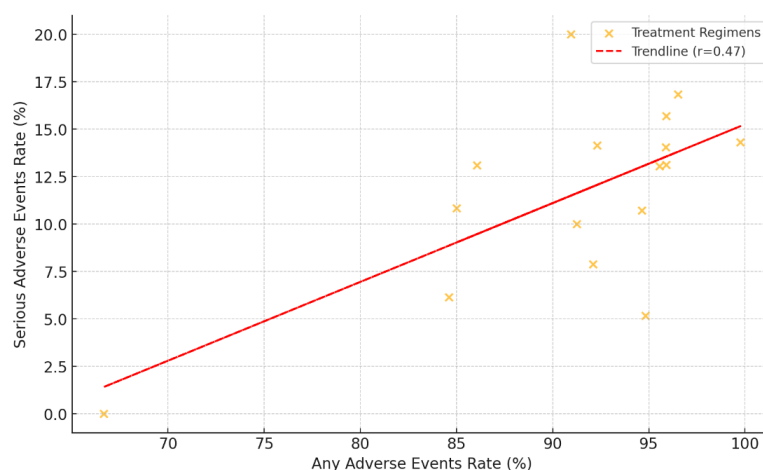


Figure 9. Correlation between any adverse events and serious adverse events in antiretroviral therapy

relationship is not highly pronounced. This points to the possibility of other factors influencing the severity and frequency of adverse events experienced by patients.

These insights not only contribute to our understanding of the safety dynamics associated with ARV treatments but also highlight the need for meticulous monitoring of patients for adverse effects. Further, it underscores the importance of thorough pre-treatment evaluations and post-treatment follow-ups to mitigate the impact of serious adverse events in the management of HIV/AIDS.

Comparative analysis of the efficacy and safety profiles of ART over time

In this comparative study, the efficacy and safety profiles of various ART interventions for HIV treatment over periods of 48 and 96 weeks were analyzed. Efficacy was determined by the percentage of participants achieving viral load suppression below 50 copies/ mL, which serves as the benchmark for successful viral suppression in HIV treatment. Safety was evaluated based on the incidence of serious adverse events. Selected efficacy parameters included viral load suppression and immune recovery indicated by CD4⁺ count improvement, while safety was assessed through serious adverse events, providing a comprehensive evaluation of treatment effectiveness. Viral suppression directly measures the regimen's ability to control HIV replication, while CD4⁺ count recovery reflects the immune system's response to treatment. These combined metrics offer a holis-

tic view of the treatment's impact on both viral control and overall immune health. At 48 weeks, data indicated a slight positive correlation between treatment efficacy and the occurrence of serious adverse events, with a correlation coefficient of 0.111. This trend persisted at 96 weeks, with a correlation coefficient of 0.063, suggesting that higher treatment efficacy is slightly associated with an increased risk of serious adverse events. However, the overall relationship between these two metrics remains weak, indicating that while both efficacy and safety are crucial considerations, they do not strongly predict each other within the context of these interventions (Figures 10 and 11). These findings underscore the importance of a balanced approach in the clinical evaluation of ART, taking into account both the benefits of viral suppression and the potential risk of adverse events.

DISCUSSION

Evaluating the efficacy and safety of antiretroviral regimens: insights from a systematic review

The systematic review and meta-analysis conducted in this study comprehensively assess the efficacy and safety of 12 ARV regimens, drawing on data from 17 meticulously chosen RCTs. Our analysis highlights the considerable variability in the efficacy of these ARV regimens, which is particularly evident in the viral suppression rates observed at the 48-week benchmark. The E/C/F/TAF regimen stands out, achieving viral suppression in 90% of participants, signifying

