Real-World Effectiveness and Tolerability of Cabotegravir + Rilpivirine Long-Acting in People Living With HIV-1: A Meta-Analysis of Real-World Evidence

eP103

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Key Takeaways

- **In real-world clinical settings, long-acting cabotegravir plus rilpivirine (CAB + RPV LA) maintained high effectiveness and tolerability in people living with HIV-1 (PWH) through 12 months post switch, with low rates of discontinuation.**
- **Overall, rates of virological failure on CAB + RPV LA were low, with few participants having resistance-associated mutations at failure.**
- **Real-world evidence of CAB + RPV LA use in broader and more diverse populations further supports findings from randomised controlled clinical trials.**

Introduction

- CAB + RPV LA is the first and only complete LA injectable regimen, administered monthly (Q1M) or every 2 months (Q2M) via gluteal intramuscular injections,[1–3] recommended by treatment guidelines for the maintenance of HIV-1 virological suppression in PWH.[4–7]
  - CAB + RPV LA offers unique benefits for PWH, including reducing the dosing frequency compared with daily oral antiretroviral therapy (ART), as well as reducing the psychological challenges and stigma associated with taking daily oral pills.[8]
- Across many real-world cohorts, CAB + RPV LA has demonstrated long-term effectiveness with low virologic failure rates in diverse populations, consistent with clinical trial outcomes.[9–17]
  - To date, no analyses have consolidated the outcomes from these cohorts to assess the real-world effectiveness and tolerability of CAB + RPV LA.
- Meta-analyses are a valuable source of real-world data as they may reduce the bias associated with individual real-world studies or specific cohorts, while also providing greater confidence and additional supporting evidence for the overall real-world effectiveness of a given intervention.
- Here, we present a meta-analysis of real-world effectiveness and tolerability outcomes in virologically suppressed PWH switching to CAB + RPV LA in a broad range of real-world settings.

Methods – Systematic Literature Review (SLR) and Meta-Analysis

- A SLR of congress abstracts and articles published between January 2020 and March 2025 was conducted to identify real-world observational cohort studies of CAB + RPV LA.
- The analysis was conducted on real-world cohorts of suppressed individuals (viral load [VL] <50 copies/mL) switching to CAB + RPV LA, in line with the licensed indication. Any studies from the literature review reporting data in a suppressed switch cohort were eligible for inclusion.
  - Studies were assessed for overlapping of cohorts to minimize double-counting of individuals in the meta-analysis.
- A single-arm meta-analysis was used to produce point-estimates at Month 12 for the proportion of individuals maintaining virological suppression, experiencing virological failure, developing resistance mutations, and discontinuing treatment, due to injection site reactions (ISRs) or other reasons, as well as the proportion of injections administered within the dosing window.
- A Freeman–Tukey double arcsine transformation was used for the meta-analysis of proportions. The Daimonian–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.
- Sensitivity analyses, including pooling studies regardless of endpoint definitions and reporting outcomes in a follow-up period of between Months 9 and 15, were conducted to assess the impact of consistency in endpoint definitions and observation window.

Results: Included Studies and Populations

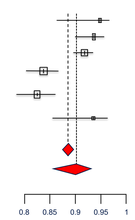
- The meta-analysis included 27 eligible studies conducted in diverse populations from Australia, Canada, France, Germany, Italy, Japan, Spain, the United Kingdom, and the United States.
- A total of 7687 virologically suppressed (HIV-1 RNA <50 copies/mL) participants at baseline who had received CAB + RPV LA were included.
- Of the 27 studies included, 15 reported only Q2M dosing, 9 reported mixed Q1M and Q2M dosing and did not stratify results, and 3 studies did not report the dosing regimen.
- Due to differences in endpoint definitions and time points used, the number of studies included for each endpoint varied, meaning not all 27 studies were included in each endpoint analysis.

