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Original Article

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Effectiveness and Tolerability of Dual Therapy with Dolutegravir Plus Darunavir/cobicistat in Treatment-Experienced Patients with HIV: A 144-Week Follow-Up

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ABSTRACT

Background: A dual regimen with dolutegravir plus cobicistat-boosted darunavir (DTG+DRV/c) is a promising alternative for patients with human immunodeficiency virus (HIV) with resistance or intolerance to nucleoside reverse transcriptase inhibitors, especially those with a history of treatment failure.

Materials and Methods: We included all treatment-experienced patients with HIV who switched to the DTG+DRV/c regimen at a tertiary university hospital. We assessed the regimen's effectiveness, safety, and tolerability through serial laboratory data and clinical findings. The primary endpoint was the proportion of patients with plasma HIV-RNA levels <50 copies/mL at week 144 post-switch. The secondary endpoints were safety and tolerability assessments.

Results: Our retrospective analysis involved 40 patients. The leading reasons for switching to DTG+DRV/c were treatment failure in 17 patients (42.5%), simplification after multiple previous regimens in 15 (37.5%), and adverse drug reactions in 8 (20.0%). Among the 17 patients in the treatment failure group, we observed enhanced viral suppression and improved CD4+ T-cell counts after initiating the dual regimen. In the non-treatment failure group (23 patients), viral suppression and CD4+ T-cell levels were consistently maintained. No significant alterations in renal function, liver function, glucose levels, or lipid profiles were observed post-switch. High tolerability was observed, with 34/40 patients (85.0%) responding well to the regimen. However, six patients discontinued treatment before reaching the 144-week mark.

Conclusion: Our findings confirm that DTG+DRV/c is an effective and well-tolerated switch therapy regimen for treatment-experienced patients with HIV, with sustained benefits observed for up to 144 weeks of follow-up. This regimen showed adaptability across different patient groups and demonstrated virological and immunological improvements, particularly in patients with a history of treatment failure.

Keywords: Human immunodeficiency virus; Treatment-experienced patients; Dolutegravir; Cobicistat-boosted darunavir; Antiretroviral therapy

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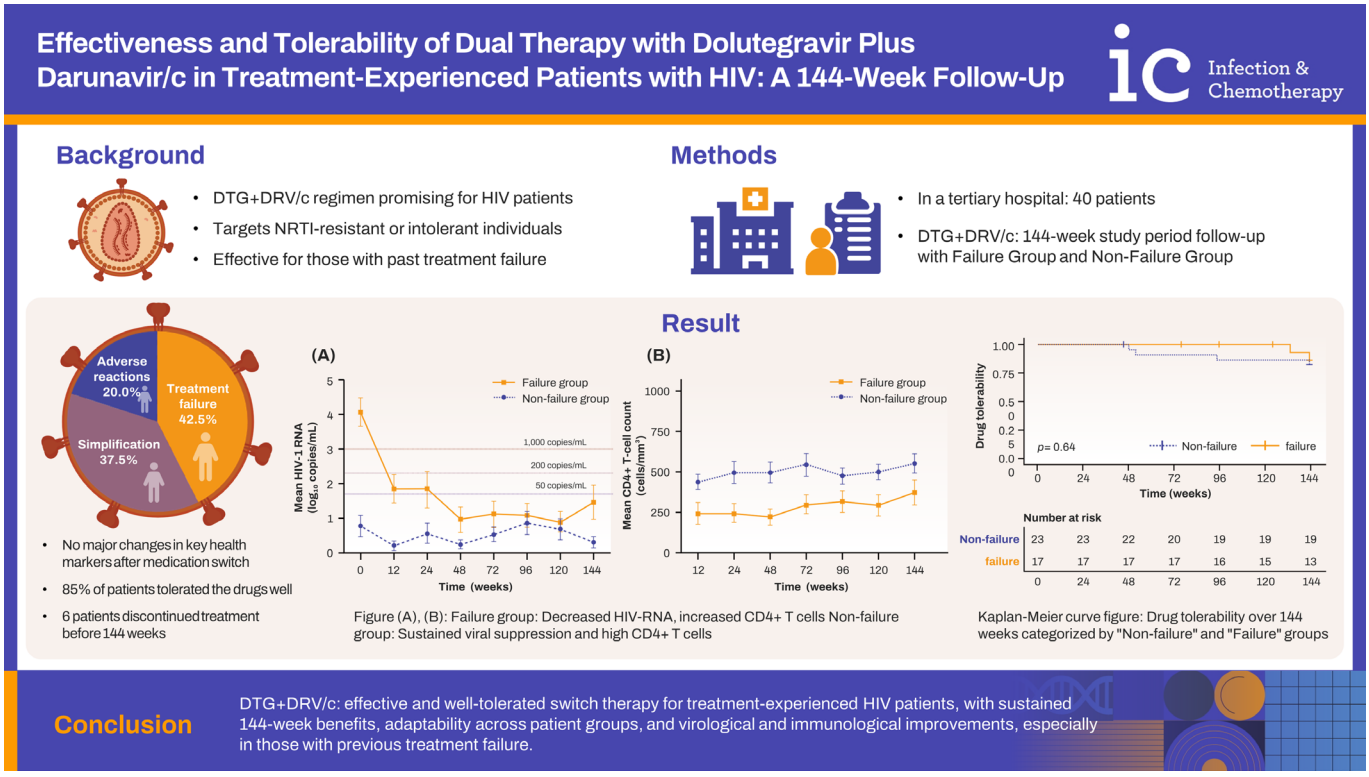
GRAPHICAL ABSTRACT