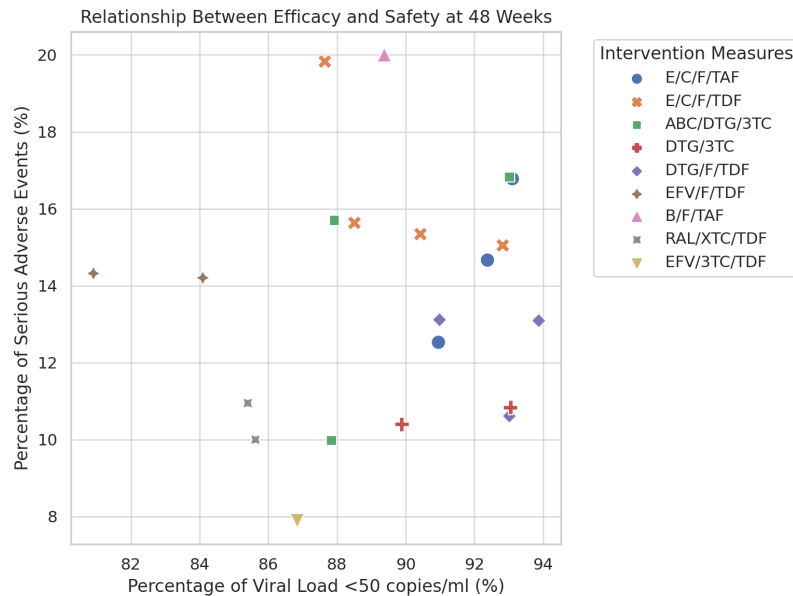


Figure 10. Relationship between efficacy and safety at 48 weeks post-treatment initiation

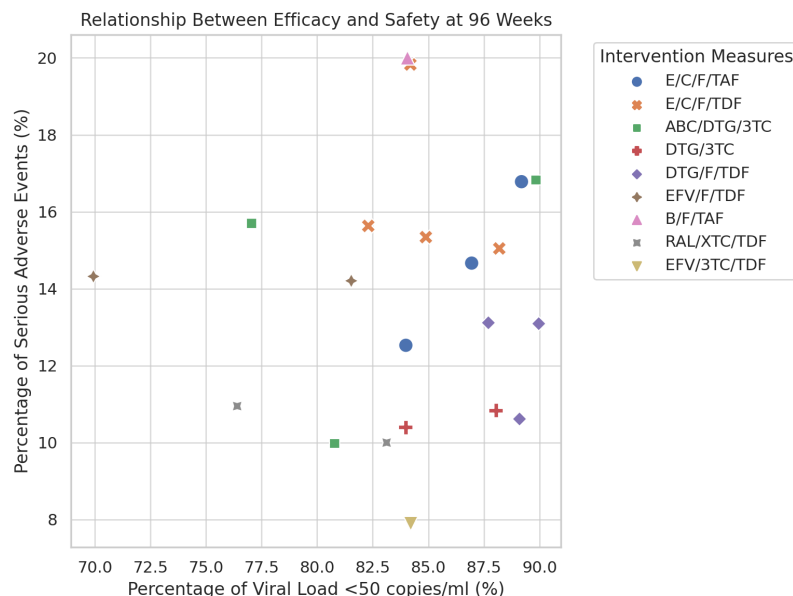


Figure 11. Relationship between efficacy and safety at 96 weeks post-treatment initiation

its potential superiority among the array of treatments studied. This observation is in line with contemporary research, which similarly identifies the high efficacy of INSTI based regimens in securing and maintaining viral suppression (18). Furthermore, the varied immune responses, as reflected in the changes in CD4⁺ cell counts at both 48 and 96 weeks, underscore the necessity for tailored treatment strategies. The notable immune rebound exhibited by certain regimens compared to others accentuates the need to factor in the individual clinical profiles of patients when formulating treatment plans (19).

The selective reporting bias identified through the quality assessment of included studies represents a potential influence on the interpretation of both efficacy and safety outcomes, echoing the wider call for standardized reporting practices in clinical trials to ensure results' reliability and comparability (20). Additionally, the adverse event profiles linked with different ARV regimens elucidate the intricacies involved in managing side effects whilst aiming for optimal efficacy. Achieving a harmonious balance between efficacy and tolerability forms the foundation of successful long-term HIV management, highlighting the ongoing necessity for research and development

within ARV therapy realms (21). This discussion not only reflects the heterogeneity in ARV regimen efficacy and safety but also the imperative for individualized treatment approaches to accommodate the diverse needs of patients living with HIV.

