12-Month Outcomes of Cabotegravir Plus Rilpivirine Long-Acting Every 2 Months in a Real-World Setting: Effectiveness, Adherence to Injections, and Patient-Reported Outcomes From People With HIV-1 in the German CARLOS Study

TUPEB095

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Key Takeaways

- **We present the Month 12 outcomes for the real-world CARLOS study; a non-interventional, 3-year, multicenter, prospective study evaluating outcomes for PWH on suppressive daily oral ART who switched to CAB + RPV LA Q2M in routine clinical care in Germany.**
- **CAB + RPV LA Q2M demonstrated high rates of virologic suppression, with low rates (1.4%) of virologic failure in the first 12 months following switch from daily oral ART.**
- **The majority of participants were adherent to injections in routine clinical practice, with 95% of injections administered within the dosing window or earlier.**
- **Switching to CAB + RPV LA Q2M was well tolerated and improved treatment satisfaction over 12 months, with most (99%) participants preferring LA therapy, primarily due to convenience and alleviations of adherence concerns.**

Background

- Cabotegravir (CAB) plus rilpivirine (RPV) is the first complete long-acting (LA) regimen administered monthly or every 2 months (Q2M) and is recommended by treatment guidelines for the maintenance of HIV-1 virologic suppression in people living with HIV (PWH).[1–3]
  - PWH may be interested in less-frequent dosing for different reasons, including convenience and better lifestyle fit. Additionally, CAB + RPV LA has been shown to help to address challenges associated with daily oral therapy, with PWH preferring the LA regimen due to improvements around their fear of disclosure, stigma, anxiety around adherence, and the daily reminder of HIV status.[4]
- The noninferior efficacy of CAB + RPV LA has been established in four large Phase 3/3b randomized noninferiority trials (ATLAS, FLAIR, ATLAS-2M, and SOLAR);[5–8] however, real-world data can help us to better understand utilization and clinical outcomes among groups of PWH who are more reflective of real-world populations.
- CARLOS is a non-interventional, 3-year, multicenter, prospective study in PWH on suppressive daily oral antiretroviral therapy (ART) who switched to CAB + RPV LA dosed Q2M in routine clinical care in Germany. Here, we present outcomes at Month 12 from the CARLOS study.

Methods

- In line with the European label, eligible participants were aged ≥18 years, had documented HIV-1 infection, and were virologically suppressed (HIV-1 RNA <50 copies/mL) on a stable ART regimen.[9,10] Participants were excluded if they had present or past evidence of viral resistance to, or prior treatment failure with, non-nucleoside reverse transcriptase inhibitors (NNRTIs) or integrase strand transfer inhibitors (INSTIs).[9,10]
- The analysis population included participants who reached the Month 12 window, as well as those who discontinued treatment but would have reached Month 12 at the time of data cut-off (November 20, 2023).
- Participant demographic data were collected from medical records during routine clinical care and patient-reported outcomes were assessed via questionnaires.
- The primary endpoint was the proportion of participants with virologic suppression (HIV RNA <50 copies/mL) at Month 12 (defined as: last available viral load at the injection 7 date ± 12-week window).
- Other endpoints assessed at Month 12 included:
  - Incidence of confirmed virologic failure (CVF; two consecutive HIV-1 RNA ≥200 copies/mL or a single HIV-1 RNA ≥200 copies/mL followed by treatment discontinuation).
  - Proportion of participants with virologic non-response (HIV-1 RNA ≥50 copies/mL).
  - Adherence to injection schedule.
  - Tolerability.
  - Patient-reported outcomes:
    - Reasons for switch: treatment satisfaction (12-item HIV Treatment Satisfaction Questionnaire status version [HIVTSQs]) and treatment preference (preference questionnaire [single question]).
- This study descriptively summarized all endpoints.
- A *post hoc* analysis using a Wilcoxon signed-rank test was performed to determine the change in total treatment satisfaction (HIVTSQs) from baseline to Month 12 for participants who completed the survey at both timepoints.
- For exploratory questions, the number of participants included in the analysis reflect the number of participants who completed the survey at the timepoint of interest.

