Use of *Cabenuva* in Patients with a Detectable HIV-1 RNA

Summary

- Use of Cabenuva (long-acting cabotegravir plus rilpivirine [CAB + RPV LA]) in patients with detectable HIV-1 RNA is not approved in any jurisdiction. Limited data are available for this patient population.
- Real-world observational cohorts have reported rates of achieving virologic suppression in treatment-experienced patients with detectable HIV-1 RNA at baseline ranging from 71 to 98%.[1-5]
    - Additionally, one cohort reported all 12 patients achieved virologic suppression.[6]
- Data from the compassionate use program reported 57% of patients had virologic suppression.[7]
- Important Safety Information can be found in the Prescribing Information and can also be accessed from Our HIV Medicines.

To access additional scientific information related to ViiV Healthcare medicines, visit the ViiV US Medical Portal at viivhcmedinfo.com.

Use of CAB + RPV LA in patients with detectable HIV-1 RNA is not approved in any jurisdiction. Limited data are available for this patient population.

WARD 86 AT UNIVERSITY OF CALIFORNIA SAN FRANCISCO (UCSF)

A retrospective cohort study was conducted of patients aged ≥ 18 years who initiated CAB + RPV LA from January 2021 through September 2024 and were viremic (HIV-1 RNA ≥ 30 copies/mL) at the time of first injection.[1] Individuals with any CAB or RPV-associated mutations were excluded. Patients were initiated on monthly dosing, with the option to transition to every-2-month dosing after viral suppression for at least 3 months.

Overall, 129 patients who were viremic at CAB + RPV LA initiation were included.[1] Select baseline demographics are summarized in Table 1.

Table 1. Select Baseline Demographics of Individuals Initiation CAB + RPV LA[1]

Characteristic	**Viremia (N = 129)**
Age, years, median (range)	48 (25–67)
Race and Ethnicity, %	
Black	25
White	43
Gender, %	
Cisgender men	86
Transgender women	11
Unstable housing, %	52
Baseline viral load, copies/mL	45,600
CD4+ count < 200 cells/mm^3, %	68
Current or past substance use, %	61

CAB + RPV LA = long-acting cabotegravir plus rilpivirine

Virologic outcomes at Week 24 and 48 are summarized in Table 2.[1] Median time to achieve an undetectable viral load in patients was 32 (95% CI 30–45) days.

Table 2. Virologic Outcomes of Patients Viremic at CAB + RPV LA Initiation[1]

Proportion of Patients, % (n/N)	Virologic Suppression (HIV-1 RNA < 30 copies/mL)	95% CI
24 Weeks[a]	97 (114/118)	93–100
48 Weeks[a]	98 (94/96)[b]	93-99

[a] ±2 weeks [b] Including 5 patients who achieved viral suppression on CAB + RPV LA but switched to oral ART due to convenience or adverse events and maintained suppression at 48 weeks.

ART = antiretroviral therapy; CAB + RPV LA = long-acting cabotegravir plus rilpivirine; CI = confidence interval

An analysis through January 26, 2025 described reasons for discontinuation stratified by viral load at CAB + RPV LA initiation.[8] Among patients with initial viremia, 22 discontinued CAB + RPV LA. Reasons for discontinuation included: lateness leading to provider discontinuation (n = 6), virologic failure (n = 6), injection site pain (n = 4), other side effect/concern (n = 3), injection site pain with other side effect/concern (n = 2), and declined antiretroviral therapy but remained in care (n = 1).

Adverse virologic outcomes were described for 13 patients who were viremic at initiation.[8] See Table 3 for additional details.

Table 3. Adverse Virologic Outcomes in Patients with Viremia at Initiation (n = 13)[8]