INTRODUCTION

The evolution of antiretroviral therapy (ART) has been pivotal in managing human immunodeficiency virus (HIV) infections [1]. The advent of integrase inhibitors marked a significant advancement, initiated in the early 2000s, and a pivotal moment occurred in 2007 when the Food and Drug Administration approved raltegravir, an inaugural integrase strand transfer inhibitor (INSTI), for HIV treatment. Subsequently, in 2012, the authorization of a once-daily regimen incorporating elvitegravir was achieved, and the introduction of bictegravir and dolutegravir (DTG)-based regimens emerged in the mid-2010s. These developments have positioned integrase inhibitors as essential components of modern HIV therapies, distinguished by their high efficacy and simplified administration [1].

Although recent advancements have significantly improved HIV treatment, this study extends beyond merely addressing the emergence of drug-resistant HIV strains in the community [2]. The selection of therapeutic agents for salvage therapy in the context of resistance poses a significant challenge because of the limited availability of suitable drugs, considerable pill burden, and scarcity of robust medical evidence and experience [2]. This study aimed to address these critical gaps by evaluating the efficacy and feasibility of alternative treatment options for managing drug-resistant HIV cases.

Drug-resistant HIV strains can emerge through various mechanisms, often involving mutations in the viral genome that confer resistance to antiretroviral drugs. These mutations can occur naturally due to error-prone replication of the HIV reverse transcriptase enzyme or may be induced by the selective pressure of ART [3, 4]. Such strains pose a severe threat to the therapeutic landscape, as they can substantially narrow treatment options and worsen patient outcomes [3].

To address these challenges, various combinations of medications exist; however, many involve a high quantity of drugs and frequent daily dosages. However, the combination of DTG and cobicistat-boosted darunavir (DRV/c) requires only two pills daily, overcoming resistance with a relatively lower pill burden. Importantly, DTG's inclusion, known for its high resistance barrier, further enhances this regimen's appeal by offering robust protection against the development of drug resistance,

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making it an optimal choice for those seeking effective and manageable HIV treatment solutions.

Preliminary research and clinical trials have underscored the efficacy and safety of the DTG+DRV/c combination. This regimen is a significant milestone, particularly benefiting patients with complications associated with nucleoside reverse transcriptase inhibitors (NRTI) resistance or drug-resistant HIV strains [4-6].

Various studies have demonstrated the efficacy of dual therapies, such as DTG+DRV/c, in specific patient populations [6-11]. Notably, research focusing on patients with a history of treatment has indicated that these therapies are effective in managing virological failure caused by drug resistance. This effectiveness extends to patients who have previously encountered challenges with ART, highlighting the potential of DTG+DRV/c as a switch therapy option for individuals with a history of treatment failure [6-11]. However, these studies reported results at 48 weeks, and none reported long-term results, such as those at over 144 weeks.