Long-term efficacy and immune restoration under arv therapy: a comprehensive analysis

Our comprehensive analysis across 96 weeks of ARV treatment highlights significant findings regarding the long-term efficacy and immune response associated with various ARV regimens. The consistent superiority of the E/C/F/TAF regimen in maintaining viral suppression and facilitating immune restoration underscores its potential as a leading long-term treatment option. This is complemented by the strong performance of ABC/DTG/3TC, which suggests these regimens' importance in achieving durable control over HIV viral loads (22). Conversely, the lower efficacy of EFV/3TC/TDF in sustaining viral suppression points to the need for careful selection of ARV therapies that not only suppress the virus initially but also maintain that suppression effectively over time. This differentiation in long-term outcomes emphasizes the critical nature of regimen selection in the context of HIV treatment sustainability (23).

Furthermore, the analysis of immune response variability, as evidenced by changes in CD4⁺ counts at 96 weeks, offers valuable insights into the disparate impacts of ARV regimens on immune system recovery. The marked variability across treatments, with some regimens like E/C/F/TAF showing significant immune system enhancement, highlights the nuanced relationship between ARV therapy and immune recovery (24). These findings underline the importance of a holistic treatment approach that considers both virological suppression and immunological health to optimize long-term patient outcomes. A holistic treatment approach in HIV/AIDS management involves not only achieving viral suppression but also ensuring immune recovery, improving the patient's overall health and quality of life, and minimizing long-term adverse effects. Tailoring ARV strategies to balance these aspects is crucial for comprehensive patient care (25).

Longitudinal efficacy of ARV regimens: implications for sustained viral suppression

The longitudinal analysis conducted in our study elucidates the variance in long-term efficacy among pre-LPV/r+3TC ARV regimens, underlining the significance of sustained viral suppression in HIV management. The E/C/F/TAF and E/C/F/TDF regimens exemplify high degrees of durability in their suppressive capacity, with only slight declines in efficacy noted over 96 weeks. These findings suggest a resilient long-term control of the viral load, pivotal for patient care strategies aiming for prolonged suppression. In contrast, regimens such as B/F/TAF and DTG/3TC demonstrate more considerable decreases in suppression rates over time, indicating potential challenges in maintaining optimal viral control with these treatments. This diversity in regimen efficacy over an extended period emphasizes the necessity of individualized treatment plans tailored to ensure sustained viral suppression, a cornerstone in the management of HIV infection. By highlighting these differences, our study contributes valuable insights for clinicians in selecting ART that offer the best chance for long-term success in viral load management (26).

Moreover, the comparative analysis of viral suppression across various regimens provides a clear visual representation of the longitudinal effectiveness of each treatment, serving as a crucial tool for clinicians in making informed decisions regarding HIV treatment strategies. The graphical depiction of suppression rates from 48 to 96 weeks facilitates a deeper understanding of each regimen's performance, aiding in the optimization of HIV care protocols to enhance patient outcomes. Such detailed long-term efficacy data are essential for advancing HIV treatment approaches, underscoring the importance of ongoing research and evaluation of ART to meet the evolving needs of patients living with HIV (27).

Integrated analysis of efficacy and safety in ART

Our comprehensive evaluation of ART across pivotal periods of 48 and 96 weeks underscores the intricate interplay between treatment efficacy and safety, revealing a nuanced balance that necessitates careful clinical consideration. The

observed variability in adverse event rates among different regimens points to the essential role of personalized treatment strategies within the HIV/AIDS management continuum. For instance, the distinct safety profiles of E/C/F/TAF and DTG/3TC regimens—where the former shows a higher incidence of adverse events, and the latter exhibits fewer serious adverse events—highlight the importance of aligning treatment choices with individual patient needs and tolerability considerations. This alignment underscores the necessity for ongoing safety monitoring and the adjustment of treatment paradigms to not only achieve viral suppression but also minimize adverse impacts on patient well-being (28).

