P-096

Switching to the combination of dolutegravir plus rilpivirine as dual therapy in the clinical setting: a prospective cohort study

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BACKGROUND

The combination of dolutegravir (DTG) plus rilpivirine (RPV) has been shown to be effective in selected patients, but there are no data in patients with hepatitis C virus (HCV) coinfection, previous toxicity or failure, or/and at risk of severe drug-drug interactions (DDI).

OBJECTIVES

To evaluate the safety and efficacy of this dual regimen in patients with toxicity or drug-drug interactions, a population not included in clinical trials.

METHODS

Prospective cohort study of 102 virologically suppressed HIV-infected patients, without previous failure to integrase inhibitors or non-nucleoside, who switched to this combination because of toxicity or interactions (**EC 280/15; NCT02491242**).

The primary study endpoint was the proportion of patients at 48 weeks who were free of treatment failure, defined as virological failure (two consecutive measurements of plasma viral load above 50 copie/mL separated at least by 2 weeks), discontinuation of any drug, or reintroduction of a three-drug regimen. Secondary end-points included the evolution of CD4 count, CD4/CD8 ratio, liver function tests, renal function (eGFR, urine parameters), bone mineral density (BMD), and lipid parameters after switching therapy, according to the previous use of TDF and other baseline factors. Patient's end of follow up was considered the date of regimen change or, if treatment continued, until 31th December 2017.

Baseline characterístics of the 102 patients included

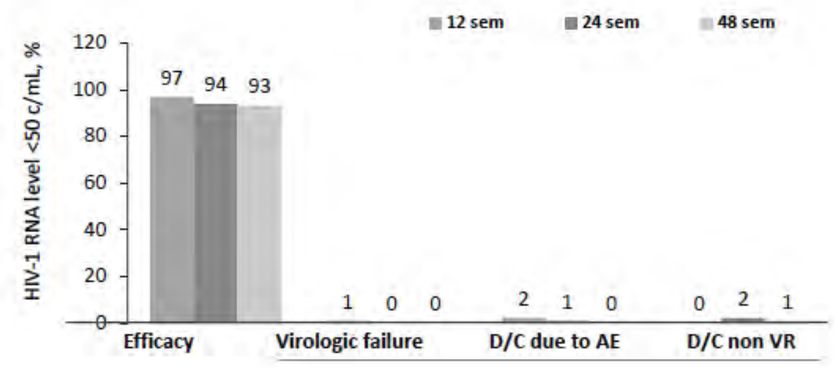
Overall, 102 patients (mean age 54 yrs, 29 women, 28%) were included and followed for a median of 25.7 months (208.2 patients-year).

Variable	Value
Mean age, years (range)	54 (31-84)
Sex male, n (%)	73 (72)
Risk factor for HIV infection	
Former IDUs, n (%)	55 (54)
MSM, n (%)	24 (24)
HCV coinfection, n (%)	57 (56)
- Fibrosis 2-3	13 (12)
- Fibrosis 4/ Cirrhosis	27 (27)
Duration of HIV infection, months	252,7 (169.9-296.7)
Previous AIDS diagnosis, n (%)	35 (34)
Nadir CD4+T-cell count, cells/ml	221 (74-305)
< 200 cells/ml	48 (47)
Prior cART, n (%)	
PI-based	28 (27)
NNRTI-based	59 (58)
- RPV	7 (7)
INI-based	15 (15)
- DTG	5 (5)
TDF-including	59 (58)
Mean number of previous regimens	6.1 (1-17)
Mean number of previous pills	2.82 (1-6)
Time in previous cART, months	52 (19-91)
Presence of genotypic resistance to NRTIs/PI	61 (60)
Mean number of primary mutations against:	
NRTIs	2.6 (1-8)
PI	2.52 (1-6)
Causes of switch, n (%)	
toxicity / intolerance	44 (43)
risk of DDI	51 (50)
non-adherence	7 (7)
Baseline CD4+ cell count, cell/ml	613 (445-833)
Mean CD4/CD8 ratio	0.82 (0.1-3.07)
< 0.3	6 (6)
Mean eGFR (CKD-epi; ml/min/1.73m2)	86 (5-139)
MAin comorbidities at inclusion; n (%)	
Lipodystrophy syndrome	36 (38)
CKD	7 (7)
Proteinuria ≥150 mg/gr creatinine	10 (10)
IHD / AMI	12 (12)
Femoral neck/Spine Osteoporosis	5/17 (5/17)
Renal/ Liver transplantation	1 / 1 (1/1)