Building on our previous work, which demonstrated the DTG+DRV/c regimen's efficacy and tolerability over 48 weeks in a 31-patient cohort [12], this study aimed to extend these findings to a 144-week observation period. We investigated the clinical applicability of the DTG+DRV/c regimen, focusing on its long-term efficacy, safety, and tolerability, particularly in treatment-experienced patients with drug-resistant HIV strains. This extended focus significantly contributes to the existing body of research, aiming to fill the gaps in our current understanding and provide actionable insights for clinicians.

MATERIALS AND METHODS

1. Patient characteristics

The study cohort comprised treatment-experienced patients with HIV-1 transitioned to combination therapy of DTG+DRV/c (DTG 50 mg, DRV 800 mg, and cobicistat 150 mg, co-formulated once or twice daily). These patients were selected from those treated at Kyungpook National University Hospital, a tertiary hospital in Daegu, Korea, between January 2016 and January 2023. For inclusion, patients must have undergone more than two drug regimen changes. Patients who switched regimens at other healthcare facilities or were not present during the study period were excluded. Patients were categorized into two groups based on the reasons for switching regimens: the treatment failure and non-failure groups. In this study, virologic failure was defined as failure to achieve or maintain a plasma viral load below 200 copies/mL after 6 months of therapy [1]. Laboratory outcomes were verified through repeated testing before determining virologic failure [1]. This clarifies the difference between transient viremic 'blips' and sustained inability to suppress the virus, ensuring the treatment failure criteria are predicated not merely on a solitary event but on a consistent pattern of inadequate viral suppression [13].

Baseline characteristics included the duration of HIV-1 infection, age, sex, and presence of other infectious diseases or underlying conditions such as diabetes and cardiovascular diseases.

2. Ethics statement

This study adhered to the principles of the Declaration of Helsinki and was approved by the Institutional Review Board of Kyungpook National University Medical Center (IRB File No. 2018-02-027). Patient consent was obtained after a detailed explanation of the study's aims, and all personal information was anonymized to ensure data privacy.

3. Laboratory Data

Hepatitis B virus, hepatitis C virus, and tuberculosis were also accounted for. The effectiveness of the DTG+DRV/c combination was measured using HIV RNA and CD4+ T cell counts collected before and after the regimen change. HIV-RNA levels were converted to $\log_{10}$ copies/mL for ease of comparison.

4. Efficacy in treatment failure and treatment non-failure groups

In the group classified as experiencing treatment failure, the study meticulously compared longitudinal changes in two key parameters: HIV-RNA viral load and CD4+ T cell count. Data were collected at multiple time points, including baseline, 12 weeks, 24 weeks, and up to 144 weeks post-regimen switch. This study aimed to determine the effectiveness of the DTG+DRV/c combination in suppressing HIV-RNA levels and facilitating immune restoration. Conversely, in the non-failure group, the focus of the investigation was twofold. First, researchers sought to determine whether the DTG+DRV/c regimen effectively suppressed HIV-RNA levels below the critical threshold of 50 copies/mL. Second, the study aimed to verify whether CD4+ T cell counts remained within the normal range, indicating immunological stability. Similar to the failure

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group, these assessments were performed at multiple time points to capture trends or fluctuations. The primary endpoints for assessing this combination therapy's effectiveness were centered on attaining HIV-RNA levels <50 copies/mL after the 144-week post-switch period.

5. Safety and tolerability assessment

In terms of safety and tolerability, several avenues were explored. Patient complaints were rigorously documented, and physician-recorded adverse effects were collected during scheduled follow-up visits. The adverse effects under examination ranged from common complaints, such as nausea and fatigue, to more severe clinical manifestations. Laboratory data play a pivotal role in safety assessments. Renal function was evaluated using the estimated glomerular filtration rate (eGFR), liver function was assessed using aspartate aminotransferase (AST) and alanine aminotransferase levels, and metabolic status was evaluated using glucose, low-density lipoprotein, high-density lipoprotein (HDL), and triglyceride (TG) levels. These results were compared at different intervals to evaluate any potential adverse effects of the medication on critical physiological functions.