Furthermore, the slight positive correlation between the efficacy of treatments and the occurrence of serious adverse events, though weak, suggests that higher efficacy does not automatically imply increased safety risks. Rather, this relationship accentuates the multifactorial nature of treatment outcomes, advocating for an integrated treatment approach informed by both efficacy and safety considerations. The need for meticulous patient monitoring, coupled with comprehensive pre-treatment evaluations and post-treatment follow-ups, becomes evident, aiming to enhance the overall quality of life for individuals living with HIV. As our knowledge and understanding advance, the development of predictive tools and the incorporation of patient-centered outcomes into clinical decision-making will be vital in optimizing HIV treatment strategies, helping ensure a balance between effective viral control and patient safety.

Limitations and future perspectives

This comprehensive review, while offering valuable insights into the comparative efficacy and safety of various HIV/AIDS treatment regimens, is not without its limitations. One such limitation is the inherent variability in the study designs of the included trials, which may affect the generalizability of the findings. Additionally, the slight positive correlation observed between treatment efficacy and the occurrence of serious adverse events, although informative, underscores the need for further research to fully understand the complexities of this relationship. These limitations

highlight the importance of advancing methodological approaches in future studies to enhance the robustness and applicability of the findings to diverse patient populations.

Looking ahead, there is a critical need for longitudinal studies that not only examine the immediate impact of ART but also their long-term effects on patient health and quality of life. Future research should also focus on the development of personalized treatment strategies, leveraging advances in genetic and biomarker research to predict individual responses to therapy. Such endeavors will not only address the gaps identified in this review but also propel the management of HIV/AIDS towards more tailored and patient-centered approaches.

CONCLUSIONS

This comprehensive review reveals key insights into the efficacy and safety of ARV regimens, particularly highlighting the superior performance of INSTI-based treatments like E/C/F/TAF and DTG/3TC in achieving sustained viral suppression. Despite a slight positive correlation between efficacy and serious adverse events, our findings underscore the necessity for personalized HIV/AIDS treatment strategies that balance efficacy with safety. These conclusions underscore the importance of careful regimen selection and ongoing patient monitoring to enhance treatment outcomes. Future research aimed at refining predictive models for treatment response is vital for advancing personalized care for individuals with HIV/AIDS. This study contributes to the evolving landscape of HIV/AIDS management, advocating for an approach that prioritizes both the effectiveness of treatment and the well-being of patients.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest related to this study. Any opinions, findings, and conclusions or recommendations expressed in this material are those of the authors and do not necessarily reflect the views of our affiliations or funding bodies.

ADDITIONAL INFORMATION

Author contributions

M.Y.: conceptualization, writing - original draft; Yp.L.: data curation, data analysis; Jy.H.: data curation, data analysis; Sy.Z.: methodology, validation; Jr.Y.: writing - original draft preparation, Writing - review & editing; Zx.Y.: writing - original draft preparation, writing - review & editing; J.Y.: supervision, funding acquisition, project administration, final approval of version to be published. All authors have read and agreed to the published version of the manuscript.

Important abbreviations

INSTIs, integrase strand transfer inhibitors; EFV, Efavirenz; 3TC, Lamivudine; TDF, tenofovir disoproxil fumarate; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; ART, antiretroviral therapy; AIDS, acquired immune deficiency syndrome; HIV, human immunodeficiency virus; RCTs, randomized controlled trials; NRTIs, nucleotide reverse transcriptase inhibitors; NNRTIs, non-nucleotide reverse transcriptase inhibitors; PIs, protease inhibitors; FIs, fusion inhibitors; STRs, single-tablet regimens; ADE, adverse drug event.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon

reasonable request.

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