Use of Long-Acting Cabotegravir and Lenacapavir, With or Without Long-Acting Rilpivirine

Summary

- Co-administration of long-acting cabotegravir (CAB LA) and lenacapavir (LEN), with or without long-acting rilpivirine (± RPV LA) has not been studied in randomized, controlled clinical trials.
- Use of CAB LA plus LEN (± RPV LA) is not approved in any jurisdiction.
- Multiple case series have reported high rates of viral suppression with use of CAB LA plus LEN, ± RPV, in patients with adherence challenges.[1-6]
- 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.

BACKGROUND

Co-administration of CAB LA plus LEN (± RPV LA), has not been studied in randomized, controlled clinical trials.

LEN is an HIV-1 capsid inhibitor studied primarily in heavily treatment-experienced adults with multidrug resistant HIV-1 infection.[7]

CLINICAL DATA

Gandhi M, et al.[1]

A case series from 4 US academic medical centers (UCSF Ward 86, UCSD Owen Clinic, MetroHealth's HIV Clinic [Cleveland, OH], and UPenn Clinic [Philadelphia, PA]) reported outcomes of patients receiving CAB LA + LEN (± RPV LA). All patients had oral antiretroviral therapy (ART) options available but reported challenges to taking oral ART which led to use of these off-label treatments. For inclusion in the case series, at least 1 viral load after starting LEN must have been available. The primary outcome was the proportion of patients who achieved virologic suppression (HIV RNA < 75 copies/mL) after initiation of CAB LA + LEN (± RPV LA).

From February to October 2023, 34 patients were included; 76% were male, 24% cis/trans female, 41% Black, with median (range) age of 47 (28–75) years; 47% (16/34) had virologic suppression prior to initiating CAB LA + LEN (± RPV LA). Most patients received every-2-month CAB (71% [24/34]) and had RPV included in the regimen (68% [23/34]).

Reported reasons for use of CAB LA + LEN were attributed to: documented or suspected non-nucleoside reverse transcriptase mutations (n = 21 [59%]), integrase strand transfer inhibitor (INSTI) mutations (n = 5 [15%]), high viral load (n = 6 [18%]), and continued viremia on CAB + RPV LA alone (n = 4 [12%]). One patient was started on CAB LA + RPV LA + LEN due to high body mass index; another patient was started on LEN due to intolerance to RPV LA (flu-like reaction).

Overall, 94% (32/34) of patients had virologic suppression (HIV-1 RNA < 75 copies/mL) after a median (range) of 8 (4–16) weeks from starting CAB LA + LEN (± RPV LA). Among patients who were not suppressed at baseline, 89% (16/18) achieved virologic suppression. Virologic suppression was achieved or maintained in all patients with documented or suspected non-nucleoside reverse transcriptase inhibitor mutations (n = 21; 11 suppressed at baseline).

Injection site reactions (ISRs) on LEN were observed in 44% of patients (grade 1: 32%, grade 2: 12%); two patients discontinued LA LEN due to ISRs. Additional safety information was not reported.

Brock JB, et al.[2]

Another case series, conducted at the University of Mississippi Medical Center, reported results from 9 patients with poor adherence to oral ART treated with CAB + RPV LA (every 2 months) and LEN. Mean (range) age was 46 (17–60) years, 6 were female, and all patients were Black/African American. Mean (range) baseline HIV-1 RNA was 36,251 (36–251,000) copies/mL and CD4 count was 420 (23–1199) cells/µL. RPV resistance associated mutations (RAMs) were identified in all 9 patients; 1 patient had CAB RAMs (N155H, T977A; low-level CAB resistance).

Through 24–36 weeks of follow-up, all patients maintained HIV-1 RNA < 200 copies/mL; no treatment-emergent resistance was identified. Absolute CD4 count increased by 208% in patients with a baseline CD4 < 200 cells/µL.

Eldib J, et al.[3]

Data from a case series of 7 extensively-treated patients from New York Presbyterian/Columbia University Medical Center with adherence challenges to oral ART were reported.[3] The age range was 30-60 years, 4 were female, and 3 were Black. Five patients had resistance to at least 2 drug classes. RPV resistance was reported in 5 patients (3 with Y181 [intermediate resistance to RPV]), and INSTI resistance in 4 patients (3 with E157Q [little to no effect on CAB]). Baseline HIV-1 RNA was between 250–150,000 copies/mL in 6 patients; 1 patient had HIV-1 RNA > 150,000 copies/mL. Most (n = 5) had a CD4 count < 200 cells/µL and 5 were perinatally infected.