6. Medication adherence and discontinuation

Another aspect of this study was the assessment of patient adherence to the DTG+DRV/c regimen. Medication dispensing records and patient interviews were used to determine the extent of medication adherence or discontinuation. The reasons for discontinuation were documented, categorized, and analyzed to understand better the barriers to the effective use of this regimen. Throughout the study, the observation span for both efficacy and safety evaluations was uniform, ensuring a consistent data collection and interpretation approach.

7. Statistical analysis

A paired *t*-test was used to compare pre- and post-regimen variables, specifically focusing on HIV RNA and CD4+ T cell counts. Kaplan–Meier estimators were used to analyze drug tolerability over time. All statistical computations were performed using R statistics, version 4.3.1, with the significance threshold set at a *P*-value=0.05.

RESULTS

1. Baseline characteristics and outcomes

The study involved 40 participants, categorized into two groups: the 'failure group' of 17 individuals who had not responded to prior treatments and the 'non-failure group' of 23 individuals, as further detailed in **Table 1**. Both groups were primarily male, with proportions of 94.1% and 87.0% in the failure and nonfailure groups, respectively. Statistical analysis confirmed no significant sex differences between the groups (*P*=0.831). The average age was slightly higher in the non-failure group than in the failure group (54.0 *vs.* 49.8 years); however, the difference was not statistically significant (*P*=0.194). Both groups were monitored for up to 144 weeks and showed similar durations of HIV infection, which was statistically validated (*P*=0.709). The prevalence rates of Hepatitis B and C were comparable between the groups. A key difference emerged in the reasons for changing treatment regimens: the failure group switched solely because of prior treatment failure, whereas the non-failure group switched for multiple reasons, including adverse drug reactions and regimen simplification, with a statistically significant difference (*P* <0.001).

The ART regimens used before switching to DTG+DRV/c in the failure group are summarized in **Table 2**.

2. Comparative biochemical parameters

Table 3 presents an in-depth comparison of the key biochemical parameters between the failure and non-failure groups. Both groups exhibited similar initial eGFR, as confirmed by the non-significant *P*-value of 0.987. Notably, the failure group had higher initial levels of AST, a difference that reached statistical significance (*P*=0.044). Similarly, the failure group's initial glucose levels were significantly lower than those in the non-failure group, supported by a *P*-value of 0.023. This gap in glucose levels was sustained in the final measurements, as evidenced by a *P*-value of 0.005. In contrast, initial HDL levels were higher in the non-failure group, with a statistically significant *P*-value of 0.041, though this significance dissipated by the end of the study period. Finally, TG levels showed no meaningful variation between the groups at either the study's inception or conclusion.

3. Virological outcomes and immunological outcomes of DTG+DRV/c regimens assessed by temporal trends in HIV-RNA and CD4+ T cell counts

Figure 1 presents a two-part examination of longitudinal changes in key markers of HIV infection: Part A focuses on HIV-RNA levels, and Part B delves into CD4+ T cell counts. In Part A, the failure group initially registered high HIV RNA levels of approximately 5 $\log_{10}$ copies/ml.

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Table 1. Comparative characteristics and outcomes between treatment failure and treatment non-failure groups in HIV-infected individuals

