

Article

Comparable Treatment Efficacy of Switching to Dolutegravir/Lamivudine Versus Triple-Drug Antiretroviral Therapy in People with HIV After 2 Years of Follow-Up: The DUALING Prospective Nationwide Matched Cohort Study

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Abstract

Background: Demonstrating durable viral suppression after switching to dolutegravir/lamivudine in clinical practice solidifies its use. **Methods:** This was a prospective cohort (DUALING) study conducted in 24 Dutch HIV treatment centers. HIV-RNA-suppressed cases undergoing triple-drug antiretroviral therapy without prior virological failure or resistance who switched to dolutegravir/lamivudine (cases) were 1:2 matched to controls, who remained on triple-drug antiretroviral therapy. Matching was stratified by dolutegravir use in the triple-drug antiretroviral therapy, and further by age, sex, HIV acquisition route, CD4⁺T-cell nadir, and HIV-RNA zenith. The primary endpoint was the treatment failure rate at 2 years, determined using intention-to-treat and on-treatment analyses with a 5% noninferiority margin. **Results:** The 2040 mostly male (84.3%) participants included 390 cases of dolutegravir-based triple-drug regimens with 680 controls, and 290 cases of non-dolutegravir-based triple-drug regimens with 580 controls. In the dolutegravir-based cases and controls, treatment failure occurred in 12.6% and 23.3% of patients in the intention-to-treat analysis (difference: −10.7%, 95%CI: −15.3% to −6.1%) and 2.6% and 2.4% of patients in the on-treatment analysis (difference: +0.2%, 95%CI −1.9% to +2.3%). The treatment failure risk in non-dolutegravir-based cases and controls was 15.2% and 19.9% in the intention-to-treat analysis (difference: −4.7, 95%CI: −10.0% to +0.6%) and 1.2% and 1.9% in the on-treatment analysis (difference +0.7%, 95%CI −2.6% to +1.1%). Therapy modifications unrelated to virological failure explained the higher treatment failure rate in the intention-to-treat analysis. In dolutegravir/lamivudine cases, a shorter time of prior triple-drug antiretroviral therapy, age < 50 years, and non-Western origin were associated with treatment failure in the multivariable analysis. Viral blips occurred in 6.8% of cases and 5.1% of controls. In the post hoc analysis, discontinuing tenofovir disoproxil fumarate-based triple-drug antiretroviral therapy led to weight gain in people with (+2.7 kg) and without (+2.3 kg) prior dolutegravir use. **Conclusions:** In this nation-

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wide clinical practice study, switching to dolutegravir/lamivudine was noninferior to continuing triple-drug antiretroviral therapy after 2 years of follow-up.

Keywords: HIV; dolutegravir; lamivudine; 2DR; real-world data; virological failure; resistance

1. Introduction

The long-term management of HIV increasingly focuses on maintaining durable viral suppression while minimizing cumulative drug exposure and toxicity. Two-drug antiretroviral regimens are a promising strategy to achieve these goals [1]. Major guidelines, such as those from the European AIDS Clinical Society and International AIDS Society, have adopted two-drug regimens as recommended therapies in people with a suppressed plasma viral load. Treatment simplification to two-drug regimens can be attractive to clinicians when managing drug toxicity or interaction risks, especially in aging populations. In addition, cost-savings and improved compliance can be relevant considerations for these regimens.

Among two-drug antiretroviral regimens, the combination of dolutegravir plus lamivudine has demonstrated high efficacy in randomized clinical trials [2,3], but evidence is needed about its durable effect outside tightly controlled trial settings in more diverse populations. Real-world evidence is particularly important for dual-therapy strategies, because treatment changes in clinical practice are often driven by factors beyond virological efficacy, including tolerability, drug–drug interactions, adherence, comorbidities, budget impact, and patient preference.

The DUALING study was designed to address this data gap by prospectively comparing outcomes of virologically suppressed people with HIV who switched from triple-drug therapy to dolutegravir/lamivudine with those who continued standard three-drug regimens within routine HIV care in the Netherlands. The year 1 analyses showed that switching to dolutegravir/lamivudine was not associated with an increased risk of treatment failure compared with remaining on triple therapy [4]. However, durability beyond the first year increases confidence in this regimen, as virological relapse, cumulative toxicity, and treatment modifications may emerge with longer follow-up. Recent data from cohorts with follow-up beyond 1 year on dolutegravir/lamivudine have suggested adequate durability but were retrospective and lacked matched controls continuing triple-drug antiretroviral therapy [5,6]. These methodological limitations leave clinicians with suboptimal data regarding the long-term effectiveness of dolutegravir/lamivudine when used in routine practice. The DUALING study directly addresses this concern.

