Original Article

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Comparative Evaluation of Longitudinal Programmatic Outcomes of Efavirenz- and Dolutegravir-Based First-Line ART during India's Adoption Period (2019–2023)

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Abstract:

Objective: To compare the programmatic outcomes—retention in care, viral suppression, adherence, and regimen durability—between individuals receiving efavirenz (EFV) and dolutegravir (DTG)-based first-line antiretroviral therapy (ART) during India's transition period (2019–2023), and to identify predictors of regimen change.

Material and Methods: A retrospective cohort study was conducted at a district ART centre in Karnataka, India, analyzing treatment-naive adults initiating first-line ART between January 2019 and December 2023. Primary outcome was time to regimen switch, with secondary outcomes including retention in care, viral load testing uptake, viral suppression rates, adherence, mortality, and loss to follow-up at 6, 12, and 24 months. Cox proportional hazards regression identified predictors of regimen switching.

Results: Among 2,709 participants, 1,740 (64.2%) initiated EFV-based and 969 (35.8%) DTG-based regimens. DTG recipients demonstrated superior 24-month retention (93.4% vs 89.8%, p-value=0.002), higher viral load testing uptake (86.0% vs 72.1%, p-value<0.001), and greater viral suppression among tested patients (96.0% vs 90.9%, p-value <0.001). DTG had consistently higher proportions of optimal adherence (≥95%) at all timepoints (85.3% vs 77.8%, p-value <0.001 at 24 months). The proportion of patients with a cumulative regimen switch was significantly lower for DTG (3.0% vs

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7.0%, p-value<0.001). In multivariable analysis, starting DTG was associated with a 45% reduced hazard of switching from the initial regimen among those ever treated with ART (adjusted HR 0.55, 95% CI: 0.42-0.72, p-value<0.001). **Conclusion:** DTG-based fixed-dose combination first-line therapy yielded better programmatic outcomes on several fronts during India's transition phase and warrants prioritization for treatment-naive patients in similar resource-limited settings.

Keywords: antiretroviral therapy, dolutegravir, efavirenz, India, programmatic outcomes, treatment success

Introduction

Human immunodeficiency virus (HIV) continues to be a public health problem in India, the country with the third largest epidemic in the world, with an estimated 2.4 million people living with HIV (PLHIV) in 2023[1]. The National HIV Control Program has made significant strides in reducing new infections and deaths, with a decline of annual new HIV infections of up to 48% since 2010. Nevertheless, maintaining long-term viral suppression of an optimal antiretroviral therapy (ART) regimen is critical for individual health and public health.

The first-line ART landscape has changed considerably in recent years, with a shift from efavirenz-based regimens to dolutegravir-containing combinations, based on World Health Organization (WHO) guideline changes[2]. This was guided by clinical trial data which showed superior efficacy, tolerability, and genetic barrier to the resistance of dolutegravir compared to efavirenz. India began implementing this transition gradually from 2021, creating a unique programmatic context between 2019 and 2023 (a transition period), during which both regimens were administered.

Efavirenz has been effective in achieving viral suppression, but it is characterised by significant central nervous system adverse effects (vivid dreams, dizziness, or neuropsychiatric symptoms), which may affect patient adherence and quality of life. Furthermore, efavirenz has a low genetic barrier to resistance, and mutations at single sites may confer reduced susceptibility[3].

In contrast, dolutegravir (DTG), a second-generation INSTI, has several pharmacotherapeutic benefits. Clinical trial data have consistently demonstrated higher rates of viral suppression, fewer discontinuations for adverse events, and better resistance profiles compared with efavirenz-based regimens[3]. Updated WHO guidelines now recommend dolutegravir as the preferred first-line option for all patient groups, including women of childbearing potential[2,4].

Although there is strong evidence from clinical trials of the benefits of dolutegravir, real-world programmatic responses during rapid expansion could differ from the controlled trial scenarios. From a programmatic perspective, patient populations vary in implementation, depending on their different healthcare infrastructure, modality of adherence support, and limitations in resources, which may affect carry-through of the treatment. In addition, the transition phase provides distinct analytical opportunities for contrasting the outcomes between regimens within the same health system.

India's National AIDS Control Organization (NACO) has suggested that key programmatic outcomes like retention in care, uptake of viral load testing and progression to viral suppression, adherence, mortality, loss to follow-up, and regimen switching be monitored[1]. These endpoints offer a holistic assessment of program effectiveness and patient health that goes beyond traditional clinical endpoints.

Earlier studies of dolutegravir rollout in resource-limited settings have found encouraging results in South Africa and elsewhere in Africa, with better retention and

viral suppression than the efavirenz-based regimen[5]. Programmatic outcomes could vary, however, depending on the epidemiology of disease and healthcare settings or patient populations. The Indian scenario has its own peculiarities, comprising diverse sociodemographic features, differing regional healthcare infrastructures, and cultural attributes that could impact treatment adherence as well as outcomes[6].

This comparison of the programmatic outcomes of dolutegravir versus efavirenz-based first-line ART fills a crucial knowledge gap in India[3,7]. The results will add to the international body of evidence around the implementation of dolutegravir and thus provide locally-relevant information regarding what might best contribute to optimising India's HIV control program. In addition, the determinants of the need for switching regimens and the visualization of time-to-event outcomes will contribute to clarifying the durability of treatment, providing insights for patient management.

