19-21 GIUGNO ROMA
UNIVERSITA' CATTOLICA DEL SACRO CUORE CENTRO CONGRESSI EUROPA
RESEARCH and CARE: FROM BENCH, TO BEDSIDE, TO COMMUNITY
Promosso da SIMIT
16° CONGRESSO NAZIONALE ICAR Italian Conference on AIDS and Antiviral Research
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POSTER 4 YOU ICAR 2024

Long-Acting injectable regimen with cabotegravir + rilpivirine in people living with HIV: real-life experience from Modena HIV

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Introduction

Long-acting injectable (LAI) regimen with cabotegravir (CAB) and rilpivirine (RPV) has been recently approved as switch strategy for virologically suppressed people living with HIV (PLWH). The aim was to describe safety and efficacy of LAI regimen in a real-life context in PLWH followed at Modena HIV Clinic.

Methods

Retrospective descriptive cohort study including PLWH switched to LAI CAB/RPV from January 2023 to February 2024. Demographic, clinical and HIV and HBV-related characteristics were collected. Data on treatment satisfaction, discontinuation reasons and side effects were gathered. Virological failure (VF) was defined as 2 consecutive HIV-RNA>20 copies/ml or a single HIV-RNA>200copies/ml. Virological suppression (VS) was defined as HIV-RNA<20 copies/ml. Individuals were compared according to regimen discontinuation using univariate analysis.

Results

Seventy-four PLWH were included with a median follow-up of 322 days (IQR 210-379): 62%males, 53 years (IQR 44-59), BMI 24 Kg/m2 (IQR 22-27), HIV duration 14 years (IQR 7-22). Six individuals had HIV-RNA>20copies/ml at switch (median 27 copies/ml, IQR 21-78), of whom 3 gained VS at follow-up; twenty-three (31%) individuals used oral lead-in. Twenty-two (30%) had positive HBcAb titre at switch: among these 4(15%) presented non-protective (<10U/ml) or negative HBsAb titre and 7(30%) switched from Tenofovir-based regimen; none of them had detectable HBV-DNA at baseline and follow-up.

More than a half (62%) of the individuals reported side effects, injection-site pain was the most represented (38 subjects, 53%).

One individual moved to another clinic, ten (13,5%) individuals discontinued LAI (median time to discontinuation [MTD] 84 days, IQR 28-196): 5(50%) because of side effects [MTD 185 days (IQR 84-196)], one had pre-existing mutations for NNRTI at genotypic resistance test (GRT) on lymphocytes (K103N, A98G, P225H; previous exposure to EFV without history of VF), 3 (30%) for patient-related logistic reasons.

One individual experienced severe and prolonged injection pain after the first administration, leading to discontinuation, and contemporary VF (HIV-RNA 4230 copies/ml) at 4 weeks. He was immediately switched to the previous oral regimen (DTG /RPV+MVC – to notice he never stopped concurrent MVC therapy) and gained VS in 2 months. The GRT performed a posteriori on plasma revealed the emergence of RAMs 181I and 190A for NNRTI and G140S and Q148H for INSTI, thus treatment was modified to DRV/c+DTG+MVC, with stable VS.

CA, men, 56 yo
Duration HIV 30 years
1ST administration LAI 16/02/2023

	WBC	HB	Plt	Linfo	CD4+ tot	CD4/CD8	HIV-VL
13/09/2023	5940	13.9	289	2520	630	0.65	20
22/06/2023	5860	13.6	299	2590	611	0.52	-1
15/03/2023							4230
19/01/2023	5860	14.7	291	2680	657	0.33	-1
18/07/2022	5390	13.9	288	2410	612	0.43	-1

From	To			
19/07/2023		DRV/C	DTG	MVC
15/03/2023	19/07/2023	DTG/RPV	MVC	
23/01/2020	15/02/2023	DTG/RPV	MVC	
29/06/2015	23/01/2020	DTG	MVC	RPV
13/11/2011	29/06/2015	DRV/R	MVC	RAL
15/02/2023	15/03/2023	CAB_LA	RPV_LA	

Data	22/06/2023	15/03/2023	04/06/2023
RT	Linfociti DNA	RNA Plasma	Linfociti DNA
SUB	B	B	B
ESITO RT	65Rw 70Rw 75Iw 77Lw 103Nw 108Iw 116Yw 138Aw 184Vw 225Hw	62Vw 65Rw 70R 75I 77L 108I 116Y 151M 181I 190A	138A
RT minori	6Dw 7Pw 20R 68Gw 123Nw 135Tw 142Vw 151Kw 151Rw 196Ew	6D 7P 20R 68G 69Nw 135M 196E 228H 245E	20Rw 35Iw 135Mw 135Tw 142Vw 245K
RT resistenza	Elevata: 3TC ABC D4T DDI FTC TDF TAF EFV NVP. Consistente: AZT DOR. Parziale: RPV. Trascurabile: ETR. Nessuna:	Elevata: 3TC ABC AZT D4T DDI FTC TDF TAF EFV ETR NVP RPV. Consistente: DOR. Parziale: . Trascurabile: . Nessuna:	Elevata: . Consistente: . Parziale: . Trascurabile: . Nessuna: 3TC ABC AZT D4T DDI FTC TDF EFV ETR NVP RPV
ESITO PRO	10Fw	73S 90M	10Fw 13V 35D 60E 63P 77Iw
PRO minori	12Pw 13V 19Iw 19Pw 19Tw 35Dw 60E 63P	10I 12P 13V 19V 35D 36I 60E 62V 63P 71V	12Pw 57Kw
PRO resistenza	Elevata: . Consistente: . Parziale: FPV/rtv NFV. Trascurabile: IDV/rtv. Nessuna: ATV/rtv DRV/rtv LPV/rtv SQV/rtv TPV/rtv	Elevata: NFV SQV/rtv. Consistente: ATV/rtv FPV/rtv IDV/rtv. Parziale: LPV/rtv. Trascurabile: . Nessuna: DRV/rtv TPV/rtv	Elevata: . Consistente: . Parziale: . Trascurabile: . Nessuna: ATV ATV/rtv DRV/rtv FPV/rtv IDV/rtv LPV/rtv NFV SQV/rtv TPV/rtv
ESITO INI	None	G140S, Q148H	None
INI minori	E11D,L28I,V31I,V32I,V37I,S39C,L101I,S119G,T124N,V201I,T218S,D253E	E11D,L28I,V31VI,V32I,V37I,S39C,L101I,T122I,T124N,V201I,T218S,D253E	D6DE, E11D, L28IM, V31IV, V32I, V37I, S39C, G47GR, G70GR, L101I, S119GS, T122IT, T124N, V201I, T218S, D253E
INI resistenza	Susceptible: BIC, CAB, DTG, EVG, RAL	High-level resistance: CAB, EVG, RAL. Intermediate: BIC, DTG	Susceptible: DTG, EVG, RAL
V3 FPR	50.6 CCR5	0	58.9 CCR5