At Month 12, the Proportion of Participants Maintaining Virologic Suppression Was High

Figure 1. Virological Suppression at Month 12

Study	Time point	Events, n	Total, N	Viral Suppresion at Month 12*	95% CI	Weight, fixed (%)	Weight, random (%)
Spampinato et al. 2024	Week 48	50	51	0.980	[0.896; 1.000]	3.0	12.7
Schneider et al. 2024	Month 12	181	187	0.968	[0.931; 0.988]	11.0	17.3
Sension et al. 2025	Month 12	511	538	0.950	[0.928; 0.967]	31.5	19.0
Sax et al. 2025	Month 12	452	520	0.869	[0.837; 0.897]	30.4	19.0
Jonsson–Oldenbüttel et al. 2024	Month 12	301	351	0.858	[0.817; 0.892]	20.5	18.5
Haser et al. 2024	Month 12	59	61	0.967	[0.887; 0.996]	3.6	13.5
Fixed effects model				**0.918**	**[0.904; 0.930]**	**100.0**	**–**
Random effects model				**0.934**	**[0.887; 0.969]**	**–**	**100.0**

Heterogeneity: I^2=89.6%, τ^2=0.0084, p<0.0001



*Virologic suppression defined as VL <50 c/mL in these 6 studies.

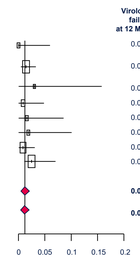
- The estimated proportion of PWH with virological suppression was **91.8% (95% confidence interval [CI] 90.4–93.0)** using the fixed-effects model and **93.4% (95% CI 88.7–96.9)** using the random-effects model (**Figure 1**).
- Sensitivity analyses showed the estimated proportions of PWH achieving virological suppression were consistent when pooling studies reporting outcomes between Months 9 and 15 with consistent outcome definitions (fixed-effects model: **93.2% [95% CI 92.1–94.2]**; random-effect model: **95.9% [95% CI 92.5–98.4]**) and when pooling all studies between Months 9 and 15 regardless of outcome definition (fixed-effects model: **94.7% (95% CI 93.8–95.5)**; random-effects model: **97.4% [95% CI 94.8–99.2]**).

Low Rates of Virological Failure Were Observed at Month 12

Figure 2. Virological Failure at Month 12

Study	Time point	Events, n	Total, N	Virological failure at 12 Months*	95% CI	Weight, fixed (%)	Weight, random (%)
John et al. 2024	Month 12	0	60	0.000	[0.000; 0.060]	4.8	4.8
Jonsson–Oldenbüttel et al. 2024	Month 12	5	351	0.014	[0.005; 0.033]	27.6	27.6
Kirk et al. 2024	Month 12	1	33	0.030	[0.001; 0.158]	2.6	2.6
Orkin et al. 2024	Month 12	1	114	0.009	[0.000; 0.048]	9.0	9.0
Haser et al. 2024	Month 12	1	63	0.016	[0.000; 0.085]	5.0	5.0
Iannone et al. 2025	Month 12	1	53	0.019	[0.000; 0.101]	4.2	4.2
Schneider et al. 2024	Month 12	2	233	0.009	[0.001; 0.031]	18.3	18.3
Hessamfar et al. 2024	Month 12	9	362	0.025	[0.011; 0.047]	28.5	28.5
Fixed effects model				**0.012**	**[0.006; 0.020]**	**100.0**	**–**
Random effects model				**0.012**	**[0.006; 0.020]**	**–**	**100.0**

Heterogeneity: I^2=0.0%, t^2=0, p=0.7102



*Virological failure definitions varied across studies and included single elevated viraemias (VL greater than a specified VL threshold) and confirmed elevated viraemias (2 consecutive VL greater than a specified VL threshold).

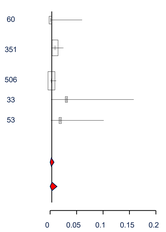
- The estimated proportion of PWH with virological failure was **1.2% (95% CI 0.6–2.0)** (both fixed-effects model and random-effects model; **Figure 2**).
- In the sensitivity analyses, pooling studies reporting outcomes between Months 9 and 15 with consistent outcome definitions, the estimated proportion of participants with virological failure was **0.6% (95% CI 0.0–2.3)** using both the fixed-effects model and random-effects model.
- In further analyses, pooling all studies between Months 9 and 15 regardless of outcome definition, the estimated proportion of PWH with virological failure was **0.7% (95% CI 0.5–1.0)** in the fixed-effects model and **0.9% (95% CI 0.5–1.3)** in the random-effects model.