Material and Methods

Study design and setting

This was a retrospective cohort study conducted at the District Antiretroviral Therapy (ART) Centre, Belagavi, Karnataka, India. Data were extracted from routinely maintained electronic medical records and patient charts covering the period January 2019 to December 2023, during which India transitioned from efavirenz (EFV) to dolutegravir (DTG)-based first-line antiretroviral regimens under the National AIDS Control Programme.

Study population

All individuals aged 15 years and above who were receiving HIV care and treatment at the District ART Centre, Belagavi, between January 2019 and December 2023 were screened for eligibility. Patients were included if they were treatment-naive adults initiating first-line ART at the same centre. Patients were grouped according to their initial regimen (EFV or DTG).

Exclusion criteria included pregnancy at ART initiation, transfer-in cases from other ART centres, and incomplete baseline demographic or clinical data (e.g., missing CD4 count, viral load, or adherence information, transfer-outs). Transfer-in patients were excluded because prior ART exposure and baseline data from referring facilities were unavailable, precluding accurate assessment of time-to-event outcomes such as retention and regimen durability.

Data collection and variables

Clinical history, pharmacy records, and laboratory data were reviewed. Recorded variables were as follows: a) demographic characteristics (age, sex, education level, occupation, and risk group); b) clinical and laboratory parameters at enrollment; c) history of previous tuberculosis opportunist infection; d) comorbidities (hypertension and diabetes mellitus); e) hepatitis B or C status; f) treatment-related data (initial regimen, scores on adherence report, following regimen substitutions and follow-up outcome).

Definitions

Retention in care was defined as being alive and on ART at the same facility at 6, 12, and 24 months after initiation. Patients who transferred out were censored at the date of transfer and excluded from non-retention counts, whereas those who died, discontinued treatment, or were lost to follow-up (LTFU; ≥90 days without a recorded ART visit) were considered not retained. Viral suppression was defined as plasma HIV RNA <1000 copies/mL, in accordance with national guidelines. Adherence was calculated based on pharmacy refill records, and ≥95% adherence was defined as optimal due to evidence associating a high level of adherence with virological success[8]. Regimen switch included modifications to second-

line medications for virological failure, toxicity, drug–drug interaction, pregnancy, programmatic stockouts, and patient preference.

Outcomes

The primary outcome was time to first regimen switch. Secondary outcomes were programmatic indicators, including retention, viral load testing coverage, viral suppression rates, adherence, mortality, loss to follow–up (LTFU), and transfers at 6, 12, and 24 months. Adverse drug reactions (ADRs) were extracted from records using NACO pharmacovigilance codes and included only clinically significant events requiring treatment change or management.

Statistical analysis

Data were cleaned and analyzed using SPSS version 25.0 (IBM, Chicago, IL, USA) and R version 4.3.0. Baseline characteristics were compared between the EFV and DTG groups using Chi–square tests for categorical variables and Student's *t*–test or Mann–Whitney U test for continuous variables, as appropriate. Programmatic outcomes were described as proportions at the specified timepoints. Kaplan–Meier survival curves were constructed to estimate time to regimen switch, and log–rank tests were used for group comparisons. Predictors of regimen switch were evaluated using Cox proportional hazards regression, with hazard ratios (HR) and 95% confidence intervals (CI) presented. Variables with p–value<0.20 in univariable analysis were entered into multivariable models. Before model fitting, multicollinearity among predictor variables was assessed using variance inflation factors (VIF), and no significant multicollinearity was observed. Sensitivity analyses were not performed, as the primary analyses included all eligible participants with complete data, and the exclusion of cases with missing records minimized potential bias.

Ethical considerations

Ethical approval was obtained from the Institutional Ethics Committee of KLE Academy of Higher Education and Research, Belagavi (Ref No: KAHER/EC/24–25/362). Permissions for data access and use were also granted by the Karnataka State AIDS Prevention Society (KSAPS) and the District AIDS Prevention and Control Office (DAPCO) under the administrative framework of the National AIDS Control Organization (NACO).

Results

Cohort characteristics and patient flow

A total of 4,853 individuals who were receiving HIV treatment at the District ART Centre, Belagavi, during the study period were screened for eligibility. Of these, 2,144 were excluded: 184 were pregnant at initiation, 526 were transfer–in cases from other ART centres, and 1,434 had incomplete baseline demographic or clinical data (such as missing CD4 count, viral load, or adherence records). The final analytic cohort included 2,709 treatment–naive adults who initiated first–line ART at the same centre, of whom 1,740 (64.2%) received efavirenz–based and 969 (35.8%) received dolutegravir–based regimens. Median follow–up was 18.3 months (IQR: 12.5–24.0). Figure 1 illustrates patient flow from screening through final analysis.

Baseline characteristics

The mean age of the entire group was 38.5±10.2 years; there was no significant age difference between groups (p–value=0.14). Males constituted 62.1% of the participants, and an increased proportion initiated efavirenz compared to dolutegravir (64.0% vs 58.5%, p–value = 0.03). There was a more significant difference in educational level reached (p–value=0.01), with dolutegravir–receivers being more likely to have graduated from schooling (29.7% versus 26.4%) (Table 1).

The route of infection was heterosexual 74.7%, MSM 9.9%, and IDU 5.0%. There were no differences between the groups in employment status or substance use characteristics. Baseline median CD4 count was 342 cells/μL (IQR: 180–525), with no difference between groups (p–value=0.40). Detectable baseline viral load occurred in 7.8% of participants, equally distributed between arms. Tuberculosis history affected 12.0% and opportunistic infections 28.0% of patients at baseline (Table 1).

