SYMTUZA® (darunavir, cobicistat, emtricitabine, and tenofovir alafenamide)
Use of SYMTUZA in Combination with Dolutegravir

SUMMARY

- There is no data specifically evaluating the use of SYMTUZA in combination with dolutegravir (DTG). Related data evaluating the use of darunavir (DRV) boosted with cobicistat (COBI) in combination with DTG are summarized below.
- In a randomized, noninferiority, multicenter study of human immunodeficiency virus (HIV)-infected adult patients who were switched to DTG (50 mg once per day) + DRV boosted with COBI (800/150 mg once per day), no significant differences was observed in the proportion of patients maintaining virologic suppression between the 2D and standard-of-care (SOC) study groups.[1]
- In an observational cohort study of HIV-infected patients with a history of virologic failure (VF) who were switched to a dual regimen with DRV/r (ritonavir) or DRV/COBI + DTG, the proportion of patients with viral load (VL) <50 copies/mL was 90% (95% confidence interval [CI], 82-99%) at week 48 (intention-to-treat [ITT] analysis, missing=failure [M=F]).[2]
- In a prospective study of HIV-infected patients who switched to a dual regimen with DRV/COBI + DTG, all 53 patients remained suppressed at week 24.[3]
- In a retrospective cohort study of highly treatment-experienced patients with HIV infection receiving the DTG + DRV-COBI regimen, 2.5% of patients experienced VF and 14.8% of patients experienced treatment discontinuation over time.[4]
- In a retrospective cohort study of highly treatment-experienced patients, bDRV and DTG dual therapy demonstrated sustained rates of viral suppression, including in those individuals who were failing therapy prior to initiating the regimen.[5]
- In a retrospective cohort study of heavily-treated, HIV-infected patients who were currently suppressed, switching to once-daily (QD) bDRV + DTG therapy was shown to be effective and well tolerated.[6]
- In a retrospective study of heavily-treated patients with HIV who were currently suppressed, switching to DRV/COBI + DTG QD maintained viral suppression without significant adverse events (AEs).[7]
- In a retrospective cohort study, patients maintained virologic suppression at 48 weeks after switching to DRV/COBI + DTG from their current antiretroviral therapy (ART).[8]

CLINICAL STUDIES WITH DRV + COBI

Prospective Studies

Santos et al (2023)[1] conducted an open-label, randomized, noninferiority, multicenter clinical trial to compare the efficacy and safety of DTG + DRV/COBI as a once-daily maintenance strategy with the continuation of previous ART in highly treatment-experienced patients with HIV-1 resistant to drugs (excluding integrase strand transfer inhibitors [INSTIs] and DRV).

Study Design/Methods

- The study was conducted between December 2018 and January 2021 across 12 HIV care centers in Spain and included 96 HIV-infected adult patients.
- **Eligibility criteria:**
  - Patients treated with at least 3 antiretroviral (ARV) drugs (protease inhibitors [PIs], nonnucleoside reverse transcriptase inhibitors (NNRTIs), nucleoside reverse transcriptase inhibitors (NRTIs), integrase inhibitors (INIs), or CCR5 receptor antagonists)
  - Patients with suppressed HIV-1 RNA levels (<50 copies/mL) for at least 6 months prior to the study

    - Patients with genotypic evidence of drug resistance mutations (DRMs) against ≥2 ARV classes
- Patients with a history of poor adherence or VF while receiving INIs, those receiving concomitant therapies with potential drug interactions with DRV/COBI or DTG, those tested positive for hepatitis B surface antigen, those having unstable liver disease or severe hepatic impairment (Child-Pugh class C), and those requiring therapy for hepatitis C coinfection during the study were excluded.
- Patients were randomized 1:1 to receive the following:
    - 2D group (n=45): dual therapy based on DTG (50 mg) + DRV/COBI (800/150 mg) once daily
    - SOC group (n=44): continuation of current ART
- **Primary endpoint:** percentage of patients with HIV-1 RNA <50 copies/mL at week 48 (time to loss of virologic response [TLOVR] analysis).
- **Secondary endpoints**: proportion of patients with HIV-1 RNA <50 copies/mL at week 48 (Food and Drug Administration [FDA] snapshot algorithm); proportion of patients with ART-related AEs leading to treatment discontinuation; changes in cluster of differentiation 4-positive ($CD4^+$) cell counts and biochemical parameters during follow-up; and emergence of new drug resistance mutations in the protease and integrase genes of HIV-1 in patients with VF.