Variables	Failure group (N=17)	Non-failure group (N=23)	Total (N=40)	*P*
Sex				0.831
- Male	16 (94.1)	20 (87.0)	36 (90.0)	
- Female	1 (5.9)	3 (13.0)	4 (10.0)	
Age	49.8±7.8	54.0±11.4	52.2±10.1	0.194
Duration of HIV infection up to 144 weeks (years)	14.9±6.2	15.6±6.4	15.3±6.2	0.709
Hepatitis B				>0.999
- Negative	16 (94.1)	21 (91.3)	37 (92.5)	
- Positive	1 (5.9)	2 (8.7)	3 (7.5)	
Hepatitis C				>0.999
- Negative	16 (94.1)	22 (95.7)	38 (95.0)	
- Positive	1 (5.9)	1 (4.3)	2 (5.0)	
Tuberculosis treatment after HIV diagnosis				0.934
- Negative	10 (58.8)	15 (65.2)	25 (62.5)	
- Positive	7 (41.2)	8 (34.8)	15 (37.5)	
Reasons for changing regimens				<0.001
- Adverse drug reaction	0	8 (34.8)	8 (20.0)	
- Simplification	0	15 (65.2)	15 (37.5)	
- Treatment failure	17 (100)	0	17 (42.5)	
HIV-RNA (Log) week 0	4.4 [3.9;4.8]	0.0 [0.0;1.3]	1.5 [0.0;4.4]	<0.001
HIV-RNA (Log) week 12	1.5 [0.7;2.2]	0.0 [0.0;0.0]	0.0 [0.0;1.5]	<0.001
HIV-RNA (Log) week 24	1.4 [0.0;2.9]	0.0 [0.0;0.0]	0.0 [0.0;1.8]	0.038
HIV-RNA (Log) week 48	0.0 [0.0;1.6]	0.0 [0.0;0.0]	0.0 [0.0;1.3]	0.096
HIV-RNA (Log) week 72	0.0 [0.0;1.6]	0.0 [0.0;1.4]	0.0 [0.0;1.5]	0.332
HIV-RNA (Log) week 96	0.8 [0.0;1.8]	0.0 [0.0;1.5]	0.0 [0.0;1.8]	0.405
HIV-RNA (Log) week 120	0.0 [0.0;1.9]	0.0 [0.0;0.7]	0.0 [0.0;1.5]	0.373
HIV-RNA (Log) week 144	1.4 [0.0;2.0]	0.0 [0.0;0.0]	0.0 [0.0;1.6]	0.025
CD4+ cells (cells/mm^3), week 0	119.0 [38.9;385.8]	417.0 [251.1;607.0]	332.0 [128.6;520.8]	0.006
CD4+ cells (cells/mm^3), week 12	168.9 [81.0;355.9]	425.2 [339.4;485.9]	352.5 [186.0;452.8]	0.003
CD4+ cells (cells/mm^3), week 24	164.4 [73.4;278.6]	421.1 [311.8;666.4]	311.8 [164.4;501.0]	0.001
CD4+ cells (cells/mm^3), week 48	233.8 [134.6;377.3]	420.6 [321.2;559.7]	347.1 [258.8;507.6]	0.010
CD4+ cells (cells/mm^3), week 72	247.0 [151.4;358.0]	417.7 [331.5;674.4]	355.2 [238.6;616.0]	0.005
CD4+ cells (cells/mm^3), week 96	219.0 [183.1;338.5]	444.7 [380.8;578.9]	379.6 [219.0;484.2]	0.005
CD4+ cells (cells/mm^3), week 120	253.5 [189.4;472.2]	457.3 [354.3;561.0]	398.5 [288.1;527.8]	0.021
CD4+ cells (cells/mm^3), week 144	241.2 [159.6;333.5]	444.9 [391.6;726.1]	403.1 [265.8;578.8]	0.002

(), percentage; [ ], interquartile range.
HIV, human immunodeficiency virus; HIV-RNA: HIV ribonucleic acid.

Table 2. Antiretroviral regimens before switching to DTG+DRV/c in the treatment failure group

Antiretroviral regimens	No. of patients
Dolutegravir, abacavir, and lamivudine	4
Raltegravir, abacavir, and lamivudine	2
Raltegravir, etravirine, darunavir, and ritonavir	2
Atazanavir, abacavir, and lamivudine	1
Bictegravir, emtricitabine, and tenofovir alafenamide	1
Darunavir, didanosine, and abacavir	1
Darunavir, ritonavir, didanosine, and abacavir	1
Elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide	1
Elvitegravir, cobicistat, emtricitabine, and tenofovir disoproxil fumarate	1
Lopinavir and ritonavir, abacavir and lamivudine	1
Raltegravir, emtricitabine and tenofovir disoproxil fumarate	1
Rilpivirine, emtricitabine and tenofovir disoproxil fumarate	1

DTG, dolutegravir; DRV/c, cobicistat-boosted darunavir.

