

SWITCHING FROM ATAZANAVIR/RITONAVIR (ATV/RTV) TO ATV/COBICISTAT (COBI) IS ASSOCIATED WITH DECREASE OF PLASMA LIPIDS AND LIVER FIBROSIS

A. Trentalange¹, C. Polifroni¹, C. Carcieri¹, C. Alcantarini¹, C. Montrucchio¹, L. Marinaro¹, N. Forni¹, A. Palazzo¹, A. Barco¹, C. Costa¹, A. Lazzaro¹, M. Tettoni¹, A. De Nicolò¹, A. D'Avolio¹, G. Di Perri¹, A. Calcagno¹, S. Bonora¹

1. Unit of Infectious Diseases, Department of Medical Sciences, University of Torino

Background

- Previous data suggested a lower dyslipidemic potential for COBI compared to RTV. (1)
- Switching from darunavir (DRV)/RTV to DRV/COBI was showed to be associated with total cholesterol (TC) and triglycerides (TG) decrease. (2)
- No virological, metabolic and PK data of switching from RTV to COBI as booster of ATV have been yet obtained in the clinical setting.
- Our aim was to study efficacy, safety and PK of switching from ATV/RTV to ATV/ COBI.

Materials and Methods

- Adult HIV+ patients who switched from ATV 300 mg/RTV 100 mg to ATV 300 mg/COBI 150 mg were enrolled;
- Demographics, virological, metabolic and PK data were recorded at baseline (BL) and 24 weeks after switching (W24).
- Hypercholesterolemia was considered as TC >190 mg/dl and/or LDL cholesterol > 115 mg/dl, and hypertriglyceridemia as TG > 180 mg/dl.
- Plasma concentrations were measured by validated HPLC methods.
- FIB-4 score was calculated as (age*AST)/(platelets*SQR(ALT)).
- Variables were described as medians (IQR) or number (%) and were compared using paired non-parametric tests (Wilcoxon's and McNemar's).

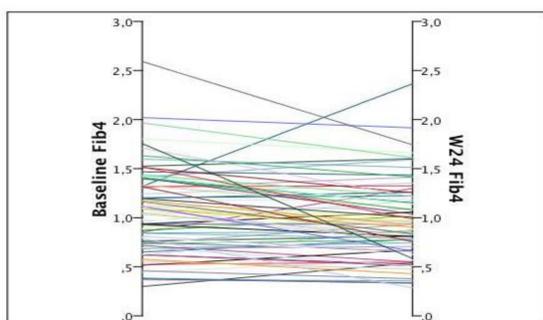
Results

We included 121 patients: BL characteristics are shown in Table 1.

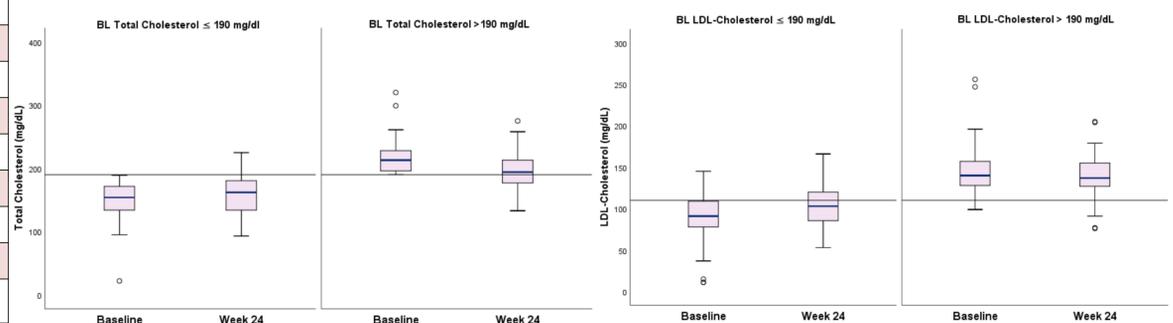
Table 1. Characteristics of study population (n=121)

Male gender, n (%)	84 (68,9)
Age*, years	48 (41-55)
CD4+ lymphocytes*, µg/ml	601 (437-820)
HIV RNA plasma < 20 cp/ml, n (%)	105 (88,2)
BMI*, Kg/m2	24,2 (21,1-26,4)
European ancestry, n (%)	100 (81,9)
CD4 lymphocytes*nadir, µg/ml	224 (129-290)
HCV+, n (%)	25 (21,9)
HBV+, n (%)	3 (2,5)
Associated antiretrovirals: NNRTIs n (%)	1 (0,8)
INSTI n (%)	26 (21,5)
NRTI n (%)	96 (79,3)
CCR5i n (%)	5 (4,1)
Comorbidities: Hypertension: n (%)	21 (21)
Diabetes: n (%)	8 (8,1)

