P086

DISCONTINUATION OF RILPIVIRINE AND CABOTEGRAVIR IN HIV-1 VIROLOGICALLY SUPPRESSED ADULTS: A MULTICENTER OBSERVATIONAL STUDY IN TUSCANY (LAHIV STUDY)

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Background: Cabotegravir (CAB) + rilpivirine (RPV), available in Italy from June 2022, dosed intramuscularly every 2 months, is the first long-acting (LA) regimen used to maintain HIV-1 virological suppression. We evaluated the durability of this regimen.

Materials and Methods: This multicenter observational study enrolled virologically suppressed adults living with HIV (HIV-RNA <50 cp/mL) from 10 Tuscan units who initiated CAB+RPV. Participants were monitored from their first injection until regimen discontinuation, death, or last visit. Discontinuation criteria included regimen switch or two consecutive missed injections. Virological failure (VF) was defined as two consecutive HIV-RNA >50 copies/mL detections or >1000 copies/mL followed by ART modification. Statistical analyses included chi-square, non-parametric tests for categorical and continuous variables, and Kaplan-Meier survival analysis for discontinuation probability estimation

Results The cohort included 129 PLWH and a combined at-risk period of 75.5 years, with a median follow-up of 28 weeks (interquartile range [IQR] 12-48). Most participants (81.4%) were male, with a median age of 51 years (IQR 42-57), and a median ART duration of 13 years (IQR 8-20). Participants discontinuing LA showed no clinical/demographic differences from those continuing, except a shorter time from the last detectable HIV-RNA and CAB+RPV introduction (0.6 [IQR 0.2-4] vs. 5 years [IQR 1-9] p=0.012) (Table 2). Ten participants discontinued CAB+RPV: 6 (4.6%) due to adverse events, 1 by patient choice, 2 (1.5%) due to VF (Table 1) and 1 lost to follow-up. Notably, one participant experiencing VF had pre-existing high-level mutations for RPV, but no mutations for CAB, and viral suppression was restored with T/F/DRVc (Table 1). The overall discontinuation rate was 13.2 per 100 person-years (95% CI 7.1-24.5), higher than reported in randomized controlled trials (RCTs), possibly due to our shorter follow-up (Figure1).

Table 1. Reasons for discontinuation of a population of adults with HIV-1, ART experienced with HIV-RNA level <50 copies/mL switching to RPV+CAB in 10 out 11 infectious diseases units in Tuscany, Italy.

Previous regimen	viremia (>50 cp/mL) less than six months ago	Subtype	BMI at BL	OLI	NNRTI or INSTI mutations on the last genotype	Cause of discontinuation	Week	Post-regimen
3TC/DTG	No	N/A	N/A	No	N/A	High fever with widespread joint pain and gluteal pain. Walking impairment	4	3TC/DTG
RPV/DTG	Yes	B	N/A	No	Not detected	Rash	28	RPV/DTG
3TC/DTG	Yes	B	29.5		98G 106I 108I 181V	Virological Failure (4930 cp/mL)	4	T/F/DRVc
RPV/DTG	Yes	N/A	20.2	No	N/A	General malaise	4	RPV/DTG
3TC/DTG	No	N/A	25.3	No	N/A	Depression	4	3TC/DTG
RPV/DTG	Yes	N/A	22	No	N/A	Lost-to follow-up	12	//
T/F/RPV	Yes	N/A	23	No	Not detected	Panic attacks	12	T/F/RPV
T/F/RPV	No	N/A	23.4	No	N/A	Excessive clinic visits, local reaction	28	T/F/RPV
T/F/DOR	No	N/A	26.6	No	Not Detected	Virological Failure (2 consecutive determinations >50 but < 200 cp/mL)	28	3TC/DTG
3TC/DTG	No		21	No	N/A	Weight gain of 10kg, worsening of depressive symptoms, insomnia, asthenia.	44	3TC/DTG

NNRTI: non-nucleoside reverse transcriptase inhibitors; INSTI: integrase strand transfer inhibitor:DTG: Dolutegravi: RPV: Rilpivirine; 3TC: Lamivudine; FTC: emtricitabine; T: TAF: F: Emtricitabine: OLI: oral lead-in: BMI: Body Mass Index: N/A: Not Available; BL Baseline

Figure 1. Probability of remaining free from treatment discontinuation for all causes in adults with HIV-1 ART experienced with HIV-RNA level <50 copies/mL switching to RPV+CAB in 10 out 11 infectious diseases units in Tuscany, Italy.

