Real-World Utilization and Effectiveness of Long-Acting Cabotegravir + Rilpivirine in Virologically Suppressed Treatment Experienced Individuals in Europe: Data from COMBINE-2 Cohort Study

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Background

- Cabotegravir (CAB) + rilpivirine (RPV) is the first complete long-acting (LA) regimen for treatment experienced virologically suppressed (HIV-1 RNA <50 copies /mL) people living with HIV without present or past evidence of viral resistance to, and no prior virological failure with NNRTI and INSTI class agents.
- This study assessed the utilization and virologic effectiveness among individuals initiating CAB+RPV LA regimen in real-world clinical practice setting in Europe.

Methods

- Adult people living with HIV who were treatment experienced, virologically suppressed, had no history of resistance or virological failure with NNRTI and INSTI classes and received CAB+RPV LA between December 2020 and September 2023 were enrolled at NEAT ID Network sites across seven European countries.
- Viral loads (VLs) were assessed from first injection until CAB+RPV LA discontinuation or at analysis.
- Confirmed virologic failure (CVF) was defined as 2 consecutive VLs ≥200 copies/mL or 1 VL ≥200 copies/mL followed by discontinuation.

Results

- A total of 472 individuals received CAB+RPV LA injection in the study period.
- All individuals were treatment experienced, had VL <50 copies/mL at initiation, had no history of resistance or virological failure with NNRTI and INSTI classes.
- Fifty-three (11%) of individuals were female, 328 (69%) were white Caucasian and median age was 44 years (IQR: 37-53).
- Nine individuals (2%) had a delayed dosing with CAB+RPV LA injection with median delay of 7 days (IQR: 7-8).
- One participant had three missed injections, did not receive oral bridging, continued CAB+RPV LA regimen and remain suppressed with VL <50 copies/mL.
- A total of 19 individuals (4%) discontinued the CAB+RPV LA regimen.
  - Twelve individuals (63%) continue to be followed within the study.
  - Seven individuals (37%) have either moved, individual's decision to discontinue or were lost to follow-up.
- Overall, 453 (96%) individuals remained on CAB+RPV LA over a median follow-up of 3.0 (IQR: 2.8, 7.1) months at the time of analysis.
- Among 374 individuals (79%) with follow-up VLs after first injection:
  - Last VL was <50 copies/mL in 365 (98%)
  - All VLs were <50 copies/mL in 359 (96%)
  - Three individuals (0.8%) had confirmed virologic failure (CVF) after initiation of CAB+RPV LA.

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

	Overall (N=472)
Age (in years), n (%)	
18-29	25 (5)
30-49	284 (60)
50+	163 (35)
Median (IQR)	44 (37-53)
Sex, n (%)	
Female	53 (11)
Male	419 (89)
Race/Ethnicity, n (%)	
White caucasian	328 (69)
White mixed	30 (6)
Asian	10 (2)
Black	25 (5)
Other	79 (17)
Route of HIV infection, n (%)	
MSM	318 (67)
Heterosexual	62 (13)
Other	46 (10)
Unknown	46 (10)
Participating country, n (%)	
Spain	280 (59)
France	58 (12)
Germany	43 (9)
Switzerland	39 (8)
Netherlands	32 (7)
Belgium	14 (3)
UK	6 (1)
Italy	0 (0)
Oral-lead in use, n (%)	150 (32)
Viral Load at initiation (copies/mL), n (%)	
<50	472 (100)
≥50	0 (0)
Median (IQR)	20 (20-49)
CD4 Cell Count at initiation (cells/µL), n (%)	
<350	15 (3)
≥350 to <500	53 (11)
≥500	404 (86)
Median (IQR)	722 (571-920)
CD4 nadir Cell Count (cells/µL), Median (IQR)	354 (230-498)
Number of years since HIV diagnosis, Median (IQR)	10.8 (6.6-16.9)
Number of years since ART initiation, Median (IQR)	9.1 (6.0-13.9)
Body mass index (BMI, kg/m²), Median (IQR)	24.7 (22.7-27.3)
HIV subtype, n (%)	
B	170 (36)
CRF02	9 (2)
A	3 (0.6)
A1	6 (1)
A2	19 (4)
A3	1 (0.2)
A6	0 (0)
Other non-B	39 (8)
Unknown	225 (48)
History of resistance testing available, n (%)	285 (60)
History of previous use of INSTI or NNRTI-based regimen, n (%)	252 (53)
Prior ARV regimen received before CAB+RPV LA, n (%)	
Bictegravir/Emtricitabine/Tenofovir alafenamide	107 (23)
Dolutegravir/Lamivudine	94 (20)
Rilpivirine/Emtricitabine/Tenofovir alafenamide	37 (8)
Cabotegravir/Rilpivirine LA prior clinical trial	36 (8)
Dolutegravir/Rilpivirine	36 (8)
Other	162 (34)
History of AIDS defining events, n (%)	32 (7)
Comorbidities, n (%)	71 (15)
HCV co-infection	43 (9)
HBV co-infection	20 (4)
NADM	9 (2)
CVD	5 (1)
CKD	1 (0.2)
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=472)
Duration of follow-up	Median months (IQR)	3.0 (2.8, 7.1)
On CAB+RPV LA at end of follow-up	n (%)	453 (96)
≥1 VL after first injection	n (%)	374 (79)
	Last VL <50 copies/mL, n (%)	365/374 (98)
	All VLs <50 copies/mL, n (%)	359/374 (96)
	Last VL <200 copies/mL, n (%)	371/374 (99)
	All VLs <200 copies/mL, n (%)	370/374 (99)
Confirmed virologic failure	n (%)	3/374 (0.8)

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 25.2 kg/m^2. They received the LA injections twice as scheduled, one month apart, with no missed or delayed doses. Baseline resistance information was not available. Resistance mutations using Stanford algorithm at failure included 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 the follow-up VL after switching is not yet available.
- 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 doses. There were no resistance mutations detected at baseline or at failure. This participant had two consecutive VLs of ≥ 200 copies/mL, switched to abacavir, lamivudine, darunavir and ritonavir and follow-up VL 18 days after switching was 109 copies/mL and 343 days after switching was 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/m^2. They received the LA injections seven times as scheduled, with no missed or delayed doses. There were no resistance mutations detected at baseline or 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, then to lamivudine, doravirine and tenofovir disoproxil fumarate a month later and the follow-up VL after switching was 0 copies/mL one- and two-months post switching.

Conclusions

- The real-world data of people living with HIV who received CAB+RPV LA in Europe, suggest that the regimen is effective among individuals virologically suppressed at initiation with high persistence and high adherence level.
- High levels of virologic control were observed with low CVF (<1%), consistent with the clinical trial data.

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