Patient	Baseline	Follow-Up
Patient 1	VL: 137,000 CD4: 15 Mutations: T97A	• VL 4400 at week 4 • Genotype with E138K (NNRTI) and R263K (INSTI). • Suppressed on BIC/TAF/FTC + LEN
Patient 2	VL: 215,000 CD4: 71 Mutations: V179I, N348I	• VL 29,000 at week 4 • Genotype new L100I, Y181I (NNRTI) • Suppressed on CAB LA + LEN LA
Patient 3	VL: 363,800 CD4: 306 Mutations: N/A	• VL: 29,000 (10-day delay of 10th injection), genotype: K101E and VL 6 days later 79; VL 4500 after 3 more injections, genotype: Q148R at 13th injection • Suppressed on CAB + RPV LA + LEN LA; discontinued LA regimen (patient preference) and started BIC/FTC/TAF (no VL after switch available)
Patient 4	VL: 140 CD4: 25 Mutations: none	• VL: 16,000 (after three on-time Q4W injections) • Switched to DRV/c/FTC/TAF and achieved viral suppression prior to obtaining genotype
Patient 5	VL: 700 CD4: 731 Mutations: K103N, T369V, I178I/M	• VL: 80 (after 8 on-time Q4W injections via home nursing); VL 1300 at 8th injection • Genotype: NNRTI, K101K/E, K103N, I178M, Y181Y/C, V189V/I, T369V; INSTI, E138E/K, Q148K • Resuppressed on DRV/c/FTC/TAF
Patient 6	VL: 309 CD4: 83 Mutations: M184V	• VL: 66 (12 days late for 4th injection of Q4W dosing), suppressed after 5th injection and transitioned to Q8W dosing; VL 137,000 (7th injection) and 256,000 (8th injection) • Genotype: M230L • Switched to DRV/c/FTC/TAF, but lost to follow-up
Patient 7	VL: 540,000 CD4: 150 Mutations: V90I	• VL: 8600 (13 days late to 9th injection; previously transitioned to Q8W at 5th injection, 9 days late to 7th injection) • Genotype: RT, I178L, F127V, M230L, K101Q; INSTI, E138E/D/K/N, G140G/S, S147S/G, Q148K • Started DRV/c/FTC/TAF + LEN LA; repeat VL not completed
Patient 8	VL: 67,000 CD4: 20 Mutations: none	• Suppressed through week 24 after 10 on-time injections but self-discontinued • Genotype (18 weeks later): NNRTI, K101E, E138K, Y181F/I/N, M230L
Patient 9	VL: 801,000 CD4: 27 Mutations: V179I	• Received 5 on-time injection (Q4W), 15 days late to 6th injection and repeated initiation dosing; then discontinued all ART and declined engagement in care • One year later: VL 226,000; genotype: NNRTI, E138A/K/T, Y181C) Started on LA CAB + LEN and re-suppressed
Patient 10	VL: 34,000 CD4: 10 Mutations: M184V	• Received 7 on-time injections (Q4W); 14 days late to 8th injection • Switched to DRV/c/FTC/TAF due to SSTI; suppressed 3 months later then discontinued ART • Genotype (14 months after last injection): K101E, V179I, Y181Y/C • Suppressed on BIC/FTC/TAF
Patient 11	VL: 114,000 CD4: 50 Mutations: none	• VL: 382 (17 Q4W injections, 6 late and one requiring re-initiation); switched to DRV/r + FTC/TAF; disengaged from care • VL: 12,000 (1 year later); genotype: K101E Started LA CAB + LEN with home nursing and had viral suppression

Patient	Baseline	Follow-Up
Patient 12	VL: 1700 CD4: 56 Mutations: NA	• VL: 99, genotype K101E (17 on-time Q4W injections, then 62 days late and re-initiated; on-time 4 weeks later then reinitiated again at 67 days late) • Disengaged from care; genotype (5 months later): NNRTI, E138K • Suppressed on DRV/c/FTC/TAF
Patient 13	VL: 18,600 CD4: 20 Mutations: none	• VL: 5000; genotype: V106V/I, Y181Y/C, H221Y, I178I/M (2 years after receiving 2 on-time injections then disengaged from care) • Suppressed on DRV/C/FTC/TAF

BIC/TAF/FTC = bictegravir/tenofovir alafenamide/emtricitabine; CAB + RPV LA = long-acting cabotegravir plus rilpivirine; DRV/c/FTC/TAF = darunavir/cobicistat/emtricitabine/tenofovir alafenamide; DRV/r = darunavir/ritonavir; INSTI = integrase strand transfer inhibitor; LEN = lenacpavir; N/A = not available; NNRTI = non-nucleoside transcriptase inhibitor; Q4W = every 4 weeks; Q8W = every 8 weeks; VL = viral load

OPERA

OPERA is a prospectively captured cohort that includes more than 150,000 people living with HIV.[2]

Adults who received at least one CAB + RPV LA injection between January 21, 2021 through December 31, 2023 and had HIV-1 RNA ≥ 50 copies/mL at first injection were included; data analysis was conducted through February 29, 2024.[2]