Number of patients stratified by end-of-follow-up week, n (%) (n=129)				
	On CAB+RPV (n=119)	Discontinued (n=10)	Tot (n=129)	(%)
• **4 weeks**	14	4	18	13.9
• **12 weeks**	39	2	41	31.8
• **28 weeks**	13	3	16	12.4
• **44 weeks**	53	1	54	41.9

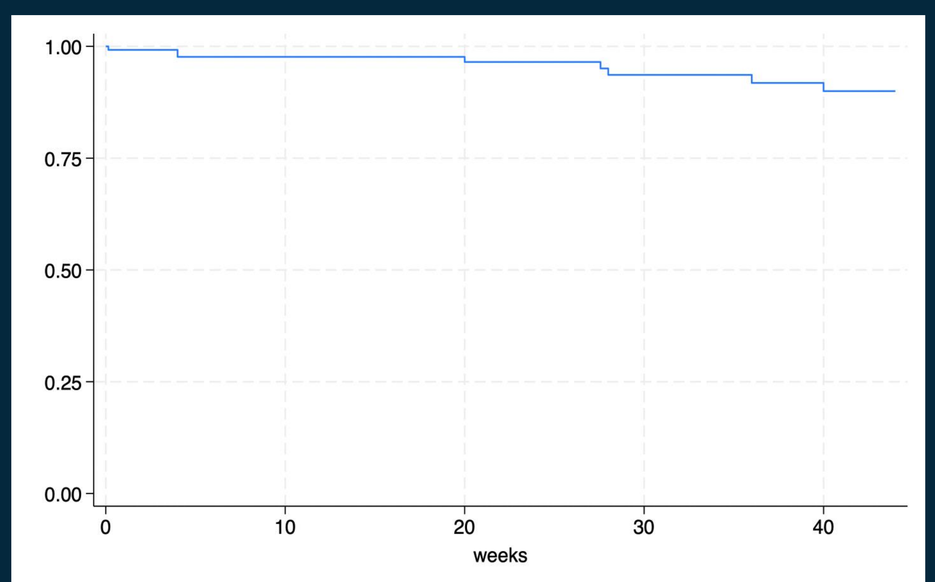

Table 2. Clinical/demographic characteristics of adults with HIV-1, ART experienced with HIV-RNA level <50 copies/mL switching to RPV+CAB in 10 out 11 infectious diseases units in Tuscany, Italy.

	On CAB+RPV (n=119)		Discontinued (n=10)		P value	TOTAL (n=129)	
Born in Italy, n (%)	104	87.3	10	100	0.232	114	88.3
Gender, n (%)					-		
• Female Cis	19	15.9	4	40.0		23	17.8
• Male Cis	99	83.2	6	60.0		105	81.4
• Female Transgender	1	0.8	0	-		1	0.8
Age in years at entry, median [IQR]	51	[42-57]	53	[49-58]	0.489	51	[42-57]
Route of HIV transmission, n (%)					-		
• Heterosexual unprotected sex	32	26.8	4	40.0		36	27.9
• MSM unprotected sex	59	49.6	6	60.0		65	50.3
• Intravenous drug users	10	8.4	0	-		10	7.7
• **Other/ Not known**	18	15.1	0	-		18	13.9
Years of undetectable viremia, median [IQR]	5	[1-9]	0.6	[0.2-4]	0.012	5	[1-10]
AIDS diagnosis, n (%)	18	15.1	1	10	0.660	19	14.7
HBc Ab, n (%)	29	24.3	1	10	0.242	39	30.2
HIV-RNA Zenit, Log_{10} copies/mL, median [IQR]]	4.8	[4.4-5.5]	5.0	[4.8-5.4]	0.460	4.9	[4.4-5.5]
Nadir CD4 (cells/mL), median [IQR]	326	[156-456]	240	[106-283]	0.230	308	[147-435]
Years of HIV, median [IQR]	12	[4-20]	17	[9-23]	0.420	13	[8-20]
CD4+ T cells at baseline/µL, median [IQR]	860	[640-1072]	786	[652-979]	0.637	850	[648-1061]
CD4/CD8 cells at baseline/µL, median [IQR]	1.0	[0.8-1.5]	1	[0.7-1.3]	0.587	1.0	[0.8-1.4]
Type of pre-switch regimen					-		
• NNRTI	50	42.0	6	60.0		56	43.4
• PI	13	10.9	-	-		13	10.0
• INSTI	85	71.4	7	70.0		92	71.3
Number of previous ART regimens, median [IQR]	4	[2-5]	4	[3-6]	0.239	4	[2-5]
Oral lead in, n (%)	23	19.3	0	-	-	23	17.8
Pre-switch regimen containing rilpivirine	46	38.7	5	50.0	0.481	51	39.5
Pre-switch regimen containing dolutegravir	56	47.1	7	70.0	0.163	63	48.8

ART: antiretroviral treatment; MSM: males who have sex with males; PI: Protease inhibitor; NNRTI: non-nucleoside reverse transcriptase inhibitors; INSTI: integrase strand transfer inhibitor

Conclusions: Early findings indicate that CAB + RPV appears to be a well-tolerated regimen. However, the overall discontinuation of CAB + RPV in real life seems to be slightly higher than those reported in trials. Discontinuation due to virological failure remains a rare event

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