Data are expressed as median, interquartile range, unless otherwise specified.

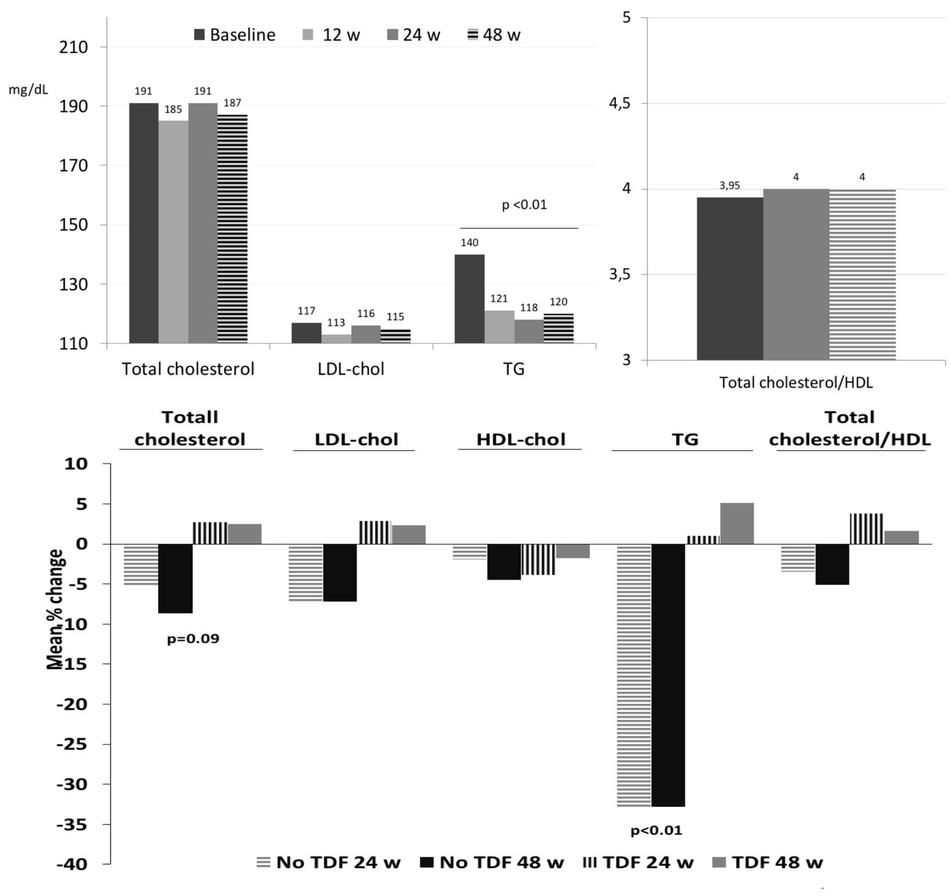
DTG, dolutegravir; RPV, rilpivirine; IDU, intravenous drug users; MSM, men having sex with men; HCV, hepatitis C virus; cART, combination antiretroviral therapy; PI, protease inhibitor; NNRTI, non nucleoside reverse transcriptase inhibitor; INI, integrase inhibitor; TDF, tenofovir disoproxil fumarate; NRTI, nucleoside reverse transcriptase inhibitor; DDI, drug-drug interaction; eGFR, estimated glomerular filtration rate; CKD, chronic kidney disease; IHD, ischemic heart disease; AMI, acute myocardial infarction.

