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Real-world Effectiveness of CAB+RPV LA in Individuals with HIV Viremia at Therapy Initiation

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Disclosures

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  - ViiV Healthcare, Gilead Sciences, Epividian

Summary

What is the main question:

Is CAB+RPV LA effective in individuals with baseline viral loads ≥ 50 copies/mL initiating the regimen?

What did we find:

CAB+RPV LA was highly effective in people with viremia in routine clinical care in the US

Why is it important:

CAB+RPV LA may be an option for individuals who are struggling with adherence or tolerability on oral therapy

Background

Potential advantages of long-acting ART

- Convenience with potential for improved adherence
- Reduced daily reminders of HIV, stigma, and disclosure
- Minimize pill burden and gastrointestinal issues

Cabotegravir + rilpivirine long-acting (CAB+RPV LA)

- 1st and currently only complete long-acting injectable ART regimen
- Indicated for ART-experienced individuals with HIV and viral loads <50 copies/mL
- Injection once a month (Q1M) or every 2 months (Q2M)

CAB+RPV LA in individuals with viremia in the US

- In real-world cohorts in the US, 9-35% of CAB+RPV LA users initiated with viremia (VL ≥ 30[1] or ≥ 50 copies/mL[2-4])

[1] Spinelli, et al. *Jama*. 2025;333(16):1451-1453; [2] Sension, et al. *Infect Dis Ther*. 2023;12:2807-2817;
[3] Elion, et al. Abstract 1592. IDWeek 2023; [4] Hickey, et al. *Clin Infect Dis.* 2025;80(4):864-870

Study Objectives

Among individuals initiating CAB+RPV LA with viremia in OPERA

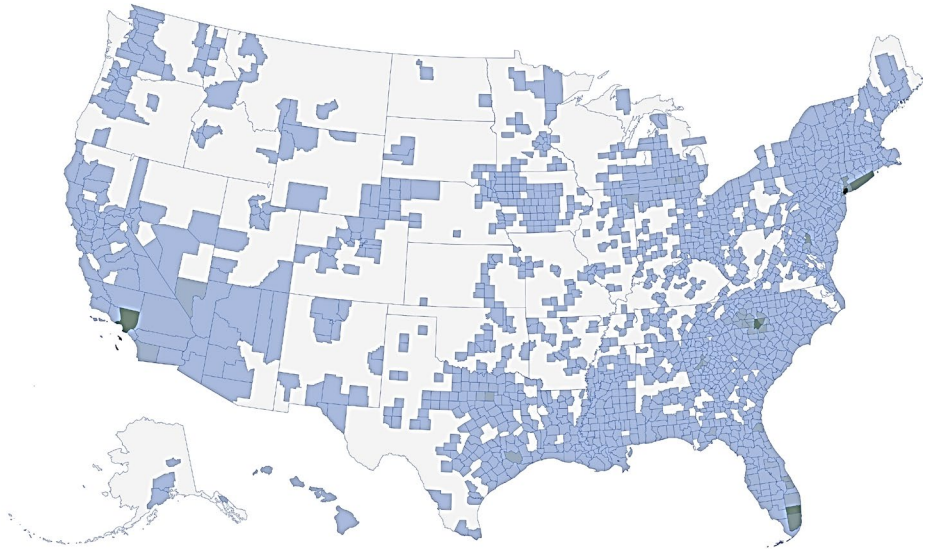
To evaluate utilization of CAB+RPV LA among people with HIV (PWH) with viral load ≥ 50 copies/mL prior to initiation

To describe adherence, persistence, and effectiveness of CAB+RPV LA within this population in real-world clinical setting

