Real world implementation of long-acting cabotegravir and rilpivirine in UK NHS HIV clinics

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Background

- Long-acting cabotegravir and rilpivirine (LA CAB/RPV) offers an alternative to daily oral antiretroviral therapy (ART) and represents a paradigm shift in HIV management[1,2,3]
- Routine use of long-acting therapy as part of UK government-approved care began in 2022[4]
- More data on the successes and challenges of implementation of LA CAB/RPV in routine care settings, and the clinical outcomes are needed
- Here we describe baseline demographics, treatment switches, missed/late injections and virological outcomes at 12 months of follow-up, from individuals enrolled in the CORAL study

Methods

- CORAL (CabOtegravir and Rilpivirine reAL world experience) is a mixed-methods, prospective cohort study conducted at ten UK NHS HIV services
- We aimed to characterise the real-world implementation, roll out, safety and patient experience of 2-monthly LA CAB/RPV
- Individuals living with HIV aged 16 or older, prospectively switching to LA CAB/RPV, or who had switched in the prior six months, were invited to participate
- A control group continuing oral ART (matched for age, sex, ethnicity, sexual orientation, ART duration) was also recruited
- Treatment decisions and clinical management were undertaken in accordance with routine care

Figure 1. CORAL Study Schematic

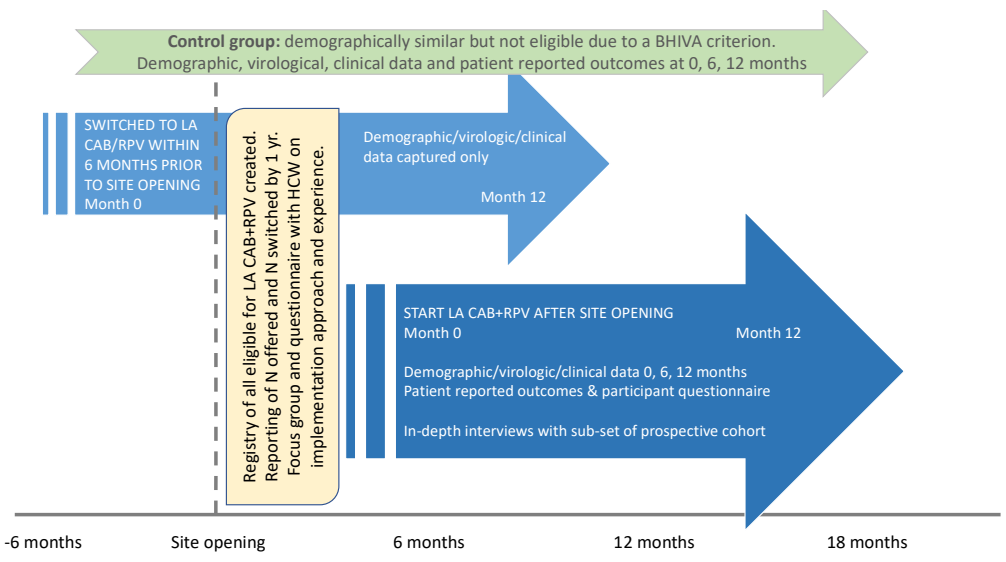

Table 1. Baseline Characteristics

		Total (n=167)	Oral (n=53)	LA CAB/RPV (n=114)
Gender, n (%)	Cisgender men	129 (77.2)	41 (77.4)	88 (77.2)
	Cisgender women	37 (22.2)	12 (22.6)	25 (21.9)
	Transgender women	1 (0.6)	0 (-)	1 (0.9)
Age, median (IQR)		46 (38-52)	46 (40-54)	45 (38-51)
Ethnicity, n (%)	White	86 (51.5)	30 (56.6)	56 (49.1)
	Black African	32 (19.2)	11 (20.8)	21 (18.4)
	Other	21 (12.6)	4 (7.6)	17 (14.9)
	Not stated	28 (16.8)	8 (15.1)	20 (17.5)
Time since HIV diagnosis at study entry, years, median (IQR)		14 (9-20)	14 (9-21)	14 (9-19)
Year of ART start, median (range)		2013 (1997-2024)	2012 (1997-2024)	2013 (1997-2024)
ART regimen*	2DR/PI monotherapy	32 (19.2)	11 (20.8)	21 (18.4)
	3DR	127 (76.1)	39 (73.6)	88 (77.2)
	Other	5 (3.0)	3 (5.7)	2 (1.8)
	Not stated	3 (1.8)	0 (-)	3 (2.6)
Number of ART regimens	1-2	61 (36.5)	19 (35.9)	42 (36.8)
	3-5	73 (43.7)	22 (41.5)	51 (44.7)
	6-10	22 (13.2)	9 (17.0)	13 (11.4)
	>10	7 (4.2)	3 (5.7)	4 (3.5)
	Not stated	4 (2.4)	0	4 (3.5)
Last CD4 count, median (IQR)†		680 (556-868)	723 (571-909)	677 (540-848)
Last HIV RNA <50c/mL†		159 (95.2)	50 (94.3)	107 (95.5)
Comorbidities, n (%)	Cardiovascular disease	11 (6.6)	5 (9.4)	6 (5.3)
	Mental health disorder	37 (22.2)	13 (24.5)	24 (21.1)
	Dyslipidaemia	13 (7.8)	9 (17.0)	4 (3.5)
	Hepatic impairment	10 (6.0)	6 (11.3)	4 (3.5)
	Diabetes Mellitus	9 (5.4)	4 (7.6)	5 (4.4)
	Substance/alcohol misuse	8 (4.8)	4 (7.6)	4 (3.5)
Hep B core Ab positive, n (%)§		32 (25%)	19 (41.3)	13 (15.9)

