Real-World Use of Long-Acting Cabotegravir Plus Rilpivirine in Virologically Suppressed People Living With HIV

Summary

- Overall, the real-world evidence (RWE) presented to date shows that the rate of maintaining virologic suppression with long-acting cabotegravir plus rilpivirine (CAB + RPV LA) is similar to what has been reported in phase 3 clinical trials.
- Below please find a summary of the data available to date from OPERA, the Trio Cohort Study, BEYOND, CARLOS, and COMBINE-2.
    - Other RWE citations can be found in the reference list below.
- Important Safety Information can be found in the Prescribing Information and can also be accessed from the Our HIV Medicines section of viivhealthcare.com/us.

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To date, more than 9000 patients receiving CAB + RPV LA have been described by various RWE cohorts.

OPERA[1]

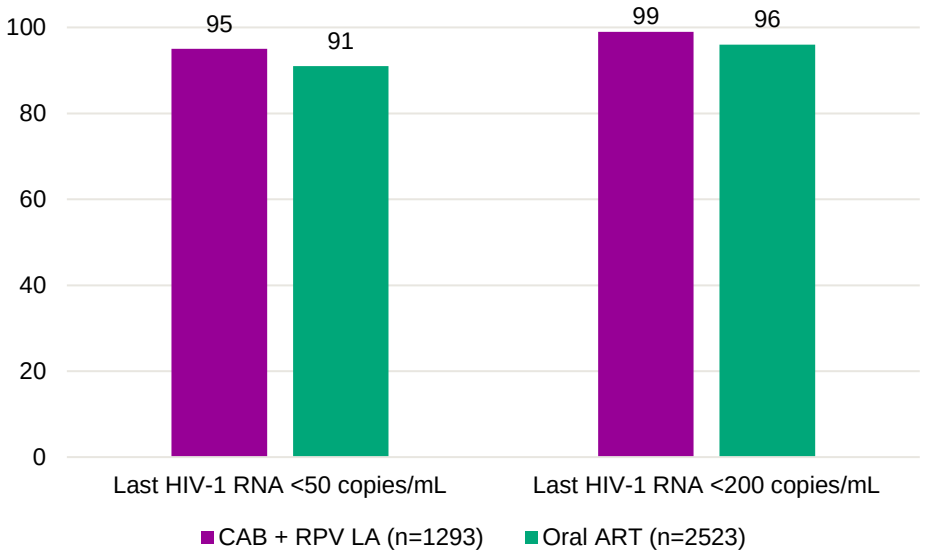
OPERA is a prospectively captured cohort that includes ~14% of people living with HIV (PLHIV) from 101 sites in the US.

Through June 2023, 1362 people had received CAB + RPV LA and were virologically suppressed at the start of the regimen; 2783 people had received oral antiretroviral therapy (ART).

Overall among the CAB + RPV LA arm, the median (interquartile range [IQR]) age was 39 (32, 52) years. Patients included were mostly male (83%); 41% were Black. The median (IQR) months of prior ART was 20 (7, 38) for the CAB + RPV LA arm and 37 (20, 55) for the oral ART arm. Prior integrase strand-transfer inhibitor (INSTI)-based regimens were most common; 74% in the CAB + RPV LA arm and 68% in the oral ART arm.

Virologic outcomes (at least 1 HIV-1 RNA after the first injections) are available for 1293 (95%) of patients treated with CAB + RPV LA and 2523 (91%) treated with oral ART.

