Long-Acting CAB+RPV for People with HIV with Adherence Challenges

We will begin shortly...

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Wednesday, February 4, 2026
Virtual Webinar

Long-Acting CAB+RPV for People with HIV with Adherence Challenges

Monica Gandhi, MD, MPH
Professor of Medicine and Associate Chief in the Division of HIV, Infectious Diseases, and Global Medicine
University of California, San Francisco (UCSF)

Director of the UCSF Center for AIDS Research (CFAR) and the Medical Director of the HIV Clinic ("Ward 86")
San Francisco General Hospital

Aadia Rana, MD
Professor of Medicine
University of Alabama-Birmingham Heersink School of Medicine, UAB 1917 Clinic

Gregory Huhn, MD, MPHTM
Regional Medical Director
ViiV Healthcare

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Background Overview

Paula Teichner, PharmD, AAHIVP
Regional Medical Lead, LAI for Treatment and Pipeline
ViiV Healthcare

CAB+RPV LA: High efficacy and a low rate of CVF has been demonstrated across a robust development program

	ATLAS	FLAIR	ATLAS-2M	SOLAR	CUSTOMIZE	CARISEL	CARES
	N=308[6]	N=283[7]	N=1045 (ITT-E)[1]	N=447 (mITT-E)[2]	N=109[3]	N=430[4]	N=255 (ITT-E)[5]
Virologically suppressed	**93%***	**94%***	**94%***	**90%***	**89%***	**87%***	**96%***
CVF	**1%** (n=3) by Week 48	**1.4%** (n=3)€ by Week 48	**1%** (n=11) by Week 48†‡	**0.4%** (n=2) by Month 12‡	**0%** No CVFs occurred by Month 12	**0.7%** (n=2) by Month 12‡	**0.8%** (n=2) by Week 48‡

N = Numbers reflect CAB/RPV treatment arms

***ATLAS, FLAIR, ATLAS-2M and CARES, VL <50 c/mL at Week 48, SOLAR, CUSTOMIZE and CARISEL, VL <50 c/mL at Month 12; †Includes one non-protocol-defined CVF; ‡ATLAS-2M: Versus 93% virologically suppressed and <1% (n=2) with CVF in the CAB + RPV LA Q4W group (n=523); CARISEL: Data from pooled Arm-S and Arm-E groups. The rate of virological suppression was 87% in both Arm-S and Arm-E. Both cases of CVF occurred in participants in Arm-E; SOLAR: Versus 93% virologically suppressed and 0% CVF in the BIC/FTC/TAF group (n=223). A third CAB + RPV LA participant in the ITT-E population met the CVF criterion at Month 3; CARES: Versus 97% and 0% CVF in the oral ART group (n=257), second virological failure occurred in the CAB + RPV LA arm (individual died before retest; HIV-unrelated cause).; € 1 additional participant failed on oral CAB before initiating injection

Arm-E, enhanced arm; **Arm-S,** standard arm; **ART,** antiretroviral therapy; **BIC,** bictegravir; **c/mL,** copies/mL; **CVF,** confirmed virologic failure; **FTC,** emtricitabine; **ITT-E,** intention-to-treat exposed; **mITT-E,** modified ITT-E; **Q4W,** every 4 weeks; **SVF,** suspected virologic failure; **VL,** viral load

1. Orkin C, et al. Clin Infect Dis 2023;77:1423–31;
2. Ramgopal MN, et al. Lancet HIV 2023;10:e566–e577;
3. Garris CP et al. Journal of the International AIDS Society 2022, 25:e26006;
4. De Wit S, et al. IDWeek 2022. Oral 1584; **4.** Orkin C, et al. Lancet HIV 2021;8:e185–96;
5. Kityo C, et al. CROI 2024. Oral 122; **6.** Swindells S, et al. N Engl J Med 2020;382:1112–23;
7. Orkin C, et al. N Engl J Med 2020;382:1124–35.

High, longer-term effectiveness and low rates of VF with resistance in real-world studies of up to 2 years

	IAS 2025	IAS 2025 2 YEARS	IAS 2025 2 YEARS	ICAR 2025 2 YEARS	ID Week 2025
	COMBINE-2 C2C[1]	**CARLOS**[2,3]	**BEYOND**[4]	**SCohoLART**[5,6]	**OPERA**[7]
	N=937 Median (IQR) follow-up: 10.2 (7.1–16.6) months* On-treatment analysis	N=351 Month 24 follow-up ITT-E analysis	N=160† Month 24 follow-up On-treatment analysis	N=549 Median (IQR) follow-up: 24 (17.0–26.8) months On-treatment analysis	N=4000 Median (IQR) follow-up: 14 (7–23) months* On-treatment analysis
Virologically suppressed‡	**99%**	**77.5%** (97.7% LOCF)	**97%**	**99%**	**95%**
Virological failure§	**0.5%** (n=5)	**2%** (n=7)¶	**1%** (n=2)	**1.1%** (n=6)	**1%** (n=43/4000)
VF with INSTI resistance	**0.2%** (n=2)	**0.9%** (n=3)	**NR**	**0.5%** (n=3)	**NR**

Presented data include real-world cohorts reporting both virologic suppression and VF, with the highest number of people with HIV and longest follow-up (≥10 months) as of March 2025 or presented at IAS or ICAR 2025
LOCF, last observation carried forward; **NR**, not reported; **VF**, virologic failure
See slide notes for footnotes

1. Pozniak A, et al. IAS 2025. Poster EP0171; **2.** Wyen C, et al. IAS 2025. Poster TUPEB035
3. Jonsson-Oldenbüttel C, et al. AIDS 2024. Poster TUPEB095; **4.** Blick G, et al. IAS 2025. Poster EP0178
5. Muccini C, et al. ICAR 2025. Abstract OC35; **6.** Muccini C, et al. ICAR 2025. Oral OC35
7. Sension M, et al. ID Week 2025. Poster P-371

CAB + RPV LA: People with HIV and HCPs have consistently reported additional benefits beyond the high effectiveness demonstrated in RCTs and RWE

WEIGHT GAIN AND METABOLIC

Neutral impact on weight and **insulin resistance,**[10,11] and **potential reduction in the risk of developing metabolic syndrome** after switching from oral ART[12]

RENAL AND BONE

Neutral impact on renal and bone biomarkers, with potential improvement in CrCl in people switching from oral ARTs, including TDF regimens†[11,13–15]

ENGAGEMENT IN CARE

High retention in care and **multiple benefits** of **increased HCP touchpoints,** including feeling **more engaged in managing HIV**[8,16,17]

QUALITY OF LIFE

High and improved quality of life,‡[8,19] including **alleviation** of **psychological challenges** and **reduced stigma**§[18,19]

*RCTs: ATLAS-2M Week 48 HCP-reported adherence: 98% (n=3,719)[1]; SOLAR Month 12 HCP-reported adherence: 93% (n=2,527)[2]; CARISEL Month 12 HCP-reported adherence: 93% (n=2,376)[3]; CARES Week 48 HCP-reported adherence: 96% (n=1,758)[4]; RWE: CARLOS Month 12 HCP-reported adherence: 89% (n=1,943)[5]; BEYOND Month 12 HCP-reported adherence: 91% (n=1,386)[6]; †BL vs 7 months: CrCl (Cockcroft-Gault) [90.9 mL/min (IQR:78.2–101.6) vs 99.1 mL/min (IQR: 85.1–110.3); p=0.0001, respectively[13]; ‡HIV-specific PozQoL [score range 13–65], and EQ-5D-5L-US [score range 0–1])[8]; perception of own quality of life changes (greater or better) at Month 6 vs BL after switching to CAB + RPV LA; HIVDQoL score 88% vs 33% (p=0.01), respectively;[19] §Switching to CAB + RPV LA helps reduce efforts to keep HIV status disclosed; HSS score at BL vs Month 6: 87.5% vs 33% (p=0.009), respectively[19]