In another subject, an HIV-RNA at 8 months after switch to LAI was 7975 copies/ml: he was switched to DRV/c/FTC/TAF rescue therapy (ongoing further HIV-RNA); at the GRT on plasma mutations 138K for NNRTI and Q148R for INSTI. He did not report any side effect neither presented previous failure risk factors.

CD, men, 48 yo
Duration HIV 22 years
1ST administration LAI 13/04/2023

	WBC	HB	Plt	Linfo	CD4+ tot	CD4/CD8	HIV-VL
17/01/2024							277
21/12/2023	7890	15.7	223	3670	1237	0.69	7975
11/05/2023	8680	15.4	234	3640	1318	1.72	-1
22/12/2022	7770	14.7	211	2570	992	1.90	20

From	To			
17/01/2024		DRV/c/FTC/TAF		
13/04/2023	17/01/2024	CAB_LA	RPV_LA	
16/03/2023	13/04/2023	CAB	RPV	
09/07/2019	16/03/2023	3TC	DRV/C	
09/12/2015	09/07/2019	3TC	DRV	RTV
16/09/2015	09/12/2015	3TC	DTG	
28/11/2011	16/09/2015	ABC/3TC	NEV	
17/09/2007	28/11/2011	FTC	NEV	TDF

Data	17/01/2024	21/12/2023	06/07/2023
RT	RNA plasma	RNA plasma	Linfociti DNA
SUB	B	B	B
ESITO RT	138K	138K	Nessuna mutazione significativa
RT minori	123E 135M 178M 179I 207A 211K 246Pw	123E 135M 178M 179I 207A 211K	35I 123E 135M 177Ew 178M 211K
RT resistenza	Resistenza prevista - Elevata: . Consistente: RPV. Parziale: . Trascurabile: EFV ETR NVP. Nessuna: 3TC ABC AZT D4T DDI FTC TDF TAF DOR	Resistenza prevista - Elevata: . Consistente: RPV. Parziale: . Trascurabile: EFV ETR NVP. Nessuna: 3TC ABC AZT D4T DDI FTC TDF TAF DOR	Resistenza prevista - Elevata: . Consistente: . Parziale: . Trascurabile: . Nessuna: 3TC ABC AZT D4T DDI FTC TDF TAF EFV ETR NVP RPV DOR
ESITO PRO	Nessuna mutazione significativa	Nessuna mutazione significativa	Nessuna mutazione significativa
PRO minori	10V 15V 35D 60E 63P 69N	10V 15V 35D 60E 63P 69N	10V 14Rw 15V 35D 37Dw 41Kw 62Vw 63P 69N 77Iw
PRO resistenza	Resistenza prevista - Elevata: . Consistente: . Parziale: . Trascurabile: . Nessuna: ATV/rtv DRV/rtv FPV/rtv IDV/rtv LPV/rtv NFV SQV/rtv TPV/rtv	Resistenza prevista - Elevata: . Consistente: . Parziale: . Trascurabile: . Nessuna: ATV/rtv DRV/rtv FPV/rtv IDV/rtv LPV/rtv NFV SQV/rtv TPV/rtv	Resistenza prevista - Elevata: . Consistente: . Parziale: . Trascurabile: . Nessuna: ATV/rtv DRV/rtv FPV/rtv IDV/rtv LPV/rtv NFV SQV/rtv TPV/rtv
ESITO INI	Q148R	Q148R	None
INI miniri	E10D,A21S,A23V,L45V,E96K,M154I,V165I,V201I,L234V	E10D,A21S,A23V,L45V,M154I,V165I,V201I,L234V	E10ED,S17SN,A21S,A23V,S119ST,M154I,V165I,V201I,L234V,S283SG
INI RESISTENZA	High-level resistance: EVG, RAL . Intermediate: CAB . Low-level: BIC, DTG	High-level resistance: EVG, RAL . Intermediate: CAB . Low-level: BIC, DTG	Susceptible BIC, CAB, DTG, EVG, RAL

Conclusion

LAI CAB/RPV regimen was safe and effective in our population. Side effects were present and led to treatment interruption in 10 cases, with prevalence similar to literature (6.5%). None of the individuals with VF had baseline known risk factors for LAI CAB+RPV failure. In the first case, the significant pain side effect could reflect incorrect injection procedure, leading presumably to inadequate drug concentration (although therapeutic drug monitoring -TDM- was not performed). Thus, we highlight the importance of correct injection administration, fundamental to maintain adequate drug concentration and reduce VF risk. Further studies could help understanding more failure mechanisms.