Figure 1. Virologic Outcomes from OPERA

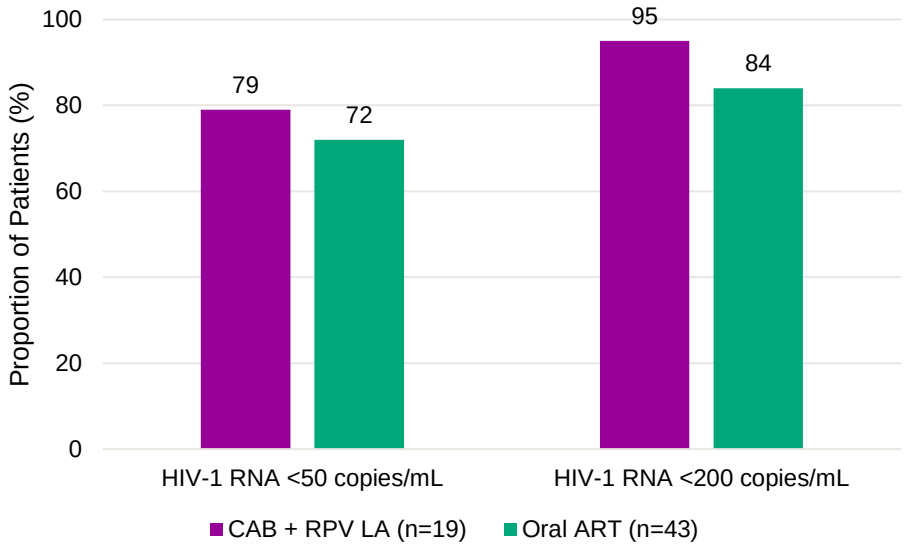


CAB + RPV LA = long-acting cabotegravir plus rilpivirine; ART = antiretroviral therapy

Confirmed virologic failure, defined as 2 consecutive HIV-1 RNA ≥200 copies/mL or 1 HIV-1 RNA ≥200 copies/mL followed by discontinuation, was reported in 2% (25/1293) of patients who received CAB + RPV LA and 3% (78/2523) who received oral ART.

Among those with CVF, the rate of subsequent virologic suppression was high.

Figure 2. Virologic Suppression Following CVF*



*among those with HIV-1 RNA available post-CVF

CVF = confirmed virologic failure; CAB + RPV LA = long-acting cabotegravir plus rilpivirine; ART = antiretroviral therapy

A logistic regression model was fit to evaluate age, sex, race, US region, injection drug use, history of AIDS-defining illness, CD4+ T-cell count, comorbid conditions, prior regimen class, and BMI as predictors of CVF. Only baseline CD4+ T-cell count was associated with CVF; every 100 cell/μL increase was associated with a 15% lower risk of CVF.

No safety data or whether resistance occurred at virologic failure is available from OPERA currently.

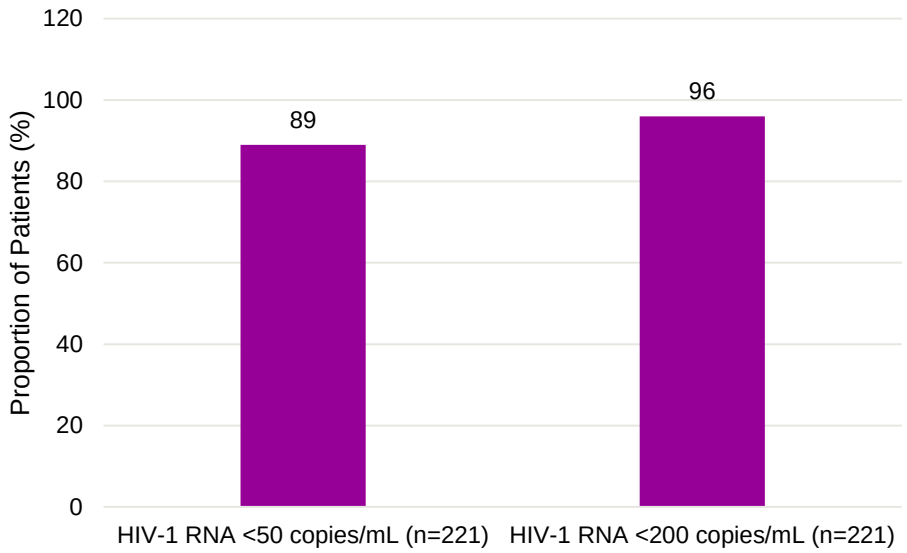
TRIO COHORT STUDY[2]

The Trio Health Cohort is an observational study that utilizes electronic medical records to prospectively collect longitudinal data. Data are available for 278 patients who were virologically suppressed at the time of switching to CAB + RPV LA.

