24-Week Viral Suppression in Patients Starting Long-Acting CAB/RPV Without HIV Viral Suppression

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BACKGROUND

- LA-CAB/RPV is FDA-approved in the United States as a switch strategy for people with HIV (PWH) who are virally suppressed on oral antiretroviral therapy (ART).
- Early data from clinical cohorts suggest that HIV viral suppression can be obtained in most patients initiating LA-CAB/RPV with an unsuppressed viral load, but there is no data on whether initial viral suppression is sustained.
- We sought to evaluate longer-term viral suppression outcomes following initiation of LA-CAB/RPV among people who were not virally suppressed at baseline.

METHODS

Viral suppression outcomes now updated to 48 weeks

- We conducted a retrospective cohort study of PWH who initiated LA-CAB/RPV at Ward 86, a teaching hospital-affiliated, publicly-funded HIV clinic in San Francisco
- We have 286 PWH who initiated LA-CAB/RPV; this analysis included those who initiated LA-CAB/RPV (without other injectable ART, e.g. lenacapavir) and with a baseline HIV viral load (VL) ≥50 copies/mL and who started prior to 5-Dec-2022 (thus having ≥56 weeks prior to database closure for outcome ascertainment)
- Our clinic protocol was to start all unsuppressed patients on every 4 week dosing, with optional change to every 8 week dosing after 3-6 months suppression
- We conducted retrospective chart review of demographics, LA-CAB/RPV injection dates, and HIV viral load measurements
- **Primary outcome:** HIV viral suppression (<50 copies/mL) and LA-CAB/RPV persistence (not discontinued or late by >14 days at 48 weeks), using closest VL to 48+/-8 weeks
- **Secondary outcomes:**
  - Any HIV viral suppression <50 copies/mL at 48 weeks (on LA-CAB/RPV or alternative ART)
  - Any HIV viral suppression <200 copies/mL at 48 weeks (on LA-CAB/RPV or alternative ART)
  - Virologic failure, defined as <2-log VL decline at 4 weeks or VL ≥200 copies/mL after initial viral suppression with emergent CAB- or RPV-associated resistance mutations
  - Proportion transitioning to every 8 week dosing
  - Proportion of patients with any injection >7 and >14 days late

Among 59 people with HIV initiating LA-CAB/RPV with HIV RNA ≥50 copies/ml, 93% were virally suppressed (<50 copies/mL) at 48 weeks (95% <200 copies/mL)

RESULTS

- 286 PWH have received ≥1 dose of LA-ART as of 31-Jan-2024 (101 with baseline VL ≥50 copies/mL and 185 with baseline VL <50); Ward 86 administers ~18 injectable medications/day in total
- 59 PWH started LA-CAB/RPV with VL ≥50 copies/mL by 5-Dec-2022 & included in analysis
- **48-week Viral Suppression:**
  - **81% (48/59) remained on LA-CAB/RPV and were virally suppressed (<50 copies/mL)**
  - **93% (55/59) were virally suppressed <50 copies/mL (LA-CAB/RPV + alternative ART)**
  - 95% (56/59) were virally suppressed <200 copies/mL (LA-CAB/RPV + alternative ART)
- **Virologic failure:** 3 patients (5%) had virologic failure with emergent resistance (see Table 3)
  - 2 within 8 weeks of initiation despite on-time injections; re-suppressed on alternative ART
  - 1 following self-discontinuation of LA-CAB/RPV, did not resume oral ART
- **Dosing interval:** 19 (32%) transitioned to every 8 week dosing by week 48
- **Late injections:** 17 (29%) had at least one injection >7 days late and 8 (14%) >14 days late
  - 3 were lost to follow-up; remainder persisted on LA-CAB/RPV and were suppressed at week 48

Figure 1. HIV Viral Suppression at 48 weeks following initiation of LA-CAB/RPV
with baseline HIV RNA ≥50 copies/mL (n=59)

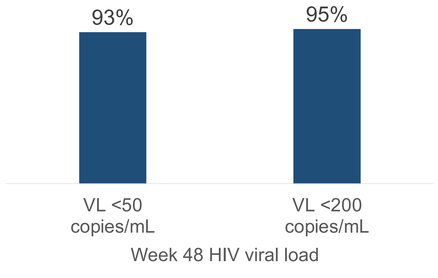

Table 2. Status at week 48*	VL <50 (N=55)	VL ≥50 (N=4)	Overall (N=59)
Remained on LA-CAB/RPV	48	1†	49 (83%)
Discontinued LA-CAB/RPV and resumed oral ART	5	-	5 (8%)
Failure with resistance • On-time injections • Lost to follow-up and off oral ART, later determined to have resistance	2 -	- 1	3 (5%)
Lost to follow up and off oral ART	-	2	2 (3%)

* Four VLs missing at week 48. Three categorized as VL ≥50 due to VL ≥50 before/after window and/or evidence off ART. One categorized as VL <50 due to VL <50 before & after window and on ART throughout.

