

Safety and Efficacy of Dual Doravirine plus Lamivudine as a Switch Strategy in HIV Patients with Metabolic or Renal Issues

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Background: dual doravirine (DOR) plus lamivudine (3TC) (DOR/3TC) regimens can maintain high levels of viral suppression in experienced patients (Perfezou et al, *J Antimicrob Chemother* 2023). This relies on the high genetic barrier and versatility of DOR.

Material and Methods: ongoing, retrospective-prospective analyses to evaluate the safety and efficacy of dual DOR/3TC started between March 2021 and July 2024 as a switch strategy in 39 HIV patients with metabolic (obesity, diabetes/prediabetes, dyslipidemia) or renal issues attended at an HIV Outpatient clinic from a tertiary hospital in Madrid, Spain.

Baseline Features and Outcomes (Overall Cohort, N=39)

Age (years, median, range)	53 (28-71)	Reason for change to DOR+3TC (%)	
Male Sex (%)	74	- CNS symptoms	15
White (%)	74	- Renal issues	46
AIDS (%)	26	- Weight gain	49
HIV Risk Factor (%)		- Other metabolic issues	8
-MSM	41	- Other	5
-IDU	41	* More than one in 5 subjects (13%)	
Years on ART (median, range)	16 (2-32)	Comorbidities (%)	85
Number of prior ART lines (median, range)	6 (2-27)	- Hypertension	38
CD4 count (cells/ml; median, range)	559 (90-1292)	- Dyslipidemia	31
Undetectable HIV RNA (%)	100	- Diabetes/prediabetes	26
Prior NNRTI experience (%)	85	- Ischemic cardiopathy	13
	No failure	- Solid organ transplant	10
		- Cancer	5
		* More than one in 20 subjects (51%)	
Prior ART (%)		HBsAb+ (%)	82
- INSTI-based	90	Isolated HBcAb (%)	10
*Long-acting C/R in 4		One HBsAg+ patient, on ETV	
- NNRTI-based	5	Baseline BMI (median, range)	28 (16-43)
- PI-based	5	GFR (ml/min; median, range)	74 (7,57-122)
Cost/day oral INSTI 186€		≤30 ml/min (%)	18
Cost/day DOR/3TC 5,86€		Haemodialysis in 2, peritoneal dialysis in one	

Safety	
Time on DOR/3TC (overall cohort) (weeks, median, range)	32 (2-147)
DOR/3TC withdrawal	N=7
Time on DOR/3TC in patients with withdrawal (weeks, median, range)	5 (2-147)
Reasons for withdrawal (N)	
- CNS symptoms	4
- Change to LA C/R	2
- Death	1
Efficacy	
- Virological failure	0
- Transient HIV RNA blip (N)	1

Baseline Features and Outcomes in patients with Renal Insufficiency (N=18)

	Patients with Renal Insufficiency (N=18)	Patients without Renal Insufficiency (N=21)	P
Age (years, mean±SD)	59±5	45±12	0.0001*
White (%)	100	52	0.001*
AIDS (%)	39	14	0.08
IDU HIV Risk Factor (%)	72	14	0.001*
Years on ART (median, range)	25±6	12±7	0.0001*
Number of prior ART lines (median, range)	13±6	5±2	0.0001*
CD4 count (cells/ml; median, range)	490±282	779±279	0.003*
BMI (mean±SD)	26±5	30±6	0.02*
GFR (mean±SD)	39±18	91±14	0.0001*
Adjusted 3TC dose (%)	39	0	0.002*
TPR (mean±SD)	62±20	----	
Comorbidities (%)	100	67	0.008*
- Hypertension	72	10	0.0001*
- Diabetes	22	29	NS
- More than one	72	33	0.015
DOR/3TC withdrawal (%)	17	14	NS

IDU: intravenous drug use; ART: antiretroviral therapy; BMI: body mass index; GFR: glomerular filtration rate; TPR: tubular phosphate resorption

Baseline Features and Outcomes in patients with Metabolic Issues (N=19)

	Patients with Metabolic Issues (N=19)	Patients without Metabolic Issues (N=20)	P
Age (years, mean±SD)	46±12	56±7	0.002*
Female (%)	26	25	NS
Hispanic (%)	47	5	0.003*
MSM HIV Risk Factor (%)	58	25	0.04*
Years on ART (median, range)	13±7	23±8	0.0001*
Number of prior ART lines (median, range)	6±4	11±6	0.003*
CD4 count (cells/ml; median, range)	807±277	493±269	0.001*
BMI (mean±SD)	32±5	25±5	0.0001*
- GLP1 analogues use (%)	16	0	NS
Comorbidities (%)	79	85	NS
- Hypertension	21	55	0.029*
- Diabetes	37	15	0.11
- Dyslipidemia	37	25	NS
- More than one	47	55	NS

MSM: homosexual; ART: antiretroviral therapy; BMI: body mass index; GFR: glomerular filtration rate; TPR: tubular phosphate resorption

Median FU 32w (2-147)	Baseline	Last available	P
CD4 count (cells/ml; median, range)	490±282	503±300	NS
BMI (mean±SD)	26±5	27±5	NS
GFR (mean±SD)	39±18	43±25	0.026
TPR (mean±SD)	62±20	68±18	0.110

FU: follow-up; BMI: body mass index; GFR: glomerular filtration rate; TPR: tubular phosphate resorption

Median FU 26w (2-96)	Baseline	Last available	P
CD4 count (cells/ml; median, range)	807±277	924±351	0.06
BMI (mean±SD)	32±5	31±5	0.01*

BMI: body mass index; FU: follow-up

Conclusions

DOR/3TC was safe and maintained viral suppression in heavily pretreated patients with metabolic issues or renal deterioration on prior INSTI-based therapies, with reduced daily costs.

These results may lead to larger comparative maintenance trials.