The median (IQR) age was 44 (35, 55) years. Patients included were mostly male (79%) and White (49%) or Black (36%). BMI was ≥30 kg/m² in 35% of patients. The median (IQR) time of follow up after the first injections was 10 (5, 13) months. The every-2-month dosing regimen was most common (82%). At the end of follow up, 88% of patients remained on CAB + RPV LA.

Of the 278 virologically suppressed patients included, 221 (80%) had a follow up HIV-1 RNA available after initiation of CAB + RPV LA.

Figure 3. Virologic Outcomes from the Trio Cohort Study



Six patients (3%) did not maintain virologic suppression (HIV-1 RNA <200 copies/mL). An additional 2 patients (0.9%) met the definition for CVF. One of these patients had high-level resistance to both nucleoside and non-nucleoside reverse transcriptase inhibitors (NNRTIs) prior to initiation of CAB + RPV LA with no resistance data at CVF available. This patient was switched to darunavir/cobicistat/emtricitabine/tenofovir alafenamide but has not had virologic re-suppression. The second CVF resuppressed with HIV-1 RNA <200 copies/mL in 3 months on bictegravir/emtricitabine/tenofovir alafenamide.

No safety data or whether resistance occurred at virologic failure is available from the Trio Cohort Study.

BEYOND[3]

BEYOND is an ongoing 2-year prospective, observational real-world study of the use of CAB + RPV LA across 27 sites in the US. Only interim data from patients who were virologically suppressed at baseline through the Month 6 cutoff are included here.

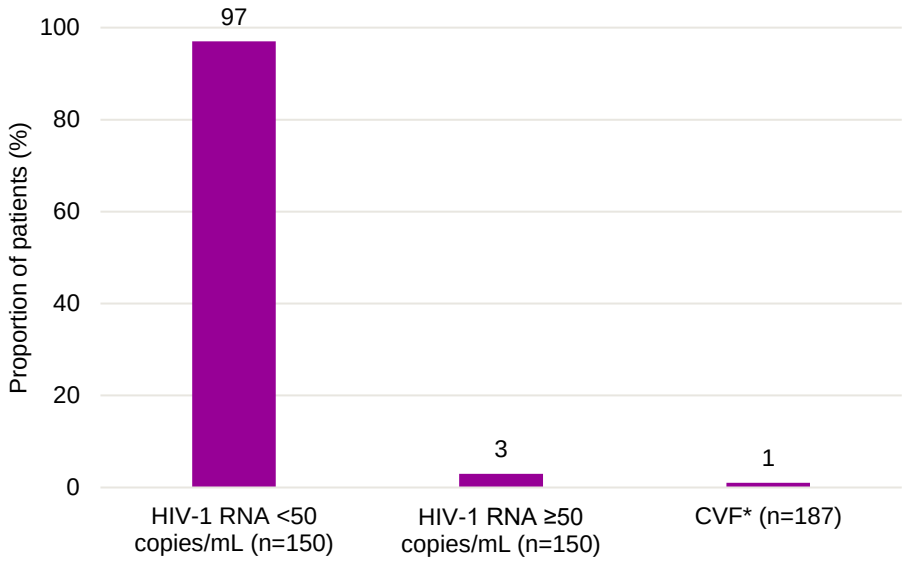
The mean (standard deviation [SD]) age was 46 (13) years. Patients included were mostly male (88%) and White (49%) or Black (39%). Half of patients included were initiated on every-2-month CAB + RPV LA. The most common prior regimen was bictegravir/tenofovir alafenamide/emtricitabine (37%).

