Why Do People With HIV Stop Long-Acting Injectable Cabotegravir-Rilpivirine and What Happens?

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BACKGROUND

- Long-acting injectable cabotegravir/rilpivirine (LA-CAB/RPV) is an important innovation in HIV antiretroviral treatment (ART)
- The Ward 86 clinic in San Francisco has one of the largest real-world cohorts of people with HIV (PWH) receiving LA-CAB/RPV.
- Little is known about why PWH discontinue LA-CAB/RPV and their subsequent clinical outcomes.

METHODS

- Retrospective chart review of the Ward 86 LA-CAB/RPV program through January 26, 2025
- Descriptive statistics summarized demographic and clinical characteristics of PWH discontinuing LA-CAB/RPV, stratified by HIV viral load (VL) at first LA-CAB/RPV injection (<50 copies/mL vs. ≥50 copies/mL)
- Discontinuation was defined as intended cessation of LA-CAB/RPV without documented plan to resume or loss to follow-up (LTFU) per clinical notes
- Viral suppression (VS) post-discontinuation was defined as HIV VL <200 copies/mL and ascertained for those with at least 90 days of follow-up post last injection.
- Reasons for discontinuation were abstracted by two coders and summarized using content analysis

RESULTS

- Of 437 PWH initiating LA-CAB/RPV with overall median time on injections 553 days (IQR 253,804 days), 69 (16%) discontinued, of whom 47 (68%) initiated with VS and 22 (32%) with viremia
- Discontinuation was similar between those starting with VS (47/287, 16%) vs. with viremia (22/150, 15%), p 0.64
- Median age 45; median CD4 478; 90% male, 33% Latino/a, 16% Black, 46% unstably housed/homeless, 35% stimulant use
- At discontinuation, median number of injections was 6 (min 1, max 32) with 30% on every 8-week dosing.
- Seven individuals (10%) discontinued after one injection and 21 (30%) after ≥10 injections.
- For those initiating with VS, the most common reason for discontinuation was pain, +/- another side effect/concern (Table 1). For those initiating with viremia, virologic failure led to discontinuation in 6 cases; NNRTI and/or INSTI RAMs developed after discontinuation in another 6 PWH who were LTFU or declined alternate ART (Table 2)
- 51/65 with ≥90 days follow-up time post-last injection had VL measured with 48/51 (94%) achieving VS (Table 3)

- Discontinuation was low (16%).
- In PWH initiating with VS, pain was the most common reason for discontinuation.
- In PWH initiating with viremia, lateness/virologic failure drove discontinuation, though most attained VS on alternate ART.

Table 1. Reasons for Discontinuation, Stratified by HIV VL at LA-CAB/RPV Initiation

Reason for Discontinuation	Overall (n=69)	HIV VL <50 copies/mL (n=47)	HIV VL ≥50 copies/mL (n=22)
Injection site pain	14	10	4
Injection site pain with other side effect/concern*	11	9	2
Other side effect/concern*	14	11	3
Residential treatment for mental health/substance use or incarceration	5	5	-
Need to come to clinic for injections	2	2	-
Allergic reaction	1	1	-
Relocation	2	2	-
Lateness leading to provider discontinuation	8	2	6
Provider discontinuation for HIV RNA blip	1	1	-
Loss to follow up	3	3	-
Virologic failure	7	1	6
Declined ART but remained in care	1	-	1

*Other side effect/concern (not mutually exclusive): flu-like symptoms (7), weight gain (2), fatigue (2), patient concern about efficacy (3), mistrust/misunderstanding (2), muscle spasms (1) injection site abscesses (1), bloating (1), sleep/appetite concern (1), patient desire for control of HIV treatment (1), feeling "stuck in a jar" (1), wanted to "take a break" (1), feeling like "too much medicine" in body (1), discomfort with subcutaneous lenacapavir injections given for intensification of treatment regimen