Programmatic outcomes

Retention and testing

Dolutegravir was linked with higher retention rates over time. At 6 months, retention was 97.5% versus 96.1% (p–value=0.057), becoming significant at 12 months (95.9% vs 93.9%, p–value=0.03) and 24 months (93.4% vs 89.8%, p–value=0.002). Viral load testing uptake was consistently higher with dolutegravir at all timepoints (all p–values<0.001): 60.4% versus 44.8% at 6 months, 78.1% versus 65.2% at 12 months, and 86.0% versus 72.1% at 24 months.

Among tested patients, dolutegravir achieved higher viral suppression rates (all p–values<0.001): 94.2% versus 87.8% at 6 months, 95.1% versus 90.0% at 12 months, and 96.0% versus 90.9% at 24 months. (Table 2)

Adherence and attrition

Optimal adherence (≥95%) was significantly higher with dolutegravir across all timepoints (all p–values<0.001): 85.1% versus 80.1% at 6 months, 86.1% versus 79.1% at 12 months, and 85.3% versus 77.8% at 24 months.

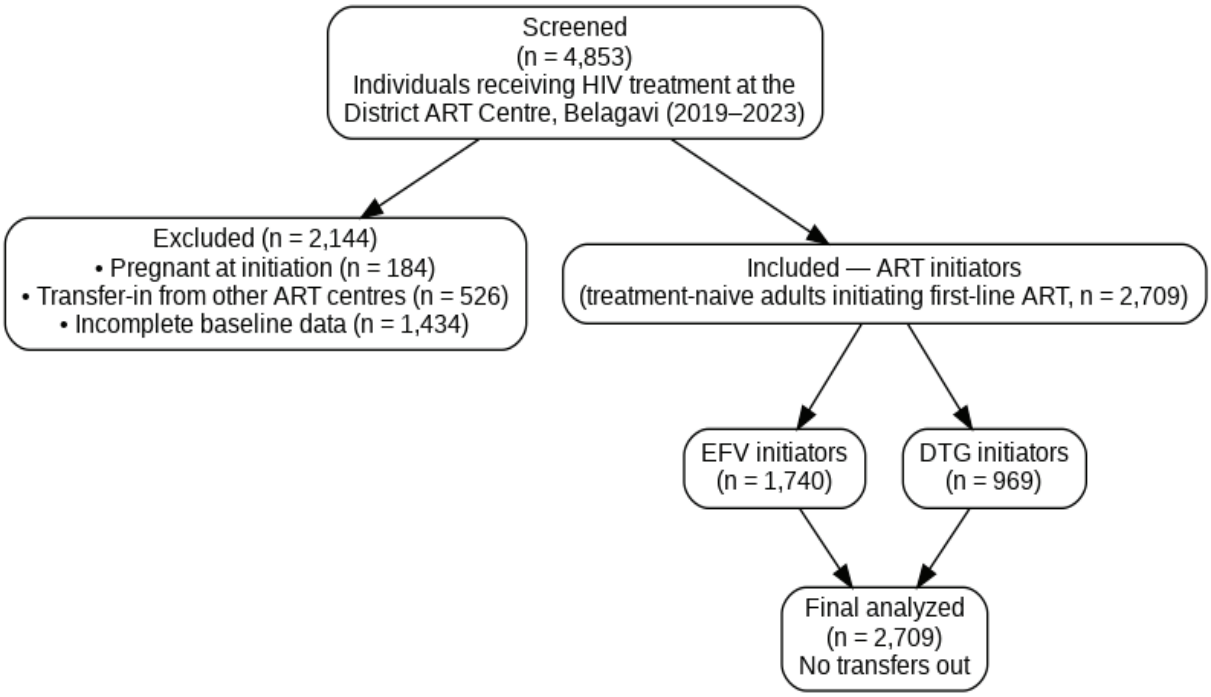

Figure 1 Patient flow from screening through final analysis

Table 1 Baseline characteristics of the cohort by initial regimen (N=2709)

Category	Variable	EFV (n=1,740)	DTG (n=969)	Total (N=2,709)	p-value
Demographic characteristics	Age (years), mean±S.D.	38.8±10.3	37.9±9.7	38.5±10.2	0.14
	Sex				0.03
	• Male	1,114 (64.0%)	567 (58.5%)	1,681 (62.1%)	
	• Female	612 (35.2%)	390 (40.3%)	1,002 (37.0%)	
	• Transgender	14 (0.8%)	12 (1.2%)	26 (1.0%)	
	Education level				0.01
	• Illiterate	503 (28.9%)	246 (25.4%)	749 (27.6%)	
	• Primary school	333 (19.1%)	196 (20.2%)	529 (19.5%)	
	• Secondary school	444 (25.5%)	239 (24.7%)	683 (25.2%)	
	• Graduate & above	460 (26.4%)	288 (29.7%)	748 (27.6%)	
Socio-behavioral characteristics	Risk group				0.74
	• Heterosexual	1,298 (74.6%)	725 (74.8%)	2,023 (74.7%)	
	• MSM	176 (10.1%)	93 (9.6%)	269 (9.9%)	
	• IDU	88 (5.1%)	47 (4.9%)	135 (5.0%)	
	• Others/Unknown	178 (10.2%)	104 (10.7%)	282 (10.4%)	
	Employment status				0.29
	• Employed	956 (54.9%)	529 (54.6%)	1,485 (54.8%)	
	• Unemployed	784 (45.1%)	440 (45.4%)	1,224 (45.2%)	
	Substance use				
	• Alcohol use (Yes)	382 (22.0%)	214 (22.1%)	596 (22.0%)	0.93
	• Smoking (Yes)	317 (18.2%)	171 (17.7%)	488 (18.0%)	0.76
	• Tobacco chewing (Yes)	437 (25.1%)	240 (24.8%)	677 (25.0%)	0.72
Clinical and laboratory parameters	Baseline CD4 (cells/μL), median (IQR)	340 (180–520)	345 (185–530)	342 (180–525)	0.40
	Detectable baseline viral load, n (%)	136 (7.8%)	74 (7.6%)	210 (7.8%)	0.91
	Tuberculosis history (Yes)	214 (12.3%)	111 (11.5%)	325 (12.0%)	0.55
	Opportunistic infections	503 (28.9%)	256 (26.4%)	759 (28.0%)	0.44
	Comorbidities				
	• Diabetes (Yes)	154 (8.9%)	90 (9.3%)	244 (9.0%)	0.21
	• Hypertension (Yes)	262 (15.1%)	144 (14.9%)	406 (15.0%)	0.87
	Hepatitis co-infection				
	• HBV positive	122 (7.0%)	67 (6.9%)	189 (7.0%)	0.96
	• HCV positive	55 (3.2%)	26 (2.7%)	81 (3.0%)	0.88