Overall 368 patients were included in the analysis; 27% were ≥ 50 years of age, 30% were female, 57% Black, and 18% Hispanic.[2] Additionally, 29% had a body mass index (BMI) ≥ 30 kg/m^2. Median (interquartile range [IQR]) time since HIV diagnosis was 9 (3, 17) years. Median (IQR) HIV-1 RNA was 120 (61, 2535) copies/mL (40% had an HIV-1 RNA ≥ 200 copies/mL) and median (IQR) CD4 cell count was 578 (353, 808) cells/µL. Prior to CAB + RPV LA, patients were on their prior regimen for a median (IQR) of 17 (8, 37) months; most (68%) were on an INSTI-based regimen. Every 2 month dosing was the most common CAB + RPV LA regimen used at initiation (80%) and at end of analysis/discontinuation (93%).

Virologic outcomes (at least 1 HIV-1 RNA after the first injections) are available for 313 patients who completed initiation injections.[2] See Figure 1 below. Twelve percent (n = 36) of patients never achieved virologic suppression (HIV-1 RNA < 50 copies/mL).

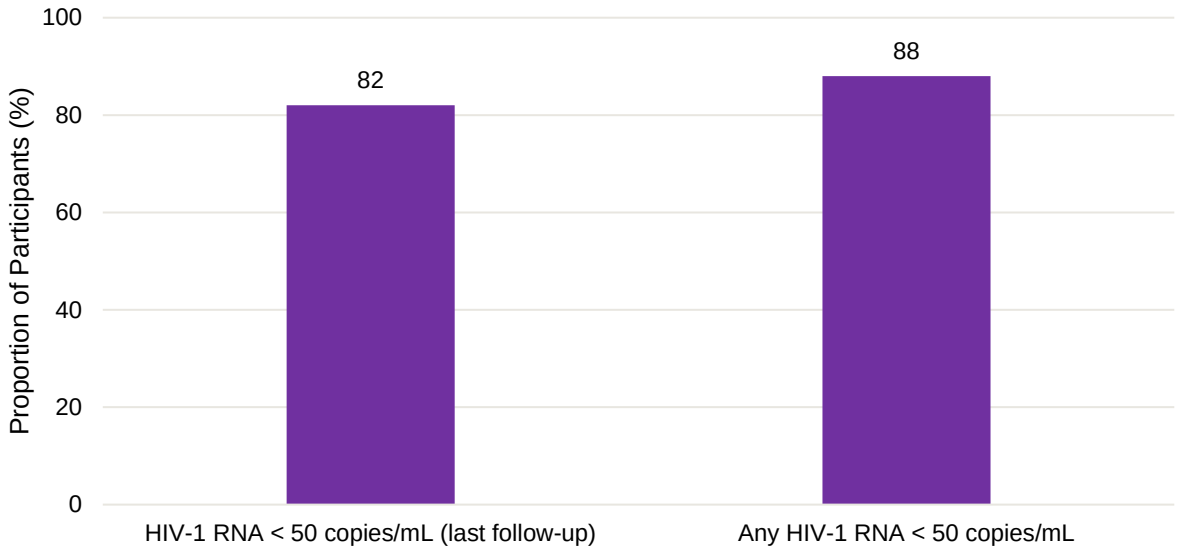
Confirmed virologic failure, defined as 2 consecutive HIV-1 RNA ≥ 200 copies/mL or 1 HIV-1 RNA ≥ 200 copies/mL followed by discontinuation within 2 (monthly dosing) or 4 (every 2 month dosing) months, was reported in 1% (n = 3/301) of patients with at least one HIV-1 RNA after virologic suppression.[2] Two patients had NNRTI and INSTI mutations at failure (the third had no genotype available).

Case 1 had a baseline HIV-1 RNA of 35,500 copies/mL 11 days prior to starting CAB + RPV LA; resistance testing showed multiple polymorphisms (not specified).[2] The patient had 2 missed doses of CAB + RPV LA prior to CVF. HIV-1 RNA was 34,600 copies/mL and resistance testing showed both NNRTI (K101P) and INSTI (L74M, G140C, Q148R) mutations. ART was changed to doravirine plus darunavir/cobicistat (HIV-1 RNA decreased to 120 copies/mL); fostemsavir was later added and HIV-1 RNA was 150 copies/mL on this regimen.