Results

- A total of 89 patients (76.4% males; median age [interquartile range; IQR], 55 [50-60] years) were included in the analysis.
    - Of these, 45 and 44 patients were included in the 2D and SOC groups, respectively.
    - Median time since HIV diagnosis was 25 (23-29) years in the 2D group and 25 (23-28) years in the SOC group.
    - The median time of virological suppression was 5 (2-9) years in the 2D group and 4 (1-9) years in the SOC group. The median (IQR) CD4+ cell count was 623 (493-901) cells/mm^3 in the 2D group and 607 (429-961) cells/mm^3 in the SOC group.
    - The median (IQR) previous exposure to ARV drugs at baseline was 14 (10-17) in the 2D group and 13 (10-17) in the SOC group.
- Before randomization, 61 patients (68%) had received boosted DRV, 59 patients (66%) were on INSTIs, and 33 patients (37.1%) were following twice-daily regimens.
- No VF was observed in the 2D group; however, 2 patients (4.5%) experienced VF in the SOC group at weeks 12 and 24.
- TLOVR analysis showed no differences in the proportion of patients maintaining HIV-1 RNA <50 copies/mL at week 48 between the 2D and SOC groups (95.5% vs 86.7%; log rank *P*=0.159).
- The estimated difference in the proportion of VF rate between the 2D and SOC groups was -8.7 (95% CI, -22.72 to 5.14).
- AEs were reported in 45 patients (91.1%) from the 2D group and 32 patients (72.7%) from the SOC group.
- A total of 111 and 81 AEs were recorded in the 2D and SOC groups, respectively (*P*=0.002).
- No serious AEs acquired immune deficiency syndrome (AIDS)-defining events, or deaths occurred during the study.
- AEs related to DTG + DRV/COBI occurred in 13 patients in the 2D group, and three of these patients developed AEs leading to treatment discontinuation.
- Ten patients from the 2D group experienced 9 drug-related AEs, and non-drug-related grade 1, 2, and 3 AEs were similar in both the groups (*P*>0.05).

Vizcarra et al (2019)[2] evaluated the efficacy and safety of a regimen consisting of DTG and DRV/r or DRV/COBI in patients with prior VF in an observational, single-center cohort study.

Study Design/Methods

- This was a phase 4, prospective, single-arm, open-label cohort study conducted at the HIV unit of a tertiary university hospital in Spain from January 2015 through December 2017.
- Patients with previous VF to different classes of ARV drugs but virologically suppressed in a salvage regimen for ≥24 weeks were included in the study if they switched to QD regimens of DTG 50 mg + DRV/r 800/100 mg or DRV/COBI 800/150 mg.
- Patients were excluded if they were pregnant, had hepatitis B virus, or previously failed integrase inhibitors.
- **Primary endpoint:** proportion of patients with VL <37 copies/mL at week 48.
- Treatment failure was defined as VF (2 consecutive detectable VL), discontinuation, or reintroduction of triple therapy.
- **Secondary endpoints**: changes in laboratory parameters.

Results

- A total of 51 patients switched to bDRV + DTG (n=29 DRV/COBI, n=22 DRV/r).
- Patients were followed for a median of 29.4 (IQR, 20.6-35.1) months.
- Baseline characteristics are noted in Table: Baseline Characteristics.
- Baseline VL was undetectable in 43 patients (83%). In 8 patients, VL was detectable due to nonadherence or recent discontinuation of the previously suppressive ARV regimen.
- At baseline, patients had received a median of 8 (IQR, 4-12) regimens over 18.4 (IQR, 13.9-21.16) years before switching and all patients had previously failed ≥2 ARV classes.
- Median time of virologic suppression with the previous regimen was 37 (IQR, 18-90) months. The reasons for switching were simplification, toxicity to NRTIs (renal/bone toxicity), and metabolic abnormalities (dyslipidemia).
- Genotypic resistance testing in 42 patients (82%) at baseline showed a mean number of primary mutations of 1.2 for NNRTIs (mostly in positions Y181 and K103), 2.4 for NRTIs (mainly in positions T215, M184, and M41), and 3.5 for PIs (mainly in positions I54 and V82).
- Five patients had reduced sensitivity to DRV.