RESULTS

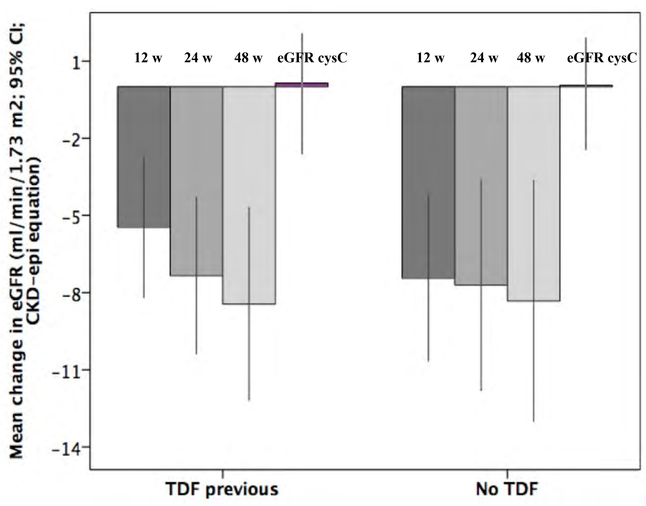


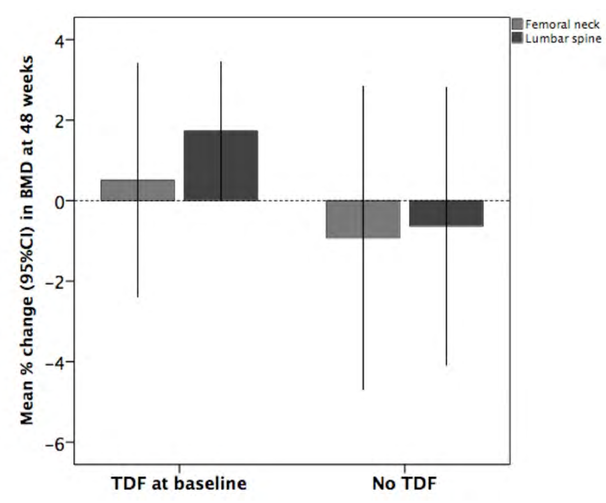
At week 48, only 1 patient had virological failure (HIV RNA level 1.93 log, CD4/CD8 ratio 0.2). Six additional patients (6%) left the regimen (3 CNS symptoms, 1 pregnancy, 1 diarrhea due to metformin, 1 alcoholism). Thus, efficacy was 93% at week 48 (95%CI, 88%-98%; ITT-e, snapshot analysis; 96%, 95% CI, 92-99%; PP analysis). Two additional patients discontinued the regimen before week 96 (1 non adherent with virological failure and emergence of E138A mutation; 1 who need prolonged omeprazole). The CD4/CD8 ratio improved from 0.76 to 0.8 (p=0.22).

Globally, lipid parameters improved (total cholesterol -2%, triglycerides -21%), and of note, there were no significant differences according to previous TDF use.



There was a significant decrease in eGFR (-8.4 ml/min at 48 weeks, -18.2 to +2.2), independently from previous TDF, without changes in eGFR cystatin-C based (0.04 ml/min at 48 weeks), and urine parameters improved or did not change (uricosuria; p=0.03). DXA scan in 89 patients showed improvement in spine in 72 patients (mean +1.15%; -0.57 to +3.3%) and in femoral neck in 56 patients (mean +0.4%; -3.3% to +2.57%), associated to previous TDF use.





CONCLUSIONS

Switching to the combination of dolutegravir plus rilpivirine is effective and safe in patients with toxicity or severe drug-drug interactions, including HCV-coinfected cirrhotic or transplant patients.

Our data corroborate the improvement in renal function as measured by urine parameters, in spite of a moderate eGFR, creatinine-based, worsening.