CrCl, creatinine clearance; **EQ-5D-5L-US,** 5-level EuroQol 5-dimensional questionnaire United States; **HIVDQoL,** HIV dependent quality of life; **HSS,** HIV stigma scale; **QoL,** quality of life

RCT, randomised controlled trial; **RWE,** real-world evidence

See slide notes for references

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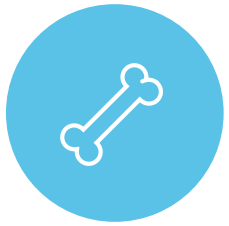

Neutral impact on renal and bone biomarkers, with potential improvement in CrCl in people switching from oral ARTs, including TDF regimens†[11,13–15]

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ADHERENCE

High, directly observed adherence to injections,*[1–7] and **higher adherence** and **persistence** vs daily oral ART (including BIC/FTC/TAF)[8,9]

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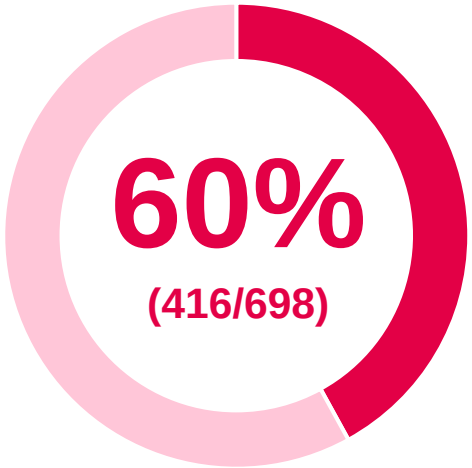
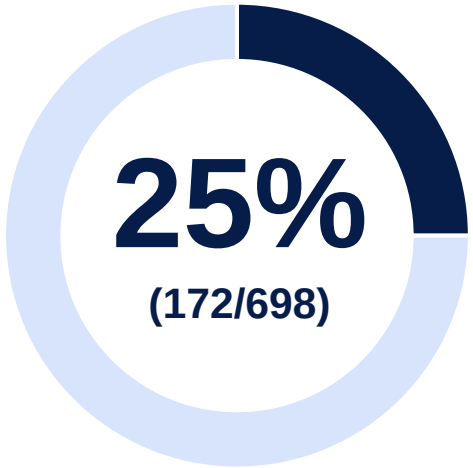
Understanding the experiences of people with HIV can identify unmet needs

The Positive Perspectives studies are a series of cross-sectional surveys that have been co-created with community representatives worldwide to capture and amplify the experiences of people with HIV[1–3]

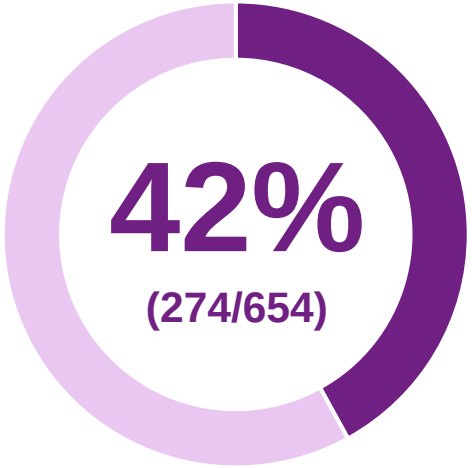
Positive Perspectives Study Wave 3 (Interim Data Analysis)[1–3]



Of people with HIV find it **difficult to start conversations** with their HCP about issues that concern them[1]



Of people with HIV reported **intentionally skipping ART** in the past 12 months prior to the interim analysis[2]



Of people with HIV **did not believe in U=U,** despite 94% surveyed having awareness of it (654/698)[3]

1. Patel R, et al. AIDSImpact 2025. Abstract 82526
2. Patel R, et al. AIDSImpact 2025. Abstract 82508
3. Patel R, et al. AIDSImpact 2025. Abstract 82532

Suboptimal adherence can lead to an increased risk of viral transmission and resistance

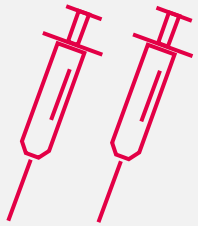
It is estimated that **38% of people with HIV** have **suboptimal adherence** to oral ART due to factors including:[1–3]

- Pill fatigue
- Emotional challenges
- Stigma
- Busy lifestyle
- Complexity of dosing schedule

DHHS Guidelines emphasise the importance of **regular assessment** of **barriers** faced by people with HIV to ensure **tailored approaches** to each person's needs, preferences and barriers to care[4]

Non-adherence to oral ART is associated with:[1,5]

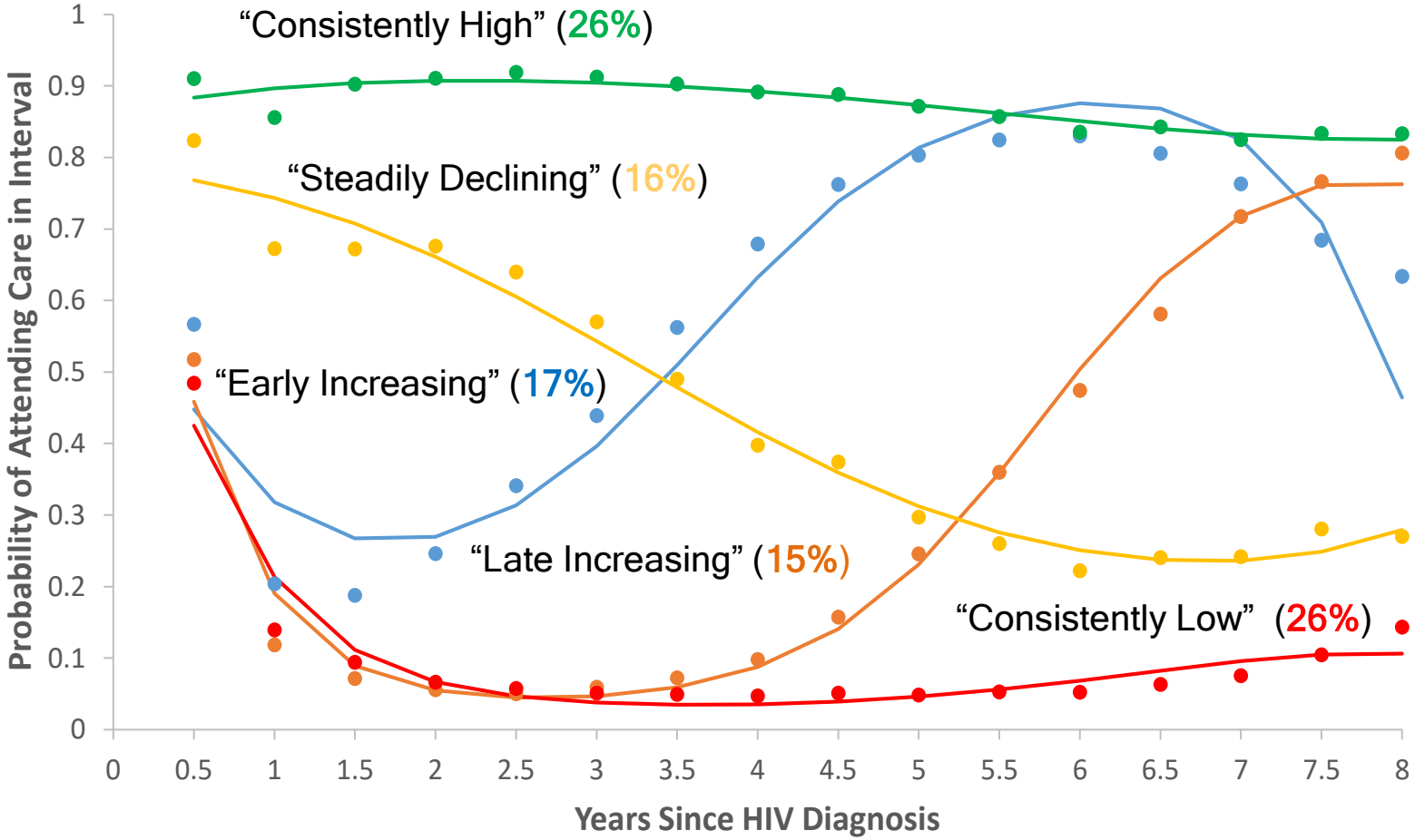
- A lower CD4 count
- AIDS-related mortality
- Increased risk of transmission
- Higher healthcare costs
- Emerging resistance