Baseline Characteristics[2]

	DTG Plus bDRV (N=51)
Mean age, years (range)	51.6 (33-66)
Male sex, n (%)	36 (71)
Risk factors for HIV infection, n (%)	
Intravenous drug use	31 (61)
Men who have sex with men	9 (18)
Heterosexual sex	11 (22)
Median duration of HIV infection, years (IQR)	23.36 (19.2-27.0)
Previous AIDS diagnosis, n (%)	31 (61)
HCV coinfection, n (%)	31 (61)
Fibrosis 4/cirrhosis, n (%)	5 (10)
Median CD4+ cell count at inclusion, cells/mm^3 (IQR)	551 (243-680)
Time on previous regimen, years (IQR)	3.08 (1.5-7.5)
Drugs in previous regimen, n (%)	
DRV/r	30 (59)
BID (600 mg/100 mg BID)	16 (31)
DRV/COBI coformulation	1 (2)
DTG	6 (12)
RAL	18 (35)
4-drugs	24 (47)
TDF	24 (47)
ETR	5 (10)

	DTG Plus bDRV (N=51)
Genotypic resistance test, n (%)	42 (82)
Resistance to 1 ARV class, n (%)	2 (4)
Resistance to 2 ARV classes, n (%)	11 (22)
Resistance to 3 ARV classes, n (%)	17 (33)
No resistance mutations, n (%)	12 (24)

Abbreviations: AIDS, acquired immune deficiency syndrome; ARV, antiretroviral; bDRV, boosted darunavir; BID, twice daily; CD4, cluster of differentiation 4; DRV, darunavir; DRV/COBI, darunavir/cobicistat; DRV/r, darunavir/ritonavir; DTG, dolutegravir; ETR, etravirine; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IQR, interquartile range; RAL, raltegravir; TDF, tenofovir disoproxil fumarate.

- At week 48, there were no VFs, 2 patients were lost to follow-up, and 3 patients discontinued the regimen due to central nervous system (CNS) AEs (insomnia, headache, and severe anxiety).
    - These patients were receiving DRV/COBI and were hepatitis C virus-coinfected, 2 of whom had fibrosis 4/cirrhosis.
- Efficacy was 90% (95% CI, 82-99%) in the ITT analysis (including all patients enrolled, M=F) and 94% (95% CI, 87-100%) in the per-protocol analysis (including only those patients who had VF or discontinuation due to AEs, M=F).
- Median CD4+ cell count increased to 650 cells/mm^3 (P=0.04).
- The proportion of patients with CD4+ cell counts <200 cells/mm^3 decreased by 16% at week 48 (P<0.01).
- Mean estimated glomerular filtration rate (eGFR) decreased by 8.8 mL/min/1.73 m^2 (P<0.01).
    - The decline in eGFR was lower in patients receiving DRV/COBI + DTG compared to DRV/r + DTG (-7.6 vs -11.9 mL/min/1.73 m^2).
- Mean proteinuria and mean tubular reabsorption of phosphate improved to 87.2 mg/dL and 80.1%, respectively.
- There were nonsignificant increases in mean total cholesterol (1.9%), low-density lipoprotein (LDL) cholesterol (1.4%), and high-density lipoprotein (HDL) cholesterol (4.3%), with a reduction in mean triglyceride levels (-10.3%).

Casado et al (2017)[3] evaluated the safety and efficacy of switching to DRV/COBI + DTG as a simplification strategy in patients who had been virologically suppressed on a multidrug salvage regimen (DOLBI Study).

Study Design/Methods

- Patients were eligible for inclusion if they met the following criteria: previous history of VF, ≥3 PI and NRTI mutations at the time of initiation of the salvage regimen, no resistance to DRV or DTG, and VL <50 copies/mL for >48 weeks.
- **Primary endpoint:** percentage of patients that maintained VL <50 copies/mL at 24 weeks.