Low Rates of Virologic Failure With Resistance Were Observed at Month 12

Figure 3. Virological Failure With Resistance at Month 12

Study	Time point	Events, n	Total, N	Virological failure at Months 12	95% CI	Weight, fixed (%)	Weight, random (%)
John et al. 2024	Month 12	0	60	0.000	[0.000; 0.060]	6.0	10.1
Jonsson–Oldenbüttel et al. 2024	Month 12	3	351	0.009	[0.002; 0.025]	35.0	34.3
Gagliardini et al. 2024	Year 1	1	506	0.002	[0.000; 0.011]	50.4	40.5
Kirk et al. 2024	Month 12	1	33	0.030	[0.001; 0.158]	3.3	6.0
Iannone et al. 2025	Month 12	1	53	0.019	[0.000; 0.101]	5.3	9.1
Fixed effects model				**0.001**	**[0.000; 0.007]**	**100.0**	**–**
Random effects model				**0.003**	**[0.000; 0.012]**	**–**	**100.0**

Heterogeneity: I^2=30.7%, t^2=0.0007, p=0.2171



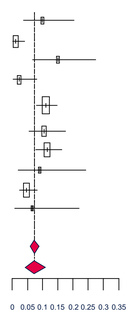
- The estimated proportion of PWH with resistance at failure was **0.1% (95% CI 0.0–0.7)** in the fixed-effects model and **0.3% (95% CI 0.0–1.2)** in the random-effects model (**Figure 3**).
- In sensitivity analyses, the estimated proportion of PWH with resistance at failure at Months 9 and 15 was **0.1% (95% CI 0.0–0.3)** using both the fixed-effects model and the random-effects model.

Low Rates of Discontinuation for Any Reason Were Observed at Month 12

Figure 4. Discontinuations For Any Reason at Month 12

Study	Time point	Events, n	Total, N	All-cause discontinuation at Month 12	95% CI	Weight, fixed (%)	Weight, random (%)
John et al. 2024	Week 48	6	60	0.100	[0.038; 0.205]	4.4	8.8
Gistand et al. 2025	Week 48	2	169	0.012	[0.001; 0.042]	12.4	11.7
Iannone et al. 2025	Week 52	8	53	0.151	[0.067; 0.276]	3.9	8.4
Spampinato et al. 2024	Month 12	2	85	0.024	[0.003; 0.082]	6.3	9.9
Jonsson–Oldenbüttel et al. 2024	Month 12	39	351	0.111	[0.080; 0.149]	25.7	12.9
Orkin et al. 2024	Month 12	12	114	0.105	[0.056; 0.177]	8.4	10.7
Schneider et al. 2024	Month 12	27	233	0.116	[0.078; 0.164]	17.1	12.3
Kirk et al. 2025	Month 12	3	33	0.091	[0.019; 0.243]	2.5	6.7
LaForty et al. 2024	Month 12	11	233	0.047	[0.024; 0.083]	17.1	12.3
Vega et al. 2024	Month 12	2	30	0.067	[0.008; 0.221]	2.2	6.4
Fixed effects model				**0.073**	**[0.059; 0.088]**	**100.0**	**–**
Random effects model				**0.073**	**[0.044; 0.109]**	**–**	**100.0**

Heterogeneity: I^2=77.4%, τ^2=0.0067, p<0.0001



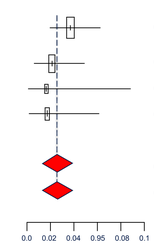
- The estimated proportion of PWH who discontinued for any reason was **7.3% (95% CI 5.9–8.8)** using the fixed-effects model and **7.3% (95% CI 4.4–10.9)** using the random-effects model (**Figure 4**).
- In sensitivity analyses, the estimated proportion of PWH who discontinued for any reason between Months 9 and 15 was **12.7% (95% CI 11.6–13.9%)** in the fixed-effects model and **9.8% (95% CI 6.4–13.6)** in the random-effects model.