This dramatically decreased to <1 $\log_{10}$ copies/mL within the first 12 weeks and remained substantially suppressed throughout the 144-week study period. Conversely, the non-failure group persistently exhibited low HIV RNA levels of approximately 1 $\log_{10}$ copies/mL, demonstrating sustained viral suppression. Remarkably, both groups

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Table 3. Comparative biochemical parameters between the treatment failure and non-failure groups

Variables	Failure group (N=17)	Non-failure group (N=23)	Total (N=40)	*P*
Initial eGFR	100.2±24.4	100.4±31.5	100.3±28.3	0.987
Last eGFR	88.3±24.7	80.2±17.0	83.6±20.6	0.288
Initial AST	29.6±11.6	22.1±10.6	25.4±11.5	0.044
Last AST	27.3±11.1	23.7±11.3	25.2±11.2	0.379
Initial ALT	32.2±24.3	24.1±13.9	27.6±19.3	0.235
Last ALT	25.5±15.8	22.6±13.3	23.8±14.2	0.574
Initial glucose	93.9±15.4	130.4±67.9	115.6±55.8	0.023
Last glucose	99.2±11.9	120.3±25.7	111.5±23.3	0.005
Initial LDL	95.1±23.9	109.2±58.8	103.4±47.6	0.343
Last LDL	92.0±33.5	106.6±68.9	100.1±55.6	0.477
Initial HDL	40.1±10.1	51.0±16.5	46.8±15.2	0.041
Last HDL	49.9±10.9	48.3±13.7	49.0±12.4	0.728
Initial TG	185.8±67.7	261.3±275.0	230.7±217.5	0.229
Last TG	182.2±108.9	262.4±190.0	227.6±162.7	0.186

±, standard deviation.
eGFR, estimated glomerular filtration rate; AST, aspartate aminotransferase; ALT, alanine aminotransferase; LDL, low-density lipoprotein; HDL, high-density lipoprotein; TG, triglyceride.

consistently maintained viral loads below the clinical threshold of 200 copies/mL, indicating the effectiveness of the treatment regimen.

In Part B, the failure group started with CD4+ T cell counts close to 250 cells/mm^3. These counts experienced a steady uptick, ultimately approaching 500 cells/mm^3 by week 144, indicative of ongoing immune restoration. Conversely, the non-failure group's CD4+ T cell counts remained stable around the 500 cells/mm^3 benchmark, signifying a sustained level of immune system stability.

In summary, our 144-week study highlighted distinct virological and immunological trajectories in the failure and non-failure groups despite starting from similar baseline characteristics. The analysis, refined to include a paired *t*-test, revealed no statistically significant differences within each group over time. This suggests that the marked improvements observed in the failure group and the sustained levels of viral suppression and immune function in the non-failure group were within the expected variability for such treatments. Consequently, both groups demonstrated resilience in managing HIV with the treatment regimen, effectively maintaining control over the virus and supporting the health of the immune system.

4. Patient drop-out and outcomes from DTG+DRV/c regimens in long-term HIV treatment management

Six patients dropped out of this treatment method: four from the non-failure group and two from the failure group. The reasons for dropping out varied from logistical issues, such as job relocation, to severe health conditions,