Long-acting injectables like CAB + RPV LA could help to overcome some of these adherence challenges, and this directly-observed therapy removes the need for adherence to daily dosing while allowing HCPs to track doses received[6]

1. Mate KKV, et al. Int J STD AIDS 2023;34:677–86; **2.** Nachega JB, et al. Lancet HIV 2023;10:e332–42
3. Akinwunmi B, et al. Eur J Public Health 2021;31:567–75
4. DHHS. Guidelines for the use of ARV agents in adults and adolescents with HIV, Sep 2025
5. Byrd KK, et al. J Acquir Immune Defic Syndr 2019;82:245–51; **6.** Davis JM, et al. Clin Infect Dis 2024:ciae557

Engagement in Care is Dynamic



Powers et al, Longitudinal HIV Care Trajectories in North Carolina *JAIDS* 2017; 74(S2)

Discussion

Polling Question #1

In your estimation, what proportion of your clinic population has challenges with adherence to oral ART?

- 0-5%
- 6-10%
- 11-15%
- 16-20%
- 21%-30%
- ≥ 31%

Polling Question #2

Are you offering CAB+RPV LA to your patients with non-adherence and/or viremia on oral ART?

- Yes, routinely in this population
- Yes, on a case-by-case basis, such as in those with significant risk for morbidity
- No

CAB+RPV LA in PWH with Adherence Challenges

CAB+RPV LA indications for HIV-1Treatment

US FDA prescribing information:

CAB + RPV LA, co-packaged for IM use[1]

Indicated as a **complete regimen** for the treatment of HIV-1 infection in **adults and adolescents** 12 years of age and older and weighing at least 35 kg **to replace the current ARV regimen** in those patients who are virologically suppressed* on a stable ARV regimen with **no history of treatment failure** and with **no known or suspected resistance** to either CAB or RPV

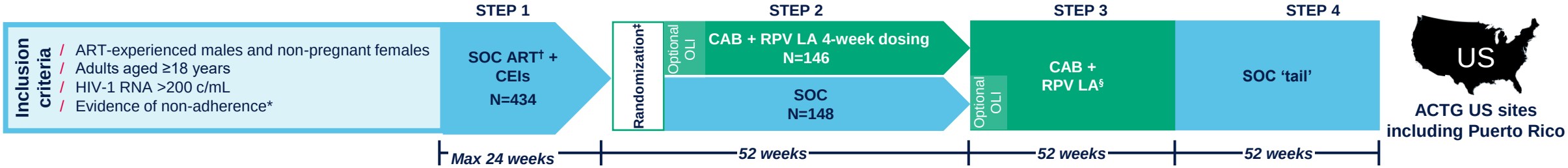
CABENUVA has not been approved by the FDA for the treatment of patients who are not virologically suppressed and the safety and efficacy of CABENUVA in such patients has not been established.

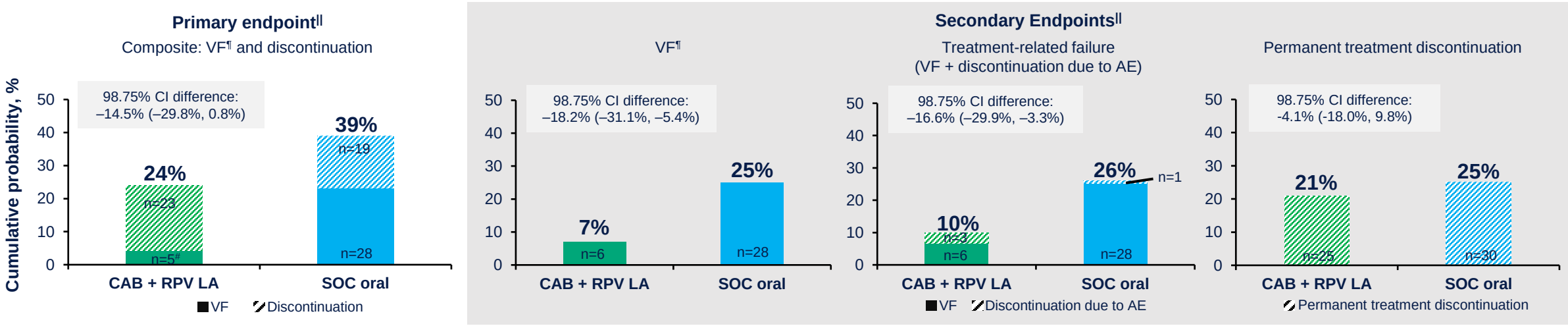
*Defined as HIV-1 RNA <50 c/mL
US FDA, United States Food and Drug Administration

1. Cabenuva US PI, ViiV Healthcare, 2025

LATITUDE (A5359) Interim analysis demonstrated superior efficacy of CAB + RPV LA compared to daily oral SOC in PLWH with adherence challenges

A Phase III prospective, randomized, open-label study to evaluate LA ART in PLWH with adherence challenges





CAB + RPV LA can help PLWH with barriers to adherence with daily oral ART to maintain an undetectable VL

*Poor viral response despite oral ART for ≥6 months or loss to clinical follow-up with ART non-adherence for ≥6 months; †Consisting of a ≥3-drug ART regimen with ≥2 drugs predicted to be fully active including a boosted protease inhibitor (PI/cobi) and/or an integrase strand transfer inhibitor for up to 24 weeks; ‡Participants who achieve viral suppression criteria at or after Step 1, Week 4, defined as: a) HIV-1 RNA ≤200 c/mL or b) HIV-1 RNA 201-399 c/mL followed by HIV-1 RNA ≤200 c/mL by Step 1 Week 24 will be eligible to enter Step 2. Participants with confirmed VF in Step 2; CAB + RPV LA (n=6), 2 with emergent RAMS (i) Week 18 E138EK; G140GS; Q148K; K103R (ii) Week 49 E138K; Q148K; K20KR; M230M; Oral SOC ART (n=28), 2 with emergent RAMs (i) Week 37, A71V; V77I; V106I (ii) Week 48, M184I; §There is an optional oral lead-in for SOC arm moving to step 3; ‖Pre-planned interim review by an independent DSMB; ¶VF, confirmed HIV-1 RNA >200 c/mL; #One participant assigned to LAI had treatment discontinuation as the primary endpoint but subsequently experienced VF, contributing to the total number of VFs; **ACTG**, AIDS Clinical Trial Group; **AE**, adverse event **CEIs**, conditional economic incentives; **cobi,** cobicistat; **DSMB**, data safety monitoring board; **LAI,** long-acting injectable; **PI,** protease inhibitor; **RAM,** resistance-associated mutation; **SOC**, standard of care; **US,** United States

UCSD Owen Clinic: Few VFs and discontinuations on CAB + RPV LA in a population with adherence challenges to oral ART

Study design:

Retrospective observational study at the UCSD Owen Clinic

Study participants

People with HIV-1 with adherence challenges to oral ART, defined as having HIV-1 VL ≥200 c/mL in the prior 12 months and either:

- Poor response to oral ART, or
- LTFU in the prior 18 months

Initiated CAB + RPV LA

Primary outcomes:

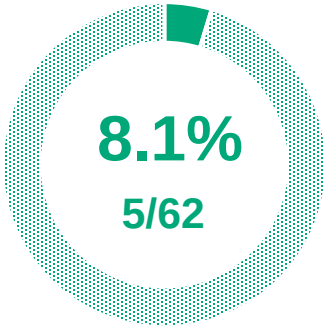
VF requiring treatment change or LTFU

48 weeks

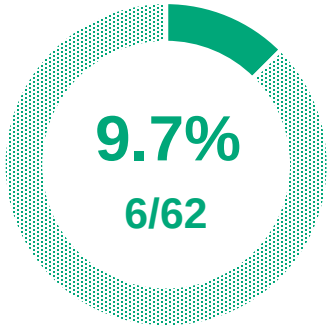
Parameter, %	N=62
Key demographics	
Male	72.6
Female	27.4
Non-binary	1.6
White	45.2
Black	16.1
Hispanic	35.5
Clinical characteristics	
Active substance use	40.3
Mental health diagnosis	56.5
VL ≥50 c/mL at initiation	43.5
VL >10,000 c/mL at initiation	11.3

Virologic outcomes, discontinuations and LTFU

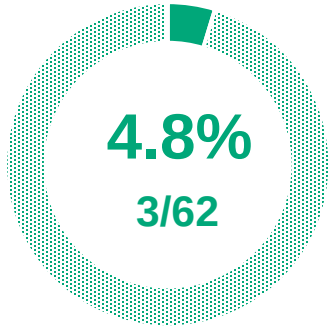
VF requiring treatment change



Discontinuations (excluding VFs)



LTFU*



Hastie E, et al. Clin Infect Dis 2025;81:543–6

High effectiveness of LA ART in people with challenges adhering to oral ART

PREFER-LA[4]	UCSD[5]	JABS[6]	Ward 86[7]	CREATE-MORE[8]	Children's National Hospital[9]
N=159 1 year	N=62 Week 48	N=60 Month 12	N=59 Week 48	N=44 ≥4 months since 1st injection	N=25 Median (range): 11.8 (0.8–31.3) months
23% (36/158)* **Unsuppressed at BL**	**44%** (27/62)* **Unsuppressed at BL**	**0%** (0/60)§ **Unsuppressed at BL**	**100%** (59/59)* **Unsuppressed at BL**	**27%** (12/44)†† **Unsuppressed at BL**	**24%** (6/25)‡‡ **Unsuppressed at BL**
98% (155/158)† **virologic suppression**	**86%** (53/62)† **virologic suppression**	**98%** (53/54)‖ **virologic suppression**	**92%** (54/59)# **virologic suppression**	**100%** (42/42)† **virologic suppression**	**100%** (25/25)§§ **virologic suppression**
VF not reported	**8.1%** (5/62)‡ **VF**	**0%** (0/54)¶ **VF**	**8.5%** (5/59)** **VF**	NR	**0%** (0/25)‖‖ **VF**

*VL ≥50 c/mL at initiation; †VL <200 c/mL; ‡Defined as VL ≥200 c/mL; §VL ≥40 c/mL. One quarter of participants had previously been identified as requiring adherence support, and 17% (10/60) had documented periods of VL >200 c/mL while receiving oral ART
‖VL <40 c/mL; ¶Defined as two VL >200 c/mL; #VL <50 c/mL (Week 48); **Defined as <2-log VL decline at 4 weeks or VL ≥200 c/mL after virologic suppression with emergent CAB or RPV RAMs; ††VL ≥200 c/mL at initiation
‡‡VL ≥20 c/mL at initiation. 10/25 (40%) had history of oral ART adherence challenges; §§VL <20 c/mL; ‖‖VF not defined

1. Vocabria EU SmPC. Sep 2025; **2.** Rekambys EU SmPC. Sep 2025; **3.** Cabenuva US PI. Apr 2025
4. Short WR, et al. IDWeek 2025. Oral 575; **5.** Hastie E, et al. Clin Infect Dis 2025;81:543–6
6. John M, et al. HIV Med 2024;25:935–45; **7.** Hickey MD, et al. Clin Infect Dis 2025;80:864–70
8. Dieterich M, et al. CROI 2025. Poster 1318; **9.** Williams T, et al. Pediatr Infect Dis J 2025;44:650–6

IMPALA: High, non-inferior efficacy with high preference for CAB + RPV LA among a diverse population with suboptimal HIV control

Study design and population[1]

Inclusion criteria

- Aged ≥18 years
- Recent VL >1,000 c/mL and/or poor engagement in care*

Screening

VL <200 c/mL for ≥3 months at the end of screening

DTG + 2NRTIs

Randomisation 1:1

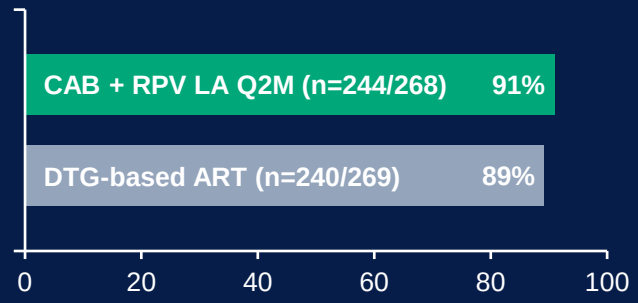
- CAB + RPV LA Q2M n=271
- DTG-based ART QD n=269

Day 1 — Week 48 (primary endpoint) — Week 96

Multi-country RCT completed in Uganda, Kenya and South Africa (N=540)[1,2]:

- **Female**: 60%
- **Median (IQR) age:** 40 (33–48) years
- **Black race**: 99.6%
- **Prior NNRTI exposure:** 78%
- **HBV:** 7.8% had evidence of vaccine-mediated immunity†

Efficacy[1]



HIV-1 RNA <50 c/mL, % (ITT-e)

1.5% (4/268)

on CAB + RPV LA experienced CVF with NNRTI and/or INSTI resistance‡

1.9% (5/268) experienced CVF on CAB + RPV LA
4 resuppressed on TLD, 1 on LPV/r + TDF/FTC
No CVFs occurred in the oral ART arm

Non-inferiority, adherence, safety and preference[1,2]

- **CAB + RPV LA was non-inferior to DTG-based ART (10% NI margin)** (91% [244/268] vs 89% [240/269]; risk difference: 1.9%; 95% CI: –3.1, 6.9)
- **CVF sensitivity analysis (CVF or 1 VL >1,000 c/mL) demonstrated superiority of CAB + RPV LA vs DTG-based ART** (2.6% [7/268] vs 6.7% [18/269]; risk difference –4.1%; 95% CI: –7.6, –0.6)
- **High adherence to injections**, with 98% of 2,159 injections given in window
- **CAB + RPV LA was well tolerated,** ISRs in 37% of participants (all Grade 1 or 2), few (n=1) Grade 3 drug-related AEs; no HBV reactivations detected
- **High preference for CAB + RPV LA and significant increase in treatment satisfaction§ with CAB + RPV LA vs DTG-based ART** (94% [249/266] of participants on CAB + RPV LA preferred LA to DTG-based ART)

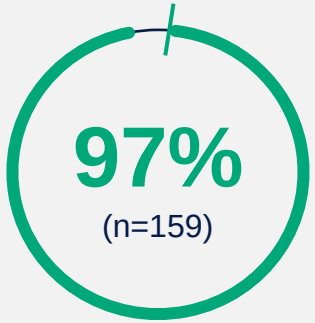
*Poor engagement in care defined as history of LTFU (>4 weeks) or unlinked to HIV care despite ≥3 months since HIV diagnosis; †HBV-related reasons precluded 84 (9.9%) from randomisation (29 [3.4%] with active HBV; 55 [6.5%] with prior infection but no immunity); ‡CVF defined as two consecutive HIV-1 RNA ≥200 c/mL. The 5th participant did not have resistance information available.
§HIVTSQc mean change +35.1 on CAB + RPV LA vs +32.3 on oral ART, p<0.0001 (BL HIVTSQs 66.1 and 64.5, respectively)
See slide notes for abbreviations

