

Preplanned Studies

Virologic Outcomes of Common First-Line Antiretroviral Regimens Among Adults with HIV — China, 2021–2023

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Summary

What is already known about this topic?

Antiretroviral therapy (ART) is the cornerstone of HIV care. In China, efavirenz-based regimens have long been widely used as first-line treatment, while integrase strand transfer inhibitor (INSTI)-based regimens are increasingly available. However, nationwide evidence on virologic outcomes across common first-line regimens remains limited.

What is added by this report?

This nationwide cohort study found higher viral suppression with EFV 400 mg-based regimens compared with EFV 600 mg- and LPV/r-based regimens, while INSTI-based regimens showed the highest suppression overall.

What are the implications for public health practice?

Findings support expanded use of INSTI-based regimens and consideration of EFV 400 mg-based regimens during ongoing optimization of first-line ART in China.

88.1% for lopinavir/ritonavir (LPV/r)-based regimens. Compared with EFV 600 mg-based regimens, EFV 400 mg-based and INSTI-based regimens were associated with higher likelihoods of viral suppression, whereas LPV/r-based regimens were associated with a lower likelihood.

Conclusion: EFV 400 mg-based regimens achieved better virologic outcomes than EFV 600 mg- and LPV/r-based regimens, while INSTI-based regimens showed the highest viral suppression. These findings support broader INSTI use where feasible and consideration of EFV 400 mg-based regimens during optimization of first-line ART in China.

Over the past decade, first-line antiretroviral therapy (ART) in China has undergone substantial changes in regimen composition and clinical practice. Since 2012, the non-nucleoside reverse transcriptase inhibitor (NNRTI) efavirenz (EFV), in combination with tenofovir disoproxil fumarate (TDF) and lamivudine (3TC), has served as the standard first-line regimen in China's National Free Antiretroviral Therapy Program (NFATP), with the EFV dose reduced from 600 mg to 400 mg in 2021 (1–2). During the same period, the protease inhibitor (PI) lopinavir/ritonavir (LPV/r) was also used as an alternative first-line option (2). Since 2018, the World Health Organization (WHO) has recommended dolutegravir (DTG), an integrase strand transfer inhibitor, as the preferred first-line ART agent (3). In routine practice, first-line ART is often tailored to patient characteristics, including baseline CD4⁺ T-cell count, viral load, comorbidities, concomitant medications, and potential drug–drug interactions, as well as regimen availability. Such individualized selection may lead to differences in baseline characteristics across treatment groups. Despite ongoing regimen optimization in China, nationwide evidence on virologic outcomes of currently used first-line regimens remains limited. A nationwide

ABSTRACT

Introduction: Evidence comparing the effectiveness of first-line antiretroviral therapy (ART) regimens in China remains limited. This study assessed viral suppression among people living with HIV receiving commonly used first-line ART regimens.

Methods: This retrospective cohort study included treatment-naïve people living with HIV who initiated ART at tertiary hospitals across China during January 2021–June 2023. Viral suppression within 18 months of ART initiation was evaluated, and adjusted sub-distribution hazard ratios (aSHR) were estimated to compare regimen effectiveness.

Results: Among 120,778 participants, per-protocol viral suppression rates at 6–18 months were 96.3% for integrase strand transfer inhibitor (INSTI)-based regimens, 93.1% for efavirenz (EFV) 400 mg-based regimens, 92.1% for EFV 600 mg-based regimens, and

retrospective cohort study was therefore conducted to compare virologic outcomes across common first-line ART regimens in Chinese adults with HIV.

All data were obtained from the Chinese National Free ART Program (NFATP) database, which contains demographic, clinical, and laboratory information on people living with HIV (PLWH) receiving ART in China. A nationwide retrospective longitudinal cohort study was conducted among treatment-naïve adults aged 18 years or older who initiated ART in tertiary hospitals between January 1, 2021 and June 30, 2023, with follow-up through December 31, 2024. Participants were classified according to initial regimen, including TDF+3TC+EFV 600 mg; TDF+3TC+EFV 400 mg; TDF/zidovudine (AZT)+3TC+LPV/r; and integrase strand transfer inhibitor (INSTI)-based regimens, including EVG/cobicistat (COBI)/emtricitabine (FTC)/tenofovir alafenamide (TAF), bictegravir (BIC)/FTC/TAF, dolutegravir (DTG)/3TC, and TDF+3TC+DTG. Participants were required to have at least one follow-up record within 18 months. The primary endpoint was virologic suppression during 6–18 months after ART initiation, defined as the first viral load (VL) <50 copies/mL within this period. Virologic failure was defined as VL ≥50 copies/mL among those with available measurements, and dropout as treatment discontinuation or loss to follow-up for more than 90 days before assessment. Fine-Gray competing risk models were used to compare virologic outcomes across regimens, with death as a competing event, yielding sub-distribution hazard ratios (SHR) and 95% confidence intervals (CI). Participants who dropped out, switched regimens, lacked virologic data, or did not achieve suppression by end of follow-up were censored. As an exploratory analysis, all available VL measurements within 18 months were used to describe suppression across 0–3, 3–6, 6–12, and 12–18 months using a missing-equals-excluded (M=E) approach. Because early viral load testing was incomplete and potentially selective, this analysis was considered descriptive. Analyses were performed using SAS (version 9.4, SAS Institute Inc., Cary, NC, USA).