Results

- A total of 53 patients were enrolled; mean age was 49.3 years, 72% of patients were male, 72% had a previous AIDS diagnosis, median time on prior combination ARV therapy was 52 months, and 94% were DRV-experienced.
- At baseline, patients had a mean of 5 NRTI resistance-associated mutations (RAMs), 3 NNRTI RAMs, and 4 PI RAMs.
- At 24 weeks, all patients maintained a VL <50 copies/mL; at 48 weeks, 1 patient was considered a failure due to loss of follow-up.
- Mean CD4+ cell count increased from 585 cells/mm^3 to 662 cells/mm^3 at 48 weeks.
- Six patients experienced moderate insomnia or CNS symptoms, but no AEs led to discontinuation.

- Mean triglyceride levels improved by a mean of -13% and cholesterol levels remained stable (slightly worsened for those previously receiving TDF).
- A decrease in mean eGFR of -13 mL/min/1.73 m^2 was observed at 48 weeks.
- An improvement in proteinuria (-22%) and fractional excretion of phosphate (-18%) was observed in patients who were previously on TDF.

Retrospective Studies

Ripamonti et al (2024)[4] conducted a multicenter, retrospective, observational study to examine the durability of a dual regimen (ie, DTG + DRV-COBI) using treatment failure over time as a composite endpoint in highly treatment-experienced patients living with HIV (PLWH; N=283).

Study Design/Methods

- PLWH who were initiated on DTG + DRV-COBI (including DTG twice daily [BID]) from 2015 onward, irrespective of the HIV RNA level, were included.
- The primary outcome was treatment failure (discontinuation for any reason) and VF (HIV RNA ≥50 copies/mL or any detectable viral load followed by a treatment switch).

Results

- The median age was 60 years, and 66.4% of patients were male. The median duration of therapy was 24 years, with 45% of patients having received ≥8 previous lines of treatment.
- At DTG + DRV-COBI treatment baseline, 57.7% of patients had a CD4+ T-cell count of >500 cells/mL and 67% of patients had HIV RNA <50 copies/mL.
- Primary RAMs were identified in 86% of patients for NRTI, 71% for NNRTI, 37% for PI, and 15% for INI. Only 2 patients were prescribed DTG BID.
- Treatment discontinuation was observed in 42 patients (14.8%) primarily due to simplification, toxicity, intolerance, or drug interactions. VF was observed in 7 patients (2.5%).
- Eighteen patients died, and 8 patients were lost to follow-up.
- The probability of treatment discontinuation after 1, 2, 3, 4, 5, 6, and 7 years of treatment was 11%, 16%, 22%, 27%, 29%, 33%, and 42%, respectively.
- Multiple logistic regression analysis revealed that a 50-unit increase in the CD4+ T-cell count was the only factor significantly linked to a reduced probability of treatment failure after 1 year (odds ratio, 0.947; 95% CI, 0.9-0.992).

Hawkins et al (2019)[5] conducted a retrospective cohort study to determine the effectiveness of bDRV + DTG in highly treatment-experienced patients.

Study Design/Methods

- All treatment-experienced patients >18 years of age who received bDRV + DTG between January 2013-December 2017 at 3 large Denver metro clinics were included.
- Patients were excluded if they had no follow-up VL or last recorded VL within 8 weeks of study regimen initiation.
- Adherence was calculated for the 6-month period prior to the last VL on the study regimen (or duration on study regimen if <6 months).
    - Patients who did not use clinic pharmacies were excluded from adherence assessments.

Results

Patient Characteristics[5]