Here, we report the year 2 outcomes of the sustained effectiveness of dolutegravir/lamivudine compared with continued triple-drug antiretroviral therapy in routine clinical practice using a nationwide cohort in the Netherlands (ATHENA).

2. Methods

Study Design and Population

DUALING is an ongoing, nationwide, prospective cohort study conducted in all 24 Dutch HIV treatment centers participating in ATHENA. A detailed description of the methodology has been published previously and is available in open access form [4]. The present analysis evaluates outcomes over 2 years of follow-up among participants who were previously enrolled at the time of switching to dolutegravir/lamivudine or who remained on triple-drug antiretroviral therapy.

Cases represent adult participants who are plasma HIV-RNA-suppressed on triple-drug antiretroviral therapy without prior virological failure or resistance who switched to dolutegravir/lamivudine as part of routine care. Controls were participants who remained on triple-drug ART. Suppression was defined as a most recent plasma HIV-RNA < 50 copies/mL, allowing for a single low-level viral blip up to 200 copies/mL prior to switch. Participants were stratified according to whether their prior triple-drug antiretroviral regimen contained dolutegravir. Exclusion criteria were a history of virological failure on a lamivudine- or emtricitabine-containing regimen with plasma HIV-RNA > 1000 copies/mL, documented resistance to lamivudine or dolutegravir, physician-reported non-adherence in the preceding three months, and chronic active hepatitis B virus coinfection in the switch group. Clinicians routinely checked daily antiretroviral regimen adherence at every clinical visit as standard of care.

Each case was matched 1:2 to controls based on current use of dolutegravir, age, sex, HIV transmission category, CD4+T-cell nadir (≤ 200 vs. > 200 cells/mm³), and HIV-RNA zenith ($\leq 100,000$ vs. $> 100,000$ copies/mL). Controls were required to have a clinic visit within 3 months of the case's switch date; follow-up for controls began at the visit closest in calendar time to that switch. This alignment minimized confounding by temporal changes in HIV care, including COVID-19-related disruptions of HIV outpatient care. When multiple controls were eligible, the closest visit date determined selection. Cases came from nine treatment centers that implemented an institutional policy to switch people with HIV to dolutegravir/lamivudine in routine care up to December 2020. Controls were selected from the remaining fifteen centers to minimize selection bias and met the same eligibility criteria for switching, but continued triple-drug antiretroviral therapy.

Treatment decisions, including whether to switch therapy, were made by the treating physician as part of standard clinical care. All participants were followed in routine clinical practice, with HIV-RNA assessed every 6 months. An additional measurement at 3 months after switching was permitted at the clinician's discretion. All participants had previously provided informed consent for inclusion in ATHENA and secondary use of their data. The study is registered at clinicaltrials.gov NCT04707326. The sponsor had no role in data collection, analysis, or manuscript preparation.

3. Outcomes

The primary endpoint for this analysis was treatment failure over 2 years of follow-up. Treatment failure was defined as either two consecutive HIV-RNA measurements > 50 copies/mL on the same regimen, or a single HIV-RNA > 50 copies/mL followed by loss to follow-up or a change in antiretroviral therapy. Outcomes were evaluated using both intention-to-treat (ITT) and on-treatment (OT) approaches. In the ITT analysis, loss to follow-up or antiretroviral therapy modification for any reason was categorized as failure. In the OT analysis, participants who changed or discontinued antiretroviral therapy while maintaining HIV-RNA ≤ 50 copies/mL or who were lost to follow-up were censored and were not considered as failures. Controls were censored at the time of switching from triple therapy to dolutegravir/lamivudine. Virological success at year 2 was defined as HIV-RNA < 50 copies/mL at the 24-month visit window. Isolated detectable HIV-RNA values without regimen change did not constitute treatment failure if they did not meet the failure definition. Loss to follow-up was defined as absence of any HIV-RNA measurement for more than 52 weeks, death or emigration. Secondary outcomes included treatment failure among participants switching from non-dolutegravir-based regimens, frequency of viral blips, and emergence of resistance mutations. Predefined subgroup analyses were performed, while body weight changes were explored post hoc.