The median (range) number of CAB + RPV LA injections administered was 4 (0-7). Eighty-two percent of patients were reported by the HCP to have received CAB + RPV LA +/-7 days from their target

treatment date. The most common reason given was the patient forgot or canceled their appointment (n=6 injection appointments) or other (n=9 injection appointments).

Virologic data was available at both baseline and Month 6 for 150 patients. See Figure 2 below.

Figure 2. Virologic Outcomes from BEYOND at Month 6 Cutoff (interim results)



*includes patients with at least 1 HIV-1 RNA available (n=187).

CVF = confirmed virologic failure (defined as 2 consecutive HIV-1 RNA ≥200 copies/mL or 1 HIV-1 RNA ≥200 copies/mL followed by discontinuation with 3 months of the test result)

Of the 248 patients who reached the Month 6 time point (those who were virologically suppressed at the start of CAB + RPV LA and those who were not), 64 adverse events were reported in 52 patients. The most common adverse events were injection site reactions (11%). Twenty-five patients (10%) discontinued CAB + RPV LA as of the data cut off including 16 who virologically suppressed at the time of CAB + RPV LA initiation. The most common reasons for discontinuation were ISRs (n=4) and medication cost/access issues (n=4).

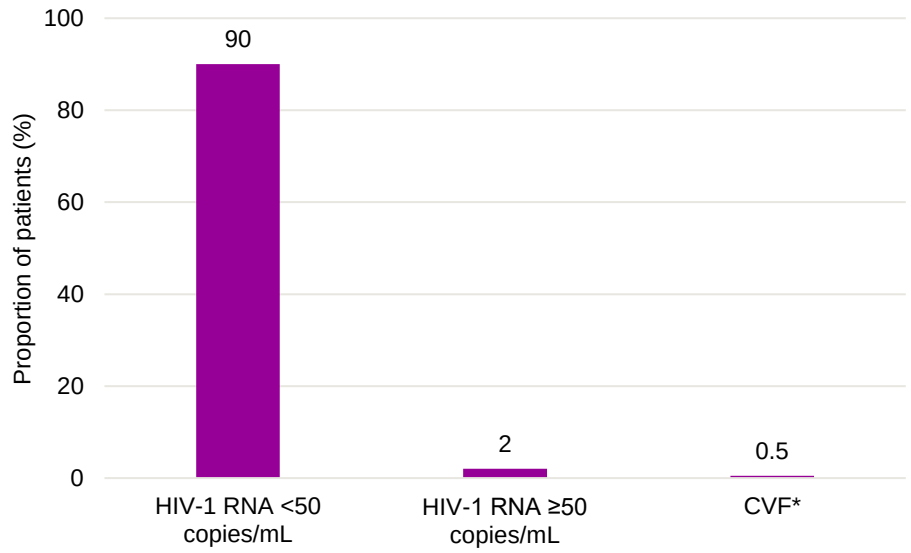
CARLOS[4]

CARLOS is a non-interventional, 3-year, multicenter, prospective German cohort study of virologically suppressed PLHIV who switched to CAB + RPV LA administered every 2 months. An interim analysis after the fourth injection (Month 6) was conducted. Data are available for 236 patients.

The median (IQR) age was 43 (36, 50) years and 75% were <50 years of age. Patients included were predominantly male (95%). BMI was ≥30 kg/m^2 in 12% of patients. The median (IQR) time of follow up was 5.1 (2.9, 8.1) months; 95% of virologically suppressed patients at initiation remained on CAB + RPV LA at the time of the analysis.

Of the 236 patients included, 230 received at least 1 round of CAB + RPV LA injections, and 200 had virologic outcome data available. See Figure 4 below.

