P080

Prevalence of virological failure and resistance patterns to Long-Acting Cabotegravir-Rilpivirine: A real life single center cohort study

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Background

There is scarce information about virological failures (VF) and resistance selection after the VF to LA-CAB/RPV. Our objective is to perform an in-depth analysis of subjects who presented a VF in a real-world setting in the 28 weeks of follow-up.

Material and Methods

Individuals starting LA-CAB/RIL at Hospital Clínic Barcelona were invited to participate in an observational, prospective single-center study. We performed an in-depth clinical and virological analysis in cases with VF (2 consecutive VL > 50 cp/mL) during LA-CAB/RPV therapy in subjects who reached week 28 . Genotypic resistance testing GRT)by Ultra Deep Sequencing (UDS) of RNA and/or DNA was conducted post-VF.

Results

Baseline characteristics

From 2Feb2023 to 2May2024, 554 people with HIV started LA-CAB/RPV (9% of total cohort), and 533 accepted to participate, 92% male. Of these, 318 (60%) reached week 28. Baseline characteristics of the 318 participants who reached w28 are shown in Table1 and Table 2. Eight (3%) participants underwent an oral lead-in (OLI) phase, 96% of injections were administered within the window period, and 2% of administrations were delayed (see more details on adherence on poster P075)

Efficacy and virological failures

- By OT, mITT and ITT, effectiveness was 98%, 92%, and 91% at W28. (see more details on efficacy on poster P075)
- Four subjects (1.25%) presented virological failure
- All were male; 3 had BMI < 30; all but one had HIV-1 subtype B (see baseline characteristics on Table 3)
- Sequence was obtained at the time of failure by UDS on peripheral blood mononuclear cell (PBMC) in 3 subjects (see Table 4)
- Two individuals achieved VL < 50 cp/mL without ART switch, and two did so after switching the ART
- Most of PBMC drug resistance mutations (DRMs) detected after VF (see Table 4) DRMs resulting from APOBEC-mediated G-to-A hypermutation

Table 1. Baseline characteristics of participants who reach week 28 (n 318)

Age, median (IQR)	45 (37 - 54)
Sex, male, n (%)	293 (92%)
Origin, n (%)	
Spanish	142 (45%)
Other European countries	43 (14%)
Latin America	104 (33%)
Other	29 (9%)
Mode of HIV acquisition, n (%)	
MSM	258 (82%)
Heterosexual	29 (9%)
IDU	21 (7%)
BMI >30 kg/m^2, n (%)	28 (11%)
Years since diagnostic, median (IQR)	12 (8 - 19)
Undetectable VL (<50cp/mL), n (%)	313 (98%)
Time with VL < 50cp/mL, median years (IQR)	8 (4 - 13)
Last CD4, cells/μL, median (IQR)	724 (563 - 938)
Nadir CD4, cells/μL, median (IQR)	335 (214 - 452)
Historic genotype available, n (%)	166 (52%)
Any non polymorphic mutation present	33 (10%)
Subtype A	4 (1%)
Years in ART, median (IQR)	9 (4 - 15)

IQR: interquartile range; MSM: men who have sex with men; IDU: injection drug user; VL: viral load.

Table 2. Previous ART

Number of previous ART	1	60 (19%)
	2-5	183 (58%)
	6-10	59 (19%)
	>10	9 (3%)
ART combination	PI based	24 (8%)
	DRVc/FTC/TAF	19 (6%)
	NNRTI based	41 (13%)
	RIL/FTC/TAF	18 (6%)
	EFV/FTC/TDF	6 (2%)
	DOR+FTC/TAF	6 (2%)
	INSTI based	206 (66%)
	BIC/FTC/TAF	90 (29%)
	DTG/3TC	64 (21%)
	EVG/FTC/TAF	22 (7%)
	Other combinations	40 (13%)
	DTG/RPV	35 (11%)

Table 3. Virological Failures (baseline characteristics and adherence)

ID	Age (Y) and sex	HIV-1 subtype	Previous genotype	Previous failures	Prior mutations	BMI	Needle	Prior ART	Baseline VL	Adherence
37	50 M	B	yes	no	no	27	23G	ABC/3TC/DTG	154	ok
142	41 M	B	no	LLV (DTG/RIL)	no	24	23G	DTG/RPV	88	ok
297	32 M	unk	no	no/ unk	no	24	23G	B/F/TAF	<50	2w delay
309	63 M	B	yes	no	no	46	21G	B/F/TAF	<50	ok

Footnote: Y: years; M: Male; BMI: body mass index;, LLV: low level viremia (>50 and < 2000 copiwes/mL); unk: unknown; G: gauge; w: week; ABC: abacavir; 3TC: lamivudine; DTG: dolutegravir; RPV: rilpivirine; B: bictegravir; F: emtricitabine; TAF: tenofovir alafenamide

Table 4. Virological Failures (results of UDS-PBMC-GRT)

ID	1st VL at VF	2nd VL at VF	Week	ART change	New ART	Drug Resistance Mutations	
37	154	137	BL	yes	DRVc/FTC/TAF	RT: 138K (20%)*, 184I (57%)*, 230I (60%) * IN: 74I (98%), 163R (4%)* PRT: 30N (6%)*, 46I (5%)*	UDS-PBMC GRT
142	88	89	BL	yes	DRVc/FTC/TAF	RT: 138K (10%)*, 184I (19%)*, 230I (21%) * IN: 140S (8%)* PRT: 90M (97%-92%)	UDS-PBMC GRT
297	210	53	12	no	-		
309	53	59	12	no	-	RT: 190E (22%) * IN: NA since 260 position	UDS-PBMC GRT

*List of APOBEC induced mutations : D30N, M46I, G48S, and G73S in PR; D67N, E138K, M184I, G190ES, and M230I in RT; and G118R, E138K, G140RS, G163KR, D232N, and R263K in IN. Chu, C., et al. (2022). Clin Microbiol Rev

Footnote: FTC: emtricitabine; TAF: tenofovir alafenamide; DRV/c: darunavir/cobicistat; UDS-PBMC-GRT: genotypic resistance test by ultra deep sequencing in peripheral blood mononuclear cell

Conclusions

In our series, at week 28 the rate of VF (2 consecutive VL > 50 cp/mL) was low (1,25%), all of them were with low level viremias (<200 copies/mL) and the resistance mutations detected in PBMC may reflect APOBEC activity and should be carefully interpreted by a resistance specialist.