Methods

OPERA®

The Longitudinal Cohort



Observational **P**harmaco-**E**pidemiology **R**esearch & **A**nalysis

>150K people with HIV in OPERA

~14% of people with HIV in the US

Study Design

Inclusion Criteria

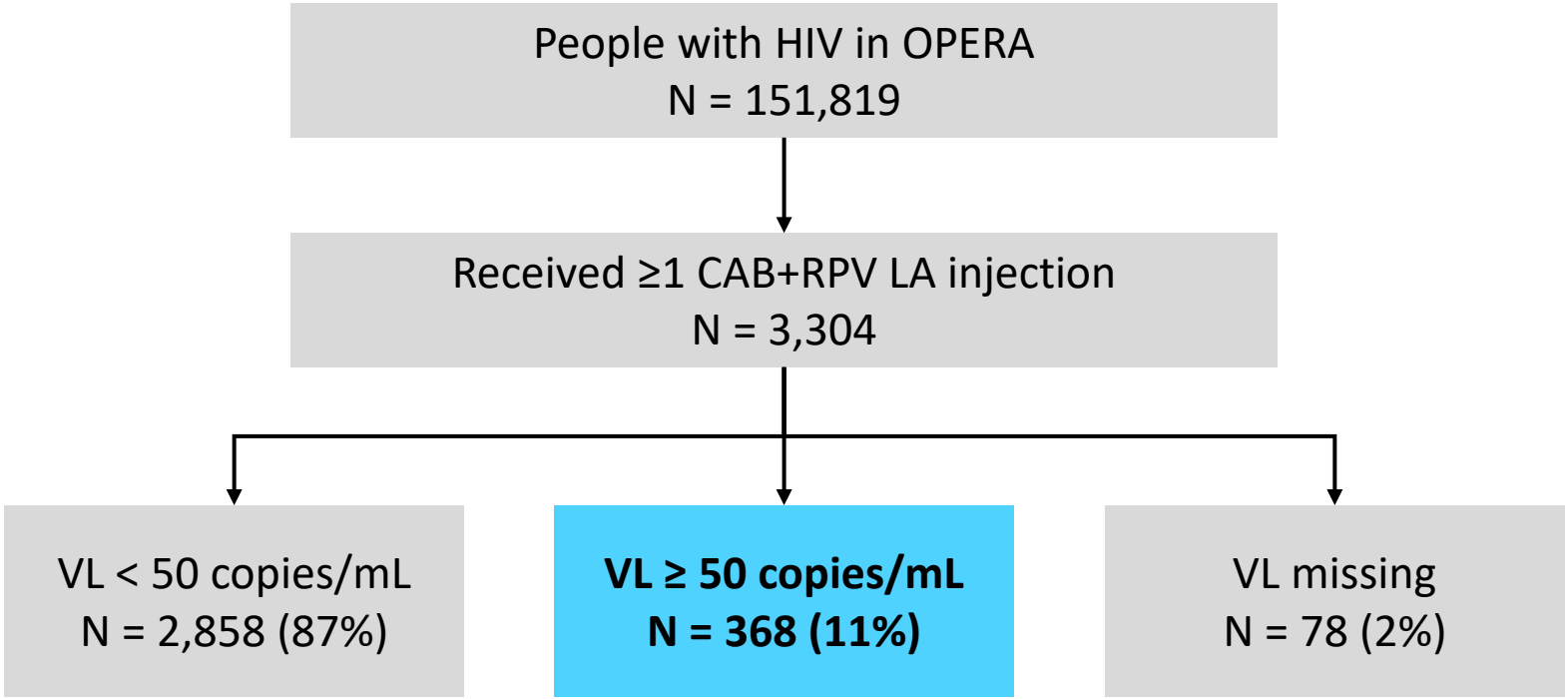
- ≥18 years old
- ART-experienced
- VL ≥ 50 copies/mL at 1st injection
- Received ≥1 CAB+RPV LA injection between 21JAN2021-31DEC2023
- Did not participate in CAB+RPV LA clinical trials

Censoring Criteria

- CAB+RPV LA discontinuation
- Lost to follow-up
- Death
- End of analysis (29FEB2024)