Results

Table 1. Baseline Characteristics

n (%) unless stated otherwise	CAB + RPV LA Q2M	n
Age		
Median years (IQR)	42 (35–50)	351
<50 years	260 (74)	
50–65 years	88 (25)	
>65 years	3 (<1)	
Sex at birth		
Male	332 (95)	351
Baseline risk factors		
BMI ≥30 kg/m^2	35 (13)	276
HIV-1 subtype A6/A1	5 (2)	226
Baseline resistance test		
No current/historical genotypic resistance test at baseline	122 (35)	351
Comorbidities with a prevalence of ≥25%		
Mental/behavioral disorders	143 (41)	351
Metabolic disorders	96 (27)	
HIV history		
Time on oral ART before switch, median years (IQR)	7.9 (4.3–11.4)	310
PWH with ≥3 prior ART regimens (excluding current daily oral)	145 (51)	284
ART regimen prior to switch (in ≥10% of participants)		
BIC/FTC/TAF	80 (23)	351
DTG/3TC	61 (17)	
DTG/3TC/ABC	36 (10)	

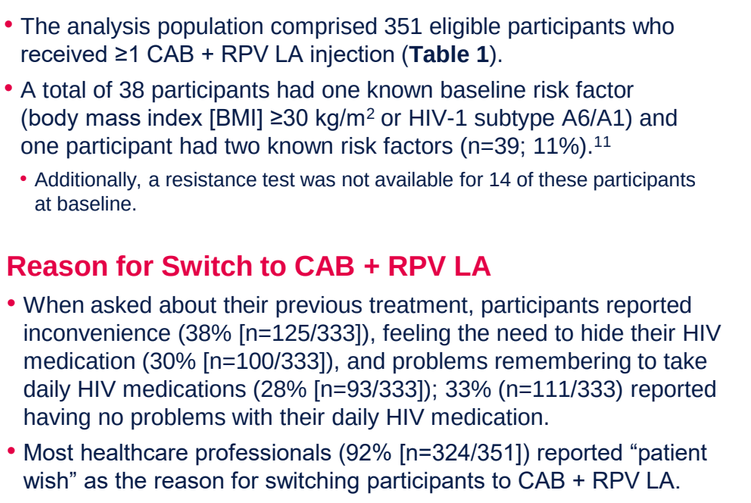
3TC, lamivudine; ABC, abacavir; BIC, bictegravir; BMI, body mass index; DTG, dolutegravir; FTC, emtricitabine; IQR, interquartile range; TAF, tenofovir alafenamide.

- The analysis population comprised 351 eligible participants who received ≥1 CAB + RPV LA injection (**Table 1**).
- A total of 38 participants had one known baseline risk factor (body mass index [BMI] ≥30 kg/m^2 or HIV-1 subtype A6/A1) and one participant had two known risk factors (n=39; 11%).[11]
  - Additionally, a resistance test was not available for 14 of these participants at baseline.

Reason for Switch to CAB + RPV LA

- When asked about their previous treatment, participants reported inconvenience (38% [n=125/333]), feeling the need to hide their HIV medication (30% [n=100/333]), and problems remembering to take daily HIV medications (28% [n=93/333]); 33% (n=111/333) reported having no problems with their daily HIV medication.
- Most healthcare professionals (92% [n=324/351]) reported "patient wish" as the reason for switching participants to CAB + RPV LA.
- The top five participant-reported reasons for switch were related to more convenient treatment option (62% [n=208/333]), pill fatigue (51% [n=170/333]), recommendation by healthcare provider (38% [n=126/333]), adherence anxiety (37% [n=123/333]), and HIV disclosure concerns (30% [n=99/333]).

Figure 1. Virologic Outcomes at Month 12



*Participant had HIV-1 RNA <50 copies/mL at injection 7 and a single viral load of 73 copies/mL at the end of the Month 12 window. †Preferred oral ART, n=11; other reason, n=7; withdrawal of consent, n=2; death, n=1. CVF, confirmed virologic failure; ISR, injection site reaction; LOCF, last observation carried forward; LTFU, lost to follow-up.