S.D.=standard deviation, IQR=interquartile range, EFV=efavirenz, DTG=dolutegravir, MSM=men who have sex with men, IDU=injecting drug user, HBV=hepatitis B virus, HCV=hepatitis C virus
Note: Values are expressed as n (%) unless otherwise specified; continuous variables are presented as mean±S.D. or median (IQR).

Mortality rates were lower with dolutegravir numerically but without statistical significance: 0.6% versus 0.8% at 6 months (p-value=0.589), 1.0% versus 1.6% at 12 months (p-value=0.264), and 1.7% versus 2.5% at 24 months (p-value=0.137). Loss to follow-up significantly favored dolutegravir at later timepoints: 12 months (1.2% vs 2.7%, p-value=0.012) and 24 months (2.6% vs 4.5%, p-value=0.013). Transfer rates were similarly lower with dolutegravir at 12 months (1.9% vs 3.4%, p-value=0.018) and 24 months (2.9% vs 4.9%, p-value=0.013) (Table 2).

Table 2 Programmatic outcomes at 6, 12, and 24 months by initial regimen

Category	Outcome (timepoint)	EFV (n=1,740)	DTG (n=969)	Total (N=2,709)	p-value
Retention in care	6 months	1,673 (96.1%)	945 (97.5%)	2,618 (96.6%)	0.057
	12 months	1,634 (93.9%)	929 (95.9%)	2,563 (94.6%)	0.03
	24 months	1,562 (89.8%)	905 (93.4%)	2,467 (91.1%)	0.002
Viral load testing	6 months	780 (44.8%)	585 (60.4%)	1,365 (50.4%)	<0.001
	12 months	1,135 (65.2%)	757 (78.1%)	1,892 (69.8%)	<0.001
	24 months	1,254 (72.1%)	833 (86.0%)	2,087 (77.0%)	<0.001
Viral suppression (among tested)	6 months	685 (87.8%)	551 (94.2%)	1,236 (90.5%)	<0.001
	12 months	1,022 (90.0%)	720 (95.1%)	1,742 (92.1%)	<0.001
	24 months	1,140 (90.9%)	800 (96.0%)	1,940 (93.0%)	<0.001
Regimen switching	6 months	44 (2.5%)	8 (0.8%)	52 (1.9%)	0.002
	12 months	70 (4.0%)	15 (1.5%)	85 (3.1%)	<0.001
	24 months	122 (7.0%)	29 (3.0%)	151 (5.6%)	<0.001
Mortality	6 months	14 (0.8%)	6 (0.6%)	20 (0.7%)	0.589
	12 months	27 (1.6%)	10 (1.0%)	37 (1.4%)	0.264
	24 months	44 (2.5%)	16 (1.7%)	60 (2.2%)	0.137
Loss to follow-up (LTFU)	6 months	26 (1.5%)	8 (0.8%)	34 (1.3%)	0.134
	12 months	47 (2.7%)	12 (1.2%)	59 (2.2%)	0.012
	24 months	78 (4.5%)	25 (2.6%)	103 (3.8%)	0.013
Transfers out	6 months	35 (2.0%)	12 (1.2%)	47 (1.7%)	0.14
	12 months	60 (3.4%)	18 (1.9%)	78 (2.9%)	0.018
	24 months	85 (4.9%)	28 (2.9%)	113 (4.2%)	0.013
Adherence ≥95%	6 months	1,393 (80.1%)	825 (85.1%)	2,218 (81.9%)	<0.001
	12 months	1,376 (79.1%)	834 (86.1%)	2,210 (81.6%)	<0.001
	24 months	1,354 (77.8%)	827 (85.3%)	2,181 (80.5%)	<0.001

VL=Viral Load, LTFU=Loss to Follow-up, Values shown as *n (%)* unless otherwise specified
Comparisons between EFV- and DTG-based groups were performed using Chi-square or Fisher's exact test, as appropriate. Statistically significant values are shown in bold.