Baseline Demographics (N=65)	
Median age, years (IQR)	55 (51, 61)
Female and male-to-female, n (%)	9 (14)
Race/ethnicity, n (%)	
Non-Latino White	31 (48)
Non-Latino Black	15 (23)
Latino	18 (28)
Other/unknown	1 (2)
Median baseline CD4+ count, cells/mm^3 (IQR)	527 (340, 767)
Baseline suppressed, n (%)	49 (75)
Study regimen characteristics (N=65)	
Boosting agent, n (%)	
Cobicistat	33 (51)
Ritonavir	32 (49)
Study regimen complexity, n (%)	
Daily	59 (91)
bDRV BID	5 (8)
DTG BID	0 (0)
bDRV and DTG BID	1 (2)
Known prior major RAMs, n (%)	
DRV (L33F, I47V, I54L, T74P, I84V)	5 (8)
DTG	0 (0)
Cumulative antiretroviral exposure and prior experience	
Median duration of prior antiretroviral therapy (years, IQR)	19 (13, 22)
Prior antiretroviral experience, n (%)	
NRTI	65 (100)
NNRTI	55 (85)
PI	58 (89)
Integrase strand transfer inhibitor	37 (57)
Reasons for use of the study regimen, n (%)	
Optimization in setting of proven or suspected TFV resistance	30 (46)
TFV toxicity or intolerance with need or desire to avoid ABC	22 (34)
CKD (including ESRD) with need or desire to avoid ABC	13 (20)

Abbreviations: ABC, abacavir; bDRV, boosted darunavir; BID, twice-daily; CKD, chronic kidney disease; DRV, darunavir; DTG, dolutegravir; ESRD, end stage renal disease; IQR, interquartile range; NNRTI, nonnucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; RAM, resistance-associated mutation; TFV, tenofovir.

- The virologic outcomes are provided in Table: Virologic Outcomes on Study Regimen.
- Use of ritonavir vs COBI, BID vs QD dosing, and preexisting DRV RAMs did not impact outcomes.
- All 7 patients with baseline suppression who developed viremia on the regimen were resuppressed with no changes to therapy.
- Median adherence was 99% (IQR 91-100%).

Virologic Outcomes on Study Regimen[5]

	n	**Follow-up Days, Median (IQR)**	**VL Ever[a] ≤50 Copies/mL, n (%)**	**Last VL[b] ≤50 Copies/mL, n (%)**
Overall	65	419 (286, 744)	62 (95)	61 (94)
Baseline suppressed	49	415 (286, 804)	49 (100)	48 (98)
Baseline not suppressed	16	511 (341, 741)	13 (81)	13 (81)

Abbreviations: bDRV, boosted darunavir; DTG, dolutegravir; IQR, interquartile range; VL, viral load.
[a]Ever refers to achieving suppression at any point while on bDRV and DTG.
[b]Last refers to the last recorded VL while on bDRV and DTG.

- The median CD4+ count increased from 527 cells/mm^3 to 585 cells/mm^3.
- Ten (15%) patients discontinued the study. Reasons for discontinuation included: drug-drug interaction with boosting agent (n=5), cardiovascular disease risk and desire to avoid DRV (n=2), low level viremia of 112 copies/mL (n=1), lost to follow up (n=1), and transition to hospice-non-HIV related (n=1).

Navarro et al (2019)[6] conducted a multicenter, retrospective cohort study designed to evaluate the efficacy of QD bDRV + DTG as a switch strategy in heavily-treated, HIV-infected patients.

Study Design/Methods

- The study was carried out across 3 university hospitals in Spain.
- Data from HIV-infected adult patients who had been receiving a stable ARV regimen with undetectable VL for ≥6 months, and who switched to a regimen consisting of bDRV + DTG (both administered QD) between January 2015-January 2018 were included.
- Patients were followed until VF or treatment discontinuation for any reason.
- The primary outcome was the percentage of patients with a VL of ≤50 copies/mL at the last follow-up visit, as measured by on-treatment analysis censoring treatment discontinuations due to switching, drug-drug interactions, AEs, or deaths.
- Secondary outcomes included safety (discontinuations due to AEs), frequency of blips (transient positive viremia), and changes in CD4+ cell count, lipid profile, and renal function.