Statistical Analysis

The original sample size calculation, based on a 95% suppression rate, a 1:2 case–control ratio, an intraclass correlation of 0.1, and a noninferiority margin of 5%, yielded a target of 390 cases for 90% power with a one-sided α of 0.05. Continuous variables are summarized using means or medians and categorical variables are summarized as proportions. Group comparisons used t-tests or Wilcoxon rank-sum tests for continuous data and chi-square tests for categorical data. The risk difference in treatment failure between cases and controls was calculated with both one-sided 90% and two-sided 95% confidence intervals. An upper confidence limit below the predefined 5% margin confirmed noninferiority. Multivariable logistic regression was used to estimate adjusted odds ratios for treatment failure among cases, including predefined HIV- and non-HIV-related covariates.

4. Results

4.1. Baseline Characteristics

The cohort characteristics have been described before [4]. Briefly, of the total 2040 people with HIV, 680 were dolutegravir/lamivudine cases matched to 1360 controls: 390 cases used a dolutegravir-based triple-drug regimen and 290 cases used a non-dolutegravir-based triple-drug regimen at the moment they switched to dolutegravir/lamivudine (Table 1). Most were men having sex with men who were born in the Netherlands, with a median age of 48 (on dolutegravir-based triple-drug regimens) and 50 (on non-dolutegravir-based triple-drug regimens) years. Apart from a shorter time on triple-drug therapy for cases, key characteristics were comparable. Most of the 390 dolutegravir-based cases had abacavir and lamivudine in their dolutegravir-based triple therapy prior to switching. Most of the 290 non-dolutegravir-based cases without dolutegravir were on non-nucleoside reverse transcriptase inhibitors.

Table 1. Baseline characteristics of the DUALING study population.

	DTG-Based ART		Non-DTG-Based ART	
	DTG/3TC (Cases) N = 390	DTG-Based Triple-Drug ART (Controls) N = 780	DTG/3TC (Cases) N = 290	Non-DTG-Based Triple-Drug ART (Controls) N = 580
Age (median years, IQR)	48 (37–57)	48 (38–57)	50 (39–59)	50 (40–59)
Male sex	344 (88.2%)	688 (88.2%)	229 (79.0%)	458 (79.0%)
Region of birth				
Netherlands	264 (67.7%)	471 (60.4%)	170 (58.6%)	344 (59.3%)
Western	45 (11.5%)	68 (8.7%)	31 (10.7%)	48 (8.3%)
Sub-Saharan Africa	19 (4.9%)	74 (9.5%)	33 (11.4%)	71 (12.2%)
Latin America/Caribbean	34 (8.7%)	100 (12.8%)	35 (12.1%)	79 (13.6%)
South Asia	19 (4.9%)	74 (9.5%)	8 (2.8%)	24 (4.1%)
Other	9 (2.3%)	34 (4.4%)	13 (4.5%)	14 (2.4%)
HIV transmission route				
MSM	283 (72.6%)	576 (73.8%)	185 (63.8%)	373 (64.3%)
Heterosexual	80 (20.5%)	170 (21.8%)	88 (30.3%)	183 (31.6%)
Intravenous drug use	3 (0.8%)	2 (0.3%)	2 (0.7%)	4 (0.7%)
Blood–blood contact	2 (0.5%)	2 (0.3%)	4 (1.4%)	2 (0.3%)
Vertical	3 (0.8%)	5 (0.6%)	1 (0.3%)	0 (0.0%)
Unknown	19 (4.9%)	25 (3.2%)	10 (3.4%)	18 (3.1%)
Prior ART use (median years, IQR)	5 (3–9)	8 (5–12)	9 (6–14)	11 (8–15)

