Superior Long-Term Real-World Adherence and Persistence With Long-Acting Cabotegravir + Rilpivirine (CAB+RPV LA) Compared With Oral Antiretroviral Therapy (ART) Among People With HIV in the US: The OPTIMIZE Study

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Key Takeaways

- **CAB+RPV LA demonstrated superior long-term real-world adherence and persistence compared with oral ART among people with HIV in the US**
- **The persistence advantage was sustained through two years of follow-up, and adherence was significantly higher at every proportion of days covered (PDC) threshold examined for both adherence periods**
- **Among the minority of individuals that discontinued CAB+RPV LA, most of them remained treated with ART by either re-initiating CAB+RPV LA or switching to oral ART**

Background

- Maintaining high adherence and persistence to ART is essential for sustained virologic control, minimizing resistance, and reducing HIV transmission to advance progress toward ending the HIV epidemic[1]
- CAB+RPV LA is the first and only complete long-acting injectable regimen dosed monthly or every 2 months that was approved in 2021 in the United States (US) for individuals with virologic suppression aged ≥12 years on a stable ART regimen[2-5]
- The real-world ABOVE study found markedly higher 12-month adherence with CAB+RPV LA vs. oral ART (proportion of days covered [PDC] ≥0.90: 74% vs. 30%; adjusted OR 8.06 [95% CI: 6.62–9.81]) and longer persistence (median 424 vs. 393 days)[1]
- The OPTIMIZE study builds on the ABOVE study with a longer, minimum 24-month follow-up period to evaluate whether the real-world adherence and persistence advantage of CAB+RPV LA is sustained over time

Objective

- To compare real-world adherence and persistence between CAB+RPV LA and oral ART regimens over a 2-year follow-up period among people with HIV in the US

Methods

Study Design and Data Source

- Retrospective cohort study using Komodo Research Database (KRD+) administrative claims between January 1, 2019 – July 31, 2025

Study Population

- Aged ≥12 years on any guideline-recommended[6] initial oral ART regimen
- ≥12 months of baseline and ≥24 months of observation period (i.e., index date to earliest of death, end of continuous enrollment, or end of data availability), unless the individual died, then ≥24 months of observation was not required, and data was censored at date of death

Study Cohorts and Index Dates

CAB+RPV LA cohort	Oral ART cohort
• Initiated CAB+RPV LA • **Index date:** first CAB+RPV LA injection on or after January 21, 2021 for adults or March 29, 2022 for adolescents	• Remained on oral ART • **Index date:** imputed based on distribution of time between the CAB+RPV LA cohort's first claim for oral ART to CAB+RPV LA initiation, on or after January 21, 2021

Outcomes

Adherence

- Measured as PDC with CAB+RPV LA or any guideline-recommended oral ART for the CAB+RPV LA or oral ART cohort, respectively: (1) over the full observation period, and (2) from index to discontinuation (or end of observation); was also dichotomized at PDC thresholds of ≥0.90, ≥0.85, and ≥0.80
- For the CAB+RPV LA cohort, only days covered by CAB+RPV LA (or label-allowed oral bridging up to 2 months) counted towards PDC; time on oral ART after discontinuing CAB+RPV LA was not counted as adherent to CAB+RPV LA
- For the oral ART cohort, any guideline-recommended oral ART regimen (not just the index regimen) was counted as being adherent and contributed to the PDC

Persistence

- Time from index date to treatment discontinuation (≥60-day gap in supply), censoring at end of observation

Treatment patterns

- **Re-initiation:** subsequent claim for the index therapy (CAB+RPV LA or oral ART) after discontinuation
- Oral ART cohort only:
  - **Switching:** claim for a different oral STR or multi-agent regimen than index therapy
  - **Duration of regimen episode:** time from treatment regimen initiation to switch, discontinuation, or end of observation