From January 1, 2021, to June 30, 2023, a total of 120,778 treatment-naïve PLWH were included. Of these, 25.7% initiated INSTI-based regimens, 29.6% EFV 400 mg-based regimens, 40.8% EFV 600 mg-based regimens, and 4.0% LPV/r-based regimens. Median follow-up of the whole cohort was 11.2 months [interquartile range (IQR): 6.8–15.5], median age was 45 years (IQR: 31–57), and median baseline

CD4⁺ T-cell count was 252 cells/μL (IQR: 134–387) (Table 1). Among 97,686 participants who continued to use the initial regimen and underwent viral load testing within 6–18 months, per-protocol viral suppression rates were 96.3% for INSTI-based regimens, 93.1% for EFV 400 mg-based regimens, 92.1% for EFV 600 mg-based regimens, and 88.1% for LPV/r-based regimens, respectively (Figure 1).

After adjustment, compared with EFV 600 mg-based regimens, INSTI-based regimens (aSHR=1.35, 95% CI: 1.33–1.38) and EFV 400 mg-based regimens (aSHR=1.22, 95% CI: 1.20–1.24) were associated with higher likelihoods of viral suppression, whereas LPV/r-based regimens were associated with a lower likelihood (aSHR=0.90, 95% CI: 0.87–0.93). Female sex, homosexual transmission, higher baseline CD4⁺ T-cell count, lower baseline viral load, and earlier ART initiation were also associated with higher likelihood of viral suppression (Table 2). In exploratory M=E analyses, INSTI-based regimens showed higher viral load testing rate and observed suppression across follow-up intervals. However, given incomplete and potentially selective testing, these findings were interpreted cautiously and not considered evidence of faster suppression (Supplementary Figure S1, available at <https://weekly.chinacdc.cn/>).

DISCUSSION

This nationwide cohort study provides large-scale evidence from China on virologic outcomes across commonly used first-line ART regimens during a period of ongoing regimen optimization. Overall, INSTI-based regimens were associated with higher likelihood of viral suppression than EFV- and LPV/r-based regimens, consistent with previous studies (4–6). These findings suggest that continued optimization of first-line ART may improve population-level treatment outcomes. As transmitted NNRTI resistance increases, the role of INSTI-based regimens is likely to expand (7). Expanding access to INSTI-based regimens may therefore further improve virologic outcomes in routine care.

Although WHO has recommended EFV 400 mg as an alternative first-line regimen (8), based largely on the ENCORE1 trial showing noninferiority to EFV 600 mg (9), this study extends those findings using nationwide real-world data. EFV 400 mg-based regimens achieved slightly better viral suppression than EFV 600 mg-based regimens. This advantage may be partly explained by ENCORE1 pharmacokinetic

TABLE 1. Baseline demographic and clinical characteristics of participants.