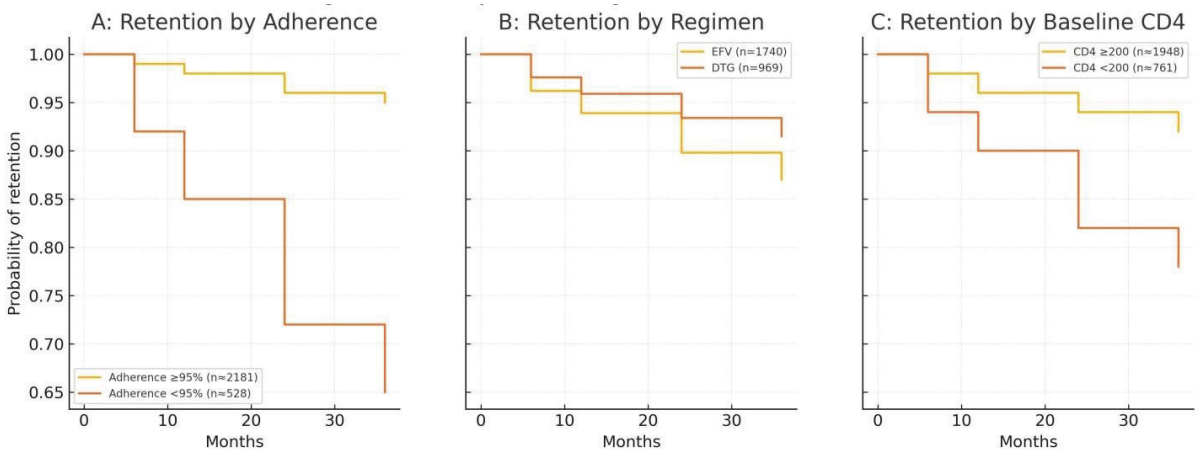

Figure 2 Retention patterns by adherence, regimen, and baseline CD4 count

Regimen Switching

Cumulative switching to second-line therapy significantly favored dolutegravir at all timepoints: 6 months (0.8% vs 2.5%, p-value=0.002), 12 months (1.5% vs 4.0%, p-value<0.001), and 24 months (3.0% vs 7.0%, p-value<0.001). Figure 3 shows Kaplan-Meier curves demonstrating consistently lower switching hazards among dolutegravir recipients throughout follow-up (log-rank p-value<0.001).

Virological failure was the leading switching reason, affecting 1.2% of dolutegravir versus 3.9% of efavirenz patients (incidence rate: 0.78 per 100 person-years). Adverse events occurred in about 6% of participants, mainly gastrointestinal (2.3%), dermatologic (1.6%), or neuropsychiatric (1.4%), predominantly among efavirenz users. Hepatic (0.6%) and metabolic (0.3%) events were rare. Toxicity-related switches were more frequent with efavirenz (3.0%) than dolutegravir (1.1%), reflecting expected tolerability differences (0.61 per 100 person-years). Drug-drug interactions occurred in 1.6% versus 2.0%, pregnancy-related switches in 1.0% versus 1.4%, programmatic factors in 0.9% versus 1.1%, and patient preference in 0.7% versus 1.0%. Overall, 6.6% of dolutegravir versus 12.5% of efavirenz patients experienced regimen modifications. (Table 3)

Predictors of regimen Switching

In univariable analysis, dolutegravir showed strong protection (HR 0.48, 95% CI: 0.37-0.63, p-value<0.001). Low baseline CD4 (<200 cells/μL) increased risk (HR 1.60, 95% CI: 1.28-2.00, p-value<0.001), as did detectable baseline viral load (HR 1.94, 95% CI: 1.36-2.75, p-value<0.001). Suboptimal adherence was the strongest predictor (HR 3.10, 95% CI: 2.40-4.01, p-value<0.001).

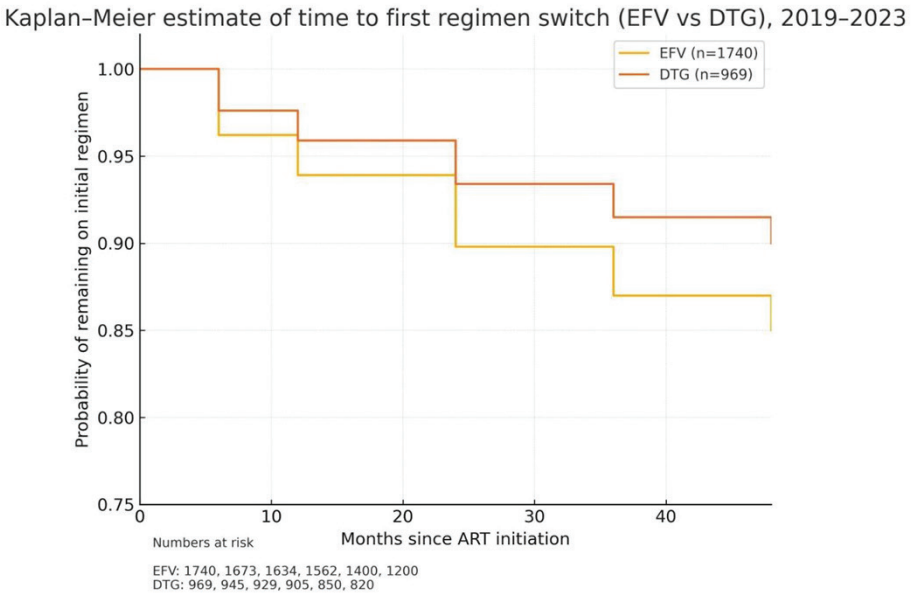

Figure 3 Kaplan–Meier estimates of time to first regimen switch

In multivariable analysis, dolutegravir use remained associated with a lower hazard of outcome (aHR: 0.55, 95% CI: 0.42–0.72) and was associated with a 45% lower hazard. Low CD4 at baseline (adjusted HR 1.42, 95% CI: 1.11–1.82), p-value=0.005, detectable VL (adjusted HR 1.76, 95%CI: 1.21–2.57), p-value=0.003, and poor adherence (<95%) remained an independent predictor of regimen switching (adjusted HR 2.85, 95% CI: 2.17–3.75, p-value<0.001) (Table 4).