Low Rates of Discontinuation Due to ISRs Were Observed at Month 12, Demonstrating the Tolerability of CAB + RPV LA in the Real-World

Figure 5. Discontinuations Due to ISRs at Month 12

Study	Time point	Events, n	Total, N	Discontinuation due to ISRs at Month 12	95% CI	Weight, fixed (%)	Weight, random (%)
Jonsson–Oldenbüttel et al. 2024	Month 12	13	351	0.037	[0.020; 0.063]	46.2	46.2
Schneider et al. 2024	Month 12	5	233	0.021	[0.007; 0.049]	30.7	30.7
John et al. 2024	Month 12	1	60	0.017	[0.000; 0.089]	8.0	8.0
Orkin et al. 2024	Month 12	2	114	0.018	[0.002; 0.062]	15.1	15.1
Fixed effects model				**0.026**	**[0.015; 0.039]**	**100.0**	**–**
Random effects model				**0.026**	**[0.015; 0.039]**	**–**	**100.0**

Heterogeneity: I^2=0.0%, τ^2=0, p =0.6728



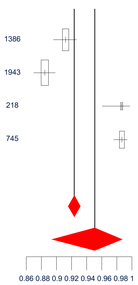
- The estimated proportion of PWH discontinuing treatment due to ISRs was **2.6% (95% CI 1.5–3.9)** (both fixed-effects model and random-effects model; **Figure 5**).
- In sensitivity analyses, the estimated proportion of PWH discontinuing treatment due to ISRs between Months 9 and 15 was **2.0% (95% CI 1.4–2.7)** using the fixed-effects model and **2.0% (95% CI 1.0–3.2)** using the random-effects model.

Most Injections up to Month 12 Were Administered Within the ±7-day Dosing Window

Figure 6. Adherence at Month 12

Study	Adherence definition	Events, n	Total, N	Adherence at Month 12	95% CI	Weight, fixed (%)	Weight, random (%)
Schneider et al. 2024	Injections on time (±7-day window)	1264	1386	0.912	[0.896; 0.926]	32.3	25.5
Jonsson–Oldenbüttel et al. 2024	Injections on time (±7-day window)	1719	1943	0.885	[0.870; 0.899]	45.3	25.6
Kirk et al. 2025	Injections within dosing window (window NR)	215	218	0.986	[0.960; 0.997]	5.1	23.6
Orkin et al. 2024	Injections on time (±7-day window)	735	745	0.987	[0.975; 0.994]	17.4	25.2
Fixed effects model				**0. 924**	**[0.915; 0.931]**	**100.0**	**–**
Random effects model				**0.951**	**[0. 893; 0.987]**	**–**	**100.0**

Heterogeneity: I^2=97.8%, t^2=0.0117, p=< 0.0001



- The estimated proportion of PWH adhering to treatment at Month 12 was **92.4% (95% CI 91.5–93.1)** using the fixed-effects model and **95.1% (95% CI 89.3–98.7)** using the random-effects model (**Figure 6**).
- In sensitivity analyses, the estimated proportion of PWH adhering to treatment between Months 9 and 15 was **96.0% (95% CI 95.6–96.3)** using the fixed-effects model and **96.1% (95% CI 93.7–98.0)** using the random-effects model.

Conclusions

- Among diverse PWH in real-world clinical settings, CAB + RPV LA maintained high rates of virological suppression and low rates of virological failure and virological failure with resistance, through 12 months following switch.
- Rates of discontinuations were low, including discontinuations due to ISRs, and most injections were administered within the ±7-day dosing window.
- These data reinforce the efficacy and tolerability seen in Phase 3/3b trials and further support CAB + RPV LA as an effective, well-tolerated, and implementable treatment option for PWH in real-world practice.

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