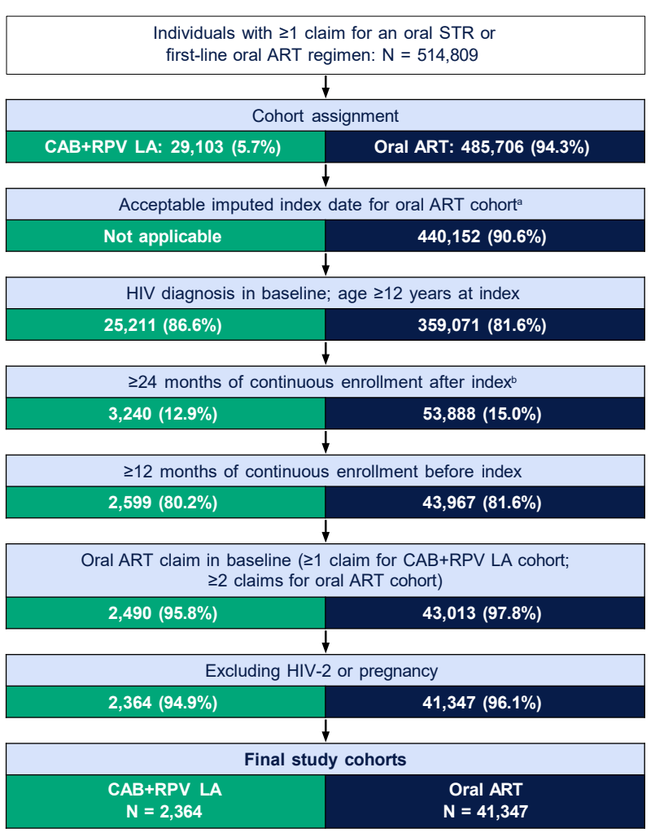
Statistical Analysis

- Descriptive statistics for continuous variables; frequency and proportion for categorical variables
- Standardized mortality ratio (SMR) weighting based on propensity scores (PS) estimated using logistic regression was applied to balance demographic and clinical characteristics between CAB+RPV LA vs. oral ART cohorts, where the CAB+RPV LA cohort individuals were assigned a weight of 1, while individuals in the oral ART cohort were assigned a weight equal to the ratio of the estimated PS/(1-PS)
- Adjusted odds ratios (aOR) for adherence were estimated using SMR-weighted logistic regression models and adjusted hazard ratios (aHR) for persistence were estimated using SMR-weighted Cox proportional hazards models, with 95% confidence intervals (CI)
- All models further adjusted for covariates with standardized difference >10% after SMR weighting

Results

- Overall, 2,364 people were included in the CAB+RPV LA cohort and 41,347 in the oral ART cohort (**Figure 1**)

Figure 1. Sample selection flowchart for CAB+RPV LA and oral ART cohorts



[a] Acceptable imputed index date: on or after the CAB+RPV LA approval date; overlapping an oral ART prescription (days' supply covering the index date); and not the individual's date of death. [b] Individuals who died within 24 months of index (n=41 CAB+RPV LA; n=2,067 oral ART) were also included.
Percentages are relative to the preceding step. HIV, human immunodeficiency virus; STR, single-tablet regimen.

Baseline Characteristics

- CAB+RPV LA cohort was more likely to be younger, with fewer comorbidities and lower baseline oral ART adherence than the oral ART cohort. After SMR-weighting, baseline characteristics between cohorts were similar (**Table 1**) and median follow up time was 32 months in both cohorts

Table 1. Select baseline demographic and clinical characteristics

Characteristic	CAB+RPV LA (N = 2,364)	Oral ART unweighted (N = 41,347)	Std. diff. (%)[a]	Oral ART SMR-weighted (N = 2,302)	Std. diff. (%)[b]
Age (years), mean ± SD [median]	46.7 ± 12.7 [46.9]	52.7 ± 12.7 [54.5]	46.8*	46.9 ± 13.3 [47.1]	1.48
Male sex, n (%)	1,804 (76.3)	31,609 (76.4)	0.32	1,743 (75.7)	1.33
Transgender women[c], n (%)	336 (14.2)	4,432 (10.7)	10.59*	303 (13.2)	3.06
Transgender men[c], n (%)	140 (5.9)	1,575 (3.8)	9.83	105 (4.6)	6.01
Elixhauser score[d], mean ± SD [median]	1.4 ± 7.4 [0.0]	3.1 ± 8.3 [0.0]	20.58*	1.5 ± 7.4 [0.0]	0.49
Elixhauser comorbidities with ≥15% prevalence in either cohort, n (%)					
Hypertension (uncomplicated and complicated)	917 (38.8)	19,234 (46.5)	15.67*	896 (38.9)	0.31
Depression	796 (33.7)	10,295 (24.9)	19.37*	711 (30.9)	5.96
Obesity	534 (22.6)	7,836 (19.0)	8.97	453 (19.7)	7.13
Chronic pulmonary disease	475 (20.1)	7,536 (18.2)	4.74	418 (18.1)	4.97
Drug abuse	372 (15.7)	5,140 (12.4)	9.51	412 (17.9)	5.84
Hepatitis C virus, n (%)	114 (4.8)	2,405 (5.8)	4.43	124 (5.4)	2.66
Hepatitis B virus, n (%)	29 (1.2)	1,383 (3.3)	14.21*	29 (1.2)	0.19
Anxiety disorders, n (%)	715 (30.2)	9,328 (22.6)	17.50 *	645 (28.0)	4.89
Substance-related/addictive disorders, n (%)	582 (24.6)	9,504 (23.0)	3.84	644 (28.0)	7.65
Baseline adherence (PDC[e]), mean ± SD [median]	0.82 ± 0.20 [0.90]	0.88 ± 0.15 [0.94]	34.20*	0.83 ± 0.20 [0.91]	2.72