Case 2 had a baseline HIV-1 RNA of 160 copies/mL and multiple polymorphisms (not specified) detected on prior archive resistance testing. HIV-1 RNA at failure was 38,600 copies/mL with NNRTI (V179I, Y181C, K101Q, V90I) and INSTI (T97A, S147G, N155H) mutations detected.[2] ART was changed to darunavir/cobicistat/emtricitabine/tenofovir alafenamide and HIV-1 RNA decreased to 140 copies/mL. ART regimen was modified to darunavir/cobicistat + lenacapavir + fostemsavir and HIV-1 RNA decreased to < 20 copies/mL.

Case 3 had a baseline HIV-1 RNA of 170 copies/mL and had multiple polymorphisms (not specified) detected prior to switch.[2] HIV-1 RNA at CVF was 930 copies/mL; resistance testing was unable to be performed. Fostemsavir was added to the regimen; subsequently CAB + RPV LA dose was changed (described as “high dose” monthly – exact dosing not specified) and virologic suppression was achieved.

Figure 1. Virologic Outcomes from OPERA (n = 313)[2]



Overall, 90% (n = 331/368) of patients completed initiation injections.[2] All maintenance injections were administered on time for 59% (n = 174/293) of patients; 33% (n = 96) had a delayed injection and 13% missed an injection.

At the end of the analysis period, 78% (n = 258/331) remained on CAB + RPV LA; median (IQR) time on this regimen was 12 (8, 19) months.[2]

A separate analysis examined outcomes among women initiating CAB + RPV LA with HIV-1 RNA ≥ 50 copies/mL from January 21, 2021 through August 31, 2023 from the OPERA cohort (n = 105).[3] Among women with at least 1 HIV-1 RNA during follow up (n = 91), 84% had last viral load < 50 copies/mL. Within 6 months, 85% had any VL < 50 copies/mL and 89% had any VL < 50 copies/mL throughout the follow-up period. CVF occurred in 2 women (3%).

No safety data is available from OPERA currently.[2,3]

TRIO COHORT STUDY[4]

The TRIO HIV Research Network Database utilizes electronic medical record data from 14 Federally Qualified Health Centers in the US. Adult people with HIV who received at least one dose CAB + RPV LA between January 2021 through March 2024 and had HIV-1 RNA ≥ 50 copies/mL prior to first injection were included.

Overall, 111 patients were included in the analysis.[4] The median (IQR) age was 44 (34, 57) years, 65% were male, and 55% were Black/African American. Thirty-two percent of patients had BMI ≥ 30 kg/m^2. At baseline HIV-1 RNA was 50–199 (51%), 200–9999 (28%), 10,000–99,999 (12%), and ≥100,000 (9%).

Most patients had prior integrase strand transfer exposure (INSTI; 91%); bictegravir/emtricitabine/tenofovir alafenamide was most common (50%). Forty-five patients had genotype test results prior to CAB + RPV LA start: no INSTI mutations were identified and non-nucleoside reverse transcriptase inhibitor were identified in 8 participants (2 had intermediate/high RPV resistance based on the Stanford HIV database algorithm).

Median (IQR) follow up time was 9 (3, 13) months. By the end of follow-up, 81% remained on CAB + RPV LA. No injection site reactions were reported based on ICD-10 codes.

Of the 81 patients (73%) with at least 1 follow-up viral load, 89% had HIV-1 RNA < 50 copies/mL. A higher proportion of patients with low-level viremia (LLV [HIV-1 RNA 50–199 copies/mL]) had virologic suppression (93%) compared with those with high-level viremia (HLV [HIV-1 RNA ≥ 200 copies/mL]; 84%). Last viral load was < 200 copies/mL in all patients with LLV and in 84% with HLV.

Two patients had confirmed virologic failure after achieving virologic suppression.

The first case had a baseline HIV-1 RNA of 590,201 copies/mL; viral load was 1210 copies/mL at 11 months and CAB + RPV LA dosing was switched from every 2 months to monthly. Virologic suppression was achieved after 3 months but then increased again to 4160 copies/mL (time to rebound not specified). No genotype was available.

The second case had a baseline HIV-1 RNA of 99,700 copies/mL and at 18 months had a viral load of 44,800 copies/mL. ART regimen was switched to darunavir/cobicistat/emtricitabine/tenofovir alafenamide and viral load was suppressed after 6 weeks. Genotype results showed baseline reverse transcriptase mutation (V179D) and emergent RPV resistance (L100I and K101E); no INSTI mutations were identified.

Discontinuation criteria was met by 19% of patients (median [IQR] time to discontinuation was 7 [5, 9] months). Two patients re-initiated CAB + RPV LA within 6 months and 4 were lost to follow-up. Last VL prior to discontinuation was < 50 copies/mL in 77% (n = 13/17) of patients with follow-up viral loads available.