- At Month 12, 86% (n=301/351) of participants maintained virologic suppression, 1.4% (n=5/351) met the CVF criterion, 0.3% (n=1/351) had a single HIV-1 RNA ≥50 copies/mL, and 13% (n=44/351) had discontinued or missing data (LOCF <50 copies/mL; **Figure 1**).
- When examining the last known viral load at Month 12 or at discontinuation (LOCF), 98% (n=345/351) of participants maintained virologic suppression.

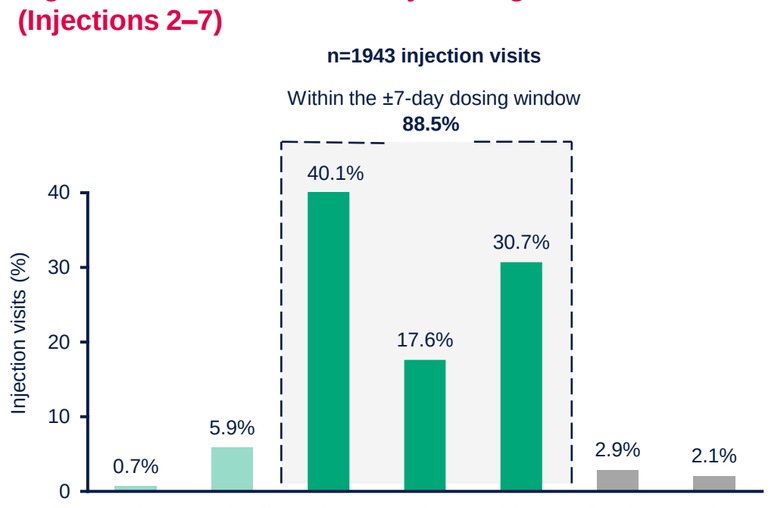
Table 2. Summary of Participants With CVF

Sex at birth, age (years)	Baseline BMI (kg/m^2)	HIV-1 subtype at baseline	Resistance at baseline	Time to failure (months); injections received	Viral load at SVF/CVF (copies/mL)	RAMs at failure	On time injections	ART following CAB + RPV LA discontinuation
Male, 41	Unknown	Unknown	Unknown	5.0; 4 injections	9620/NA	NNRTI: E138K INSTI: Q148R	Yes	DRV/COBI/FTC/TAF
Male, 45	29	B	No resistance at baseline	5.1; 4 injections	2510/NA	NNRTI: None INSTI: None	No, injection 3 received late (+10 days)	BIC/FTC/TAF
Male, 44	23	B	No resistance at baseline	5.0; 4 injections	12,315/330	NNRTI: Y181C INSTI: T97A, E138K, Q148R, N155H	Yes	DRV/COBI/FTC/TAF
Male, 26	23	B	No resistance at baseline	12.2; 7 injections	578/NA	NNRTI: None INSTI: None	No, injections 6 (+16 days) and 7 (+21 days) received late	BIC/FTC/TAF
Male, 43	26	Unknown	No resistance at baseline	13.4; 7 injections	845/3500	NNRTI: K101E INSTI: None	Yes	DRV/COBI/FTC/TAF

COBI, cobicistat; CVF, confirmed virologic failure; DRV, darunavir; NA, not available; RAM, resistance-associated mutation; SVF, suspected virologic failure.

- Overall, five participants (n=5/351; 1.4%) met the CVF criterion through Month 12.
  - For three participants, NNRTI resistance-associated mutations (RAMs; E138K, K101E, Y181C) and/or INSTI RAMs (Q148R, T97A, E138K, N155H) were observed at failure (**Table 2**).
- Previously reported: One additional participant was excluded from the analysis population for off-label use of CAB + RPV LA (discovered *post hoc*; prior virologic failure with an agent of NNRTI class) had CVF with NNRTI RAMs (K101E, Y181C, G190A) detected at failure. The participant had HIV-1 subtype C, a BMI of 20 kg/m^2, and on-time injections.[12]

Figure 2. Adherence to ±7-Day Dosing Window (Injections 2–7)



- Overall, 95% (n=1847/1943) of CAB + RPV LA maintenance injections were administered within the dosing window or earlier; 5% (n=96/1943) occurred late (**Figure 2**).
- The most common reasons for injection deviations were missed appointments (n=131) and last-minute travel (n=30).
- Oral therapy was administered on 21 occasions for a median (IQR) duration of 2.7 weeks (1.7–4.1).
- Four participants received new loading doses due to delayed injections.

