EFFICACY AND DURABILITY OF FOSTEMSAVIR, IBALIZUMAB, OR LENACAPAVIR-INCLUDING REGIMENS IN PEOPLE LIVING WITH MULTIDRUG-RESISTANT HIV-1: RESULTS FROM THE PRESTIGIO REGISTRY

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BACKGROUND AND AIMS

Heavily treatment-experienced people living with HIV (HTE-PLWH) often have few, if any, treatment options due to archived drug resistance mutations and/or intolerance to therapy[1,2]. Therefore, the availability of drugs with novel mechanisms of action in this population is essential to achieve viral suppression, restore immune function and prevent clinical progression[3]. The aim of this study was therefore to describe the efficacy and durability of fostemsavir (FTR), ibalizumab (IBA) or lenacapavir (LEN) containing regimens in people living with 4-drug class resistant HIV (4DR-PLWH) in a real-life setting.

STUDY DESIGN AND METHODS

We included 4DR-PLWH from the PRESTIGIO registry (NCT04098315) treated with a regimen containing FTR, IBA or LEN and with documented resistance to NRTIs, NNRTIs, PIs or INSTIs. FTR, IBA or LEN discontinuation was defined as interruption of the drug for any reason. Follow-up (FU) started from the date of initiation of FTR, LEN or IBA (baseline; BL) until discontinuation of FTR, IBA, or LEN or death/freezing date (30 June 2023).

Descriptions are reported as median (IQR) or frequency (%). The genotypic susceptibility score for the optimized background therapy introduced with FTR, LEN, or IBA was estimated according to the cumulative data of the available plasma genotyping resistance tests recorded for each patient.

RESULTS

Among 35 4DR-PLWH, we considered 27, 11 and 10 FTR-, IBA- and LEN-including regimens, respectively (Table 1).

FTR-including regimens: at the end of FU [median duration 18.7 (5.6-82.7) months], virological efficacy (VE; HIV-RNA <200 copies/mL) was 66.7% (18/27); 8/27 (29.6%) regimens had been discontinued. Among those still in a FTR-including regimen, the median change in CD4+ was +97 (-38/+182) cells/mm^3 (p=0.064).

IBA-including regimens: median FU 14.1 (5.6 -39.1) months, VE was 63.6% (7/11); 4/11 (36%) regimens had been discontinued. Median CD4+ change, in those still on treatment with IBA, was +63 (-38/+122) cells/mm^3 (p=0.109).

LEN including regimens: median FU 30.3 (18.7-33.5) months, VE was 90% (9/10); 2/10 (20%) regimens had been discontinued. Median CD4+ change was +5 (-48/+101) cells/mm^3 (p=0.742).

Regimens including a concomitant administration of FTR, IBA or LEN (n=4) are described in Table 2.

CONCLUSIONS

- In 4DR-PLWH, the overall efficacy and durability of FTR, IBA or LEN-including regimens were good.
- Efficacy and safety data on combination regimens including entry and capsid inhibitors are urgently needed in this fragile population.

Table 1: Characteristics of PWH at baseline (Panel A) and at the end of follow-up (Panel B).

Panel A

Characteristic	Category	FTR-including regimens (n=27)	IBA-including regimens (n=11)	LEN-including regimens (n=10)
Age (years) at baseline		54.3 (47.6 - 58.6)	55.1 (31.7 - 58.2)	52.1 (45.4 – 65.3)
Years of HIV infection at baseline		26.6 (21.4 - 33.1)	28.8 (25.9 - 33.3)	28.8 (22.8 - 30.7)
Years of ART at baseline		23.2 (19.2 - 25.9)	26.5 (23.9 - 31.6)	25.4 (22.6 – 28.7)
Viral Subtype				
	B	21 (78.3%)	8 (72.7%)	8 (80%)
	Non-B	6 (21.7%)	3 (27.2%)	2 (20%)
R5 tropism at baseline		11 (41%)	5 (45%)	4 (40%)
Nadir CD4+ (cells/mm^3)		144.5 (29 - 204)	29 (5 - 137)	40.5 (3 - 137)
Baseline HIV-RNA (log_{10} copies/mL)		3.86 (2.09 - 4.91)	4.43 (3.47 - 5.06)	3.46 (3.05 - 4.33)
Baseline CD4+ (cells/mm^3)		244 (141 - 641)	167 (9 - 324)	287 (173 - 593)
OBT GSS		1.5 (1 - 2)	1.5 (1 - 2.5)	2 (1 – 2.5)