1. Cresswell FV, et al. IAS 2025. Oral OAB0106LB
2. Bahemuka U, et al. IAS 2025. Oral OAB01

Discussion

PREFER LA: Strong preference for CAB + RPV LA among people with HIV with prior adherence challenges to oral ART

Preference and benefits for people with HIV



preferred CAB + RPV LA versus daily oral ART

mainly due to believing injections are more reliable than daily oral ART to keep VL undetectable (71%), and not having to worry about others seeing/finding their HIV pills (71%)

Impact that switching to CAB + RPV LA from daily oral ART has had on people with HIV (n=159):

- **Positive impact on overall health (67%)**
- **Positive impact on QoL (79%)**
- **Helped control HIV better (79%)**
- **Fits better with daily life/ everyday activities (83%)**

→ **90% (n=159) of people with HIV were very likely to recommend CAB + RPV LA to other people with adherence challenges,** and most people reported overall positive feelings toward CAB + RPV LA and more positive feelings towards themselves since switching

HCP perspectives on persistence and benefits for adherence-challenged people with HIV

The **most common reason** among both HCPs and people with HIV for switching to CAB + RPV LA was to **improve treatment adherence**

95% (n=151) of HCPs reported that they foresee people with HIV remaining on CAB + RPV LA long term, mainly driven by the regimen fitting with people's lifestyle, people being more adherent to treatment and personal preference

HCP-reported benefits of implementing CAB + RPV LA for people with adherence challenges (n=13)*

- **100%** Person's HIV is better controlled
- **77%** Assurance of people with HIV adherence to ART
- **92%** People with HIV have better overall engagement with care
- **69%** People are more present for vaccines and screening tests

***Responses not mutually exclusive, only the four more frequently reported reflected here**
QoL, quality of life

CAB+RPV LA in PWH with Viremia

High effectiveness of LA ART in people with viremia at initiation

OPERA[1]	TRIO[2]	Ward 86[3]	Dat'AIDS[4]	Whitman-Walker Health[5]	Chaudhuri 2025[6]
N=502 Median (IQR) follow-up 12 (7–22) months	N=111 Median (IQR) follow-up 9 (3–13) months	N=96 Week 48 (±2)	N=86 Median (IQR) follow-up 11 (5–24) months	N=31 NR (latest drawn)	N=20 Week 24
79% (399/502)* **virologic suppression**	**84%** (68/81)‡ **virologic suppression**	**98%** (94/96)§ **virologic suppression**	**86%** (74/86)‖ **virologic suppression**	**94%** (29/31)¶ **virologic suppression**	**85%** (17/20)# **virologic suppression**
2% (7/355)† **CVF**	**2%** (2/111)† **CVF**	NR	**12.8%** (11/86)† **VF**	NR	NR

*VL <50 c/mL at time of analysis among those who completed initiation and had ≥1 follow-up VL; †OPERA: CVF defined as two consecutive VL ≥200 c/mL or single VL ≥200 c/mL followed by discontinuation within 2 (Q1M) or 4 (Q2M) months after suppressing to VL <50 c/mL, TRIO: NR, Dat'AIDS: VL >200 c/mL after viral suppression, 2 consecutive VL >50 c/mL after viral suppression, or failure to reach viral suppression by 6 months
‡Last VL <50 c/mL (93% had last VL <200 c/mL); §VL ≤200 c/mL; ‖Proportion who achieved viral suppression <50 c/mL
¶VL ≤50 c/mL; #VL <20 c/mL (100% achieved VL <200 c/mL)
NR, not reported

1. Sension M, et al. IDWeek 2025. Poster P-371; **2.** Elion R, et al. LAAI 2025. Oral abstract 2
3. Gistand N, et al. CROI 2025. Poster 689; **4.** Deschanvres C, et al. EACS 2025. Poster eP.LB003
5. Fessler D, et al. CROI 2024. Poster 1235; **6.** Chaudhuri S, et al. IAS 2025. Poster EP0199

OPERA: High effectiveness and persistence on CAB+RPV LA in >5,000 people across diverse adult age groups, including people with viremia

Study population and design[1]

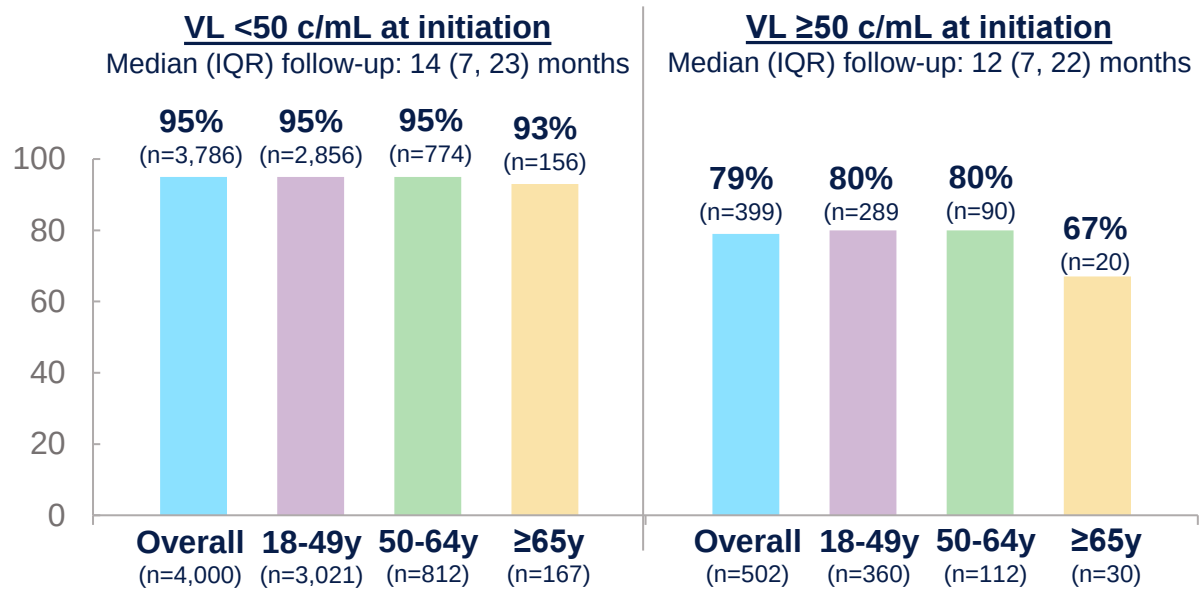
Demographic and clinical characteristics at CAB+RPV LA initiation (N=5,264)*

- **VL <50 c/mL:** 87%
- **VL ≥50 c/mL:** 11%
- **Median (IQR) age:** 38 (32, 50) years
- **Female:** 16%
- **Black race:** 44%
- **Switch from INSTI:** 76%

Effectiveness & Persistence

- The **majority** (**79%**, 3,731/4,748) of complete initiators alive and in care at time of analysis **remained on CAB+RPV LA**, and those aged ≥50 years had slightly longer cumulative months on CAB+RPV LA than those aged 18-49†
- **VL <50 c/mL at initiation: most (93-95%) remained suppressed at last VL across age groups and CVF was rare (1%)**, with no individuals aged ≥65 years experiencing CVF
- **VL ≥50 c/mL at initiation: virologic suppression at last measure ranged from 67%-80%**. Among those who suppressed, **CVF was rare (2%)**, with no individuals aged 50-64 years experiencing CVF

Virologic suppression (VL <50 c/mL) among complete initiators with ≥1 follow-up VL



WARD 86: High effectiveness of CAB + RPV LA in a vulnerable population, irrespective of virologic suppression at initiation