Table 3. Drug-Related AEs and ISRs Through Month 12

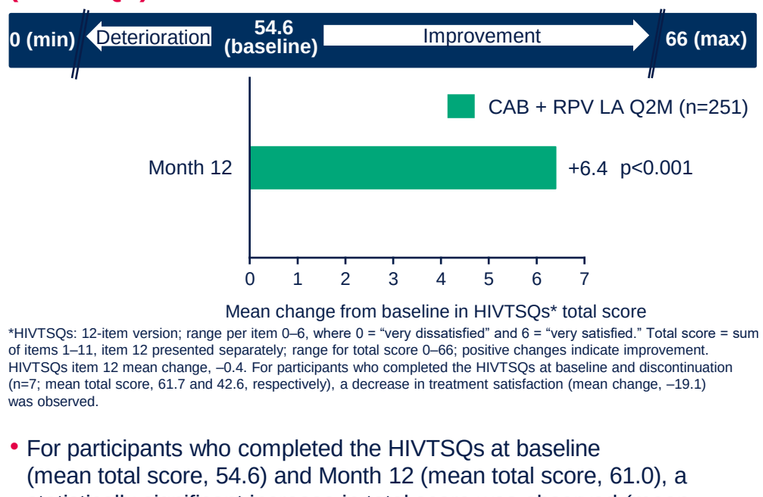
Drug-related AEs (excluding ISRs)	CAB + RPV LA Q2M n=351
Drug-related AEs, n	41
Grade 1–2 events	39
Serious drug-related AEs, n	1*
Grade 3 events	1
Discontinuation due to drug-related AEs, n (%)	4†

ISRs	CAB + RPV LA Q2M n=351
Number of injections, n	2294
ISR events, n	268
Pain, n (% of injections)‡	233 (10)
Nodule, n (% of injections)‡	13 (<1)
Swelling, n (% of injections)‡	11 (<1)
Grade 3 events, n (% of ISR events)	4 (1)
Median duration (IQR), days	3 (2–6)
Discontinuation due to ISRs, n (%)	13 (4%)§

*Anxiety disorder, n=1. †Headache (Grade 2, n=1), syncope (Grade 2, n=1), anxiety disorder (Grade 3, n=1), and pyrexia (Grade 2, n=1). ‡Top 3 most-commonly reported ISRs listed. Participants may have multiple ISR events following a single injection. §Includes 10 participants who withdrew with the primary reason as no longer tolerating injection pain/ISRs. Three additional participants withdrew citing injection-related reasons/ISRs as a secondary reason (patient prefers oral ART, n=1; safety/tolerability concerns other than ISRs, n=1; withdrawal of consent, n=1).
AE, adverse event.

- The most common (≥3 events) non-serious drug-related adverse events, excluding injection site reactions (ISRs), were pyrexia (n=13), pain (n=9), headache (n=7), nausea (n=5), pain in extremity (n=4), fatigue (n=3), and sleep disorder (n=3).
- Most ISRs were Grade 1–2 (n=264/268; 99%).
- Pain was the most common ISR reported, with a few participants (4%) discontinuing due to injection-related reasons (**Table 3**).