Results

Study Population at Regimen Initiation



Demographic Characteristics
at 1st Injection

	CAB+RPV LA users with viremia (N = 368)
Age, ≥50 years, n (%)	101 (27%)
Female sex, n (%)	109 (30%)
Black race, n (%)	208 (57%)
Hispanic ethnicity, n (%)	66 (18%)
Single, n (%)	263 (71%)
Men who have sex with men, n (%)	182 (49%)
Southern USA, n (%)	233 (63%)

Clinical Characteristics
at 1st Injection

	CAB+RPV LA users with viremia (N = 368)
BMI, >30 kg/m^2, n (%)	106 (29%)
Years since HIV diagnosis, median (IQR)	9 (3, 17)
History of AIDS-defined events, n (%)	126 (34%)
HIV viral load, median copies/mL (IQR)	120 (61, 2535)
HIV viral load ≥200 copies/mL, n (%)	148 (40%)
CD4 cell count, median cells/µL (IQR)	578 (353, 808)
Any comorbidities, n (%)	295 (80%)

Oral ART

Prior to 1st Injection

	CAB+RPV LA users with viremia (N = 368)
Duration of prior regimen, median months (IQR)	17 (8, 37)
Prior core agent class, n (%)	
INSTI	252 (68%)
PI	32 (9%)
NNRTI	28 (8%)
≥ 2 core agents	46 (12%)
Other	≤ 5
Missing	8 (2%)

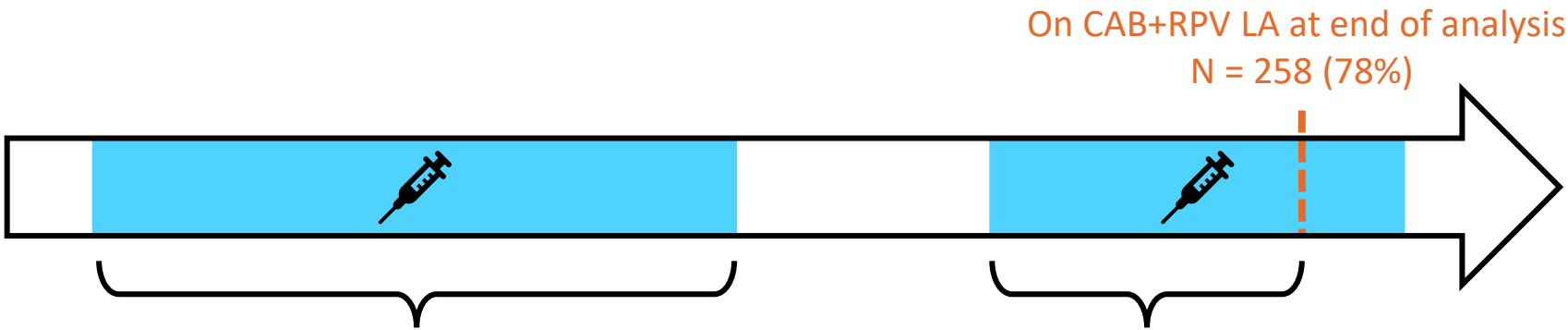
Adherence to Injection Schedule

		Days between injection	n (%)
Initiation injection N = 368	Complete	Q1M & Q2M: ≤67 days	331 (90%)
	Incomplete	Q1M & Q2M: >67 days	37 (10%)
Maintenance injections N = 293	All on-time	Q1M: 23-67 days Q2M: 53-67 days	174 (59%)
	Delayed	Q1M: 38-52 days Q2M: 68-112 days	96 (33%) Median 1 delay (IQR: 1, 2)
	Missed	Q1M: 53-67 days Q2M: 113-127 days	38 (13%) Median 1 missed (IQR: 1, 1)

Q2M at initiation: n = 264 (80%)
Q2M at end of analysis or discontinuation: n = 307 (93%)