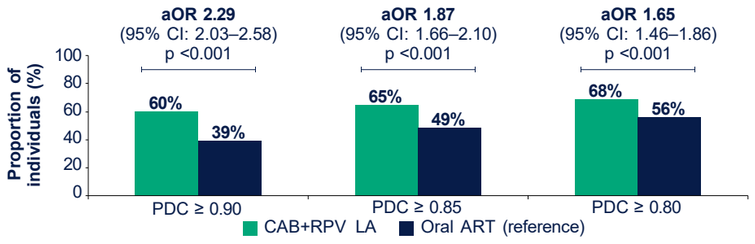
*Absolute standardized difference >10%, considered an imbalance between cohorts.
All characteristics were assessed during the 12-month baseline period unless otherwise specified.
[a] Compares the unweighted CAB+RPV LA (N = 2,364) and oral ART (N = 41,347) cohorts. [b] Compares the CAB+RPV LA cohort with the SMR-weighted oral ART cohort, whose reported N is the sum of weights (effective sample size 22,550). [c] Transgender experience identified over the study period from ICD-10-CM diagnosis, CPT gender-affirming surgery, and NDC medication codes. [d] Elixhauser scores reflect overall comorbidity burden, with higher scores indicating greater comorbidity burden. [e] PDC evaluated over the baseline period.
CPT, Current Procedural Terminology; ICD-10-CM, International Classification of Diseases, 10th Revision, Clinical Modification; NDC, National Drug Code; PDC, proportion of days covered; SD, standard deviation; SMR, standardized mortality ratio; Std. diff., standardized difference.

Treatment Adherence

- In the weighted analysis, a greater proportion of people in the CAB+RPV LA cohort achieved PDC ≥0.90 than the oral ART cohort over both adherence periods (observation period: 60% vs. 39%, **Figure 2a**; to discontinuation: 92% vs 79%, **Figure 2b**)
- CAB+RPV LA cohort vs oral ART cohort was significantly more likely to be adherent across all three PDC thresholds for both adherence periods (observation period: [aORs 1.65-2.29]; to discontinuation: [aORs 2.14-3.16])
- For the CAB+RPV LA cohort, 365 (15.4%) people received ≥1 oral bridging therapy on ≥1 occasion between consecutive CAB+RPV injections

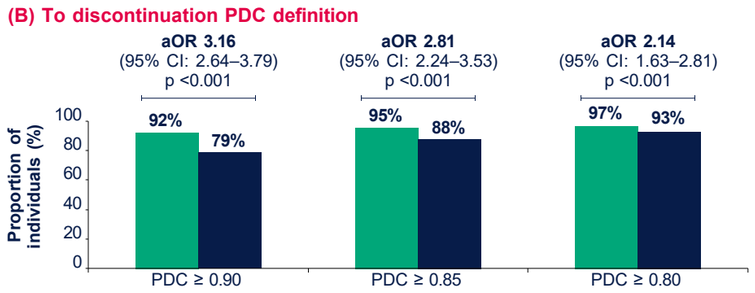
Figure 2. Higher adherence in CAB+RPV LA vs. oral ART cohorts across all PDC thresholds and both adherence periods; SMR-weighted sample

(A) Observation period PDC definition



Continuous PDC	CAB+RPV LA (N = 2,364)	Oral ART, unweighted (N = 41,347)	Oral ART, SMR-weighted (N = 2,302)
Mean ± SD; median [IQR]	0.77 ± 0.32; 0.95 [0.59–1.00]	0.77 ± 0.26; 0.89 [0.67–0.95]	0.72 ± 0.28; 0.84 [0.56–0.94]

(B) To discontinuation PDC definition



Continuous PDC	CAB+RPV LA (N = 2,364)	Oral ART, unweighted (N = 41,347)	Oral ART, SMR-weighted (N = 2,302)
Mean ± SD; median [IQR]	0.96 ± 0.12; 0.99 [0.96–1.00]	0.94 ± 0.08; 0.96 [0.92–1.00]	0.94 ± 0.09; 0.97 [0.91–1.00]

aOR, adjusted odds ratio; CI, confidence interval; PDC, proportion of days covered; SMR, standardized mortality ratio.

