Safety and Efficacy of Doravirine plus TAF/FTC/BICTEGRAVIR in Heavily Pretreated Patients

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Background: Doravirine (DOR) is a versatile antiretroviral drug that may be used in combination beyond standard triple therapy.

Material and Methods: ongoing, retrospective-prospective analyses to evaluate the safety and efficacy of DOR pus TAF/FTC/BIC started between November 2022 and July 2024 in 26 HIV patients attended at an HIV Outpatient clinic from a tertiary hospital in Madrid, Spain, due to viral failure, drug interactions or optimization.

Baseline Features (N=26)

Age (years, median, range)	58 (35-77)
Male Sex (N, %)	17 (65)
White (N, %)	19 (73)
AIDS (N, %)	11 (42)
MSM HIV Risk Factor (N, %)	13 (50)
Years on ART (median, range)	25 (1-32)
Number of prior ART lines (median, range)	10 (1-40)
CD4 count (cells/ml; median, range)	567 (119-1398)
Detectable HIV RNA (N, %) -HIV RNA (log_{10} copies/ml; median, range)	19 (73) 1.83 (1.57-2.90)
Prior NNRTI experience (N, %) - EFV - NVP - ETRA - RPV - More than one - Failure on NNRTI - Evidence of resistance to NNRTIs	20 (77) 13 (50) 13 (50) 6 (23) 5 (19) 12 (46) 10 (38) 7 (27)

Prior ART (N, %) - INSTI-based *BIC/TAF/FTC *Long-acting C/R - INSTI+b/PI - MRV use - more than 3 ARV drugs in previous regimen	14 (54) 10 1 11 (42) 3 8
Reason for change to DOR+BIC/TAF/FTC (N, %)	
- Virological Failure - Toxicity - Optimization - Drug interactions	19 (73) 1 (4) 4 (15) 2 (8)
Comorbidities (%) - Hypertension - Dyslipidemia - Diabetes - Cancer * *More than one in 15 subjects (58%)*	86 50 46 11 11
Baseline BMI (median, range)	25 (16-34)
GFR (ml/min; median, range)	88 (36-128)

Outcomes (N=26)

Time on DOR/BIC/TAF/FTC (overall cohort) (weeks, median, range)	69 (6-94)
DOR/BIC/TAF/FTC withdrawal	6 (23)
Time on DOR/BIC/TAF/FTC in patients with withdrawal (weeks, median, range)	51 (14-76)
Reasons for withdrawal (N) - Viral failure with successful change to LA C/R - Change to LA C/R with undetectable HIV RNA - Simplification to BIC/LENA in clinical trial (ARTISTRY) - Death due to urotelial cancer	6 2 2 1 1
Efficacy - Virological failure (N,%) ** Two subjects maintained therapy despite detectable HIV RNA with last values of 1.91 and 3.29 Log respectively*	4 (15)
Safety *- NO WITHDRAWALS DUE TO SAFETY ISSUES*	

LA C/R: long-acting cabotegravir plus rilpivirin;
BIC/LENA: coformulated oral bictegravir/lenacapavir

Features and Outcomes in Patients with Resistance Mutations and/or Baseline Detectable HIV RNA

	Archived Mutations	DOR	FTC	TDF	INSTI	Prior ART	Baseline HIV RNA	Last HIV RNA
P1	M41L, E44D,D67N,L74V,**L100I**, **K103N**,V118I,L210W, T215Y,K219N	Intermediate R	Low level R	High level R	S	c/EVG/TAF/FTC plus DRV plus MRV	1.88 Log	<1.30 Log 76w
P2	M41L,E44D,K65T,D67N, S68C,**K101E**,V118I	Potential low level R	S	Potential low level R	S	c/DRV/TAF/FTC plus DTG	1.83 Log	<1.30 Log 93w
P3	M41L,E44A,D67G,L74V, V118I,M184V,L210W, T215Y,K219D,V90I, **L100I**,**K103N**	Intermediate R	High level R	High level R	S	c/EVG/TAF/FTC plus DRV	<1.30 Log *Optimization*	<1.30 Log 90w
&P4	E138A **T97A in INSTI***	S	S	S	BIC S	c/DRV/TAF/FTC plus DRV plus MRV	2.90 Log	1.65 Log 79w
P5	M41L, D67N/S, L210W,T215Y,A98S	S	Low level R	High level R	S	RTV/DRV plus DTG	1.73 Log	<1.30 Log 72w
P6	M41R, T69D,M184I V118I, **Y181C**	S	High level R	S	S	c/DRV/TAF/FTC plus DTG	1.70 Log	<1.30 Log 56w
P7	M41L, T69i, L74V, M184V, L210W, T215Y, **Y181C**, **G190A**, **A98G**, K101Q	Intermediate R	High level R	High level R	S	RTV/DRV plus DTG	<1.30 Log *Severe lipodistrophy*	<1.30 Log 6w

&P4Patient with archived PRO mutations (L90M):
*BIC/CAB/DTG S; EVG/RAL potential low-level resistance
DRV S: *cob/DRV added to DOR/BIC/TAF/FTC after 40w due to viral rebound (5,7 Log) due to treatment discontinuation. Patient with intermitent adherence issues*
According to Stanford University HIV Drug Resistance Database

	Archived Mutations	DOR	FTC	TDF	INSTI	Prior ART	Baseline HIV RNA	Last HIV RNA
P8	NO	S	S	S	S	BIC/TAF/FTC	2.04 Log	1.43 Log* 61w
P9	NO	S	S	S	S	BIC/TAF/FTC	1.96 Log	<1,30 Log 89w
P10	NO	S	S	S	S	c/DRV plus BIC/TAF/FTC	1.59 Log	<1.30 Log 85w
P11	NO	S	S	S	S	BIC/TAF/FTC	2.61 Log	<1.30 Log 77w
P12	NO	S	S	S	S	DTG/RPV	1.57 Log	<1.30 Log* 51w
P13	NO	S	S	S	S	BIC/TAF/FTC	1.61 Log	<1.30 Log* 14w
P14	NO	S	S	S	S	BIC/TAF/FTC	2.30 Log	<1.30 Log 66w
P15	NO	S	S	S	S	BIC/TAF/FTC	1.80 Log	<1.30 Log 64w
P16	NO	S	S	S	S	BIC/TAF/FTC	1.82 Log	<1.30 Log 62w
P17	D67N,K70R,V90I,T215Y	S	S	Low level R	S	BIC/TAF/FTC	2.15 Log	1.91 Log 43w
P18	NO	S	S	S	S	LA C/R	2.66 Log	<1.30 Log 8w
P19	NO	S	S	S	S	BIC/TAF/FTC	1.74 Log	<1.30 Log 8w
P20	NO	S	S	S	S	BIC/TAF/FTC	1.96 Log	<1.30 Log 90w
P21	NO	S	S	S	S	DTG/RPV	1.77 Log	<1,88 Log* 51w

* Change to LA C/R

Conclusions

The use of DOR plus TAF/FTC/BIC in heavily pretreated patients was safe –no withdrawals due to toxicity- and led to undetectable HIV RNA in 79% of patients with prior viral failure.