Persistence of All CAB+RPV LA Exposures

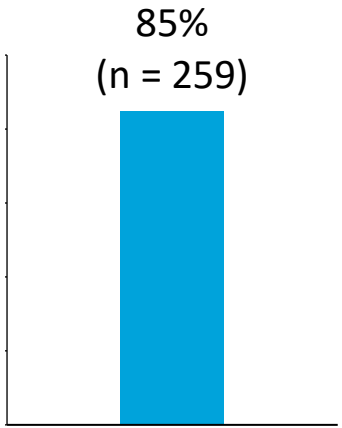
Among All CAB+RPV LA Initiators (N = 331)



Median 12 cumulative months (IQR: 8, 19) on CAB+RPV LA from 1st injection to end of analysis among those on CAB+RPV at end of analysis

Virologic Outcomes

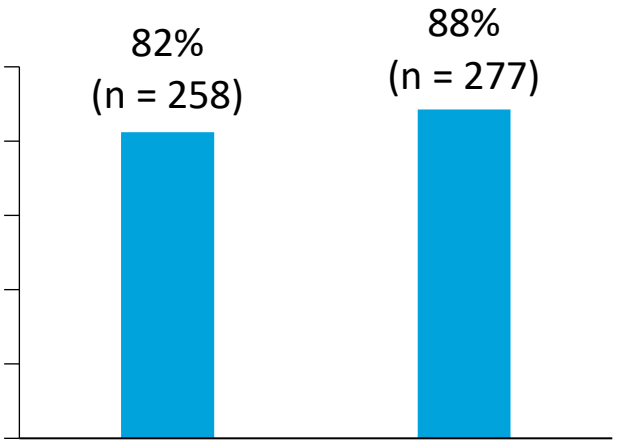
Complete initiators, ≥ 1 VL within 6 months (N = 306)



VL < 50 c/mL within 6 months[†]

[†] + 30 days grace period

Complete initiators, ≥ 1 VL during follow-up (N = 313)

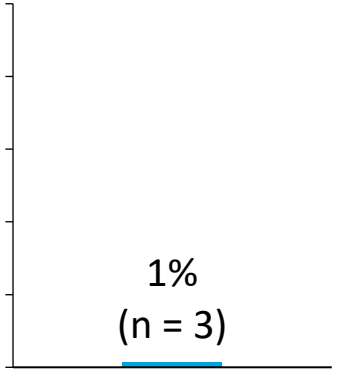


VL < 50 c/mL at last follow-up

Any VL < 50 c/mL*

* 12% (n = 36) never suppressed to < 50 copies/mL

Complete initiators, ≥ 1 VL after suppression (N = 301)



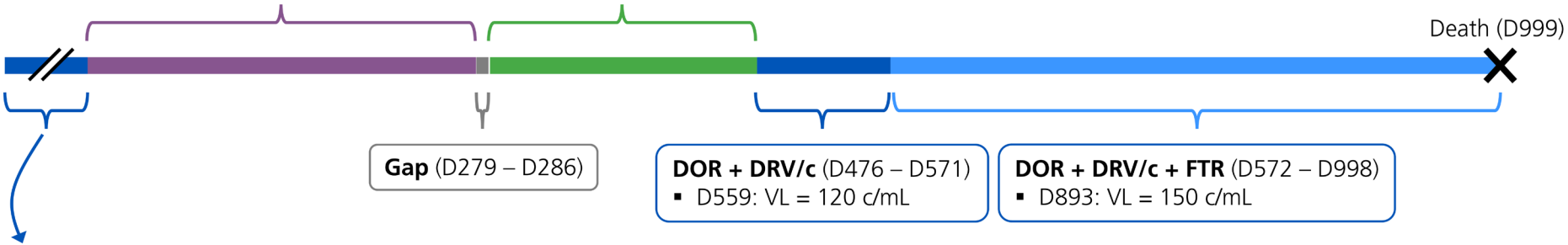
Confirmed virologic failure[‡]

[‡] 2 consecutive VLs ≥ 200 c/mL or 1 VL ≥ 200 c/mL + discontinuation within 2 (Q1M) or 4 (Q2M) months

CVF Case #1

CAB+RPV LA Q1M (D0 – D278)
- D209: Last dose
  - Missed 2 doses (due ~D239 & ~D269), CVF
- D266: VL = 69,700 c/mL

