Long-Acting Cabotegravir Plus Rilpivirine Was Effective and Well-Tolerated by Adults ≥60 Years of Age With HIV: A Pooled Analysis of Phase 3 Studies

Dennis Rice,[1] Patricia de los Rios,[1] Marius Sieverding,[2] Richard Grove,[3] Ines Augusto,[4] Lori A. Gordon,[1] Lionel Tan,[5] Bryn Jones[5]

[1]ViiV Healthcare, Durham, NC, USA; [2]Veramed, Frankfurt, Germany; [3]GSK, London, UK; [4]ViiV Healthcare, Algés, Portugal; [5]ViiV Healthcare, London, UK

Key Takeaways

- **Older adults with HIV-1 are an increasing and important group that faces increased risk of comorbidities and polypharmacy; long-acting injectable regimens can help address limitations of oral therapy, including adherence challenges[1]**
- **In a pooled analysis of phase 3 studies, long-acting cabotegravir plus rilpivirine (CAB+RPV LA) was highly efficacious and well tolerated in older adults with HIV-1 (aged ≥60 years) and was associated with improved treatment satisfaction**
- **These findings support the use of CAB+RPV LA for maintenance of virologic suppression in older adults with HIV-1**

Introduction

- Advances in antiretroviral therapy (ART) have enabled people with HIV-1 to live longer, healthier lives, and a growing proportion of individuals are reaching older age[1]
  - By 2030, an estimated 50% to 70% of people with HIV-1 will be aged ≥50 years[1-3]
- Older adults with HIV-1 experience a higher burden of comorbidities compared with older adults without HIV-1, which can lead to increased polypharmacy and challenges with ART adherence[2,4]
- Long-acting injectable regimens can help address limitations of oral therapy, including adherence challenges[4]
- Phase 3 clinical trials demonstrated that CAB+RPV LA was non-inferior to daily oral ART for the maintenance of virologic suppression in adults with HIV-1[5-7]
- Currently, data on the efficacy and safety of long-acting injectable ART regimens in older adults with HIV-1 (aged ≥60 years) are limited. We present a pooled post hoc analysis assessing the efficacy and safety of CAB+RPV LA in older adults with HIV-1 from phase 3 clinical trials to address this evidence gap

Methods

- Pooled data from adult participants aged ≥60 years who were virologically suppressed and switched to CAB+RPV LA dosed once-monthly (Q1M) or every-2-months (Q2M), or continued their current oral antiretroviral regimen (CAR) from FLAIR (NCT02938520), ATLAS (NCT02951052), ATLAS-2M (NCT03299049), and SOLAR (NCT04542070) were assessed post hoc
- The primary objective was to describe the Week 48 efficacy endpoints (FDA Snapshot) of participants from the FLAIR, ATLAS, ATLAS-2M, and SOLAR trials
- Secondary objectives at Week 48 (except where noted) included description of:
  - Virologic efficacy at Week 96 across FLAIR and ATLAS-2M
  - Confirmed virologic failure (2 consecutive measurements of viral load ≥200 copies/mL)
  - Safety outcomes
  - Change from baseline in CD4+ T-cell cell count and CD4/CD8 ratio
  - Change from baseline in body mass index (BMI), weight, lipids, and eGFR
  - Change from baseline in treatment satisfaction using the HIV Treatment Satisfaction Questionnaire, status version (HIVTSQs)
- An intent-to-treat-exposed (ITT-E) population was employed for all analyses[a,b]

[a]The ITT-E population employed for ATLAS-2M excluded participants with prior CAB+RPV LA exposure in ATLAS. [b]The modified ITT-E population employed for SOLAR excluded 11 participants from 1 study site that had significant and persistent non-compliance to protocol entry requirements.