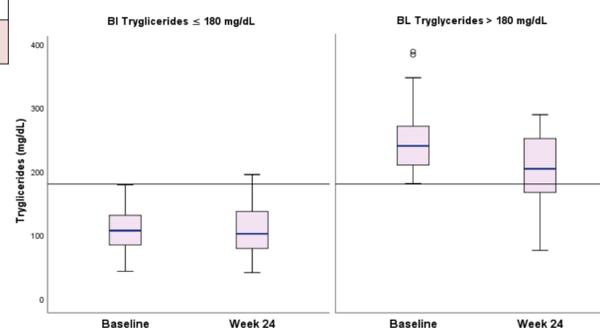
- Fifteen (12.3%) patients discontinued ATV/c.
- BL and W24 HIV RNA was <20 copies/ml in 88.2% and 82.1% of participants (p=0.38).
- A small although significant increase in serum creatinine at W24 (0.1 mg/dl [p<0.001]) was observed with no change in total or indirect bilirubin.
- No significant differences were found in atazanavir Ctrough, pre and post switch (p=0.56).



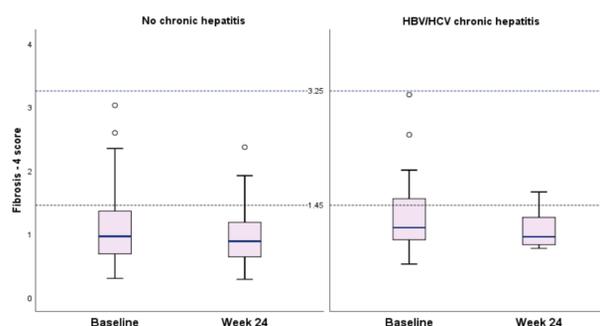
- We observed non significant changes in **Total cholesterol** [from 183 mg/dl (151-210) to 173 mg/dl (147-204)], **LDL-cholesterol** [117 mg/dl (87-140) to 118 mg/dl (94-146)] and **Triglycerides** [125 mg/dl (92-192) to 121 mg/dl (81-175)] (p=0.08, p= 0.1 and p= 0.1).



- **In patients with BL hypercholesterolemia (44,6%)** total cholesterol decreased from 213 mg/dl (196-228) to 194 mg/dl (175-213) (p<0.001) and LDL-cholesterol from 140 mg/dl (130-155) to 137 mg/dl (120-155) (p=0.05).



- **In patients with baseline hypertriglyceridemia (27,5%)** Triglycerides decreased from 240 mg/dl (207-276) to 204 mg/dl (159-252) (p=0.01).



- **Fib-4** value decreased from 1.04 (0.73-1.41) to 0.93 (0.67-1.21) (p=0.001). This finding was confirmed even in HCV/HBV-negative patients [0.96 (0.68-1.39) to 0.90 (0.63-1.20), p=0.01]

Conclusions

- This is the first report on switching from ATV/r to ATV/c in the clinical setting.
- Virological efficacy was maintained and substantial PK equivalence was confirmed.
- Switch from RTV to COBI as ATV booster was associated with significant decrease of LDL cholesterol and TGL in patients with dyslipidemia at baseline, and significant decrease of liver fibrosis in the whole population. These findings support a lower metabolic impact of COBI as compared to RTV when associated with ATV and deserve further investigation.

References

1. Garcia G, Duenas C, Aleman Ana, et al. Lipid profile in HIV patients who switch from ritonavir to cobicistat. P1926. ECCMID 21-24 April 2018
2. Echeverria P, Bonjocj A, Puig J, et al. Significant improvement in triglyceride levels after switching from ritonavir to cobicistat in suppressed HIV-1-infected subject with dyslipidaemia. HIV Med. 2017 Nov; 18(10):782-786. doi: 10.1111/hiv.12530, Epub 2017 Jul 3.

Contact: Dr. Alice Trentalange, Unit of Infectious Diseases, Department of Medical Sciences, University of Torino, alicentrenta@gmail.com; +393463518210