Characteristics	Total, N (%)	INSTI, N (%)	EFV400, N (%)	EFV600, N (%)	LPV/r, N (%)	P
Overall	120,778 (100)	31,004 (25.67)	35,709 (29.57)	49,250 (40.78)	4,815 (3.99)	
Follow-up duration						
Median (months)	11.2 (6.8–15.5)	9.4 (5.8–14.6)	10.7 (6.9–14.7)	12.1 (8.3–16.6)	11.1 (6.7–15.4)	<0.001
Sex						
Male	97,710 (80.9)	26,587 (85.8)	27,130 (76.0)	40,430 (82.1)	3,563 (74.0)	<0.001
Female	23,068 (19.1)	4,417 (14.3)	8,579 (24.0)	8,820 (17.9)	1,252 (26.0)	
Age (years)						
Median (years)	45 (31–57)	38 (29–54)	49 (32–59)	46 (31–57)	46 (32–59)	<0.001
<30	27,420 (22.7)	8,432 (27.2)	7,338 (20.6)	10,673 (21.7)	977 (20.3)	<0.001
30–49	43,450 (36.0)	12,762 (41.2)	11,215 (31.4)	17,779 (36.1)	1,694 (35.2)	
≥50	49,908 (41.3)	9,810 (31.6)	17,156 (48.0)	20,798 (42.2)	2,144 (44.5)	
BMI (kg/m ²)						
<18.5	13,755 (11.4)	3,666 (11.8)	5,143 (14.4)	4,207 (8.5)	739 (15.4)	<0.001
18.5–23.9	70,003 (58.0)	18,204 (58.7)	21,643 (60.6)	27,305 (55.4)	2,851 (59.2)	
24.0–27.9	23,114 (19.1)	6,398 (20.6)	5,924 (16.6)	10,023 (20.4)	769 (16.0)	
≥28.0	5,646 (4.7)	1,583 (5.1)	1,243 (3.5)	2,595 (5.3)	225 (4.7)	
Not tested	8,260 (6.8)	1,153 (3.7)	1,756 (4.9)	5,120 (10.4)	231 (4.8)	
Time of ART initiation (days)						
Median (days)	13 (6–29)	14 (7–31)	13 (6–27)	13 (6–30)	15 (7–41)	<0.001
≤7	37,721 (31.2)	9,310 (30.0)	11,343 (31.8)	15,717 (31.9)	1,351 (28.1)	<0.001
8–30	53,543 (44.3)	13,941 (45.0)	16,289 (45.6)	21,300 (43.3)	2,013 (41.8)	
>30	29,514 (24.4)	7,753 (25.0)	8,077 (22.6)	12,233 (24.8)	1,451 (30.1)	
Transmission route						
Heterosexual contact	73,434 (60.8)	14,845 (47.9)	24,665 (69.1)	30,642 (62.2)	3,282 (68.2)	<0.001
Homosexual contact	42,024 (34.8)	14,896 (48.1)	9,705 (27.2)	16,198 (32.9)	1,225 (25.4)	
Other	5,320 (4.4)	1,263 (4.1)	1,339 (3.8)	2,410 (4.9)	308 (6.4)	
Baseline CD4 ⁺ T-cell count (cells/μL)						
Median (cells/μL)	252 (134–387)	236 (100–382)	248 (141–376)	266 (154–400)	219 (87–365)	<0.001
<200	41,283 (34.2)	12,398 (40.0)	12,301 (34.5)	14,586 (29.6)	1,999 (41.5)	
200–349	33,552 (27.8)	8,001 (25.8)	10,647 (29.8)	13,762 (27.9)	1,142 (23.7)	
350–499	19,329 (16.0)	4,845 (15.6)	5,763 (16.1)	8,055 (16.7)	666 (13.8)	
≥500	13,901 (11.5)	3,766 (12.2)	3,727 (10.4)	5,895 (12.0)	513 (10.7)	<0.001
Not tested	12,713 (10.5)	1,994 (6.4)	3,271 (9.2)	6,953 (14.1)	495 (10.3)	
Baseline viral load (copies/mL)						
≤100,000	34,559 (28.6)	12,839 (41.4)	9,313 (26.1)	11,357 (23.1)	1,050 (21.8)	<0.001
>100,000	19,381 (16.1)	8,798 (28.4)	4,867 (13.6)	4,886 (9.9)	830 (17.2)	
Not tested	66,838 (55.3)	9,367 (30.2)	21,529 (60.3)	33,007 (67.0)	2,935 (61.0)	

Note: INSTIs=EVG/COBI/FTC/TAF, BIC/FTC/TAF, DTG/3TC and TDF+3TC+DTG; EFV400=TDF+3TC+EFV (400 mg); EFV600=TDF+3TC+EFV (600 mg); LPV/r (lopinavir/ritonavir)=TDF/ AZT+3TC +LPV/r; IQR=Interquartile Range; Time of ART initiation=Time from HIV diagnosis to ART initiation; Baseline CD4⁺ T-cell count refers to CD4⁺ T-cell count testing results before ART initiation; Baseline viral load refers to viral load testing results before ART initiation.

