P-1051

Real-World Virologic Effectiveness Outcomes With Long-Acting Cabotegravir Plus Rilpivirine in People Who Are Treatment-Experienced With Viremia: A Systematic Literature Review and Meta-Analysis

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Key Takeaways

- **In real-world clinical settings, long-acting cabotegravir plus rilpivirine (CAB+ RPV LA) maintained high effectiveness in people with HIV-1 with viremia at initiation through 12 months post-switch, with low rates of discontinuation throughout follow-up**
- **Overall, rates of virologic failure on CAB+RPV LA were low, with few participants having resistance-associated mutations at failure**
- **These findings help address an important evidence gap by expanding the real-world evidence on outcomes with CAB+RPV LA among people with HIV and viremia at initiation, a population with substantial unmet need**

Plain Language Summary

- This review looked at data from routine clinic visits in everyday life all over the world to study how well long-acting cabotegravir + rilpivirine, an HIV-1 treatment given 6 or 12 times a year as injections, works for people with a detectable level of virus in the blood, called viremia
- Researchers found 20 publications in medical databases and conferences, collecting results on 1438 people who had previously used another type of HIV medication and who had viremia at CAB+RPV LA initiation across North America and Europe
- When results of the different publications were added together across various time points, analyses estimated that the virus was not detectable in 91% of people (17 publications in 1106 people) and was detectable in 4% (11 publications in 984 people); and 13% of people stopped using long-acting cabotegravir + rilpivirine (7 publications in 451 people)

Introduction

- Suboptimal adherence to oral antiretroviral therapy (ART) can lead to virologic, inflammatory, and clinical implications, including serious non-AIDS events[1-4]
- Evidence from recent randomized clinical trials has expanded understanding of CAB+RPV LA in people with current or previous adherence challenges, including people with viremia, while selected guidelines now include recommendations for its use in some people with viremia[5-11]
  - LATITUDE and SUPLA demonstrated superior efficacy of CAB+RPV LA versus oral ART,[9,10] while IMPALA demonstrated long-term non-inferior efficacy and superiority over oral ART for the outcome of clinically relevant viremia (confirmed virologic failure or viral load [VL] ≥1,000 c/mL),[11] among people with adherence and/or engagement challenges
- We conducted a systematic literature review (SLR) and single-arm meta-analysis to characterize virologic outcomes, resistance-associated mutations at virologic failure, and treatment discontinuation among people with HIV-1 who were treatment experienced and had viremia at CAB+RPV LA initiation in routine clinical practice

Methods

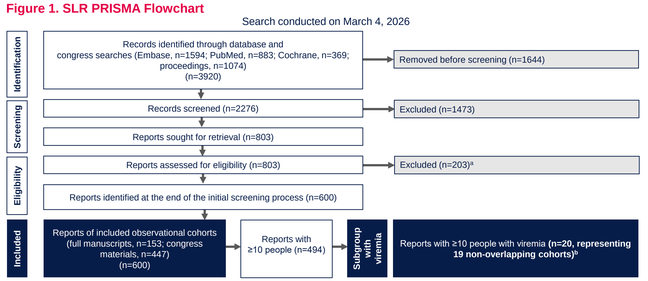
Systematic Literature Review

- An SLR of real-world evidence (RWE) was conducted following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines
- Literature searches were conducted in Embase®, PubMed®, and Cochrane Library databases, as well as major international HIV congress proceedings, to capture both journal articles and congress proceedings from January 2020 to March 2026 (Figure 1)
- Eligible RWE publications reported relevant outcomes for ≥10 people who did not have suppressed VL at CAB+RPV LA initiation as determined by the VL thresholds reported in the source publications
- Publications, defined here as peer-reviewed manuscripts and congress proceedings, were assessed for potential overlap across cohorts to minimize double-counting

Meta-Analyses

- Single-arm meta-analyses were used to produce point estimates at Month 12 and across all publication-reported time points for the proportions of individuals with virologic suppression or experiencing virologic failure, irrespective of outcome definitions in the source publications
  - Point estimates for virologic failure with resistance and treatment discontinuation, either all-cause or due to virologic failure, were produced across all publication-reported time points only, as Month 12 analyses were not feasible
- Freeman-Tukey double-arcsine transformation was used for meta-analyses of proportions, Clopper-Pearson CIs were calculated for individual publications, and the DerSimonian-Laird estimator was used for the τ^2 calculation
- Estimates were calculated using both a random-effects model, where the model allowed for variation between studies, and a fixed-effects model, where the model assumed all studies estimated the same effect, with differences due to chance

