PE8/26

Effectiveness and safety of fixed dose ABC/3TC plus Rilpivirine in a multicenter cohort of HIV-infected patients. SIMRIKI Study. GESIDA-8314

J. Troya[1], P. Ryan[1], E. Ribera[2], D. Podzamczer[3], V. Hontañón[4], J.A. Terrón[5], V. Boix[6], S. Moreno[7], P. Barrufet[8], M. Castaño[9], A. Carrero[10], J. Galindo[11], M. Raffo[12], H. Knobel[13], H. Esteban[14], GESIDA-8314

[1]Hospital Universitario Infanta Leonor, Madrid, Spain, [2]Hospital Universitario Vall d´Hebrón, Barcelona, Spain, [3]Hospital Universitario de Bellvitge, Barcelona, Spain, [4]Hospital Universitario La Paz, Madrid, Spain, [5]Hospital Jerez de la Frontera, Jerez de la Frontera, Spain, [6]Hospital General Universitario de Alicante, Alicante, Spain, [7]Hospital Universitario Ramón y Cajal, Madrid, Spain, [8]Hospital de Mataró, Mataró, Spain, [9]Hospital Carlos Haya, Málaga, Spain, [10]Hospital Universitario Gregorio Marañón, Madrid, Spain, [11]Hospital Clínico de Valencia, Valencia, Spain, [12]Hospital Universitario Infanta Elena, Huelva, Spain, [13]Hospital del Mar, Barcelona, Spain, [14]Fundación SEIMC-GESIDA, Madrid, Spain

EACS European AIDS Clinical Society

OBJECTIVES

Little information has been published to date about the combination ABC/3TC+RPV as a switching strategy, nevertheless its use is increasing in Spain. The aim of this study was to evaluate effectiveness and safety with real world data in virologically supressed HIV-1 adult patients switching to ABC/3TC+RPV.

METHODS

Retrospective, multicenter cohort study with HIV-1 adult patients, who started ABC/3TC+RPV as a switching strategy at least 48 weeks before the start of the study and with previous HIV RNA of less than 50 copies per mL for at least 24 weeks. Effectiveness was analyzed by intention-to-treat (ITT) (non complete/missing=failure) and on-treatment (OT).

RESULTS

205 patients were included. 75.6% were male, median age 49 (41-54) years, 23.4% AIDS and 20% HCV PCR+. Median CD4+ lymphocyte count at baseline 667 (471.5, 870) cells per uL. Median follow-up with HIV RNA <50 copies per mL previous to switching 74.8 (35.8, 117) months. The reasons for switching to ABC/3TC+RPV were drug toxicity/tolerability (60.5%), regimen simplification (20%),other physician´s criteria (11.2%), cost saving reasons (1.5%) and unknown reasons (6.8%).

The primary end point was achieved by 187 out of 205 patients (91.2%; [95% CI: 86.5-94.7]) by ITT analysis, and by 187 out of 192 patients (97.4% [95% CI: 94-99.1]) by OT analysis. Overall, 18 (8.8%) patients experienced therapeutic failure, including 15 patients who discontinued ABC/3TC+RPV during the 48 weeks study period. Reasons for discontinuation were toxicity/tolerability: 4 (2%), virological failure: 2 (1%), other medical decision: 3 (1.5%), loss of follow-up or patient´s decision: 3 (1.5%), death: 1 (0.5%) and no clinical data: 2 (1%). At week 48, 5 (2.4%) patients experienced protocol defined virological failure. Of these 5 patients, 2 continued with ABC/3TC+RPV after 2 consecutive low-level HIV RNA determinations (at weeks 6 and 24, respectively) despite of which both had HIV RNA <50 copies per mL at week 48. The other 3 patients had consistent HIV RNA > 50 copies per mL (2 patients between weeks 4-8, and one patient at week 48).

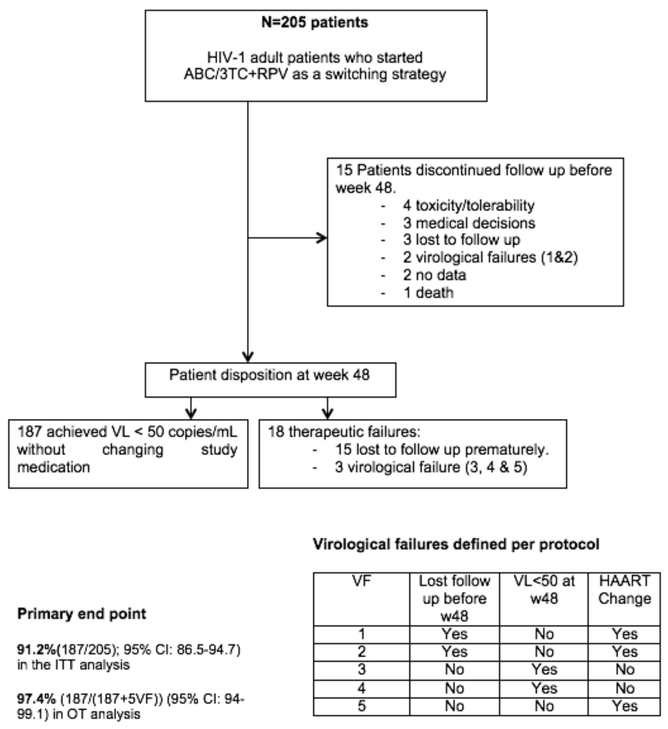
Median CD4+ lymphocyte count increase was 48 (-50, +189) cells per uL and percentage of CD4+ lymphocyte an increase of 1.2 % (-1.3, +4.1), *P*< 0.001.

