High Virologic Suppression and few Virologic Failures with Long-Acting Cabotegravir + Rilpivirine in Treatment Experienced Virologically Suppressed Individuals from COMBINE-2 cohort in Europe

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Background

- Cabotegravir (CAB) + rilpivirine (RPV) is the first and only complete long-acting (LA) regimen indicated for virologically suppressed (viral load (VL) <50 copies /mL) people with HIV (PWH) on stable antiretroviral regimen without viral resistance to, and no prior virological failure with NNRTI and INI class.

- The study assessed clinical outcomes among individuals initiating CAB+RPV LA regimen in real-world settings in Europe.

Methods

- Treatment experienced, virologically suppressed PWH with no history of resistance or virological failure with NNRTI and INSTI classes initiating CAB+RPV LA at NEAT-ID Network sites across seven European countries between December 2020 and May 2024 were included.

- VLs were assessed from first injection until discontinuation or time of analysis.

- Confirmed virologic failure (CVF; 2 VL ≥200 copies/mL or 1 VL ≥200 copies/mL + discontinuation) was assessed among those with follow-up VL.

Results

- All 956 individuals initiating CAB+RPV LA were treatment experienced, had VL <50 copies/mL at initiation, no previous virologic failure or history of NNRTI or INSTI mutations among those with history available (62%).

- Median age was 45 years (IQR: 37-53), 85% males and 10% with BMI ≥30 kg/m^2 at initiation.

- 919 individuals (96%) had on-time injections with 25 individuals (3%) having delayed doses and 7 individuals (1%) with missed injections.

- At time of analysis, 882 individuals (92%) remained on CAB+RPV LA regimen with median follow-up of 10.2 months (IQR: 7.1, 16.6).

- A total of 74 individuals (8%) discontinued the CAB+RPV LA regimen.
  - 48 individuals (65%) continue to be followed within the study.
  - The rest of the 26 individuals (35%) were not followed and have either moved, decided to leave the study, were lost to follow-up, regimen stopped by physician or withdrawn consent

- Among 937 individuals with follow-up VLs, 925 (99%) had last measured VL <50 copies/mL.

- Of those with 6, 12, and 24-month VLs, 97%, 96% and 94%, respectively had follow-up VLs <50 copies/mL.

- Virologic control was similar regardless of BMI at initiation (last VL <50 copies/mL 99% vs. 99% and all VL <50 copies/mL 94% vs. 97% among BMI <30 kg/m^2 and ≥30 kg/m^2 respectively).

- Five individuals (0.5%) had CVF after initiation of CAB+RPV LA with history of resistance data unavailable.

Conclusions

- This real-world data on PWH virologically suppressed at initiation on CAB+RPV LA in Europe demonstrated high levels of virologic control with low CVF.

- These data demonstrate high levels of adherence and persistence to the regimen.

- Among few with CVF, suppression was achieved after switching to PI or INI-based regimen.

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Table 1: Baseline Demographic and Clinical Characteristics of individuals initiating CAB+RPV LA regimen

	Overall (N=956)
Age (in years), n (%)	
18-29	59 (6)
30-49	551 (58)
50+	346 (36)
Median (IQR)	45 (37-53)
Sex, n (%)	
Female	141 (15)
Male	815 (85)
Race/Ethnicity, n (%)	
White caucasian	612 (64)
Black	104 (11)
White mixed	69 (7)
Asian	11 (1)
Other	160 (17)
Route of HIV infection, n (%)	
MSM	606 (63)
Heterosexual	169 (18)
Other	94 (10)
Unknown	87 (9)
Participating country, n (%)	
Spain	511 (54)
France	230 (24)
Germany	78 (8)
Belgium	53 (6)
Switzerland	39 (4)
Netherlands	32 (3)
UK	13 (1)
Body mass index (BMI, kg/m^2)	
<30	734 (77)
30-34.9	77 (8)
35-39.9	11 (1)
≥40	6 (1)
Unknown	128 (13)
Median (IQR)	24.9 (22.8-27.5)
Oral-lead in use, n (%)	301 (32)
Viral Load at initiation (copies/mL), n (%)	
<50	956 (100)
≥50	0 (0)
Median (IQR)	20 (20-49)
CD4 Cell Count at initiation (cells/µL), n (%)	
<350	49 (5)
≥350 to <500	117 (12)
≥500	789 (83)
Unknown	1 (0.1)
Median (IQR)	726 (555-921)
CD4 nadir Cell Count (cells/µL), Median (IQR)	346 (221-499)
Number of years since HIV diagnosis, Median (IQR)	10.9 (6.8-17.1)
Number of years since ART initiation, Median (IQR)	9.4 (6.0-14.2)
HIV subtype, n (%)	
B	338 (35.4)
CRF02	43 (4.5)
A	8 (0.8)
A1	13 (1.4)
A2	25 (2.6)
A3	1 (0.1)
A6	1 (0.1)
Other non-B	103 (10.8)
Unknown	424 (44.4)
History of resistance testing available, n (%)	594 (62)
History of previous use of INSTI or NNRTI-based regimen, n (%)	916 (96)
Prior ARV regimen received before CAB+RPV LA, n (%)	
Bictegravir/Emtricitabine/Tenofovir alafenamide	207 (22)
Dolutegravir/Lamivudine	172 (18)
Dolutegravir/Rilpivirine	89 (9)
Rilpivirine/Emtricitabine/Tenofovir alafenamide	79 (8)
Cabotegravir/Rilpivirine LA prior clinical trial	77 (8)
Other	332 (35)
History of AIDS defining events, n (%)	76 (8)
Comorbidities, n (%)	144 (15)
HCV co-infection	87 (9)
HBV co-infection	31 (3)
NADM	17 (2)
CVD	13 (1)
CKD	9 (1)
ESLD	0 (0)