Results

- The analysis included 115 participants; 79 switched to CAB+RPV LA (Q2M, 42; Q1M, 37) and 36 continued CAR (Table 1)
- Participants had considerable burdens of comorbidity at baseline; the most prevalent comorbidities included
  - Cardiovascular risk factors, of which hypertension was the most prevalent
  - Metabolism and nutrition disorders, of which hypercholesterolemia was the most prevalent
  - Psychiatric disorders, of which depression was the most prevalent
- All participants in the CAB+RPV LA groups and 97% in the CAR group were on concomitant medication(s)

Table 1. Baseline Demographics and Clinical Characteristics

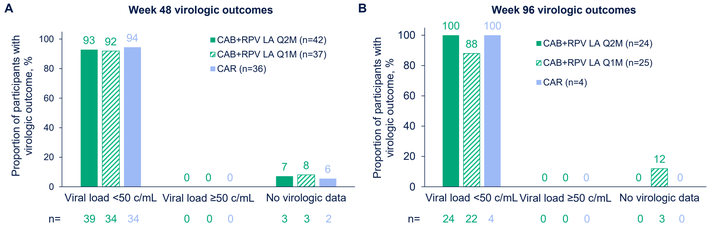
	CAB+RPV LA Q2M (n=42)	CAB+RPV LA Q1M (n=37)	CAR (n=36)
Median age (range), y	64 (60-83)	63 (60-74)	63 (60-82)
Assigned male sex at birth, n (%)	29 (69)	25 (68)	22 (61)
Race, n (%)			
White	32 (76)	26 (70)	20 (56)
Black/African American	6 (14)	6 (16)	12 (33)
Other races	4 (10)	5 (14)	4 (11)
Ethnicity, n (%)			
Hispanic or Latine	1 (2)	1 (3)	1 (3)
Median time on prior ART (IQR), mo	49.2 (27.6-81.7)	51.2 (23.4-87.8)	50.9 (26.2-83.5)
BMI category at baseline, n (%)			
≥30 kg/m^2	13 (31)	4 (11)	10 (28)
Number of comorbidities at baseline, n (%)			
0	5 (12)	3 (8)	6 (17)
1	5 (12)	3 (8)	5 (14)
2	8 (19)	5 (14)	6 (17)
≥3	24 (57)	26 (70)	19 (53)
Baseline comorbidities, n (%)[a]			
Cardiovascular risk factor	24 (57)	19 (51)	20 (56)
Metabolism and nutrition disorder	19 (45)	16 (43)	12 (33)
Psychiatric disorder	11 (26)	18 (49)	13 (36)
Musculoskeletal and connective tissue disorder	11 (26)	13 (35)	13 (36)
Nervous system disorder	4 (10)	11 (30)	7 (19)
Concomitant medication use, n (%)	42 (100)	37 (100)	35 (97)

ART, antiretroviral therapy; BMI, body mass index; CAB+RPV LA, long-acting cabotegravir plus rilpivirine; CAR, current antiretroviral regimen; IQR, interquartile range; Q1M, monthly; Q2M, every 2 months. [a]Comorbidities occurring in ≥30% of any group are shown.

Virologic and Immunologic Outcomes

- CAB+RPV LA demonstrated high efficacy at Weeks 48 and 96 in older adults with HIV-1 (Figure 1)
- No participants had viral load ≥50 c/mL at Week 48 or Week 96, and no cases of confirmed virologic failure were reported
- Immunologic parameters (CD4+/CD8+ ratio and CD4+ T-cell counts) remained stable in all groups through Week 48 (Table 2)

Figure 1. Pooled Snapshot Virologic Outcomes at (A) Week 48 Across FLAIR, ATLAS, ATLAS-2M, and SOLAR and (B) Week 96 Across FLAIR and ATLAS-2M



Missing virologic data were due to study discontinuations (due to adverse events, death, or other reasons). One participant in the CAB+RPV LA cohort had withdrawn before Week 48 due to meeting protocol-specific withdrawal criteria (liver chemistry changes).