Injections were administered on time (± 7 days from target date) in 95% of patients (2nd initiation injection; n = 96/101 with ≥ 2 injections) and 64% (n = 55/86 with ≥ 3 injections) of patients for continuation injections. Thirty-six percent (n = 31/86) had at least 1 delayed continuation injection and no missed injections were reported.

NEW YORK CITY HEALTH + HOSPITALS (NYC H+H)

A retrospective cohort was reported among patients with HIV with at least 1 primary care visit at the NYC H+H system and received at least 1 dose of CAB + RPV LA from January 2024 through December 2024, including patients with viremia at initiation.[5]

Overall, 328 patients were identified; among these, 17 were viremic (HIV-1 RNA ≥ 200 copies/mL) at baseline.[5] Most identified as female (65%); 53% of patients were Black and 47% were Hispanic. Compared with patients who were virologically suppressed at baseline, those with viremia were more likely to have baseline CD4 < 200 cells/mm^3 (63% vs 5%) and to screen positive for a social determinant of health need (paying for healthcare need, housing instability, employment need, financial insecurity; 29% vs 15%). Median baseline viral load was 21,045 copies/mL.

Among patients with viremia at baseline, 76% and 71% had their most recent viral load < 200 copies/mL and < 50 copies/mL, respectively.[5]

UNIVERSITY OF MISSISSIPPI MEDICAL CENTER

A retrospective case series reported the results of 12 patients with viremia who were initiated on CAB + RPV LA between February 2022 and June 2023.[6] The median (range) age was 42 (28–61) years, 7 patients were cisgender females, and 11 were Black/African American. Four patients had NNRTI mutations present at baseline (K103N [n = 2], V106I [n = 1], P225H [n = 1]) and 5 had INSTI mutations present (D232N [n = 1], N155H [n = 1] E157Q [n = 3]). Mean (range) baseline viral load was 152,657 copies/mL (2410–566,000); absolute mean (range) CD4 count was 233 (131–475) cells/µL.

Six patients had at least 12 months of follow-up.[6] Monthly dosing was started in 6 patients who were all transitioned to every-2-month; the remaining 6 patients directly initiated every-2-month dosing. Of the 82 injection visits, 5 were administered outside of the scheduled dosing window; a repeat loading dose was administered within 1 month for these patients.

Within 3 months of CAB + RPV LA initiation, all 12 patients achieved virologic suppression (HIV-1 RNA < 50 copies/mL). Mean (range) CD4 increase was 184 (26–414) cells/µL; patients with CD4 < 200 cells/µL at baseline had a mean increase of 308%. No discontinuations or virologic failure occurred during the follow up period. Additional safety information was not reported.

COMPASSIONATE USE PROGRAM

Under special circumstances, where benefits may outweigh the risks, new antiretroviral drugs can be made available before they are approved to patients with serious or life-threatening conditions who are unable to participate in ongoing clinical trials. Such access to investigational drugs is typically limited to these programs.

Physicians could request compassionate use of CAB + RPV LA through an expanded access program.[7] Criteria for granting requests included the need for parenteral therapy, advanced disease, absence of key resistance associated mutations (RAMs) associated with resistance to cabotegravir or rilpivirine, and established retention in care.

All patients received one-time initiation doses of CAB 600 mg and RPV 900 mg followed by every-4-week maintenance doses of CAB 400 mg and RPV 600 mg.[7]

Of the 28 patients with detectable viremia upon entering the compassionate use program, 16 (57%) had HIV-1 RNA < 50 copies/mL at the time of this analysis.[7] The median (range) duration of follow-up was 11 months (1–47). The median (interquartile range [IQR]) time to virologic suppression, as reflected in the quarterly clinical updates, was 5 months (1, 31).

Of the 7 patients who had an incomplete virologic response leading to withdrawal, 6 had detectable HIV-1 RNA at initiation with CAB + RPV LA.[7] All patients were subsequently start on boosted protease inhibitor- or integrase strand-transfer inhibitor (INSTI)-based regimens.

Detailed safety assessments were not available for all patients. The most frequently reported adverse event was injection site reactions.[7]

ONGOING STUDIES

CROWN (NCT06694805) is a phase 3b, open-label, randomized, multicenter, superiority study which aims to evaluate the efficacy, safety, and tolerability of CAB + RPV LA in viremic patients living with HIV.[9]

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