CAB+RPV LA Q2M (D287 – D475)
- No initiation dose
- D406: VL = 34,600 c/mL
- D411: GenoSure PRIme
  - NNRTI – **K101P** (sensitive to DOR; resistant to all other NNRTI)
  - INSTI – **L74M, G140C, Q148R** (pan resistant)



Prior ART: LPV/r + ATV + DTG (31 months)
- Median VL = 47,000 c/mL (range: 270 – 187, 000 c/mL)
- 31 day before CAB+RPV LA: GenoSure PRIme, Subgroup B, multiple polymorphisms
- 11 days before CAB+RPV LA: VL = 35,500 c/mL

CVF Case #2

CAB+RPV LA Q1M (D0 – D208)
- D0: VL = 160 c/mL
- D14: GenoSure Archive: multiple polymorphisms
- D57 – D176: VL < 50 c/mL

DRV/c/FTC/TAF (D457 – D601)
- D470: GenoSure PRIme
  - NNRTI – **V179I, Y181C, K101Q, V90I** (resistance)
  - INSTI – **T97A, S147G, N155H** (possible resistance)
- D503: VL = 390 c/mL
- D539: VL = 230 c/mL
- D580: VL = 140 c/mL

CAB+RPV LA Q2M (D209 – D455)
- D271: VL < 20 c/mL
- D454: VL = 38,600 c/mL , last dose
- D456: Discontinuation, CVF

LEN + DRV/c + FTR (D602 – D1049)
- D649: VL < 20 c/mL
- D685 – D1049: Median VL = 30 c/mL (range < 20 – 80 c/mL)

Prior ART: DRV/c + DTG BID (>48 months)
- Median VL = 20 c/mL (range: <20 – 620 c/mL)
- 645 & 127 days before CAB+RPV LA: GenoSure Archive, multiple polymorphisms

CVF Case #3

CAB+RPV LA Q1M (D0 – D188)
- D0: VL = 170 c/mL
- D95: VL < 20 c/mL

CAB+RPV LA Q2M + FTR (D416 – D461)

CAB+RPV LA Q2M (D189 – D415)
- D249: VL = 360 c/mL
- D371: VL = 930 c/mL, CVF
- D389: VL = 360 c/mL, GenoSure PRIme could not be run (VL too low)

CAB+RPV LA Q1M (high dose) + FTR (D462 – D1223)
- D502: VL = 20 c/mL
- Median VL = 19 c/mL (range: 19 – 70 c/mL)

Prior ART: B/F/TAF (26 months)
- Median VL = 445,000 c/mL (range: 320 – 973,000 c/mL)
- 191 days before CAB+RPV LA: Subgroup B, multiple polymorphisms

Discussion

Key Findings

368 individuals (11%) initiated CAB+RPV LA with viremia (off-label) in the OPERA cohort during the first 3 years of availability in the US

High persistence with moderate adherence on CAB+RPV LA

- 258 (78%) remained on CAB+RPV LA at the time of analysis
- 174 (59%) were fully adherent to injection schedule

CAB+RPV LA demonstrated high effectiveness in people with viremia

- 259 (85%) achieved suppression to <50 copies/mL by 6 months
- 3 (1%) experienced confirmed virologic failure, after which 2 had major NNRTI & INSTI resistance, 1 had no genotyping

Strengths & Limitations

Strengths

- Large population of individuals initiating CAB+RPV LA while viremic
- Regionally diverse representation of people with HIV in the US
- Real-world data captured through electronic health records

Limitations

- Possible misclassification of adherence and non-persistence due to:
  - Incomplete documentation of oral bridging in EHR
  - Loss to care (e.g., care interruption, transfer to a non-OPERA clinic)

Conclusion

Given the high effectiveness observed in a real-world setting in the US, CAB+RPV LA may have a role for individuals with VL ≥ 50 copies/mL who may be struggling with adherence or tolerability to oral therapy

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