Table 2. Change From Baseline to Week 48 in Immunologic Outcomes

	CAB+RPV LA Q2M (n=42)	CAB+RPV LA Q1M (n=37)	CAR (n=36)
Baseline CD4+/CD8+ ratio, median (IQR)	1.06 (0.66, 1.76)	0.76 (0.50, 1.24)	0.92 (0.68, 1.54)
Change from baseline to Week 48, median (IQR)	0.04 (−0.04, 0.08)	0.05 (−0.05, 0.18)	0.03 (−0.06, 0.13)
Baseline CD4+ T-cell counts, median (IQR)	638 (430, 897)	526 (445, 743)	631 (424, 824)
Change from baseline to Week 48, median (IQR)	9 (−89, 65)	−10 (−111, 47)	−3 (−75, 19)

IQR, interquartile range.

Metabolic Outcomes

- At Month 12, both BMI and weight in all groups remained stable relative to baseline (Table 3)

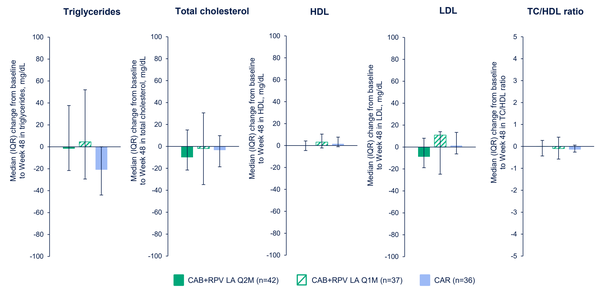
Table 3. Change From Baseline to Week 48 in BMI and Weight

	CAB+RPV LA Q2M (n=42)	CAB+RPV LA Q1M (n=37)	CAR (n=36)
Baseline BMI, median (IQR), kg/m^2	27.2 (24.2, 31.4)	26.6 (24.9, 27.9)	27.0 (23.6, 31.0)
Change from baseline to Week 48, median (IQR)	−0.04 (−0.5, 1.0)	0.5 (−0.1, 1.3)	−0.05 (−0.9, 0.8)
Baseline weight, median (IQR), kg	78.7 (69.0, 89.6)	76.8 (66.0, 84.2)	78.0 (72.8, 86.8)
Change from baseline to Week 48, median (IQR)	−0.2 (−1.4, 2.8)	1.8 (−0.3, 3.0)	−0.1 (−2.4, 2.0)

BMI, body mass index; IQR, interquartile range.

- Median changes from baseline to Week 48 in metabolic health parameters were generally small (Figure 2)

Figure 2. Median Change From Baseline in Fasting Lipids Through Week 48



HDL, high density lipoprotein; IQR, interquartile range; LDL, low density lipoprotein; TC, total cholesterol.

- Median changes from baseline in eGFR (CAB+RPV LA Q2M, −1%; CAB+RPV LA Q1M, +2%; CAR, +3%) were not clinically relevant

Safety

- CAB+RPV LA had a well-tolerated safety profile, with 1 drug-related adverse event (AE) leading to withdrawal in the CAB+RPV LA Q1M group (Table 4)
- Grade ≥3 AEs and serious adverse events were infrequent

Table 4. Summary of Systemic (Non-ISR) Safety Profile Through Week 48

Event, n (%)	CAB+RPV LA Q2M (n=42)	CAB+RPV LA Q1M (n=37)	CAR (n=36)
Any AE[a]	28 (67)	31 (84)	30 (83)
Infections and infestations	14 (33)	18 (49)	21 (58)
Musculoskeletal and connective tissue disorders	9 (21)	10 (27)	7 (19)
Gastrointestinal disorders	6 (14)	10 (27)	7 (19)
Any drug-related AE	8 (19)	11 (30)	2 (6)
Any grade ≥3 AE	2 (5)	2 (5)	5 (14)
Any grade ≥3 drug-related AE	2 (5)	0	0
Any AE leading to withdrawal	0	2 (5)	2 (6)
Any drug-related AEs leading to withdrawal[b]	0	1 (3)	0
Any SAE	2 (5)	2 (5)	2 (6)
Drug-related SAEs	1 (2)	0	0
Fatal SAEs	0	0	0

ISR, injection site reaction. [a]AEs occurring in ≥20% of any group are shown. [b]One participant in the Q1M group withdrew due to increased alanine transaminase.