Results

- A total of 50 patients (64% males; median age [IQR], 52 [45-55] years) were included in the analysis.
  - Of these, 44 (88%) were boosted with COBI.
- Median (IQR) time of viral suppression was 52 (18-103) months, and median (IQR) CD4+ cell count was 565 (335-850) cells/mm^3.
- Reasons for initiating QD bDRV + DTG included treatment simplification (42 patients [84%]), bone toxicity (4 patients [8%]), renal toxicity (3 patients [6%]), and drug-drug interactions with hepatitis C treatment (1 patient [2.6%]).
- Patients had a median (IQR) of 8 (4-11) previous ARV therapy combinations.
- All patients had a history of VF, with a median (IQR) of 3 (2-8) VFs.
- Histological genotypes available in 44 patients (88%) showed that 41 (93.2%) patients had NRTI RAMs, 32 (72.7%) had NNRTI RAMs, and 12 (27.3%) had primary RAMs to PIs, of which 7 patients (15.9%) had DRV RAMs. No patients were reported to have INSTI RAMs.
  - Thirty-seven (84.1%) of the 44 patients had RAMs to ≥2 ARV classes.
- After a median (IQR) follow-up of 25 (17-28) months, 49 of 50 (98%) patients maintained a VL ≤50 copies/mL (95% CI, 89.5-99.6%).
- Ten patients (20%) experienced blips during follow-up.
- VF occurred in 1 patient (2%) who discontinued treatment and was lost to follow-up; when the patient returned to the clinic, the same regimen was reintroduced and VL was suppressed.
- There were 4 other treatment discontinuations (8%), with all of them occurring with the last VL ≤50 copies/mL: 1 patient (2%) with persistent insomnia that led to ARV therapy change, 1 patient (2%) had their treatment switched to tenofovir alafenamide/emtricitabine/elvitegravir-COBI to improve adherence, and 2 patients (4%) died due to bacterial peritonitis and pancreatic neoplasm, respectively.
- There were 37 patients (74%) with RAMs to ≥2 ARV classes, including 12 patients (24%) with PI RAMs. At the end of follow-up, all of these patients maintained suppressed viremia.

- Serum creatinine increased by a median (IQR) of 0.12 (0.03-0.23) mg/dL (*P*=0.011) and eGFR decreased by 1.4 (0-18.5) mL/minute (*P*=0.013) at week 4 and remained stable during follow-up.
- An increase in total cholesterol level (median 9 mg/dL; *P*=0.019) and LDL (median 16 mg/dL; *P*=0.019) was observed at the end of follow-up.
- No significant changes were observed in CD4+ cell count, HDL, or triglycerides.

Vassilios et al (2019)[7] conducted a retrospective study to evaluate the efficacy and safety of switching to dual therapy with DRV/COBI + DTG as a simplification strategy in heavily-treated patients with HIV.

Study Design/Methods

- The study was conducted between March 2017 and January 2018.
- Patients were included if they were receiving salvage ART, had an undetectable VL (<20 copies/mL) for ≥12 months, had >1 treatment failure due to treatment resistance in the past, had multiple mutations in several drug categories, and were willing to change therapy.

Results

- A total of 16 patients were included and were switched to dual therapy with DRV/COBI and DTG QD.
- All patients were men having sex with men with a median age of 49 years.
- All patients were receiving ≥3 drugs from different ARV classes.
- Patients had been followed for their HIV infection for 14-27 (median: 21) years.
- Patients had received 4-14 (median: 8) different ARV regimens.
- Historical genotypes from the 16 patients showed 6 (37.5%) patients with NRTI and NNRTI RAMs; 7 (44%) with NRTI, NNRTI, and PI RAMs; and 3 (19%) with NRTI and PI RAMs.
- After a median 15 (range 12-17) month follow-up, all 16 patients remained undetectable (VL <20 copies/mL).
- CD4+ cell counts were 686±380 cells/μL at the beginning of the study and 709±301 cells/μL at the end of the study (*P*=0.86).
- There were no AEs or changes in metabolic profile or renal function.

Lee et al (2018)[8] conducted a retrospective cohort study to evaluate the effectiveness, safety, and tolerability of switching to dual therapy with DRV/COBI + DTG in treatment-experienced patients with HIV.

Study Design/Methods

- This was a retrospective cohort switch study conducted at a tertiary hospital in Korea between 2016 and December 2017 in treatment experienced patients (>2 years) who switched to DRV/COBI + DTG.
- The study divided the patients into a treatment failure group (≥50 copies/mL) and a nonfailure group (defined as patients who changed their regimen due to adverse drug reactions [ADRs] or therapy simplification).
- Patients were excluded if their regimen was switched at a previous hospital.
- **Primary endpoint:** proportion of patients with virologic suppression 48 weeks after switch.
- **Secondary endpoints**: safety and tolerability.