Panel B

Characteristic	Category	FTR-including regimens (n=27)	IBA-including regimens (n=11)	LEN-including regimens (n=10)
HIV-RNA at last visit (copies/mL)				
	<50	13 (48.2%)	5 (45.5%)	7 (70%)
	≥50 - <200	5 (18.5%)	2 (18.2%)	2 (20%)
	≥200	9 (33.3%)	4 (36.3%)	1(10%)
CD4+ at last visit (cells/mm^3)		328.5 (208 - 616)	131 (105 - 230)	282 (159 - 630)
Change in CD4+ during FU (cells/mm^3)	Among those still on treatment	97 (-38/+182)	63 (-38/122)	5 (-48/+101)
Duration of FTR, IBA or LEN-regimen (months)		18.7 (5.6 - 82.7)	14.1 (5.6 - 39.1)	30.3 (18.7 – 33.5)
Discontinuation of FTR, IBA or LEN-regimen		8 (29.6%)	4 (36.4%)	2 (20%)
Reasons of discontinuation				
	Virological failure	5 (63%)	1(25%)	0
	Toxicities/Other	3 (37%)	3 (75%)	2 (100%)

OBT-GSS: optimized background therapy-genotypic susceptibility score ;FTR: fostemsavir; IBA: ibalizumab; LEN: lenacapavir

Table 2: Regimens including a concomitant administration of fostemsavir (FTR), ibalizumab (IBA) or lenacapavir (LEN)

ID PLWH	New drugs Combination	Optimized backgroung treatment (OBT)	Baseline Cumulative Genotype	Date of start	Date of stop	OBT GSS	BL HIV-RNA (copies/mL)	Last HIV-RNA (copies/mL)	BL CD4+ (cells/µL)	Last CD4+ (cells/µL)	Duration (months)	Discontinuation (reason)
104-002	IBA+LEN	FTC, TAF, DOR, DRV/c, MVC	RT:41L,74V,138A,181CIV,184V,190A,210W,215F,215Y,219E,230L PRO:32I,33F,46I,46L,54A,54L,54T,54V,82F,84V,90M IN: 140S,148H	26 Oct 2020	17 May 2022	1.0	26800	<1	42	159	18.7	Yes, only LEN: patient's decision
108-0021	IBA+FTR+LEN	3TC, TDF, DOR, MVC	RT: 67N,70R,138K, 181C, 184V,190A, 215F,215Y,219Q PRO: 32I,46I,76V,82A,84V IN: 138T,140S,143C,148H	18 Jan 2021	ongoing	1.5	2982	52	734	721	28.7	No
120-001	IBA+FTR	FTC, TAF, DRV/r, DTG, MVC	RT:67N,70R,181CI, 184V,190A, 219Q PRO:47V,50V,54V IN:140S,148H	22 Dec 2022	ongoing	2.5	396	23	324	286	5.6	No
134-005	IBA+FTR+LEN	FTC, TAF, DRV/r, DTG	RT:41L,74V,103N,181C, 184V,215Y PRO:33F,84V,90M IN:138K,140S,148H	12 Sep 2022	ongoing	1.0	2400	20	296	230	8.9	No

GSS: susceptibility score; RT: reverse transcriptase; PRO: protease; IN: integrase

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