- Injection site reactions (ISRs) associated with CAB+RPV LA were predominantly grade 1 in severity and transient (median duration of 3 days in each group; Table 5)
- Grade 3 ISRs were infrequent, no grade ≥4 ISRs were reported, and no ISRs led to withdrawal
- Injection site pain was the most commonly reported ISR (109 and 108 events in the Q2M and Q1M groups, respectively)

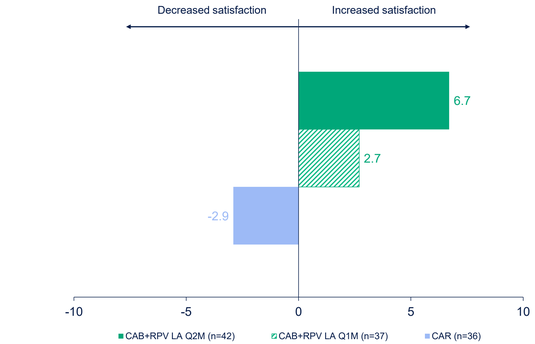
Table 5. Summary of ISRs Through Week 48

Event, n (%)	CAB+RPV LA Q2M (n=42)	CAB+RPV LA Q1M (n=37)
Number of injections received	550	848
Number of ISR events	131	135
Grade 1	113 (86)	106 (79)
Grade 2	17 (13)	28 (21)
Grade 3[a]	1 (<1)	1 (<1)
Grade 4	0	0
ISRs leading to withdrawal	0	0
Median (range) duration of grade 1 or 2 ISRs, days	3 (1-29)	3 (1-443)

ISR, injection site reaction. [a]1 grade 3 ISR of injection site pain occurred in each CAB+RPV LA group, with a median duration of 6 days each.

- Total treatment satisfaction scores improved from baseline with CAB+RPV LA at Week 48, with a greater increase in the Q2M group (Figure 3)

Figure 3. Mean Change From Baseline in HIVTSQs Score at Week 48[a]



[a]Mean (SD) baseline HIVTSQs scores were 58.6 (9.3) for CAB+RPV LA Q2M, 56.8 (9.0) for CAB+RPV LA Q1M, and 58.1 (8.2) for CAR.

Conclusions

- In this pooled analysis of phase 3 studies, CAB+RPV LA was highly efficacious at maintaining virologic suppression and was well tolerated in older adults (aged ≥60 years) with HIV-1
  - No participants experienced confirmed virologic failure through 96 weeks, and drug-related AEs leading to discontinuation were rare
  - The safety profile in older adults with HIV-1 was consistent with the characterized profile of CAB+RPV LA in the general population
- Metabolic parameters generally remained stable in a population with a high baseline comorbidity burden
- Treatment satisfaction scores improved among individuals receiving CAB+RPV LA at Week 48, demonstrating the regimen's high long-term acceptability
- These results support the use of CAB+RPV LA for the maintenance of virologic suppression in older adults with HIV-1, a group with a high burden of multiple comorbidities and taking concomitant medications
- These findings are reinforced by real-world studies showing that CAB+RPV LA is highly effective and generally well tolerated among older adults[8,9]

Acknowledgments: This study was funded by ViiV Healthcare. Editorial assistance and graphic design support for this poster were provided under the direction of the authors by Fingerpaint Medical and funded by ViiV Healthcare.

References: 1. Althoff et al. *AIDS*. 2022;36:459-471. **2.** Marty et al. *J Int AIDS Soc*. 2022;25:e25986. **3.** Smit et al. *Lancet Infect Dis*. 2015;15:810-818. **4.** O'Shea et al. *AIDS*. 2023;37:2271-2286. **5.** Orkin et al. *Lancet HIV*. 2021;8:e185-e196. **6.** Swindells et al. *N Engl J Med*. 2020;382:1112-1123. **7.** Ramgopal et al. *Lancet HIV*. 2023;10:e566-e577. **8.** Focà et al. *Sex Transm Infect*. 2025;101. **9.** Troya et al. *HIV Med*. 2026;27:58-73.

Presenting author: Dennis Rice; dennis.a.rice@viivhealthcare.com