CD4+ T-cell count nadir (median cells/mm³, IQR)	330 (200–485)	310 (190–471)	290 (180–437)	270 (170–380)
HIV-RNA zenith (median log₁₀ c/mL, IQR)	4.9 (4.4–5.3)	4.8 (4.3–5.4)	5.0 (4.4–5.3)	5.0 (4.5–5.4)
Prior AIDS diagnosis	52 (13.3%)	138 (17.7%)	31 (10.7%)	96 (16.6%)
CD4+T-cell count current (median cell/mm³, IQR)	690 (500–890)	736 (561–934)	750 (540–950)	730 (569–930)
HIV-RNA 50–200 c/mL (blip) at start follow-up	8 (2.1%)	11 (1.4%)	3 (1.0%)	5 (0.9%)
Prior ART regimens (median, IQR)	2 (1–3)	2 (1–3)	2 (1–3)	2 (1–3)
NRTI backbone				
3TC	390 (100%)	0 (0%)	290 (100%)	0 (0%)
ABC/3TC	0 (0%)	600 (76.9%)	0 (0%)	28 (4.3%)
TDF/FTC	0 (0%)	105 (13.5%)	0 (0%)	233 (40.2%)
TDF/3TC	0 (0%)	1 (0.1%)	0 (0%)	49 (8.4%)
TAF/FTC	0 (0%)	74 (9.5%)	0 (0%)	269 (46.4%)
TAF/3TC	0 (0%)	0 (0%)	0 (0%)	1 (0.1%)
Anchor drug class				
INSTI	390 (100%)	780 (100%)	290 (100%)	182 (31.4%)
NNRTI	0 (0%)	0 (0%)	0 (0%)	332 (57.2%)
PI	0 (0%)	0 (0%)	0 (0%)	66 (11.4%)
Reasons to switch to DTG/3TC ¹				
ART simplification	216 (55.4%)		109 (37.6%)	
New treatment option	96 (24.6%)		25 (8.6%)	
Toxicity	56 (14.4%)		126 (43.5%)	
Drug–drug interaction	0 (0%)		10 (3.4%)	
Other	13 (3.3%)		13 (4.5%)	
Unknown	9 (2.3%)		7 (2.4%)	
Comorbidities				
Hepatitis B Ag positive	0 (0%)	24 (3.1%)	0 (0%)	27 (4.7%)
Hepatitis C IgG positive	28 (7.2%)	70 (9.0%)	27 (9.3%)	53 (9.1%)
Obesity	44 (11.3%)	93 (11.9%)	34 (11.7%)	69 (11.9%)
Diabetes mellitus 2	12 (3.1%)	24 (3.1%)	16 (5.5%)	29 (5.0%)
Hypertension	141 (36.2%)	245 (31.4%)	94 (32.4%)	151 (26.0%)
Chronic kidney disease	42 (10.8%)	92 (11.8%)	17 (5.9%)	33 (5.7%)
Cardiovascular disease	10 (2.6%)	25 (3.2%)	12 (4.1%)	25 (4.3%)
Stroke	4 (1.0%)	8 (1.0%)	3 (1.0%)	8 (1.4%)
Non-AIDS malignancy	15 (3.8%)	29 (3.7%)	9 (3.1%)	23 (4.0%)

¹ Reasons to switch: new treatment category is defined by patient preference; other reasons include pill size and aging; unknown is defined when the treating physician did not specify a reason for the switch. Abbreviations: 3TC, lamivudine; ABC, abacavir; ART, antiretroviral therapy; DTG, dolutegravir; FTC, emtricitabine; INSTI, integrase strand transfer inhibitor; MSM, men who have sex with men; (N)NRTI, (non-)nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; TDF, tenofovir disoproxil fumarate; TAF, tenofovir alafenamide.

4.2. Treatment Outcomes

The treatment failure rate (Figure 1) in the dolutegravir-based stratum after 2 years in the OT analysis was 2.6% in cases and 2.4% in controls (difference 0.2%, 95%CI: −1.9% to +2.3%). ITT analysis found less treatment failure in cases (12.6%) than controls (23.3%, difference −10.7%, 95%CI: −15.3% to −6.1%), which is attributable to more treatment switches (n = 256) without plasma viral rebound above 50 copies/mL in controls. The treatment failure rate in the non-dolutegravir-based stratum after 2 years in the OT analysis

was 1.2% in cases and 1.9% in controls (difference +0.7%, 95%CI: −2.6% to +1.1%). ITT analysis found a lower rate of treatment failure (difference −4.7%, 95%CI −10.0% to +0.6%) in cases (15.2%) than controls (19.9%). Also here, therapy modifications unrelated to virological failure (n = 95) explained the higher rate of treatment failure in controls. In the ITT analysis of the 680 pooled dolutegravir/lamivudine cases using multivariable logistic regression, a shorter time on triple-drug antiretroviral therapy, age < 50 years, and non-Western origin were independently associated with treatment failure (Figure 2).

In total, 22 cases and 38 controls were lost to follow-up, including only one control with a last plasma viral load above 50 copies/mL at the last measurement. Follow-up was limited in 9 cases and 14 controls who had died within 2 years of the start of follow-up. Virological failure, defined as two consecutive plasma viral load above 50 copies/mL, occurred in 25 people, including nine cases (only one in the non-dolutegravir stratum) and 16 controls. The year 2 treatment success rate excluding censored individuals with a plasma viral load below 50 copies/mL was above 97% across all groups. In both control groups, antiretroviral therapy modifications occurred frequently, with 135 and 11 controls censored due to dolutegravir/lamivudine initiation in the dolutegravir and non-dolutegravir strata, respectively.