Table 3 Reasons for Regimen Switch and Incidence Rates by Initial Regimen

Reason for Switch	EFV (n=1,740)	DTG (n=969)	Total (N=2709)	Incidence Rate (per 100 PY)
Virological failure	68 (3.9%)	12 (1.2%)	80 (3.0%)	0.78
Toxicity/adverse events	52 (3.0%)	11 (1.1%)	63 (2.3%)	0.61
Drug–drug interactions (e.g., TB)	35 (2.0%)	15 (1.6%)	50 (1.8%)	0.48
Pregnancy-related switch	25 (1.4%)	10 (1.0%)	35 (1.3%)	0.32
Programmatic/stock-out	20 (1.1%)	9 (0.9%)	29 (1.1%)	0.28
Patient preference/others	18 (1.0%)	7 (0.7%)	25 (0.9%)	0.24
Total switched	218 (12.5%)	64 (6.6%)	282 (10.4%)	2.71

PY=Per year, TB=Tuberculosis

Table 4 Cox regression predictors of regimen switch in the cohort (N=2,709, events=282)

Predictor	Unadjusted HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
Initial regimen				
EFV (ref)	1.00	–	1.00	–
DTG	0.48 (0.37–0.63)	<0.001	0.55 (0.42–0.72)	<0.001
Demographic				
Age (per 10y ↑)	1.05 (0.94–1.18)	0.35	1.08 (0.96–1.22)	0.19
Female vs Male	0.90 (0.70–1.16)	0.42	0.92 (0.71–1.20)	0.54
Clinical				
CD4 <200 vs ≥200	1.60 (1.28–2.00)	<0.001	1.42 (1.11–1.82)	0.005
VL detectable vs undetectable	1.94 (1.36–2.75)	<0.001	1.76 (1.21–2.57)	0.003
TB history (Yes vs No)	1.33 (0.99–1.78)	0.06	1.29 (0.94–1.78)	0.11
Comorbidities				
Diabetes (Yes vs No)	1.12 (0.78–1.61)	0.55	1.05 (0.72–1.54)	0.80
Hypertension (Yes vs No)	0.94 (0.67–1.32)	0.72	0.97 (0.69–1.36)	0.86
Treatment-related				
Adherence <95% vs ≥95%	3.10 (2.40–4.01)	<0.001	2.85 (2.17–3.75)	<0.001

HR=Hazard Ratio, CI=Confidence Interval, VL=Viral Load
All variables with p-value<0.20 in univariable models were considered in the multivariable model.

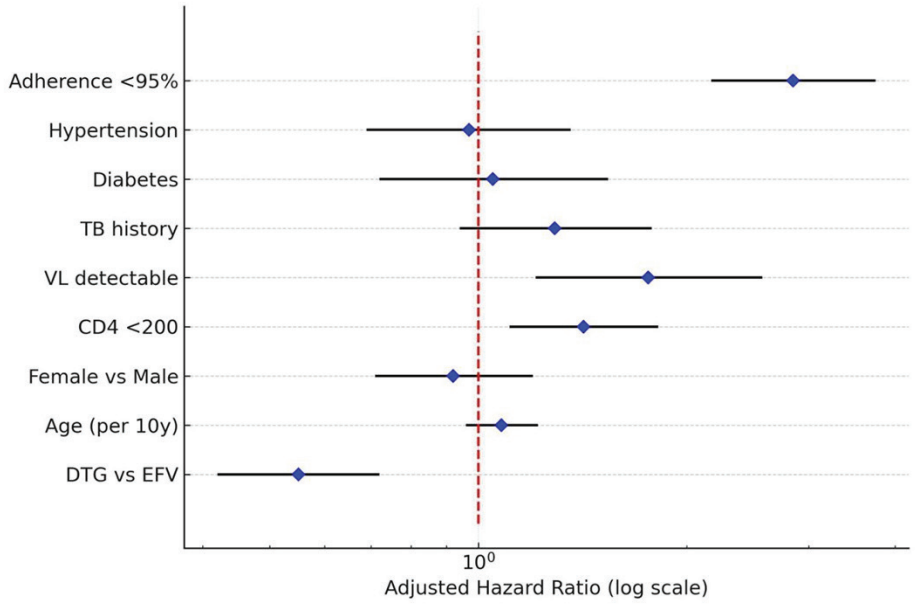

Figure 4 Forest plot of adjusted hazard ratios for predictors of regimen switching