† Intensified to LA-CAB/RPV + Lenacapavir for low-level viremia. Week 48 VL <200 copies/mL.

Reasons for discontinuation and switching to oral ART: side effects (n=3), provider-initiated switch due to viremia associated with incorrect needle length in patient with BMI ≥30 kg/m^2 (no resistance; n=1), transfer to another clinic that did not have LA-CAB/RPV available (n=1).

Reasons for discontinuation/loss to follow-up and not taking oral ART: fixed belief that cured from HIV (n=1), psychosis (n=1), depression (n=1)

Table 1. Baseline characteristics (n=59)		
Gender	Female	5 (8.5%)
	Male	53 (89.8%)
	Gender minority	1 (1.7%)
Age	18-29	2 (3.4%)
	30-49	29 (49.2%)
	50+	28 (47.5%)
Race/ Ethnicity	White	24 (40.7%)
	Black/AA	14 (23.7%)
	Latino	17 (28.8%)
	Other	4 (6.8%)
Housing status	Stable	28 (47.5%)
	Unstable	26 (44.1%)
	Homeless	5 (8.5%)
Substance use	Methamphetamine/cocaine	36 (61.0%)
	Opioids	6 (10.2%)
CD4 count	<50	9 (15.3%)
	50-199	20 (33.9%)
	200-349	13 (22.0%)
	350-499	7 (11.9%)
	>=500	10 (16.9%)
HIV viral load	50 to <200	3 (5.1%)
	200 to <1,000	5 (8.5%)
	1,000 to <10,000	10 (16.9%)
	10,000 to <100,000	22 (37.3%)
	>=100,000	19 (32.2%)

Table 3. Adverse virologic outcomes (n=6)

Patient	Baseline	Follow-up	Week 48 status
Patient 1 (Failure despite on-time injections)	VL: 137,000 CD4: 15 Mutations: T97A (minor INSTI)	VL 4,400 at week 4 (<2 log decline), genotype with E138K (NNRTI) and R263K (INSTI). Disengaged from care, but later returned and re-suppressed on BIC/TAF/FTC + LEN	Suppressed on BIC/TAF/FTC + LEN
Patient 2 (Failure despite on-time injections)	VL: 215,000 CD4: 71 Mutations: N348I (minor NNRTI)	VL 39,000 at week 4 (<2 log decline). Genotype new L100I, Y181I (NNRTI). Disengaged from care but later returned and re-suppressed on CAB+LEN.	Suppressed on CAB + LEN
Patient 3 (Failure after discontinuation)	VL: 67,000 CD4: 20 Mutations: none	Received 10 on-time injections, VL <200 by week 4 and <50 by week 24. Discontinued due to severe depression. Genotype 18 weeks after discontinuation with new K101E, E138K, Y181F/I/N, M230L (extensive NNRTI mutations)	Emergent resistance after discontinuation, presumed viremic
Patient 4 (discontinued, lost)	VL: 19,000 CD4: 20 Mutations: none	Received 2 injections, suppressed by week 4. Discontinued LA-CAB/RPV due to psychosis. At week 36, VL from the emergency department 32,000 (no genotype).	Lost to follow-up, presumed viremic
Patient 5 (discontinued, lost)	VL: 801,000 CD4: 27 Mutations: none	Received 6 on-time injections, then discontinued all ART due to patient's belief they were cured of HIV. Declined all subsequent laboratory testing or care engagement.	Lost to follow-up, presumed viremic
Patient 6 (on LA-CAB/RPV + LEN, VL ≥50)	VL: 284,000 CD4: 118 Mutations: none	VL 418 after 8 weeks. Persistent low-level viremia (range 94-614). VL 614 at 6th injection prompted addition of lenacapavir. Continued low-level viremia (VL 126 at wk 48)	Low-level viremia on LA-CAB/RPV+LEN

SUMMARY AND CONCLUSION

- Ward 86 started a LA-ART program for those without & with adherence challenges in 2021, now with 286 PWH
- Among those initiating LA-CAB/RPV with HIV RNA ≥50 copies/mL, 48-week viral suppression to <50 copies/ml was 93%, with 81% persisting on LA-CAB/RPV
- In population facing significant psychosocial challenges, loss to follow-up was low following LA-CAB/RPV initiation
- LA-ART can be an important tool for improving viral suppression among patients facing adherence challenges

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