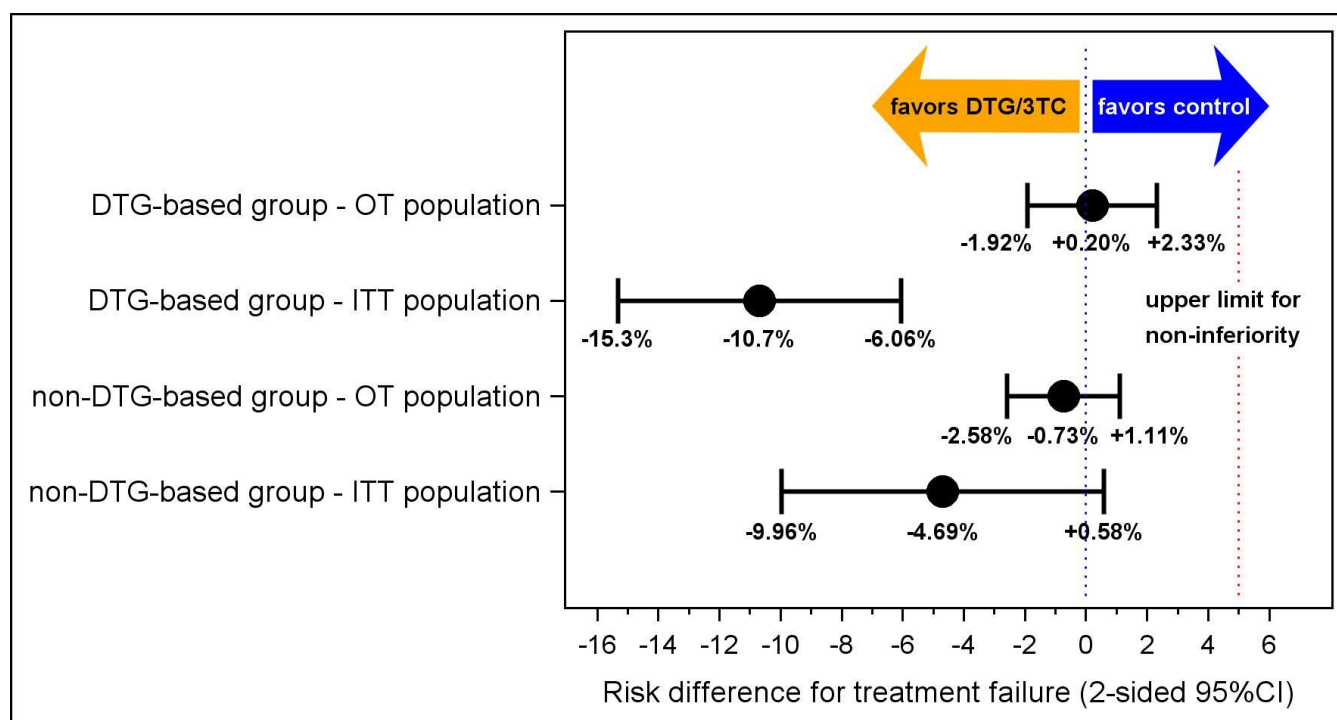


Figure 1. Treatment failure risk difference between cases on dolutegravir/lamivudine and controls on triple-drug antiretroviral regimens at 2 years of follow up. Table of failure risk difference with two-sided 95% CI at 2 year of follow-up between cases and controls who were virologically suppressed on either a dolutegravir- or a non-dolutegravir-based triple-drug antiretroviral regimen and started dolutegravir/lamivudine or continued triple-drug antiretroviral regimens, studied using on-treatment and intention-to-treat analysis. The vertical blue dotted line indicates no risk difference and the vertical red dotted line indicates the 5% noninferiority margin. Abbreviations: CI, confidence interval; DTG, dolutegravir; OT, on-treatment; ITT, intention-to-treat.