Five patients received CAB LA plus LEN and 2 patients received CAB + RPV LA and LEN. At or after Week 26, all patients had HIV-1 RNA < 200 copies/mL; 5 had HIV-1 RNA < 50 copies/mL and 3 had HIV-1 RNA < 20 copies/mL. Five patients had CD4 count > 200 cells/µL at Week 26; an additional patient had CD4 count > 200 cells/µL after 1 year of LEN.

Palich R, et al.[4]

A report from 2 French hospitals described 8 patients who were virologically suppressed with RPV resistance and started on LA CAB (every-2-month) + LEN. All patients had difficulty with acceptance of HIV status and problems with adherence. Patients were monitored for at least 6 months (3 were monitored for 12 months).

Median (IQR) age was 56 (44, 58) years and half were female. Median (IQR) time from ART initiation and duration of viral suppression were 25 (18, 32) years and 32 (7, 59) months, respectively. CD4 T-cell count was < 200 cells/µL for 4 patients at the time of LA CAB + LEN initiation.

All patients remained virologically suppressed (HIV-1 RNA < 50 copies/ml) during follow-up.[4] No serious adverse events or discontinuations were reported.

National Clinician Consultation Center[5]

The National Clinician Consultation Center is a US-based clinical resource that offers provider-to-provider teleconsultation, education, and capacity-building. Calls received from December 1, 2022 through August 30, 2024 were identified in which providers were considering potential ART changes to LEN + CAB, LEN + CAB/RPV, or LEN + RPV. Case providers were provided an 18-question survey to inquire about long-acting ART changes. Potential overlap between cases reported here and other cohorts cannot be ruled out.

Overall, 10 cases were identified in which ART was switched to LA LEN + CAB ± RPV with follow-up information available. The mean age (standard deviation) was 51 (14) years, 60% were cisgender men, and 30% were Black/African American. Seven cases reported a history of NNRTI mutations and 6 reported INSTI mutations. Six cases received CAB monthly and 4 were on every-2-month dosing. Reasons for ART change included: detectable viral load on oral ART (n = 6), documented/suspected NNRTI resistance (n = 3), inability/refusal to take oral ART (n = 3), documented/suspected INSTI mutations (n = 2), and persistent viremia on CAB + RPV LA alone (n = 2).

Within a median (range) of 56 (29–166) days, viral load decreased by a mean of 3.88 $\log_{10}$ copies/mL. Viral load was < 200 copies/mL in 8 individuals; the remaining 2 individuals' viral loads decreased from 2,640,00 copies/mL to 313 copies/mL and 4,280,000 copies/mL to 210 copies/mL after 48 and 153 days, respectively. Additional details for the reported cases are summarized in Table 1.

Five individuals reported ISRs to either CAB + RPV, LEN, or all three; all were rated by the provider as "not at all" or "slightly" problematic. One individual had delayed/missed CAB/RPV injection and none had delayed/missed LEN injections. All individuals (except for one case due to patient death for unstated reason) reported wanting to continue with the LA regimen.

Chaudhuri S, et al.[6]

A retrospective case series described 27 viremic patients treated with LA ART, 7 of which received LA LEN + CAB ± RPV. Of the overall cohort, 52% were male, 67% Black, 41% had perinatal HIV, 56% had CD4 cell count < 200 cells/mm^3 (26% had CD4 < 50 cells/mm^3). At baseline, all patients receiving LA LEN + CAB ± RPV had baseline NNRTI and/or INSTI mutations.

All patients in the LA LEN + CAB ± RPV achieved virologic suppression (HIV-1 RNA < 200 copies/mL); median time to suppression was 7.9 weeks. All 7 patients remained on treatment at 24 weeks.

This information is scientific and non-promotional in nature and is not intended for further distribution.

The described use of this product has not been approved by the FDA; therefore, no conclusions should be drawn about the safety or efficacy of this product. This information is not intended to offer recommendations for using this product in a manner inconsistent with its approved labeling. Please consult the applicable Prescribing Information. For ViiV to monitor the safety of our products, we encourage healthcare professionals to report adverse events or suspected overdoses to the company at 877-844-8872.

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

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