*ART regimen prior to switch for those switching to LA CAB/RPV

†Last CD4 and HIV RNA before switch for those switching to LA CAB/RPV; last CD4 and HIV RNA pre-date of consent for matched controls; HIV RNA data missing for two in LA cohort

§Data missing for 32 in LA cohort and 7 in matched oral cohort

Results

Baseline

- A total of 167 participants were included: 114 receiving LA CAB/RPV (52 prospective and 62 retrospective) and 53 control participants receiving oral ART (**Table 1**)
- The majority (77%; 129/167) were cisgender men, median age was 46 years [IQR 38-54], just over half (52%; 86/167) were of white ethnicity and for almost all (95%; 159/167) the last HIV RNA reading prior to treatment switch (LA cohort) or study entry (oral cohort) was <50 c/mL
- In the LA cohort, no participants had prior evidence of resistance to integrase inhibitors, but one participant had prior known non-nucleoside reverse transcriptase inhibitor resistance, although this was a K103N which does not preclude CAB/RPV use

After 12 months of follow up (Table 2)

Virological Effectiveness

- 17/114 (14.9%) participants in the LA cohort had at least one HIV RNA 50-199 c/mL, with 10/114 (8.8%) having multiple readings in this range
- 4/53 (7.5%) participants in the oral cohort had at least one HIV RNA 50-199 c/mL, one (1.9%) of whom also had one HIV RNA ≥200 c/mL
- No HIV RNA readings ≥200 c/mL were observed in the LA cohort
- No virological failure was observed

Safety and Tolerability:

- 3/114 (2.6%) in the LA cohort had switched therapy, primarily due to injection site reactions
- 4.53 (7.5%) in the oral cohort had switched treatment, primarily citing drug-drug interactions and adherence challenges
- No drug-related serious adverse events were reported

Injection Schedule Adherence:

- Nine out of 736 (1.2%) of injections were administered out of the 7-day window, five of which were late, three were early, and for one it was not specified if this was early or late
- Three participants had one missed injection each, and all received oral bridging therapy accordingly

Table 2. Month 12 Outcomes

		Total (n=167)	Oral (n=53)	LA CAB/RPV (n=114)
At least one HIV RNA ≥50-199 c/mL		21 (12.8)	4 (7.5)	17 (14.5)
Multiple HIV RNA ≥50-199 c/mL		12 (7.2)	2 (3.8)	10 (8.8)
At least one HIV RNA ≥200 c/mL		0 (0.6)	1 (1.9)	0 (0.0)
Confirmed virological failure		0 (0.0)	0 (0.0)	0 (0.0)
Participants who had switched to alternative regimen		7 (4.2)	4 (7.5)	3 (2.6)
Drug-related serious adverse events		0 (0.0)	0 (0.0)	0 (0.0)
Participants with out of window injections‡	Early		-	3 (2.6)
	Late		-	5 (4.4)
	Not stated		-	1 (0.9)
Participants with missed injections‡			-	3 (2.6)

‡Each participant experienced only one out of window or missed injection

Key Messages

- **No virological failure** was observed at 12 months of follow up, **No HIV RNA readings ≥200** c/mL were observed in the LA cohort
- The proportion of individuals with **viral blips appeared higher** in the LA cohort, but this is likely to be explained by guidance around **increased testing frequency** in those receiving LA CAB/RPV (2-monthly) as compared to those receiving oral ART (6-monthly)
- **Over 98%** of injections were administered within window
- **All participants** who missed an injection were provided with **oral bridging therapy**
- **Injection site reactions rarely led to treatment switches** off LA CAB/RPV

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2. Swindells S, et al. Long-Acting Cabotegravir and Rilpivirine for Maintenance of HIV-1 Suppression. The New England Journal of Medicine. 2020;382(12):1112-23
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4. Overview | Cabotegravir with rilpivirine for treating HIV-1 | Guidance | NICE

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