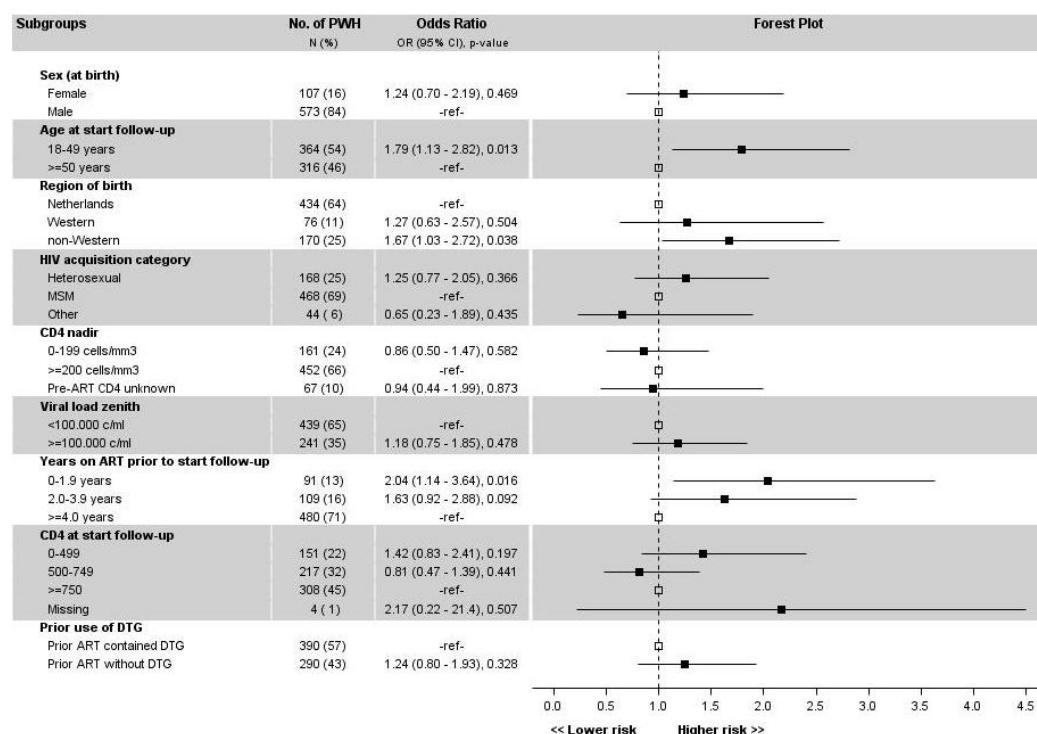


Figure 2. Subgroup analysis of treatment failure at 2-year follow-up in 680 cases on dolutegravir/lamivudine. Square markers denote the odds ratio (OR). The vertical dashed line at OR = 1 is the line of no effect. Upper calipers are capped at value 4.5. The reference category uses open square markers at OR = 1. The filled black squares shows the OR point estimate of the variables of interest. Abbreviations: ART, antiretroviral therapy; CI, confidence interval; DTG, dolutegravir; HIV, human immunodeficiency virus; MSM, men who have sex with men; OR, odds ratio; PWH, people with human immunodeficiency virus; REF, reference category.

While four cases had protocol-defined virological failure at 1 year of follow-up as reported, the current year 2 timepoint analysis showed nine cases meeting the virological failure criteria. Of these, two cases had plasma viral loads above 200 copies/mL, and the remaining seven had low-level viremia between 50 and 200 copies/mL. Seven switched to triple-drug antiretroviral therapy, of whom in six the low-level viremia persisted after the switch. The remaining two continued dolutegravir/lamivudine with low-level viremia below 200 copies/mL. No genotypic resistance was documented in the ATHENA database for these individuals. Of the people without protocol-defined virological failure during the 2-year follow-up period, 6.8% of cases and 5.1% of controls had a viral blip. Blips above 200 copies/mL occurred at a comparable rate in dolutegravir-based cases and controls (1.8% and 1.7%) and non-dolutegravir-based cases and controls (1.4% and 2.4%).

At year 2, weight measurements before and after the therapy switch were available for more cases (254 from the dolutegravir stratum and 201 from non-dolutegravir stratum) and matched controls (475 and 377, respectively). Similar trends were observed as in year 1. The mean weight gain was higher in the dolutegravir and non-dolutegravir cases (1.6 kg in both) than in controls (1.1 kg and 0.5 kg, respectively). These gains were driven by the discontinuation of tenofovir disoproxil fumarate, with a mean 2.7 kg and 2.3 kg weight gain in the dolutegravir and non-dolutegravir strata, respectively.