Table 2. Adverse Virologic Outcomes

	Case Description
Initiated with VS – Had Virologic Failure with Late Injections	
Patient 1	Initiated q4 week dosing, late at 4th, 6th injections, reloaded when 50 d late for 8th->q8week dosing, 11d late to 11th injection, 42d late to 14th- and VL=62 with K101E. Started TAF/FTC/DRV/c and has had continuous VS
Initiated with Viremia	
Patient 2 (failure w/ on-time inj.)	VL 137,000; CD4: 15; mutations: T97A (minor INSTI) VL 4,400 at wk 4; genotype with E138 K (NNRTI) and R263K (INSTI); disengaged from care but returned and resuppressed on BIC/TAF/FTC + LEN
Patient 3 (failure with on-time injections)	VL 215,000; CD4 cell count 71; mutations: V179I and N348I (minor NNRTI) VL 29,000 at wk 4; genotype showed new L100I and Y181I mutations (NNRTI); disengaged from care but later returned, resuppressed on CAB + LEN
Patient 4 (failure with late injections)	VL 363,800; CD4 cell count 306; mutations: n/a. Had 9 on-time q4week injections then -> q8 wk; 10d late to 10th injection; VL 29,000; gt: K101E. Repeat VL 6 days later 79. Thought to be a lab error/patient wanted to continue LA-CAB/RPV. Subsequently received 3 on-time q8-wk injections but had VL 4500 c/mL with new Q148R at the 13th injection (wk 68). Unwilling to take oral ART but resuppressed with subcutaneous LEN (CAB/RPV + LEN) Ultimately discontinued because did not like LEN injection and started TAF/FTC/BIC; in touch with care team but has not yet had VL measurement.
Patient 5 (viremia)	VL 140; CD4 cell count 25; no mutations. Received 3 on-time q4week injections, VL at third injection came back at 16,000. Immediately started TAF/FTC/DRV/c and suppressed before genotype obtained.
Patient 6 (failure with on time injections)	VL 700; CD4 731; mutations K103N, T369V, I178I/M. Received 8 on-time q4 week injections via home nursing. At 5th injection VL 80. At 8th injection noted to have VL 1,300. Genotype: NNRTI: K101K/E, K103N, I178M, Y181Y/C, V189V/I, T369V INSTI E138E/K, Q148K. Resuppressed on TAF/FTC/DRV/c.
Patient 7 (failure with late injections)	VL 309; CD4 83/μL; mutations M184V. Initiated with q4week injections. Was 12d late for 4th injection and had VL 66; genotype failed. VS at 5th injection->q8week dosing. At 7th injection VL 137,000; at 8th injection VL 256,000 and genotype with M230L. Care team confirmed patient picked up TAF/FTC/DRV/c at pharmacy but patient LTFU.
Patient 8 (failure with late injections)	VL 540,000; CD4 150; mutations V90I. Initiated q4week then VS, had blips of 88 and 33 but moved to q8week at 5th injection. VS at 6thinjection. 9 d late to 7th injection, 13 d late to 9th injection and VL 8,600. Genotype RT I178L, F127V, M230L, K101Q, INSTI: E138E/D/K/N, G140G/S, S147S/G, Q148K. Started TAF/FTC/DRV/c + LEN. Repeat VL ordered but not yet completed.
Initiated with Viremia and Developed Resistance After Discontinuation	
Patient 9	VL 67,000; CD4 cell count 20; mutations: none Received 10 on-time injections; VL <200 copies/mL wk 4 and <50 wk 24; self-dc due to severe depression; genotype 18 wk later NNRTI: K101E, E138 K, Y181F/I/N, M230L
Patient 10	VL 801,000; CD4 cell count: 27; mutations: V179I. Received 5 on-time q4week injections; was 15 d late to 6th and received reloading. Presented on time for 7th injection but left without being seen, then discontinued all ART due to belief they were cured of HIV; declined all care engagement until 1 y later; VL 226,000; genotype RT E138A/K/T and Y181C; patient resumed CAB + LEN and had resuppression.
Patient 11	VL 34,000; CD4 10, mutations: M184V. Received 7 on-time q4 week injections; 14 d late to 8th injection and when came to clinic -> TAF/FTC/DRV/c due to c/f SSTI. VS observed 3 months later, then patient discontinued oral ART. Genotype 14 months after last injection: K101E, V179I, Y181Y/C. Now VS on TAF/FTC/BIC.
Patient 12	VL 114,000; CD4 50; mutations: none. Had 17 q4 week injections with 6 late, one requiring a reloading. VL 382 and switched to TAF/FTC/DRV/r due to concern for resistance. Patient disengaged from care and presented one year later with VL 12,000. Genotype K101E. Started CAB/LEN with home nursing and has VS.
Patient 13	VL 1,700; CD4 56; mutations: n/a. History of TDF/FTC/RPV use. Had 17 on-time q4week inj., then 62 d late, reloaded; on-time at 4 weeks; then reloaded at 67d late. At last injection VL 99; genotype K101E. Disengaged from care then genotype 5 months later showed NNRTI: E138K. Now suppressed on TAF/FTC/DRV/c.
Patient 14	VL 18,600; CD4 20; mutations: n/a. Had 2 on-time injections and then disengaged. Returned to clinic two years later with VL 5,000; genotype: V106VI, Y181Y/C, H221Y, I178I/M. Now suppressed on TAF/FTC/DRV/c.

*Cases shaded in blue described in Hickey et. al., CID 2024, Gandhi et. al., Annals Int Med, 2023, and Christopoulos et. al., CID 2022.

Table 3. Viral Load Outcomes Post Discontinuation, Stratified by HIV VL at LA-CAB/RPV Initiation

	Overall (n=69) N(%)	VL <50 c/mL(n=47) N(%)	VL ≥50 c/mL (n=22) N(%)
Has ≥90 days follow-up until database closure	65/69 (94.2)	45/47 (95.7)	20/22 (90.9)
Has VL measure after discontinuation	51/65 (78.5)	34/45 (75.6)	17/20 (85.0)
Last VL <200 copies/mL	48/51 (94.1)	34/34 (100)	14/17 (82.4)
Has >365 days since last injection	44/69 (63.8)	29/47 (61.7)	15/22 (68.2)
Has VL measure >365 days after last injection	26/44 (59.1)	13/29 (44.8)	13/15 (86.7)
Last VL >365 days from last injection with VS	24/26 (92.3)	13/13 (100%)	11/13 (84.6%)

Reasons for absence of follow-up VL in those with >90 days since last injection: LTFU (7), relocation (3) awaiting labs (3), and incarceration (1)

CONCLUSIONS

- In a large cohort of LA-CAB/RPV users with median time on injections of ~18 months, discontinuation was low (16%).
- In PWH initiating LA-CAB/RPV with VS the most common reason was injection site pain +/- other side effect/concern.
- In PWH initiating LA-CAB/RPV with viremia due to adherence challenges, virologic failure and care disengagement drove discontinuation; however, most achieved VS on alternate ART.
- Nearly one-third (30%) discontinued after ≥10 injections so continued inquiry into discontinuation will be important.

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Acknowledgments: We would like to acknowledge the patients and clinical staff of the Ward 86 Special Program on Long-Acting Antiretrovirals to Stop HIV (SPLASH) program, as well as R01 MH123396 for supporting this analysis.