Results

- A total of 31 patients were analyzed, with 13 patients in the treatment failure group and 18 patients in the non-failure group.
- Patients were followed for 44.8±13.5 weeks after switch to DRV/COBI + DTG.
- Baseline characteristics are defined in the Table: Baseline Characteristics.

- Of the 13 patients in the treatment failure group, the percentage of patients with a VL <50 copies/mL was 0% of patients at week 0, 45% of patients at week 4, 50% of patients at week 12, 50% of patients at week 24, and 66.7% of patients at week 48.
- Of the 18 patients in the non-failure group, virologic suppression was maintained at <50 copies/mL for all periods, and the average number of CD4+ T cells was 408 cells/mm^3 (maintained at >200 cells/mm^3).
- Of the 31 patients, 2 patients experienced a VF.
- Of the 13 patients in the treatment failure group, 4 patients were found to be resistant to lamivudine, rilpivirine, emtricitabine, didanosine, abacavir, etravirine, efavirenz, and nevirapine.
- During the follow-up period (44.8±13.5 weeks), DRV/COBI + DTG was relatively well tolerated.
    - AEs reported (all Grade 1) included itching, acne, weight loss, constipation, and general weakness.
    - One patient experienced persistent renal insufficiency and was switched to an unspecified therapy.
- There were no reports of neuropsychiatric ADRs such as depression, suicidality, and sleep disturbances.
- Lab values are defined in the Table: Lab Values Before and After Regimen Change.

Baseline Characteristics[8]

Variables	Failure Group (n=13)	Non-Failure Group (n=18)	Total (n=31)
Male sex (%)	12 (92.3%)	16 (88.9%)	28 (90.3%)
Age (years)	44.8±8.8	50.2±8.6	47.9±8.9
Duration with HIV-1 infection (years)	14.4±5.4	13.3±7.0	13.7±6.3
Coinfection with HBV (%)	1 (7.7%)	2 (11.1%)	3 (9.7%)
Coinfection with HCV (%)	1 (7.7%)	1 (5.6%)	2 (6.5%)
Coinfection with TB (%)	5 (38.5%)	6 (33.3%)	11 (35.5%)
Reasons for changing regimen			
Treatment failure	13 (100%)	0 (0.0%)	13 (41.9%)
Simplification	0 (0.0%)	6 (33.3%)	6 (19.4%)
Adverse drug reaction	0 (0.0%)	12 (66.7%)	12 (38.7%)

Abbreviations: HBV, hepatitis B virus; HCV, hepatitis C virus; HIV-1, human immunodeficiency virus type 1; TB, tuberculosis.

Lab Values Before and After Regimen Changes[8]

Variables	Failure Group (n=13)	Non-Failure Group (n=18)	Total (n=31)
Initial eGFR (mL/min/BSA)	107.9±33.6	108.4±29.6	108.2±30.8
Last eGFR (mL/min/BSA)	77.9±17.0	103.1±35.5	88.5±30.8
Initial glucose (mg/dL)	144.3±85.8	87.9±16.9	117.4±68.1
Last glucose (mg/dL)	121.5±55.1	98.5±16.8	92.3±45.2
Initial LDL (mg/dL)	87.1±56.9	98.7±27.1	92.3±45.2
Last LDL (mg/dL)	116.3±60.3	103.0±39.4	110.7±52.2
Initial HDL (mg/dL)	52.8±19.1	47.9±16.5	49.3±13.6
Last HDL (mg/dL)	47.9±11.3	51.2±16.6	49.3±13.6
Initial TG (mg/dL)	329.4±369.4	145.8±69.4	242.0±281.4
Last TG (mg/dL)	268.6±223.1	143.0±87.0	215.9±187.6

Abbreviations: BSA, body surface area; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglycerides.

LITERATURE SEARCH

A literature search of MEDLINE®, EMBASE®, BIOSIS Previews®, and DERWENT® (and/or other resources, including internal/external databases) pertaining to this topic was

conducted on 07 February 2025. Clinical studies specifically evaluating the efficacy of DRV+COBI+DTG are summarized.

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