Abbreviation: ART=antiretroviral therapy; INSTIs=integrase strand transfer inhibitors; EVG/COBI/FTC/TAF=elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide; BIC/FTC/TAF=bictegravir/emtricitabine/tenofovir alafenamide; DTG/3TC=dolutegravir/lamivudine; TDF=tenofovir disoproxil fumarate; EFV=efavirenz; LPV/r=lopinavir/ritonavir; AZT=zidovudine; BMI=Body Mass Index.

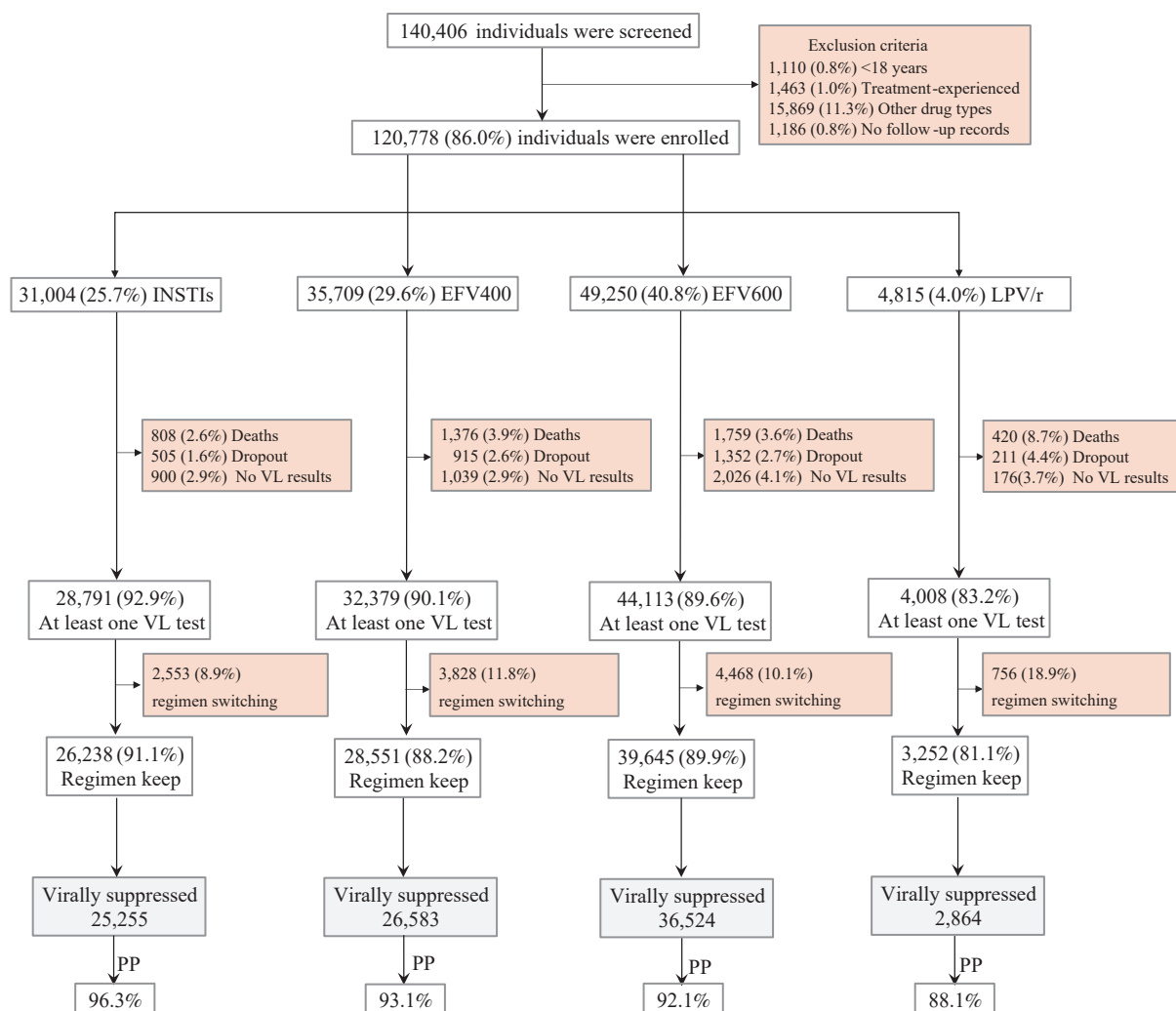


FIGURE 1. Flowchart of the cohort of adults with HIV initiating first-line ART.

