BACKGROUND

Dual therapy in HIV represents an attractive opportunity for HIV-infected people in virologic suppression. Dual therapy regimens should achieve and maintain viral suppression and immunologic control while minimizing short- and long-term AEs, improve adherence and convenience, and reduce drug-drug interactions and costs. To date, there are few clinical data to support a dual regimen with dolutegravir and doravirine [1]. The individual efficacy of both doravirine and dolutegravir suggests that concomitant administration of these two molecules as part of an NRTI-sparing regimen could be a viable option, although to date there are no studies in the HIV-infected population. The aim of our study is to investigate whether a dual therapy regimen containing dolutegravir and doravirine is effective and safe.

METHODS

A prospective observational study lasting 24 months (February 2021-February 2023) is conducted at the Infectious Diseases Unit of University of Palermo to evaluate the efficacy, safety and tolerability of a two-drug antiretroviral scheme, containing dolutegravir and doravirine, in a cohort of patients with HIV infection and already on effective antiretroviral therapy.

The primary endpoint of the study is maintenance of viral suppression at 48 weeks (±6 weeks) with HIV-1 RNA <50 copies/mL. Secondary endpoints are: 1) percentage of participants without virological failure; 2) strategy success rate, defined as the percentage of participants without virological failure without interruption of study treatment; 3) genotypic resistance profile in case of virologic failure; 4) changes in CD4 cell counts, CD4/CD8 ratio, neutrophil-to-lymphocyte ratio (NLR) as a marker of systemic inflammation; 5) Estimated Glomerular Filtration Rate (eGFR), lipid profile, fasting glucose 6) clinical and laboratory adverse events.

RESULTS

Fifteen patients were included in this analysis, 10 (67%) males and 5 (33%) women. Mean age was 50.4 years (SD 13.2), with a mean length of HIV disease of 13.2 years (SD 7.94), mean nadir CD4 was 379/mmc (SD 201). Most frequent comorbidities were hypertension (40%), dyslipidemia (46%), osteoporosis and chronic kidney disease (13.3%), NCS disorders, metabolic syndrome, diabetes and HCV coinfection (6.7%). Switch to DOR and DTG were mainly due to high CV and metabolic risk (9/15, 60%). Antiretrovirals that patients were switched off were mostly integrase inhibitors (7/15, 46.7%), followed by boosted protease inhibitors (8/15, 53.3%). All 15 patients meets baseline criteria for HIV-RNA viremia <50 copies, 9/15 (60%) had complete suppression (TND). After 48 weeks, we observed a maintenance in viral suppression among all those who were undetectable at the baseline, 11/15 obtained TND. 1 patients stopped DOR and DTG regimen for sleep disorders before the follow-up analysis, resolved after switch to PI regimen, maintaining viroemia undetectability. No significant changes in CD4, CD4/CD8 ratio, lipid profile, renal function and neutrophil-to-lymphocyte ratio were observed from the baseline.

CONCLUSIONS

Combination strategies with a good tolerability profile, an high genetic barrier and also the ability to be administered once-daily should be preferred in a setting such as the current SARS-CoV-2 pandemic. Doravirine is presented as a versatile molecule, the main feature of which is the low impact on serum lipids and carbohydrate profile, together with a distinctive resistance pattern. The combination of doravirine together with dolutegravir, a drug characterized by an excellent profile of potency, safety and long-term tolerability, appears to be a potential strategy in the setting of patients who require a regimen which maintains high virologic efficacy but reduces long-term toxicity and pharmacological potentials.

References