CAB + RPV LA in people with and without detectable viremia

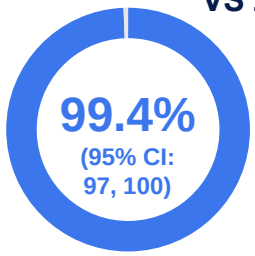
Spinelli et al.[1]

Study design: Retrospective study using EMR data of people with HIV who initiated CAB + RPV LA between January 2021 and September 2024 in the SPLASH program

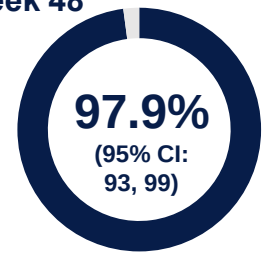
370 individuals: 129 with viremia**, 241 virologically suppressed

- Median age 45 years (range 21-70), 82% cisgender men, 15% transgender women
- 41% White, 23% Black, 52% CD4⁺ T-cell count <200 cells/mm³
- 44% unstable housing, 46% with current or past substance use
- Median time to achieve VS (≤200 c/mL) in participants with viremia was 32 days
- **Median baseline VL 45,600** copies/mL (for those with viremia at baseline)

VS ≤30 c/mL at Week 48



Virologically suppressed at BL
n=168/169



Viremic at BL
n=94/96

CAB + RPV LA in people who were viremic at switch

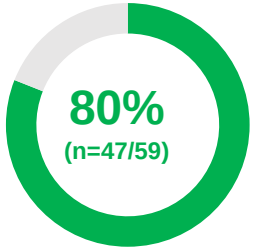
Hickey et al.[2]

Study design: Retrospective cohort study of people with HIV viremia (≥50 c/mL) who started CAB + RPV LA before December 2022 in the SPLASH progam

59 individuals started Q1M dosing with optional switch to Q2M after 3–6 months of maintained VS

- 48% age ≥50 years old
- 90% male, 41% White, 24% Black
- 49% CD4⁺ T-cell count <200 cells/mm³
- 53% unstable housing or homeless, 71% with substance use
- **Median baseline VL 42,900 copies/mL** (IQR 5,272-139,038); 69% VL ≥ 10,000

Status at Week 48 (n=59)



VS

- n=5 **VF with resistance**
- n=5 **Discontinued and remained virally suppressed on oral ART**
- n=1 **LTFU**
- n=1 **Intensified to CAB + RPV LA + LEN***

CAB + RPV LA was highly effective in a cohort of people with HIV with high rates of unstable housing, substance use and low CD4⁺ T-cell counts, irrespective of VS at initiation

*Intensified to CAB + RPV LA + LEN for low-level viremia without CAB or RPV associated resistance mutations; **viremia defined as ≥ 30 copies/mL
EMR, electronic medical record; **SPLASH,** Special Programs to Stop HIV Using Long-Acting ART

1. Spinelli MA, et al. JAMA 2025;333:1451–3
2. Hickey MD, et al. Clin Infect Dis 2025;80:864–70

CAB + RPV LA may be a viable treatment option for people with HIV and viremia: data from a SLR and meta-analysis

Study design and population

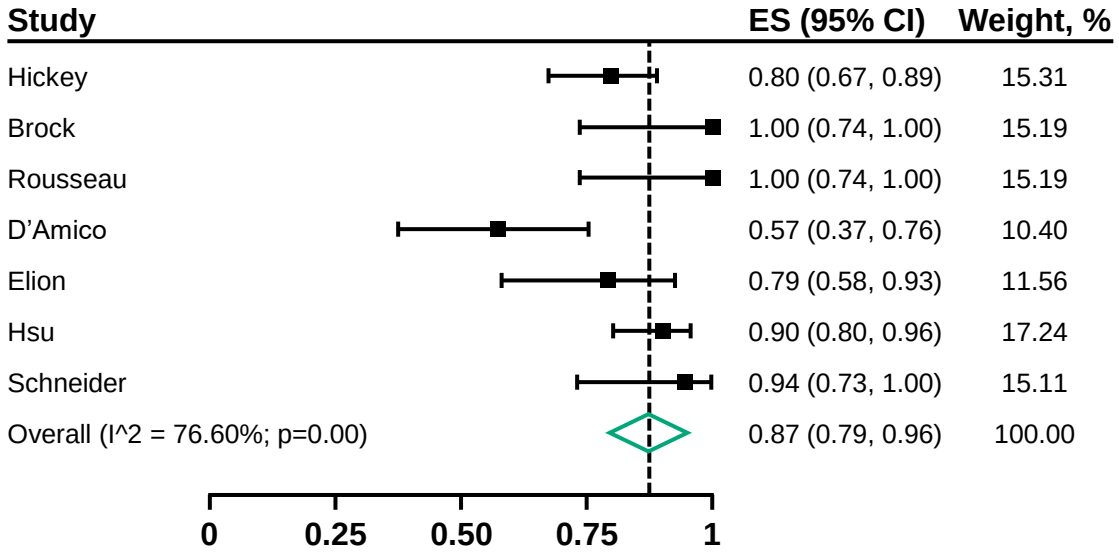
SLR and meta-analysis of CAB + RPV LA in people living with HIV and viremia (VL >50 c/mL; N=244)

- 8 studies (5 manuscripts and 3 abstracts) were included
- **Primary outcome:** virologic success as defined by each study*

Virologic success, adherence and tolerability

- The cumulative probability of achieving virologic success with CAB + RPV LA was **87% (95% CI, 79%–95%)**
  - Results were consistent when assessing all studies (N=14) or when excluding a study where individuals also received LEN
- **Most individuals** maintained **adherence rates above 90%** to their schedules injections visit†
- **No cases of treatment discontinuation** due to **treatment-related toxicity** reported across the studies

Forest plot of CAB + RPV LA achieving virologic success



*Defined as either HIV RNA <50 c/mL sustained for 48 weeks after initiating CAB + RPV LA, or virologic undetectability (HIV-RNA <50 c/mL) and suppression (HIV-RNA <200 c/mL) at the last available VL, or undetectable viraemia during follow-up, or a threshold of 75 copies/mL to define virologic response; †Though not consistently reported across all manuscripts, most patients maintained adherence rates above 90% to their scheduled injection visits

Barda B, et al. HIV Med 2025;26:993–1003

MORE: CAB + RPV LA at-home administration for people with adherence challenges

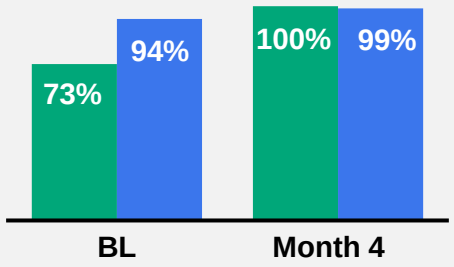
Mobile Outreach Retention and Engagement (MORE) programme initiated in 2016 to support people with HIV with adherence challenges (VL >200 c/mL and/or no medical visits in 6 months)
MORE offers mobile care navigator support, transportation assistance and physician assistant-led home medical visits. **In 2023, at-home maintenance injections were added as an optional service**

Study design: Effectiveness–implementation hybrid type-2 study comparing people with HIV receiving CAB + RPV LA with Mobile Outreach Retention and Engagement (MORE) programme support to a 2:1 matched comparison group of people receiving CAB + RPV LA in clinic without MORE support

Effectiveness[1]

- N=44 started CAB + RPV LA through MORE between November 2023 and September 2024; 63% (28/44) chose home injections
- Median age 44 years, 39% cis female, 11% trans female and 93% Black

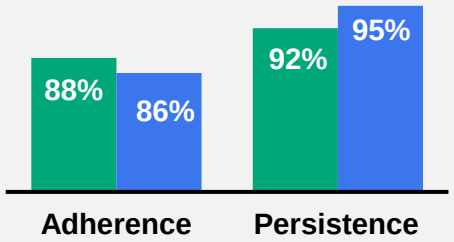
BL and Month 4 virologic suppression (<200 c/mL)