Discussion

This large assessment of the HIV treatment programme in India during the transition from efavirenz to dolutegravir for first-line therapy offers real-world evidence supporting the programmatic benefits of dolutegravir as a component of first-line regimens. Our results show good performance across a wide array of indicators, which include retention in care, viral suppression rates, level of adherence, and durability of regimens. These findings provide important characterisation for maximising antiretroviral therapy programmes in low-resource settings, and add to the body of evidence on the dolutegravir rollout globally. The retention rates observed are in favor of dolutegravir at all time points, with statistical significance reached from 12 months onward. The 3.6 percentage point gap in 24-month retention amounts to a large programmatic advantage that is likely to be experienced by thousands of patients over time. These results are consistent with the recent reports from randomized trials and real-world cohort studies showing greater therapeutic durability with dolutegravir-based regimens[9]. The better retention may also be a result of better tolerability, as adherence rates were consistently higher in dolutegravir recipients at all timepoints. The time ordering of retention differences indicates that early treatment tolerability has large effects on the long-term participation in care. Although initial differences were modest, the increasing divergence suggests that the accumulated weight of efavirenz-related side effects may become more important in terms of patient willingness to take therapy. The 24-month retention (91%) and viral suppression (93%) rates observed in this cohort are higher than the national programmatic averages reported by NACO and UNAIDS for the same period, which ranged from 82% to 85% for retention and 89% to 91% for viral suppression. This underscores the strength of consistent ART delivery and adherence support at the study site. There was a substantial gap in viral load testing uptake between dolutegravir users and non-users, with differences

from 15.6 percentage points at 6 months to 13.9 percentage points by 24 months. This unexpected finding points to potential programmatic elements that are not related to the medication itself, such as differential engagement of patients, healthcare provider behaviours, or systematic variations in care delivery around the transition. The increased testing among those taking dolutegravir may also be indicative of greater provider confidence in the more modern regimen and/or increased patient acceptance of monitoring with better-tolerated ART.

Viral response rates with dolutegravir were higher at 6, 12, and 24 months (sustained differences: 5.1–6.4 percentage points) among tested patients. These data support the findings seen in clinical trials such as those from NAMSAL and ADVANCE, where dolutegravir-based regimens were observed to have better virological outcomes[3,10]. The continued benefit over the follow-up is indicative of long-term efficacy advantages leading to substantial programmatic impact. The persistence of this advantage at various time points argues in favor of the intrinsic virological superiority of dolutegravir compared to temporal confounding.

The patterns of adherence we observed in our cohort suggest that dolutegravir appears to have long-term benefits for adherence compared with efavirenz, with between 5 and 7 percentage point differences across the follow-up period. The better adherence could probably be explained by the better tolerability profile of dolutegravir when compared with efavirenz, especially in terms of its CNS-related adverse effects, which may significantly affect patient quality of life and treatment continuation[11]. The consistency of benefits in adherence at all timepoints indicates that this benefit is not a transient effect but could be lasting.

The observed adherence trends also illustrate the intricate inter-dependence between tolerability, experience, and engagement. Greater rates of adherence to dolutegravir presumably lead to the superior viral suppression, thus generating a virtuous cycle whereby treatment success and retention in care are mutually reinforcing. Switching patterns confirm what may be the most demonstrable advantage of dolutegravir for programs. A 2.3-fold increase in the 24-month switch rates (7.0% vs 3.0%) is associated with considerable cost and treatment continuance benefits. Virological failure was found to be the leading cause of switch seen, nearly three times as often in efavirenz versus dolutegravir recipients. Regimen change due to toxicity occurred 2.7 times more frequently with efavirenz, consistent with known tolerability differences between these agent classes.

The switch patterns provide valuable insight regarding the durability of treatment in clinical practice. Early separation of the KM curves indicates that tolerability problems develop rapidly following initiation of therapy, whereas virological failures are more gradual. Rates of drug-drug interaction with concomitant tuberculosis treatment were equivalent between regimens, indicating both regimens can be used in this important comorbid population.

Cox regression analysis reveals definite predictors of regimen change, with dolutegravir initiation resulting in a 45% risk reduction in multivariate analyses. Conversely, bad baseline prognostic factors of low CD4 and detectable viral load increased switch risk as anticipated. In contrast, suboptimal adherence became the most important predictor and was associated with an almost three times higher hazard. This finding underscores the crucial role of adherence support interventions in program settings, irrespective of regimen selection. The interaction of baseline factors and dolutegravir-containing treatment regimens indicates that although dolutegravir offers benefits across patient subsets, the greatest advantages may be experienced in patients with suboptimal baseline properties. Several study limitations warrant consideration. The design was retrospective in nature and utilized routinely collected data, some of which were incomplete or unavailable

for certain variables, most notably laboratory tests and records on adherence. There may be a selection bias for non-random allocation in the transition phase. Variability in the duration of program implementation over time, provider practice, and patient population also may affect adherence when comparing outcomes. Despite adjustments for covariates using multivariable analysis, the presence of residual confounding by unmeasured variables cannot be ruled out. Long-term durability and resistance may not be captured by the short follow-up. Lastly, as the study was from a single ART centre, it may only be representative of the setting where it was performed. Adherence was assessed using pharmacy refill records, which may not fully capture true medication consumption. The proportional hazards assumption was not formally tested, which may affect the interpretation of time-to-event estimates.

The discrepancy in baseline characteristics between the two arms of treatment, although statistically adjusted for in regression analyses, may be a result of unreported confounding that may affect the outcomes. There are programmatic implications of our findings, not only for the individual patient but also at the level of population health and resource allocation. The increased virological suppression and retention on therapy as a result of dolutegravir use contribute to reduced risk of transmission, quality-adjusted life years, and burden on the healthcare system. Real-world evidence has shown high rates of virologic suppression and low rates of virologic failure with DTG-based regimens[12].