5. Discussion

In this nationwide cohort study, virologically suppressed people with HIV who switched to dolutegravir/lamivudine maintained durable viral control similar to matched controls who stayed on triple-drug therapy through two years of follow-up in routine

clinical care. Across both dolutegravir-based and non-dolutegravir-based strata, treatment success remained high, protocol-defined virological failure was uncommon, and no emergent genotypic resistance was observed. On-treatment analyses showed nearly identical failure rates between dual therapy and continued triple-drug regimens, while ITT analyses favored dolutegravir/lamivudine due to fewer treatment modifications, mostly for antiretroviral therapy simplification unrelated to viral rebound. Together, these findings confirm the sustained effectiveness of dolutegravir/lamivudine in clinical practice beyond the first year after switching.

While additional protocol-defined virological failures accumulated during the second year, absolute numbers remained low and reflected mostly low-level viremia of unclear clinical relevance. The overall treatment success rate at two years exceeded 97%, building on the high rate observed at year 1. The difference between cases and controls in the ITT analysis was driven by more regimen changes in controls. This indicates that long-term treatment stability rather than virological efficacy alone distinguishes dual therapy in routine care.

Our findings in clinical practice are concordant with phase III/IV randomized trials, including TANGO, SALSA, RUMBA and PASO-DOBLE [3,7–9], reporting the high effectiveness of dolutegravir/lamivudine as maintenance therapy in virologically suppressed populations up to 144 weeks in TANGO. In addition, our data align with observational cohort studies from Europe with long-term follow-up, reporting low rates of virological failure, rare resistance emergence, and comparable viral blip frequencies on dolutegravir/lamivudine [5,6]. Our study's nationwide coverage and superior design including matched controls not on dolutegravir/lamivudine add significant weight to the expanding evidence base on the safety of using this regimen in routine clinical practice. Similar to these Italian and Spanish cohorts, we found that age below 50 increased the treatment failure risk, confirming the trend observed at our year 1 timepoint analysis. A shorter time on antiretroviral therapy and non-Western origin remained associated with treatment failure at both year 1 and year 2. Contextual factors rather than regimen potency possibly explain these patterns. Weight gain trajectories observed at year 2 were consistent with year 1 findings and support the dominant role of discontinuing tenofovir disoproxil fumarate.

Several limitations should be considered. Despite using a matching strategy that is unique in real-world studies on dolutegravir/lamivudine efficacy and that allows for a more robust controlled analysis, the non-randomized design cannot fully exclude residual confounding or selection bias, particularly favoring switches in individuals expected to do well on dual therapy. Although calendar-time alignment reduced bias from evolving clinical practices, treatment strategies may have differed across centers. Some clinically relevant subgroups, such as individuals with advanced immunosuppression, remained underrepresented. A follow-up beyond 2 years would further strengthen conclusions on long-term efficacy. With a planned 5-year follow-up of the ongoing DUALING study, these data are expected. Weight outcomes were explored post hoc and should therefore be interpreted cautiously. Key strengths include the national coverage of all Dutch HIV treatment centers, prospective data collection within a well-established cohort, matched controls, and extended follow-up, capturing clinically meaningful outcomes beyond the first year.

6. Conclusions

This two-year analysis of the DUALING study demonstrates that switching to dolutegravir/lamivudine provides durable viral suppression in routine care, supporting its continued use as a long-term maintenance antiretroviral treatment strategy.

Author Contributions: Conceptualization: F.W.N.M.W., M.v.d.V., B.J.A.R. and C.R. Methodology: F.W.N.M.W., M.v.d.V., B.J.A.R. and C.R. Investigation: All authors. Visualization: F.W.N.M.W. and C.R. Funding acquisition: B.J.A.R. and C.R. Project administration: C.R. Supervision: F.W.N.M.W. and C.R. Writing—original draft: C.R. Writing—review and editing: All authors. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki. People entering HIV care receive written material about participation in the ATHENA cohort, after which they are asked to consent verbally to the use of their routinely collected medical data for research and monitoring (i.e., an “opt-in” procedure). Participants can withdraw their consent at any time. Data collection was approved by boards of all participating centres. Routinely collected data were used for this analysis and therefore no additional review or consent was required. This study was approved by the Dutch Ministry of Health, Welfare and Sports (approval number GZB/GZ-2232379, 19 November 2001).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data are available upon reasonable request to the corresponding author.