Thirty-eight adverse effects (AE) were described in 32 patients (15.6%) with no clinical intervention in 33. Clinical resolution was achieved in 25 patients. Drug withdrawal was carried out in 3 (1.5%) patients (insomnia/depression, dizziness, epigastralgia). No direct correlation was found between AE and treatment in 25 patients.

Age (years); median (IQR)	49 (41- 54)
Gender	
Males n (%)	155 (75.6)
Females n (%)	50 (24.4)
HIV risk factors	
MSM; n (%)	62 (30.2)
Heterosexual; n (%)	65 (31.7)
IDU; n (%)	61 (29.7)
Other/Unknown; n (%)	17 (8.3)
Baseline CD4	
CD4 count (cells/ µL); median (IQR)	667 (471-870)
CD4 %; median (IQR)	31 (23-38)
Nadir CD4; (cells/µL); median (IQR)	198 (87-288)
AIDS diagnosis; n (%)	54 (26.3)
Time since HIV diagnosis; (years); median (IQR)	13.1 (6.1-18.7)
Months since undetectable viral load (<50 copies/mL); median (IQR)	74.8 (35.8-117.0)
Comorbilities	
HBV (Hbsag +); n (%)	4 (2)
HCV (PCR +); n (%)	41 (20)
Hypertension; n (%)	44 (22.5)
Diabetes mellitus; n (%)	19 (9.3)
Dyslipidemia; n (%)	59 (28.8)
Isquemic heart disease; n (%)	12 (5.9)
Kidney disease; n (%)	10 (4.9)
Previous Nucleos(t)ide	
Abacavir; n (%)	144 (70.2)
Tenofovir; n (%)	53 (25.8)
Other; n (%)	4 (1.9)

MSM: men who have sex with men, IDU: injected drug user; AIDS: Acquired Inmune Deficiency Syndrome, HBV: hepatitis B virus, HCV: Hepatitis C virus. Data are Median (IQR) or n (%).

Baseline characteristics



Primary end point

91.2%(187/205); 95% CI: 86.5-94.7) in the ITT analysis

97.4% (187/(187+5VF)) (95% CI: 94-99.1) in OT analysis

Virological failures defined per protocol

VF	Lost follow up before w48	VL<50 at w48	HAART Change
1	Yes	No	Yes
2	Yes	No	Yes
3	No	Yes	No
4	No	Yes	No
5	No	No	Yes

Flowchart of included patients

Summary of adverse effects	
Patients with ≥ 1 AE	32
Total Number of AE	38
Patients with ≥1 Grade 3-4 AE	4
Total number of Grade 3 or 4 AE	5
Patients with serious AE	1
Total number of serious AE	1
Discontinuation due to AE	3*
Deaths	1
Type of Adverse effects	
Digestive AE	11
Neuropsyquiatric AE	7
Infectious AE	7
Systemic AE	7
Dermatological AE	3
Cardiovascular AE	3
Causality with combination RIL + ABC/3TC	
Related	2
Likely	5
Possible	3
Unlikely	3
Not related	25

AE: adverse effects
* insomnia/depression, dizziness, epigastralgia

Adverse events overview

The median estimated glomerular filtration rate (MDRD equation) at week 48 was 89.4 (74.6, 99.6) mL/min/1.73 m^2. This is a mild increase of 1.1 (-4.8, +10) mL/min/1.73 m^2, *P*<0.001. Taking into account the previous backbone, fifty-five patients were taking TDF before the switch and had a median increase in glomerular filtration rate of 7 (-5.8, +13,1) mL/min/1.73 m^2 at the end of the follow-up, *P*<0.001 and 150 patients in the group without TDF a non significant increase of 0.1 (-3, 6.6) mL/min/1.73 m^2, *P*=0.196.

No changes in liver enzyme levels (AST, ALT, bilirubin) were observed at week 48, except for a slight decrease in gamma-glutamyl transpetidata (GGT), [29 (21- 53) UI/L] of -7 (-26, -2) UI/L, *P*<0.001 and alkaline phosphatase [75 (62, 90) UI/L] of -12 (-29, -1) UI/L, *P*<0.001.

The lipid profile showed a small but significant decrease including total cholesterol of -9.1 [186 (158-209) mg/dl], low-density lipoprotein cholesterol of -8.9 [113.8 (91-135) mg/dl], high-density lipoprotein cholesterol of -7 [46 (39-58) mg/dl] and triglycerides of -15 [108 (75.5-163.5) mg/dl], all of them *P*<0.001.

CONCLUSIONS

In this cohort, ABC/3TC+RPV was found to have high effectiveness, safety and tolerability in treatment of patients with previous virologically stable HIV-1 Infection.

BIBLIOGRAPHY

- Cohen CJ, Andrade-Villanueva J, Clotet B, Fourie J et al. Rilpivirine versus efavirenz with two background nucleoside or nucleotide reverse transcriptase inhibitors in treatment-naive adults infected with HIV-1 (THRIVE): a phase 3, randomised, non-inferiority trial. *Lancet* 2011;378:229-237.
- Nelson MR, Bion RA, Cohen CJ et al. Rilpivirine versus efavirenz in HIV-1-infected subjects receiving emtricitabine/tenofovirDF: pooled 96-week data from ECHO and THRIVE Studies. *HIV Clin Trials* 2013;14(3):81-91.
- Nachega JB, Mugavero MJ, Zeier M, Vitória M, Gallant JE. Treatment simplification in HIV-infected adults as a strategy to prevent toxicity, improve adherence, quality of life and decrease healthcare costs. *Patient Prefer Adherence* 2011;5:357-367.

GeSIDA GRUPO DE ESTUDIO DEL SIDA-SEIMC