BL viraemia (≥200 c/mL) in MORE group (27%) versus comparison group (6%) (p<0.001)

MORE group (n=42)
Comparison (in clinic) (n=82)

Adherence and persistence at Month 4*



MORE group (n=42)
Comparison (in clinic) (n=84)

Implementation[2]

- N=45 completed BL survey between November 2023 and February 2025
- Acceptability (AIM), feasibility (FIM) and appropriateness (IAM) of intervention assessment tools used for BL survey, qualitative interviews also conducted

Agreement of acceptability, feasibility and appropriateness of MORE programme and home injections†

MORE programme offers **trust**, **flexibility**, **choice** and **privacy**

67% were willing to receive home injections at BL
31% received at least one home injection

***MORE group had 2 ISR-related discontinuations and 2 missed injections due to insurance lapse who restarted; MORE group had no late injections or LTFU due to missed injections; comparison group, had 5 late injections and 2 LTFU due to missed injections; †Agreement defined as cumulative percentage of "agree/strongly agree"
AIM, Acceptability of Intervention Measure; **FIM,** Feasibility of Intervention Measure; **IAM,** Intervention Appropriateness Measure

1. Dieterich M, et al. CROI 2025. Poster 1318
2. Dieterich M, et al. IDWeek 2025. Oral presentation 577

Treatment guidelines: CAB + RPV LA can be used to achieve virologic suppression in people with detectable viremia

Data for CAB + RPV LA in people with viremia are emerging, and the IAS–USA, DHHS, BHIVA and WHO guidelines have been updated to reflect growing interest in its use in this population[1–4]

IAS–USA guidelines[1]	DHHS guidelines[2]	BHIVA guidelines[3]	WHO guidelines[4]
May be considered for people with viraemia who are **unable to take oral ART consistently**, are at **high risk of HIV disease progression** and have **no resistance to CAB or RPV**	On a **case-by-case basis** in select individuals with **persistent VF** despite intensive adherence support on oral ART, who have **no evidence of resistance to RPV or CAB**, and with **shared-decision making** between providers and people with HIV	Can be **used with caution** in people who **continue to have a detectable VL** on oral ART despite extensive support, are at **high risk of disease progression** based on CD4 count and/or HIV-related conditions, can **commit** to regular appointments, **do not have resistance** to CAB and/or RPV and are willing to accept the **possibility of resistance** emergence and limitation of treatment options	**LAI CAB + RPV** can be used as an **alternative switching option** for adults and adolescents with **undetectable HIV VL** on oral ART and without active hepatitis B infection This includes use to support people with HIV facing **adherence challenges to oral regimens**

VL, viral load; **WHO,** World Health Organization

1. Gandhi RT, et al. JAMA 2025;333:609–28
2. DHHS. Guidelines for the use of antiretroviral agents in adults and adolescents with HIV, Sep 2025
3. BHIVA. Guidelines on antiretroviral treatment for adults living with HIV-1 2022, 2025 interim update
4. WHO. Overview of WHO recommendations on HIV and sexually transmitted infection testing, prevention, treatment, care and service delivery. 2025

Discussion

Modelling suggests that CAB + RPV LA can increase viral suppression rates in PWH with and without persistent viraemia

Impact of increased LAI uptake on HIV incidence and VS in the United States under 2021 FDA guidelines[1]

HOPE compartmental modelling simulated CAB + RPV LA use (2023–2035) across two scenarios*

1. Improved duration of VS post-cessation of ART use (vs oral ART)

2. Scenario 1 with additional improvement in adherence (vs oral ART)

Impact of delayed CAB + RPV LA implementation in people with HIV and persistent viremia in the US[2]

Microsimulation¶ assessed two approaches for PWH with persistent viraemia and intermittent care engagement:

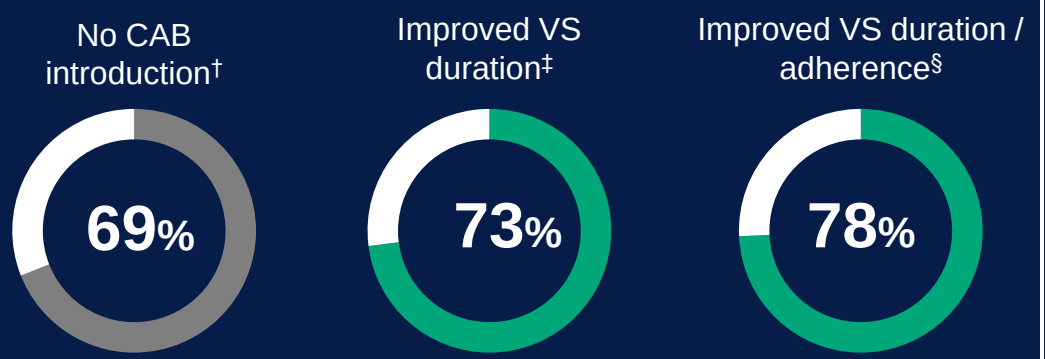
1. Daily first-line oral ART, or

2. CAB + RPV LA assessed across four implementation scenarios#

Impact of CAB + RPV LA on VS rates

Baseline simulation

CAB + RPV LA simulations:



Modelling suggested that CAB + RPV LA use would increase population levels of VS. Expanding use beyond 2021 FDA guidelines (e.g., in viraemic individuals) could increase the impact of CAB + RPV LA on VS levels

Impact of CAB + RPV LA on VSPY by implementation scenario**

1. **Current practice**: **35,810 VSPY** among PWH with persistent viraemia
2. **Complete (immediate or delayed) implementation**: **immediate** implementation **increased VSPY by 26,830**; **delayed** implementation **decreased VSPY by 5,370**
3. **Post-trial implementation**: **VSPY increased by 1,690 and 1,280** in post-one-arm and post-randomized trial scenarios, respectively
4. **Immediate incomplete implementation**: **VSPY increased** comparable to post-trial implementation††

Modelling suggested that increased CAB + RPV LA implementation in PWH with persistent viraemia / intermittent care engagement would increase VS and decrease mortality versus waiting for clinical trial data

See slide notes for footnotes

VS, virological suppression; **VSPY**, virologically-suppressed patient years

1. Viguerie A et al. AIDS 2025;39:1024-32;
2. Pei PP et al. Clin Infect Dis 2025; Epub ahead of print: doi: 10.1093/cid/ciaf428

What's Next?

CROWN: Upcoming study in people with HIV with detectable viremia

CROWN Protocol 221611

Phase IIIb, open-label, randomised, multicentre, superiority study of CAB + RPV LA in viremic participants

Inclusion criteria

- ≥12 years of age
- ≥35 kg
- HIV-1 RNA >1,000 c/mL at screening
- Evidence of insufficient virologic response to oral ART*

Exclusion criteria

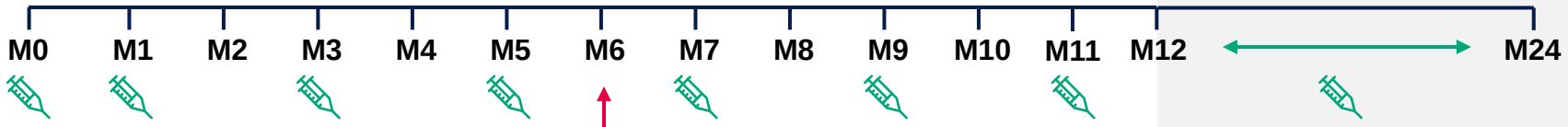
- HBV coinfection
- HIV subtype A6
- Evidence of INSTI or clinically significant NNRTI resistance

Randomisation 3:1

CAB + RPV LA IM Q2M (N=249) → **Long-term treatment**

ART oral QD (N=83)