Figure 4. Virologic Outcomes from CARLOS at Month 6 (interim results; n=200)



CVF = confirmed virologic failure (confirmed HIV-1 RNA ≥200 copies/mL or a single HIV-1 RNA ≥200 copies/mL followed by treatment discontinuation

The single CVF occurred in the setting of on-time injections and was associated with INSTI (L74I, T97A, E138K, Q148R, and N155H) and NNRTI (Y181C) resistance associated mutations (RAMs).

The most common (>2 events) drug-related adverse events (AEs) excluding injection site reactions (ISRs) were pyrexia (n=10), pain (n=6), headache (n=6), pain in extremity (n=3), nausea (n=3), fatigue (n=3), and sleep disorder (n=3). Six patients (6/200, 2.5%) discontinued the study due to drug-related AEs and an additional 6 patients (6/230, 2.6%) discontinued due to ISRs.

Overall, 97.2% (615/633 injection visits) of injections occurred within the dosing window or earlier (± 7 days from the target treatment date). Of the 18 late injections, 6 were covered with oral therapy.

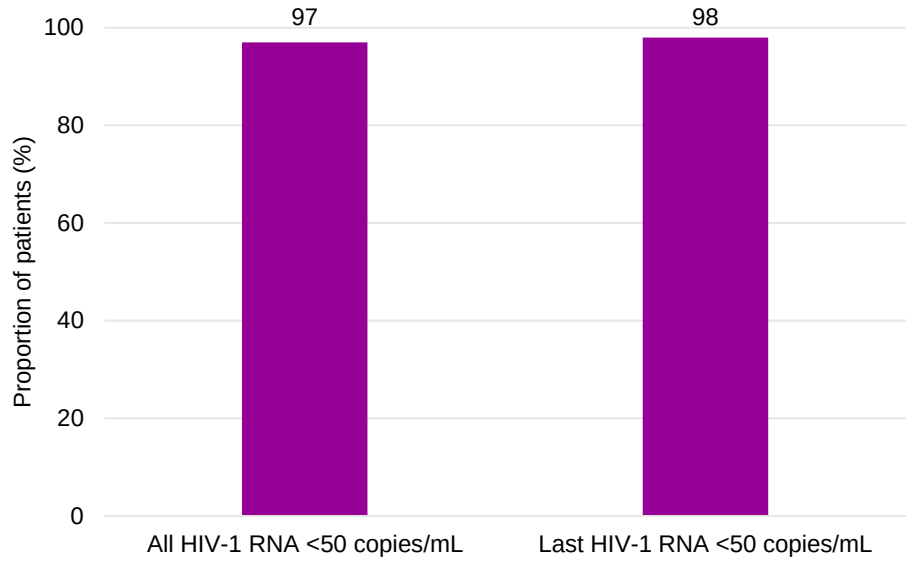
COMBINE-2[5]

COMBINE-2 includes virologically suppressed patients enrolled at NEAT ID Network sites from 5 European countries. Patients received CAB + RPV LA every 2 months from June 2021 through April 2023.

The median (IQR) age was 47 (39, 54) years and 36% were >50 years of age. Patients included were predominantly male (83%) and White (78%). BMI was ≥30 kg/m^2 in 8% of patients. The median (IQR) time of follow up was 5.2 (1.0, 10.8) months. Nine patients had a prior history virologic failure; 4 had a history of INSTI or NNRTI RAMs.

Among the 120 patients included, 89 had an HIV-1 RNA available after the first injections. See Figure 5 below.

Figure 5. Virologic Outcomes from COMBINE-2 (n=89)



There was 1 CVF reported 35 days after the initiation of CAB + RPV LA. The NNRTI RAM E138A was detected at failure. No INSTI RAMs were detected. This patient was switched to darunavir/cobicistat/emtricitabine/tenofovir alafenamide; no outcome information is available.

No safety data is available from COMBINE-2.

OTHER STUDIES REPORTING REAL WORLD EVIDENCE

Please see the reference list below for other RWE presentations or publications.[6-31]

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Selection of references follows principles of evidence-based medicine and, therefore, references may not be all inclusive.

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