Abbreviation: HIV=human immunodeficiency virus; VL=viral load; INSTI=integrase strand transfer inhibitor; EVG/COBI/FTC/TAF=elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide; BIC/FTC/TAF=bictegravir/emtricitabine/tenofovir alafenamide; DTG/3TC=dolutegravir/lamivudine; TDF=tenofovir disoproxil fumarate; EFV=efavirenz; LPV/r=lopinavir/ritonavir; AZT=zidovudine; PP=per-protocol.

findings indicating that, despite lower overall exposure, EFV 400 mg maintained trough concentrations above levels required for virologic efficacy. The lower dose may be associated with improved tolerability and adherence, as suggested by previous studies (ENCORE1), which could contribute to better virologic outcomes in routine practice (10). At the population level, these findings support broader use of INSTI-based regimens where feasible and suggest EFV 400 mg-based regimens as a practical alternative during transition in treatment strategies. Overall, the results provide real-world evidence to inform optimization of first-line ART in China.

This study has some limitations. First, as treatment was not randomized, residual confounding, including

confounding by indication, may persist despite adjustment. In addition, limited availability of covariates prevented adjustment for lifestyle factors, comorbidities, concomitant medications, and other potential confounders. Adherence data were also unavailable, although adherence is a major determinant of viral suppression and may differ across regimens due to pill burden, tolerability, and accessibility. Adverse events were not systematically recorded in sufficient detail and, therefore, could not be adequately evaluated, limiting a more comprehensive assessment of regimen safety and overall clinical value. Second, incomplete and non-random viral load testing may have introduced selection bias. Early VL monitoring was limited under routine practice, and missingness

TABLE 2. Determinants of viral suppression (VL<50 copies/mL) among participants.

Characteristics	Unadjusted SHR (95% CI)	P	Adjusted SHR (95% CI)	P
Sex				
Male	Reference		Reference	
Female	1.01 (1.00–1.03)	0.116	1.13 (1.11–1.15)	<0.001
Age (years)				
<30	Reference		Reference	
30–49	0.92 (0.91–0.94)	<0.001	0.99 (0.97–1.01)	0.254
≥50	0.77 (0.76–0.78)	<0.001	0.88 (0.87–0.90)	<0.001
BMI (kg/m ²)				
<18.5	0.83 (0.81–0.85)	<0.001	0.85 (0.83–0.87)	<0.001
18.5–23.9	Reference		Reference	
24.0–27.9	1.12 (1.11–1.14)	<0.001	1.09 (1.07–1.11)	<0.001
≥28.0	1.13 (1.10–1.17)	<0.001	1.07 (1.04–1.10)	<0.001
Not tested	0.76 (0.74–0.78)	<0.001	0.83 (0.81–0.85)	<0.001
Time of ART initiation (days)				
≤7	1.17 (1.15–1.20)	<0.001	1.18 (1.16–1.21)	<0.001
8–30	1.15 (1.13–1.17)	<0.001	1.13 (1.11–1.15)	<0.001
>30	Reference		Reference	
Transmission route				
Heterosexual contact	Reference		Reference	
Homosexual contact	1.28 (1.27–1.30)	<0.001	1.13 (1.11–1.15)	<0.001
Other	0.91 (0.88–0.94)	<0.001	0.92 (0.89–0.95)	<0.001
Drug type				
INSTIs	1.48 (1.46–1.51)	<0.001	1.35 (1.33–1.38)	<0.001
EFV400	1.21 (1.19–1.23)	<0.001	1.22 (1.20–1.24)	<0.001
EFV600	Reference		Reference	
LPV/r	0.87 (0.84–0.90)	<0.001	0.90 (0.87–0.93)	<0.001
Baseline CD4 ⁺ T-cell count (cells/μL)				
<200	Reference		Reference	
200–349	1.23 (1.21–1.25)	<0.001	1.17 (1.15–1.19)	<0.001
350–499	1.29 (1.26–1.31)	<0.001	1.20 (1.18–1.22)	<0.001
≥500	1.31 (1.28–1.34)	<0.001	1.20 (1.18–1.23)	<0.001
Not tested	0.90 (0.88–0.92)	<0.001	1.01 (0.98–1.03)	0.640
Baseline viral load (copies/mL)				
≤100,000	1.19 (1.17–1.21)	<0.001	1.12 (1.09–1.14)	<0.001
>100,000	Reference		Reference	
Not tested	0.80 (0.79–0.82)	<0.001	0.87 (0.86–0.89)	<0.001

Note: INSTIs=EVG/COBI/FTC/TAF, BIC/FTC/TAF, DTG/3TC and TDF+3TC+DTG; EFV400=TDF+3TC+EFV (400 mg); EFV600=TDF+3TC+EFV (600 mg); LPV/r (lopinavir/ritonavir)=TDF/ AZT+3TC +LPV/r; IQR=Interquartile Range; Time of ART initiation=Time from HIV diagnosis to ART initiation; Baseline CD4⁺ T-cell count refers to CD4⁺ T-cell count testing results before ART initiation; Baseline viral load refers to viral load testing results before ART initiation.