Figure 1. SLR PRISMA Flowchart



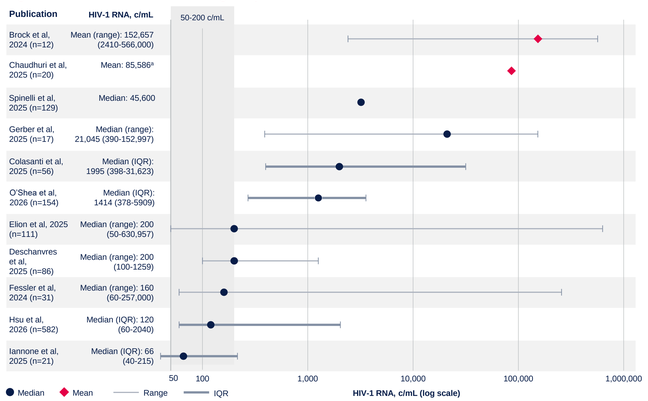
[a]Reasons for exclusion: intervention, n=50; study design, n=33; publication type, n=55; outcomes, n=36; lack of sufficient information for individuals using CAB+RPV LA, n=20; presentation was withdrawn or presumed to have been withdrawn from congress, n=4; full text was not available or encore included instead, n=2; abstract or final presentation with incomplete data, n=1; unclear if the study included individuals using CAB+RPV LA, n=1. individual in the study died from other complications soon after starting CAB+RPV LA, n=1. [b]One additional eligible report was identified through author review and included following assessment against the prespecified eligibility criteria.

Results

Overview of Included RWE

- The SLR identified 494 publications reporting CAB+RPV LA use in ≥10 people, representing 133 cohorts and 45,596 people with HIV-1
- Overall, 20 eligible publications,[12-31] representing 19 non-overlapping cohorts, reported relevant outcomes for 1438 people who were treatment-experienced and had viremia at CAB+RPV LA initiation and, as such, were included in this analysis
- The included cohorts represented routine clinical practice, comprising 15 from the United States,[12-14,17-23,25,26,28-31] 2 from France,[24,27] 1 from Italy,[16] and 1 from Poland[15]
- Publications contributing to each outcome varied according to the outcomes and follow-up reported; where a cohort was represented by multiple publications, only 1 publication was selected for each outcome
- HIV-1 RNA at CAB+RPV LA initiation varied substantially across the 1219 people with viremia included in the 11 publications reporting these data (Figure 2)

Figure 2. Baseline HIV-1 RNA Among People With Viremia at CAB+RPV LA Initiation

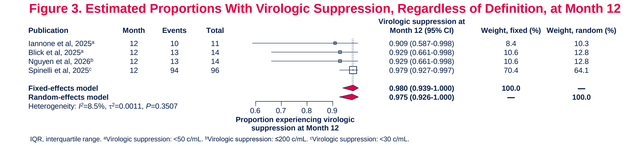


IQR, interquartile range; LEN, lenacapavir. [a]Mean HIV-1 RNA includes 7 people who were using LEN/CAB±RPV.

High Virologic Suppression Through Month 12 and All Available Follow-Up Time Points After CAB+RPV LA Initiation

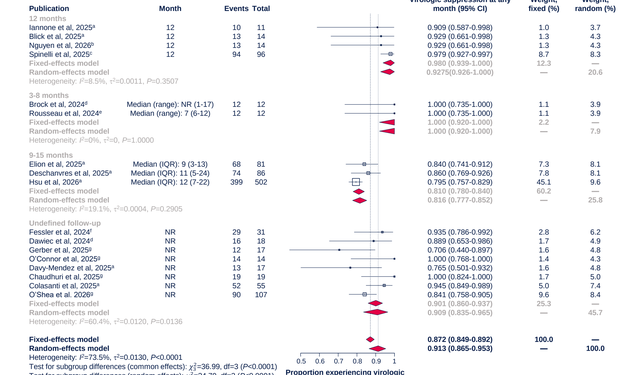
- Across publications reporting virologic suppression at Month 12, the estimated proportion of people with virologic suppression was **97.5% (95% CI, 92.6%-100.0%)** using the random-effects models, regardless of outcome definition (Figure 3)
- Using virologic suppression data reported across all available follow-up time points, the random-effects model estimated that **91.3%** of people had virologic suppression **(95% CI, 86.5%-95.3%)**, irrespective of the outcome definitions used (Figure 4)

Figure 3. Estimated Proportions With Virologic Suppression, Regardless of Definition, at Month 12



IQR, interquartile range. [a]Virologic suppression: <50 c/mL. [b]Virologic suppression: ≤200 c/mL. [c]Virologic suppression: <30 c/mL.

Figure 4. Estimated Proportions With Virologic Suppression, Regardless of Definition, at All Time Points

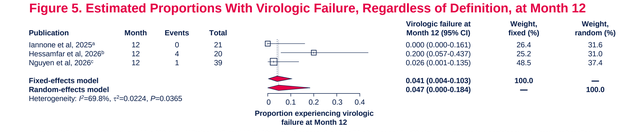


IQR, interquartile range. [a]Virologic suppression: <50 c/mL. [b]Virologic suppression: ≤200 c/mL. [c]Virologic suppression: <30 c/mL. [d]Virologic suppression not defined. [e]Virologic suppression: <20 c/mL. [f]Virologic suppression: ≤50 c/mL. [g]Virologic suppression: <200 c/mL.