HCV, Hepatitis C virus; HBV, Hepatitis B virus; NADM, Non-AIDS Defining Malignancy; CVD, Cardiovascular disease; CKD, Chronic kidney disease; ESLD, End-stage liver disease

Table 2. Virologic outcomes among individuals initiating CAB+RPV LA regimen

		Overall (N=956)
Duration of follow-up	**Median months (IQR)**	10.2 (7.1, 16.6)
On CAB+RPV LA at end of follow-up	**n (%)**	882 (92)
≥1 VL after first injection	**n (%)**	937 (98)
	Last VL <50 copies/mL, n (%)	925/937 (99)
	All VLs <50 copies/mL, n (%)	880/937 (94)
	VL <50 copies/mL at month 6, n (%)	841/871 (97)
	VL <50 copies/mL at month 12, n (%)	350/366 (96)
	VL <50 copies/mL at month 24, n (%)	46/49 (94)
Confirmed virologic failure	**n (%)**	5/937 (0.5)

Resistance Narratives

- The first individual had CVF 35 days after initiation of CAB+RPV LA. This individual was male, had HIV sub-type B and BMI was 25.3 kg/m^2. They received the LA injections twice as scheduled, one month apart, with no missed or delayed injections. Baseline resistance information was not available. Resistance mutations using Stanford algorithm at failure included NNRTI mutation (V179I), low-level resistance to rilpivirine (E138A), no INSTI mutations and potential low-level resistance to lopinavir and atazanavir (M46I, M36I, L63P, I64L, V77I, I93L). This participant had two consecutive VLs of ≥ 200 copies/mL, switched to darunavir, cobicistat, emtricitabine and tenofovir alafenamide and follow-up VL after switching was 20 copies/mL.

- The second individual had CVF 96 days after initiation of CAB+RPV LA. This individual was female, had HIV sub-type D and BMI was 23.5 kg/m^2. They received the LA injections three times as scheduled, with no missed or delayed injections. Baseline resistance information was not available. There was no resistance mutations detected at failure. This participant had two consecutive VLs of ≥ 200 copies/mL, switched to abacavir, lamivudine, darunavir and ritonavir and follow-up VL after switching was 109 copies/mL. This individual then switched to bictegravir, emtricitabine and tenofovir alafenamide and follow-up VL after switching was 30 copies/mL. Following that, this individual switched to dolutegravir and lamivudine and follow-up VL after switching continues to stay at 30 copies/mL.

- The third individual had CVF 402 days after initiation of CAB+RPV LA. This individual was male, had HIV sub-type B and BMI was 25.1 kg/m2. They received the LA injections eight times as scheduled, with no missed or delayed injections. Baseline resistance information was not available. There was no resistance mutations detected at failure. This participant had one VL ≥ 200 copies/mL followed by treatment discontinuation within 4 months, switched to darunavir, cobicistat, emtricitabine and tenofovir alafenamide and follow-up VL after switching was 1 copies/mL. This individual then switched to tenofovir disoproxil fumarate, lamivudine and doravirine and follow-up VL after switching was 1 copies/mL.

- The fourth individual, had CVF 120 days after initiation of CAB+RPV LA. This individual was male, had HIV sub-type H and BMI was 29.0 kg/m^2. They received the LA injections three times as scheduled, with no missed or delayed injections. Baseline resistance information was not available. Resistance mutations using Stanford algorithm at failure included NNRTI mutations (K101E, E138G and G190S), INSTI mutations (L74M, Q148R and T97A) and NRTI mutations (D67N, K70R and K219E). This participant had two consecutive VLs of ≥ 200 copies/mL, switched to darunavir, ritonavir, emtricitabine and tenofovir disoproxil fumarate and the most recent follow-up VL after switching was 20 copies/mL.

- The fifth individual, had CVF 582 days after initiation of CAB+RPV LA. This individual was male, had HIV sub-type 01_AE and BMI was unknown. They received the LA injections eleven times as scheduled, with no missed or delayed injections. Baseline resistance information was not available. Resistance mutations using Stanford algorithm at failure included NNRTI mutation (E138K) and INSTI mutation (N155H). This participant had two consecutive VLs of ≥ 200 copies/mL, switched to darunavir, cobicistat, emtricitabine and tenofovir alafenamide and follow-up VL after switching is not available yet.

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