Abbreviation: ART=antiretroviral therapy; INSTIs=integrase strand transfer inhibitors; CI=confidence interval; EVG/COBI/FTC/TAF=elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide; BIC/FTC/TAF=bictegravir/emtricitabine/tenofovir alafenamide; DTG/3TC=dolutegravir/lamivudine; TDF=tenofovir disoproxil fumarate; EFV=efavirenz; LPV/r=lopinavir/ritonavir; AZT=azidothymidine; BMI=Body Mass Index.

was unlikely to be random. Accordingly, exploratory analyses of early suppression may overestimate virologic response and should be interpreted cautiously.

Conflicts of interest: No conflicts of interest.

Ethical statement: Approved by the Institutional Review Board of the National Center for AIDS/STD Control and Prevention, China CDC (Number: KX20260210742). Patient information was de-identified for data analysis.

Funding: This work was supported by Prevention and Technology Research Project of NCAIDS (grant number NCAIDS2025K008).

doi: 10.46234/ccdcw2026.137

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Submitted: March 23, 2026

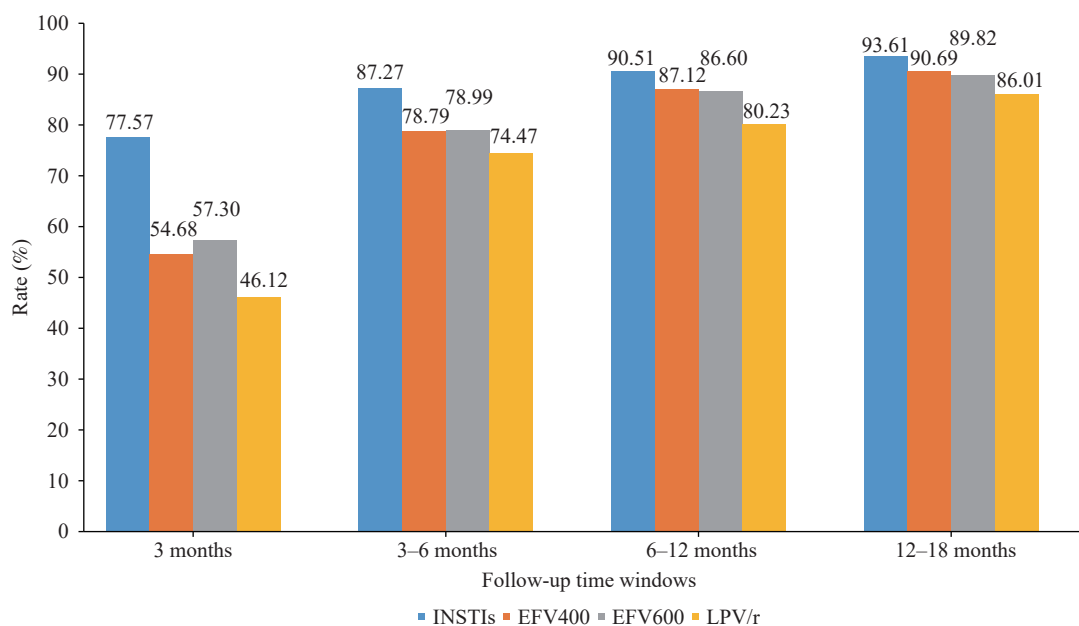
Accepted: May 26, 2026

Issued: July 03, 2026

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SUPPLEMENTARY MATERIAL



SUPPLEMENTARY FIGURE S1. Exploratory observed viral suppression rates across follow-up intervals by antiretroviral regimen.

Note: Percentages of participants achieving viral load <50 copies/mL at each visit, using a missing-equals-excluded (M=E) analysis.

Abbreviation: INSTI=integrase strand transfer inhibitor; EVG/COBI/FTC/TAF=elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide; BIC/FTC/TAF=bictegravir/emtricitabine/tenofovir alafenamide; DTG/3TC=dolutegravir/lamivudine; TDF=tenofovir disoproxil fumarate; EFV=efavirenz; LPV/r=lopinavir/ritonavir; AZT=zidovudine.