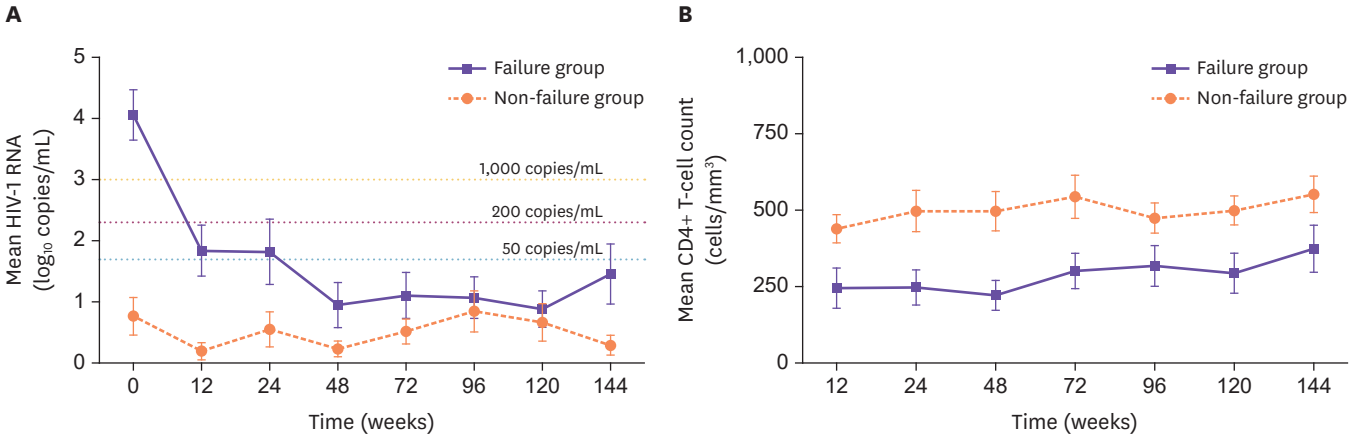

Figure 1. Mean changes in HIV-RNA titer (A) and CD4 + T cell count (B). In the failure group, suppression of the HIV-RNA titer decreased, and CD4 + T cell count increased. In the non-failure group, virus suppression and high CD4 + T cell levels are maintained.

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Table 4. Outcomes of patients with HIV who dropped out and regimen changes over 144 weeks

Group	Date of dual regimen start	Week at drop-out	Sex	Age	Changed regimen and brief course of patient	Cause of drop-out	Viral suppression after 3 months post drop-out
Non-failure group	Apr 2017	52.0	Male	59	Switched to DTG + DRV + ritonavir; expired due to cancer	L-tube feeding required due to advanced colon cancer	Yes
Non-failure group	Jun 2018	48.4	Male	73	-	No visit	Unknown
Non-failure group	Aug 2016	94.9	Male	49	-	Transferred to another region due to job issues	Unknown
Non-failure group	Feb 2017	143.6	Male	60	Bictegravir/emtricitabine/tenofovir alafenamide	Wanted to change due to weakness of lower extremities	Yes
Failure group	Aug 2017	143.6	Male	54	Switched to etravirine + raltegravir + DRV + ritonavir and Bictegravir/emtricitabine/tenofovir alafenamide after 1.5 years	Hemodialysis due to renal failure	Yes
Failure group	Jul 2020	133.4	Male	45	Switched to rilpivirine QD, lamivudine/zidovudine BID, DRV BID, then to rilpivirine + DRV QD after 2 years	Wanted simplification	Yes

DTG, dolutegravir; DRV; darunavir; QD, once daily; BID, twice daily.

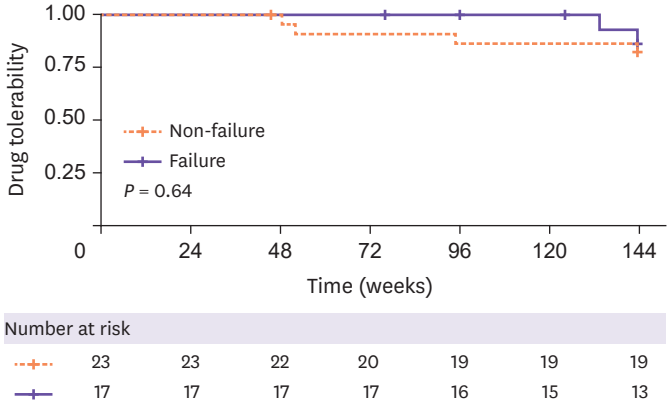

Figure 2. Kaplan–Meier curve of drug tolerability over 144 weeks categorized by "Non-failure" and "Failure" groups.

such as advanced colon cancer (**Table 4**). Most patients with HIV who changed or discontinued this regimen for various reasons maintained viral suppression after 3 months, indicating the effectiveness of the treatment program (**Fig. 2**).

DISCUSSION

This study builds on a previous research involving 31 participants that demonstrated good efficacy and safety. We further examined these patients over an extended follow-up period and included additional individuals who began taking medication after the initial study. Forty participants were enrolled for this extended duration. In this study, the DTG+DRV/c combination showed a high treatment success rate and safety over the 144-week period.

The primary endpoint of our study was the proportion of patients with plasma HIV-RNA levels of <50 copies/mL at week 144 post-switch. This metric is crucial in HIV research, as it gauges long-term virological suppression, which is essential for enhancing clinical outcomes, reducing transmission, and preventing drug resistance [14, 15]. This measure reflects the chronic nature of the HIV infection and underscores the importance of sustained and effective ART. Its standardization also facilitates comparability and contributes to the understanding of the long-term efficacy of HIV treatment [14, 15].