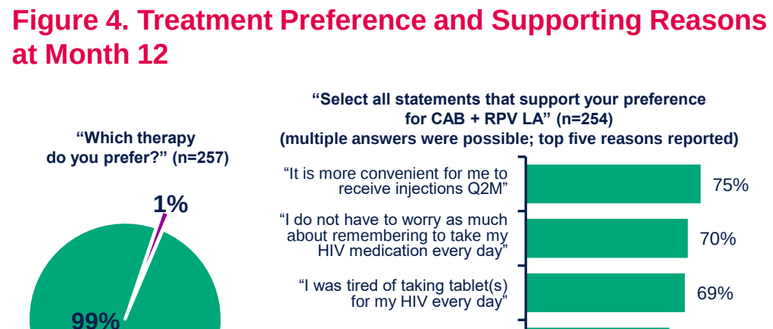
Figure 3. Change in Total Treatment Satisfaction (HIVTSQs) at Month 12



*HIVTSQs: 12-item version; range per item 0–6, where 0 = "very dissatisfied" and 6 = "very satisfied." Total score = sum of items 1–11, item 12 presented separately; range for total score 0–66; positive changes indicate improvement. HIVTSQs item 12 mean change, –0.4. For participants who completed the HIVTSQs at baseline and discontinuation (n=7; mean total score, 61.7 and 42.6, respectively), a decrease in treatment satisfaction (mean change, –19.1) was observed.

- For participants who completed the HIVTSQs at baseline (mean total score, 54.6) and Month 12 (mean total score, 61.0), a statistically significant increase in total score was observed (mean change, +6.4; p<0.001) (**Figure 3**).
  - Mean change in HIVTSQs total score was greater than half of the baseline standard deviation (10.0); meeting the threshold for minimum clinically important difference.[13]

Figure 4. Treatment Preference and Supporting Reasons at Month 12



- At Month 12, CAB + RPV LA was preferred by 99% (n=254/257) of participants responding to the preference questionnaire; 1% (n=3/257) reported no preference (**Figure 4**).
- Supporting reasons for LA treatment preference included "convenience" (n=191/254 [75%]), "not having to worry about remembering to take HIV medicine" (n=177/254 [70%]), and "being tired of taking tablet(s) every day" (n=174/254 [69%]).
- For the seven participants who responded to the preference questionnaire at treatment discontinuation, 86% (n=6/7) indicated a preference for daily oral HIV medication with the remaining participant preferring CAB + RPV LA (14% [n=1/7]); supporting reasons for daily oral therapy preference included "injection pain" (83% [n=5/6]).

Conclusions

- In this real-world study, CAB + RPV LA maintained high levels of effectiveness and was well tolerated in the first 12 months following the switch from daily oral therapy to CAB + RPV LA, consistent with data collected in Phase 3/3b clinical trials.[5–8]
  - The majority (86%) of participants remained suppressed at Month 12.
  - Virologic failure was infrequent, with five participants (1.4%) meeting the CVF criterion through Month 12.
  - Participants demonstrated high rates of adherence to injection visits, with 95% of injections administered within the dosing window or earlier.
  - CAB + RPV LA was well tolerated, with most (99%) ISRs being mild to moderate in severity, and infrequently leading to withdrawal (4%).
- Despite high baseline satisfaction, a statistically significant and clinically meaningful improvement in treatment satisfaction was observed after switching to CAB + RPV LA.
- Most participants responding to the questionnaire at Month 12 preferred CAB + RPV LA (99%), primarily due to the convenience of Q2M injections and having fewer concerns about adherence.

Acknowledgments: We thank everyone who has contributed to the success of the study; all study participants, investigators, and the staff at the CARLOS study centers: Infektiologisches Zentrum Steglitz/Berlin; Klinikum Osnabrueck; MVZ am Isartor/Munich; MVZ München am Goetheplatz/Munich; Novopraxis/Berlin; Praxis an der Kulturbrauerei/Berlin; Praxis am Ebertplatz/Cologne; Praxis City Ost/Berlin; Praxis Cordes/Berlin; Praxis Goldstein/Berlin; Praxis Knechten/Aachen; Praxis Schöneberg/Berlin; Praxis Seidel/Weimar; Praxis UBN/Berlin; prinzmed/Munich; Scholten & Schneeweiß GbR/Cologne; Universitätsklinikum Bonn; ViRo Schillerkiez/Berlin; WIR, Walk In Ruhr/Bochum. The CARLOS study is sponsored by ViiV Healthcare, Germany. Statistical analysis was provided by MUC Research GmbH; editorial assistance was provided by Poppy Mashilo of Nucleus Global, with funding provided by ViiV Healthcare.

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