Cost considerations, though beyond the scope of this study, favor DTG on cost-effectiveness with lower rates of switching, better retention, and higher viral suppression. The reduced requirement for second-line therapy switches is cost-saving, which can be particularly relevant in resource-constrained settings. Better tolerability might also result in lower healthcare utilization for the management of adverse events. Our findings have important implications in terms of treatment guidelines and programmatic implementation. The data are in favor of dolutegravir-containing regimens for treatment-naive patients but highlight the relevance of adherence counseling and support. Programs should expect better results following the switch to dolutegravir, but will require strong monitoring systems to demonstrate them[13].

The transition period analysis offers novel perspectives on programmatic change management, showing that treatment enhancements can be effectively introduced under current healthcare conditions. Such experience may be useful for future challenges or treatment optimization, when new therapeutic strategies appear. Further research should investigate such long-term outcomes as the development of resistance, cardiovascular and metabolic effects, and measures of treatment satisfaction. Continued surveillance of safety, in particular around pregnancy outcomes and concerns about weight gain associated with dolutegravir use, is critical as the global footprint of dolutegravir continues to grow[14].

In conclusion, our detailed review provides evidence of substantial programmatic benefits associated with dolutegravir-based first-line treatment over multiple outcomes. These align with the National AIDS Control Organisation (NACO) 2021 and 2025 Guidelines, highlighting the role of dolutegravir and emphasising the need for ongoing programmatic investment in adherence support, monitoring systems, and further optimisation strategies.

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Conflict of interest

The authors declare that they have no financial or non-financial competing interests that could have influenced the conduct, outcomes, or reporting of this research.

References

1. National AIDS Control Organization. National guidelines for HIV care and treatment 2021. Ministry of Health and Family Welfare, Government of India [homepage on the Internet]. New Delhi: Government of India; 2021 [cited 2025 Oct 7]. Available from: https://naco.gov.in/sites/default/files/National_Guidelines_for_HIV_Care_and_Treatment_2021.pdf
2. World Health Organization. WHO released updated guideline on HIV service delivery [homepage on the Internet]. Geneva: WHO; 2025 Sep 11 [cited 2025 Oct 7]. Available from: https://www.who.int/news/item/12-09-2025-who-released-updated-guideline-on-hiv-service-delivery
3. Mahale PR, Patel KR, Raval RR, Vyas JR, Mehta AR. Treatment outcomes of dolutegravir- versus efavirenz-based antiretroviral therapy regimens among people living with HIV in India: a retrospective study. J Family Med Prim Care 2023;12:1032–40. doi: 10.4103/jfmpc.jfmpc_567_23.
4. Kanters S, Vitoria M, Zoratti M, Doherty M, Socías ME, Ford N, et al. Comparative efficacy, tolerability and safety of dolutegravir and efavirenz: systematic review and network meta-analysis. EBioMedicine 2020;55:102779. doi: 10.1016/j.ebiom.2020.102779.
5. Kamori D, Barabona G, Maokola W, Rugemalila J, Mahiti M, Mizinduko M, et al. HIV viral suppression in the era of dolutegravir use: findings from a national survey in Tanzania. PLoS One 2024;19:e0307003. doi:10.1371/journal.pone.0307003.
6. Joshi RK, Mehendale SM. Determinants of consistently high HIV prevalence in Indian districts. PLoS One 2019;14:e0216321.
7. Kumar P, Das C, Deo V, Chaturvedi HK, Biswas S, Priyam N, et al. Progress and challenges towards eliminating vertical transmission of HIV in India. Sci Rep 2025;15:25004. doi: 10.1038/s41598-025-09481-2.
8. Basu S, Garg S. Methods for estimating medication adherence to antiretroviral therapy: response to Mehta et al. Indian J Community Med 2017;42:49-51.
9. Ayal MA, Berha AB. Comparative safety and changes in immunologic and virologic parameters of dolutegravir versus efavirenz-based antiretroviral therapies among HIV patients: a retrospective cohort study. HIV AIDS (Auckl) 2023;15:173-90. doi: 10.2147/HIV.S396420.
10. Pepperrell T, Venter WDF, McCann K, Bosch B, Tibbatts M, Woods J, et al. Participants on dolutegravir resuppress human immunodeficiency virus RNA after virologic failure: updated data from the ADVANCE trial. Clin Infect Dis 2021;73:e1008-10. doi: 10.1093/cid/ciab086.
11. Majula RT, Mweya CN. Brief communication: long-term treatment outcomes of transitioning to dolutegravir-based ART from efavirenz in HIV study participants in Mbeya, Tanzania. AIDS Res Ther 2024;21:98. doi: 10.1186/s12981-024-00662-z.
12. Doblado-Maldonado A, Ooi AYR, Cheng CY, Sun W, Letang E, Moorhouse M, et al. Dolutegravir + lamivudine effectiveness and tolerability in real-world cohorts with HIV-1 across Asia and South America: a systematic literature review. *Med (Baltimore)* 2025;104:e43558. doi:10.1097/MD.0000000000043558. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC12366928/
13. Skrivankova VW, Huwa J, Muula G, Chiwaya GD, Banda E, Buleya S, et al. Virologic failure and drug resistance after programmatic switching to dolutegravir-based first-line antiretroviral therapy in Malawi and Zambia. Clin Infect Dis 2025;80:120-8. doi: 10.1093/cid/ciae261.
14. Kourtis AP, Zhu W, Lampe MA, Huang YA, Hoover KW. Dolutegravir and pregnancy outcomes including neural tube defects in the USA during 2008–20: a national cohort study. Lancet HIV 2023;10:e588-e596. doi:10.1016/S2352-3018(23)00108-X.