Control arm to switch to CAB + RPV LA if suppressed



Endpoint

Primary endpoint: HIV-1 RNA <50 c/mL on CAB + RPV LA versus oral ART at Month 6

*At least one of the following: a) <1 $\log_{10}$ decrease in HIV-1 RNA or HIV-1 RNA >200 c/mL at two time points at least 4 weeks apart in individuals who have been prescribed oral ART for at least 3 consecutive months, b) a documented lapse in current oral ART regimen usage expected to result in HIV-1 viraemia (defined as at least a 30-day consecutive period of non-use of oral ART), c) a documented need for change from oral ART regimen that the investigator attributes as the primary reason for insufficient virologic response (e.g. safety findings and/or limited tolerability, clinically relevant DDIs)

HBV, hepatitis B virus; **QD,** once daily

CROWN (NCT06694805). Available at: https://clinicaltrials.gov/study/NCT06694805 (accessed Feb 2025)

Discussion/Q&A

Appendix

Case series reports of LA combination of CAB + LEN ± RPV

	N=34 Gandhi et al.[1] California, Pennsylvania, Ohio	N=22 Colasanti et al.[2] Atlanta, GA	N=10 Saberi et al.[3] NCCC, 7 US states	N=9 Brock et al.[4] Jackson, MS	N=8 Palich et al.[5] Paris, France
Population	People with adherence challenges prescribed either **CAB LA + LEN ± RPV LA** in 4 clinics across 3 states	People with HIV and viraemia at initiation of **CAB LA ± RPV LA** and **LEN**	People who switched to **CAB LA + LEN ± RPV LA**, based on calls received by the NCCC	People with persistent viraemia, RAMs to CAB or RPV, and prescribed **CAB LA + RPV LA + LEN**	People who were virologically suppressed with RPV resistance, started on **CAB LA + LEN**
Key BL characteristics	Median age 47 years, 76% male, 42% Black, 36% Hispanic **Reasons for use of CAB LA + LEN ± RPV LA:** / RAMs: NNRTI (21), INSTI (5)* / High VL (6) / Viraemia on CAB + RPV LA (5)	Median age 43 years; 40% cisgender women; 96% Black / RAMS (either documented or suspected): NNRTI (11), INSTI (4), ≥2 classes (2)	Mean age 51 years; 60% male **Reasons for use of CAB LA + LEN ± RPV LA:** / Viraemia (6) / RAMs: NNRTI (3), INSTI (2)* / Can't/won't take oral ART (3) / Viraemia on CAB + RPV LA (2)	Mean age 46 years, 33% male, 100% Black RAMs: RPV only (8), CAB and RPV (1)†	Median age 56 years; 50% male Median 25 years on ART RAMs: RPV (8) based on archived genotype

CAB LA + LEN ± RPV LA

Effectiveness	**94% virally suppressed** <75 c/mL on CAB + RPV LA + LEN (23) or CAB LA + LEN (11) within a median of 8 weeks All with NNRTI RAMs achieved virologic suppression	**92% virally suppressed** <50 c/mL after median of 1 injection and sustained through follow-up	**80% virally suppressed** <200 c/mL on CAB + RPV LA + LEN (7) or CAB LA + LEN (1) within a median of 56 days In 2, VL decreased from >6.2 $\log_{10}$ to 210 and 313 c/mL	**100% virally suppressed** <200 c/mL on CAB + RPV LA + LEN during follow-up (Week 24–36) Those with BL CD4 <200 cells/mm^3 had 208% increase in absolute CD4	**100% virally suppressed** <50 c/mL on CAB LA + LEN during follow-up (8 at least 6 months and 3 at 12 months)

See slide notes for footnotes
GA, Georgia; **MS,** Mississippi; **NCCC,** National Clinician Consultation Center

1. Gandhi M, et al. Open Forum Infect Dis. 2024;11:ofae125; **2.** Colasanti JA, et al. Clin Infect Dis 2025 (online ahead of print)
3. Saberi P, et al. IAS 2025. Poster EP0190; **4.** Brock JB, et al. IDWeek 2024. Poster P-558
5. Palich R, et al. HIV Glasgow 2024. Poster P058

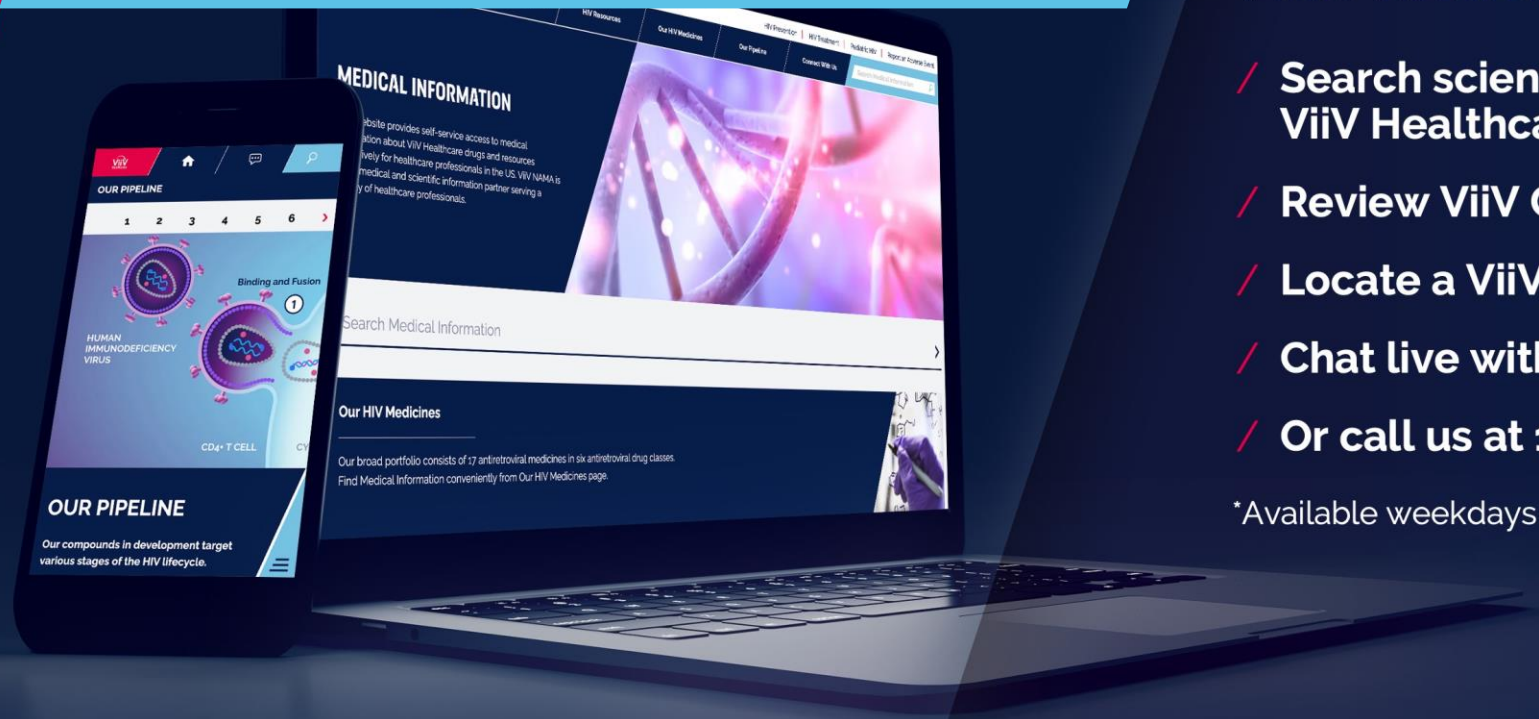
Q & a

- Please use the Q&A function to submit comments and questions
- If we are unable to get to your question, we will ensure to follow up with you!

FEEDBACK

Tell us what you think of today's program

Thank You!



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