Low Incidence of Virologic Failure Through Month 12 and All Available Follow-Up Time Points After CAB+RPV LA Initiation

- From the publications contributing data to the Month 12 virologic failure analysis, an estimated **4.7% (95% CI, 0.0%-18.4%)** of people experienced virologic failure under the random-effects model, although definitions differed between publications (Figure 5)

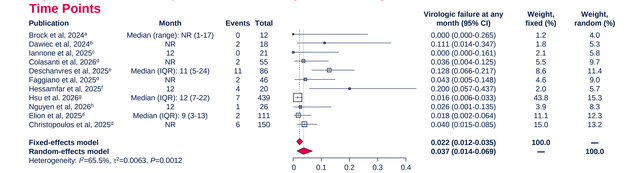
Figure 5. Estimated Proportions With Virologic Failure, Regardless of Definition, at Month 12



[a]Virologic failure: 2 VL >50 c/mL or a VL >200 c/mL. [b]Virologic failure: 1 VL >1000 c/mL, 2 consecutive VLs >50 c/mL, or no VL <50 c/mL by 6 months in a participant with viremia at baseline. [c]Virologic failure: 1 VL >1000 c/mL or 2 consecutive VLs >200 c/mL.

- Across publications contributing virologic failure data at all available follow-up time points, the estimated proportion of people experiencing virologic failure was consistent, with an estimated **3.7% (95% CI, 1.4%-6.9%)** under the random-effects model, based on varying follow-up periods and definitions (Figure 6)

Figure 6. Estimated Proportions With Virologic Failure, Regardless of Definition, at All Time Points

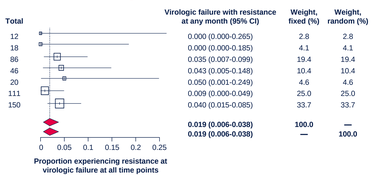


IQR, interquartile range. [a]Virologic failure: VL ≥200 c/mL. [b]Virologic failure: VL >1000 c/mL. [c]Virologic failure: 2 VL >50 c/mL or a VL >200 c/mL. [d]Virologic failure not defined. [e]Virologic failure: 1 VL >200 c/mL after virologic suppression, 2 consecutive VLs >50 c/mL after virologic suppression, or failure to reach virologic suppression by 6 months. [f]Virologic failure: 1 VL >1000 c/mL, 2 consecutive VLs >50 c/mL, or no VL <50 c/mL by 6 months in a participant with viremia at baseline. [g]Virologic failure: 2 consecutive VLs ≥200 c/mL or discontinuation of CAB+RPV LA after a VL ≥200 c/mL assessed after virologic suppression to <50 c/mL. [h]Virologic failure: 1 VL >1000 c/mL or 2 consecutive VLs >200 c/mL.

Low Incidence of Virologic Failure With Resistance Across all Available Follow-Up Time Points After CAB+RPV LA Initiation

- Among publications contributing data on virologic failure with resistance-associated mutations, the random-effects estimated proportion of people experiencing this outcome across all reported time points was **1.9% (95% CI, 0.6%-3.8%;** Figure 7)
  - Specifically, across these 7 publications, the estimated proportion was **0.5% (95% CI, 0.0%-1.9%)** for integrase strand transfer inhibitors and **1.4% (95% CI, 0.3%-3.1%)** for non-nucleoside reverse transcriptase inhibitors using the random-effects model

Figure 7. Estimated Proportions With Resistance at Virologic Failure: All Time Points

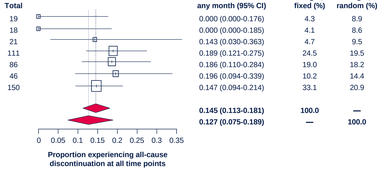


IQR, interquartile range.

Low Incidence of Treatment Discontinuation, Including Discontinuation Due to Virologic Failure

- Across publications contributing all-cause discontinuation data, the random-effects model estimated that **12.7% (95% CI, 7.5%-18.9%)** of people discontinued CAB+RPV LA for any reason during the reported follow-up periods (Figure 8)
  - Discontinuation specifically due to virologic failure was estimated at **2.3% (95% CI, 0.8%-4.2%)**, based on 7 publications[12,16,18,21,24,25,27] including 446 people

Figure 8. Estimated Proportions With All-Cause Discontinuation: All Time Points



IQR, interquartile range.

Conclusions

- Across real-world publications, CAB+RPV LA was associated with high effectiveness in people with viremia who were treatment-experienced at initiation
- Virologic failure, virologic failure with resistance, and discontinuations due to virologic failure were uncommon; all-cause discontinuation rates were low in this population
- Taken together, these findings suggest that CAB+RPV LA may offer meaningful benefits for people with viremia, including those experiencing challenges with adherence to daily oral ART, and may help address an important unmet treatment need in appropriately selected individuals
- Further evidence generation is ongoing, including the phase 3b CROWN study (NCT06694805) in people who are treatment-experienced with detectable viremia

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