The inclusion of antiretroviral agents, such as DTG, which is a high-barrier-to-resistance second-generation INSTI, has been highly successful in the treatment of HIV. It demonstrates high efficacy, a favorable resistance profile, and minimal side effects. Endorsed by the World Health Organization, DTG's use in HIV care has been further validated, emphasizing its role in switch therapy approaches. Previous studies have shown that DTG-based therapies significantly reduce viral loads and improve CD4 counts, providing a solid basis for its adoption [16-18].

Although DTG in combination with lamivudine shows promise as a switch therapy for treatment-naïve patients, decision-making becomes more complex for treatment-experienced patients or those who have failed previous regimens. The combination of DTG and boosted DRV has proven effective in combating resistance in more challenging cases, as evidenced by existing studies, particularly in real-world settings [6, 10, 19-21].

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Switch therapy plays a crucial role in managing HIV by allowing changes in medication regimens to either improve therapeutic outcomes or manage side effects. Our work suggests that the DTG+DRV/c regimen is effective and well-tolerated, especially in treatment-experienced patients. This aligns with the existing studies and contributes to a growing body of evidence supporting its utility [22].

Transitioning to a combination of DTG and boosted DRV has demonstrated promising results in terms of effectiveness and tolerability, particularly in heavily treated patients with HIV. Our recent study involving 31 HIV patients undergoing switch therapy confirmed these observations [12]. Studies with a follow-up period of 48 weeks have consistently demonstrated the efficacy of this regimen. Additionally, a 68-week follow-up study suggested its potential, particularly in individuals with undetectable HIV RNA levels at baseline [6, 10, 11, 19-21]. Regarding long-term treatment, our study extended the follow-up period to 144 weeks, offering a comprehensive comparison with previous short-term studies. Our report on the 144-week effectiveness and stability is, to our knowledge, the first of its kind and represents the most significant contribution of this study. This extended duration allowed us to explore the potentially delayed adverse reactions and long-term sustainability of viral suppression. Notably, our study included both treatment failure and non-failure groups, demonstrating the efficacy, safety, and tolerability of the DTG+DRV/c combination.

At the molecular level, DTG, an integrase inhibitor, prevents the integration of viral DNA into the host genome, showing promise in overcoming drug resistance. The addition of cobicistat enhanced the effectiveness of DRV and boosted the overall potency of the regimen [23].

From an economic perspective, dual therapies, such as DTG+DRV/c, are gaining attention for their cost-effectiveness, an increasingly vital consideration for healthcare policymakers. Phase I pharmacokinetic studies further supported the potential of this combination as an NRTI-sparing and/or salvage strategy, opening pathways for future exploration, especially in treatment-experienced HIV patients [24].

When examining the six individuals who dropped out of this treatment, it was apparent that the patients' age and serious health conditions may have significantly impacted the continuation of the treatment plan. Personal circumstances such as job changes should also be considered in long-term treatment strategies. Additionally, the lack of visits or the unclear status of some patients poses a challenge for the long-term follow-up and management of patients with HIV, which is crucial to ensure continued treatment success. Future studies should focus on observing the success of simplification in patients who are stable with this regimen. These results indicated that virological suppression can be sustained in patients who discontinue this regimen for various reasons. However, this aspect of the research remains unanswered.

This study was an independent research project not sponsored or influenced by any pharmaceutical company. Although our study contributes significantly to the existing literature, we acknowledge its limitations. These included a relatively small patient cohort, the inclusion of patients from a previous study for long-term follow-up, and the retrospective nature of our study. Each of these points emphasizes the necessity for further investigation with larger and more diverse patient cohorts, as well as prospective study designs, to validate our findings more robustly.

In conclusion, our study indicates that the DTG+DRV/c regimen offers a simplified yet effective treatment option for managing HIV infections, particularly in treatment-experienced patients. However, given the limitations of our study, further research involving larger and more diverse patient cohorts is essential to substantiate these findings and ensure their applicability in real-world settings.

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Conceptualization: SWK. Formal analysis and data curation: SWK. Validation: HWJ, SWK. Investigation: SWK, HWJ, HHJ. Supervision: SWK. Writing - Original Draft: HWJ, YJK, SHB, SWK. Writing - Review & Editing: HWJ, YJK, SHB, HHJ, SWK.

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