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References

1. Gibas, K.M.; Kelly, S.G.; Arribas, J.R.; Cahn, P.; Orkin, C.; Daar, E.S.; Sax, P.E.; Taiwo, B.O. Two-drug regimens for HIV treatment. *Lancet HIV* **2022**, *9*, e868–e883.
2. van Wyk, J.; Ajana, F.; Bisshop, F.; De Wit, S.; Osiyemi, O.; Portilla Sogorb, J.; Routy, J.P.; Wyen, C.; Ait-Khaled, M.; Nascimento, M.C.; et al. Efficacy and safety of switching to dolutegravir/lamivudine fixed-dose 2-drug regimen vs continuing a tenofovir alafenamide-based 3-or 4-drug regimen for maintenance of virologic suppression in adults living with human immunodeficiency virus type 1: Phase 3, randomized, noninferiority TANGO Study. *Clin. Infect. Dis.* **2020**, *71*, 1920–1929.
3. Llibre, J.M.; Brites, C.; Cheng, C.Y.; Osiyemi, O.; Galera, C.; Hocqueloux, L.; Maggiolo, F.; Degen, O.; Taylor, S.; Blair, E.; et al. Efficacy and Safety of Switching to the 2-Drug Regimen Dolutegravir/Lamivudine Versus Continuing a 3- or 4-Drug Regimen for Maintaining Virologic Suppression in Adults Living With Human Immunodeficiency Virus 1 (HIV-1): Week 48 Results From the Phase 3, Noninferiority SALSA Randomized Trial. *Clin. Infect. Dis.* **2023**, *76*, 720–729.
4. Vasylyev, M.; Wit, F.W.N.M.; Jordans, C.C.E.; Soetekouw, R.; van Lelyveld, S.F.L.; Kootstra, G.J.; Delsing, C.E.; Ammerlaan, H.S.M.; van Kasteren, M.E.E.; Brouwer, A.E.; et al. Dolutegravir/lamivudine is noninferior to continuing dolutegravir- and non-dolutegravir-based triple-drug antiretroviral therapy in virologically suppressed people with human immunodeficiency virus: DUALING prospective nationwide matched cohort study. *Open Forum Infect. Dis.* **2024**, *11*, ofae160.

5. Baldin, G.; Salvo, P.F.; Passerotto, R.A.; Iannone, V.; Lamanna, F.; Carbone, A.; Farinacci, D.; Lombardi, F.; Borghetti, A.; Di Giambenedetto, S.; et al. "With age comes wisdom": Effectiveness and tolerability of dolutegravir + lamivudine in virologically-suppressed people with HIV. *AIDS* **2025**, *39*, 1014–1017.
6. Suárez-García, I.; Alejos, B.; Moreno, C.; de Miguel, R.; Aldámiz-Echevarría, T.; García-Fraile, L.J.; Tacias Pitarch, M.; Pérez Martínez, D.; Antela, A.; Moreno, S.; et al. Effectiveness and tolerability of dolutegravir/lamivudine in virologically suppressed people with HIV at 96 weeks in a multicentre cohort. *HIV Med.* **2026**, *27*, 546–559.
7. Olayemi, O.; De Wit, S.; Ajana, F.; Bisshop, F.; Portilla, J.; Routy, J.P.; Wyen, C.; Ait-Khaled, M.; Leone, P.; Pappa, K.A.; et al. Efficacy and safety of switching to dolutegravir/lamivudine versus continuing a tenofovir alafenamide-based 3- or 4-drug regimen for maintenance of virologic suppression in adults living with human immunodeficiency virus type 1: Results through week 144 from the phase 3, noninferiority TANGO randomized trial. *Clin Infect. Dis.* **2022**, *75*, 975–986.
8. De Scheerder, M.A.; Degroote, S.; Delporte, M.; Kiselina, M.; Trypsteen, W.; Vincke, L.; De Smet, E.; Van Den Eeckhout, B.; Schrooyen, L.; Verschoore, M.; et al. In-depth analysis of the HIV reservoir confirms the safety of dolutegravir/lamivudine in a phase 4 randomized controlled switch trial (RUMBA). *J. Infect. Dis.* **2024**, *231*, e91–e100.
9. Ryan, P.; Blanco, J.L.; Masia, M.; Garcia-Fraile, L.; Crusells, M.J.; Domingo, P.; Curran, A.; Guerri-Fernandez, R.; Bernal, E.; Bravo, J.; et al. Maintenance therapy with dolutegravir and lamivudine versus bicitgravir, emtricitabine, and tenofovir alafenamide in people with HIV (PASO-DOBLE): 48-week results from a randomized, multicentre, open-label, non-inferiority trial. *Lancet HIV* **2025**, *12*, e473–e484.

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