Treatment Persistence and Reinitiation

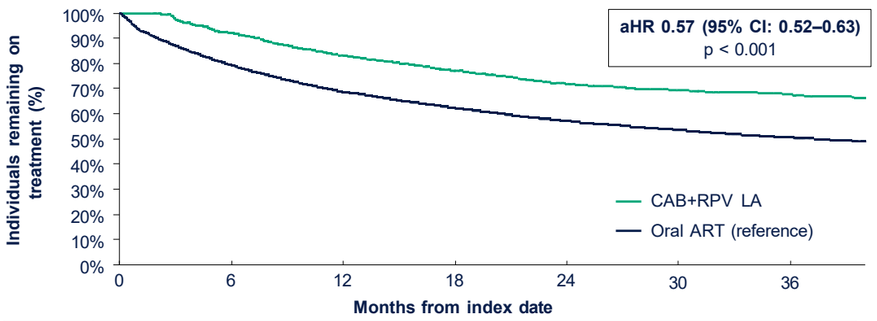
Persistence

- At 24 months: 72.0% of the CAB+RPV LA cohort remained persistent vs. 57.2% of the SMR-weighted oral ART cohort (**Figure 3**)
- Over follow-up, CAB+RPV LA was associated with a 43% lower rate of discontinuation versus oral ART
- Median time to discontinuation for the SMR-weighted oral ART cohort was 37.4 months and median time to CAB+RPV LA discontinuation was not reached in this analysis

Reinitiation

- Among 668 people who discontinued CAB+RPV LA, 86.7% either re-initiated CAB+RPV LA (35.5%) and/or switched to oral ART (62.9%)
- Among the 1,070 people who discontinued in the oral ART cohort (SMR-weighted), 76.3% re-initiated any oral ART

Figure 3. Kaplan-Meier curve showing greater persistence with CAB+RPV LA vs. oral ART (SMR-weighted sample)



	Individuals remaining on treatment (Kaplan-Meier persistence), %						
	Month 0	Month 6	Month 12	Month 18	Month 24	Month 30	Month 36
CAB+RPV LA cohort[a] (N = 2,137)	100.0%	92.1%	83.2%	77.1%	72.0%	69.3%	67.7%
Oral ART cohort (N = 2,302)	100.0%	79.3%	68.8%	62.3%	57.2%	53.6%	50.6%

[a] For the persistence analysis only, a second CAB+RPV injection was required within 21 days to 3 months after index for the CAB+RPV LA cohort to capture individuals fully initiated on CAB+RPV LA.
aHR, adjusted hazard ratio.

Oral ART Treatment Patterns

- Most people in the SMR-weighted oral ART cohort did not switch regimens during the observation period: 84.8% had no regimen switches, while 11.7% had one switch and 3.4% had ≥2 switches (**Table 2**)
- The median number of oral ART regimen episodes per person was 1.0 (IQR: 1.0, 2.0)
- Oral ART regimen episodes lasted a median of 9.3 months (IQR: 2.9, 25.4)

Table 2. Oral ART treatment patterns

	Oral ART unweighted (N = 41,347)	Oral ART SMR-weighted (N = 2,302)
Number of oral ART regimen switches, n (%)		
0 switches	34,558 (83.6)	1,953 (84.8)
1 switch	5,311 (12.8)	270 (11.7)
2 switches	790 (1.9)	44 (1.9)
≥3 switches	688 (1.7)	35 (1.5)
Number of oral ART regimen episodes per individual		
Mean ± SD	1.7 ± 1.3	1.8 ± 1.3
Median [IQR]	1.0 [1.0, 2.0]	1.0 [1.0, 2.0]
Duration per regimen episode (months)		
Mean ± SD	16.4 ± 13.8	14.1 ± 12.9
Median [IQR]	12.7 [3.4, 27.7]	9.3 [2.8, 25.4]

IQR, interquartile range; SD, standard deviation; SMR, standardized mortality ratio.

Conclusions

- CAB+RPV LA was associated with superior adherence compared to oral ART across all PDC thresholds examined
- Persistence was greater for CAB+RPV LA compared to oral ART over ≥24 month follow-up period
- OPTIMIZE extends the findings from ABOVE, providing long-term evidence of the sustained advantage of CAB+RPV LA over oral ART to address real-world adherence and persistence challenges

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