Virological Outcomes After Late CAB+RPV LA Injections in Newly Suppressed People With HIV-1: 11-Month Results From the VOLITION Study

P059

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Key Takeaways

- **In VOLITION, 58% of participants naive to treatment received cabotegravir plus rilpivirine (CAB+RPV LA) injections early or on time after suppression on DTG/3TC**
- **Short (>7 days) injection delays were not associated with loss of virologic suppression**
- **In participants who are naive to treatment while receiving first-line therapy, CAB+RPV LA provides therapeutic forgiveness when short scheduling delays occur when receiving second-line therapy**

Plain Language Summary

- Long-acting cabotegravir plus rilpivirine (CAB+RPV LA) offers the convenience of injections 6 times a year instead of daily pills
- When a CAB+RPV LA injection appointment needs to be delayed due to unforeseen events such as travel, this can be a potential concern for healthcare professionals and people with HIV
- This study examined whether CAB+RPV LA suppressed the amount of HIV-1 in the blood of study participants receiving CAB+RPV LA who had at least one injection more than 7 days after their planned appointment
- The results showed that HIV-1 levels in the blood remained low at Month 11/12, including in people who had short delays (>7 days) in getting their next injection

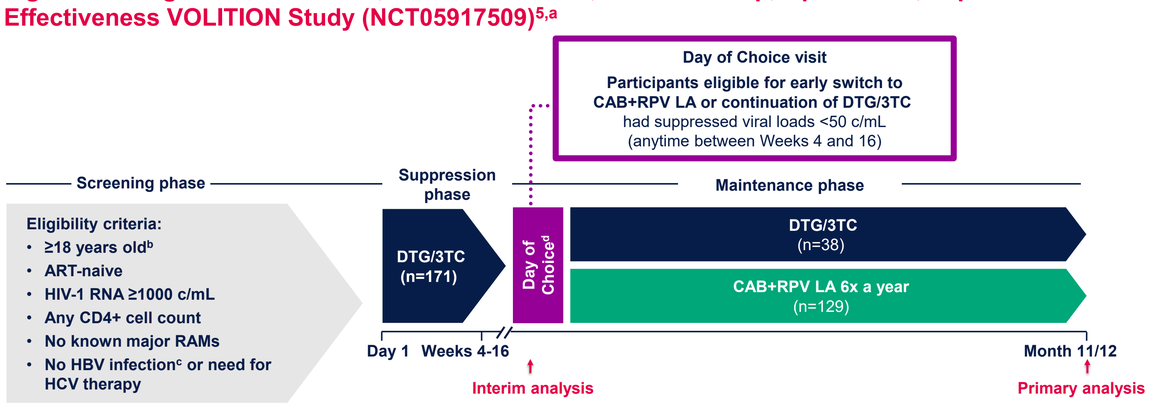
Introduction

- Long-acting cabotegravir plus rilpivirine (CAB+RPV LA) is the first and only complete long-acting injectable regimen that delivers high efficacy and durable virologic suppression in clinical trials, with direct (healthcare professional–confirmed) observation in clinical settings[1,2]; however, real-world scheduling variability can occur and concerns about the impact of a late injection remain a potential barrier to broader uptake
- While CAB+RPV LA can be given 7 days before or after the target injection date,[2-4] clinical outcomes data on injections administered beyond this window (ie, delays due to life circumstances) remain limited, and the degree of therapeutic forgiveness for people newly suppressed on CAB+RPV LA is unclear
- The VOLITION study (NCT05917509) evaluated optional early switch to CAB+RPV LA through shared decision-making after dolutegravir plus lamivudine (DTG/3TC) suppressed viral load (median time to suppression was 4.1 weeks) in adults with HIV-1 who were naive to treatment[5]
  - This provided a unique opportunity to assess the clinical impact of late injections (>7 days after the target injection date) of CAB+RPV LA in individuals with newly suppressed viral loads who experienced dosing delays[5]

Methods

- The design of the VOLITION study is shown in Figure 1[5]
- This post-hoc analysis of VOLITION data included participants who chose to switch to CAB+RPV LA after having initially suppressed viral loads on oral DTG/3TC
- Participants were categorized according to injection adherence: "early/on-time" (no injections >7 days late, no missed injections, no oral bridging) or "late" (≥1 injection >7 days late, ≥1 missed injection, or oral bridging therapy required)
  - Total number of expected dosing visits after the first injection were based on each participant's length of time on-study
  - Days were calculated using "actual injection visit date minus the projected visit date from first injection"
  - Each injection visit was counted only once
- Virologic Snapshot outcomes (HIV-1 RNA <50 copies/mL), confirmed virologic failure (CVF; defined as 2 consecutive plasma HIV-1 RNA values ≥200 copies/mL after prior suppression to <50 copies/mL), and safety outcomes were evaluated through Month 11/12[5]

Figure 1. Design of the Phase 3b, Non-Randomized, Parallel Group, Open-Label, Implementation-Effectiveness VOLITION Study (NCT05917509)[5,a]



ALT, alanine transaminase; anti-HBc, hepatitis B core antibody; anti-HBs, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCV; hepatitis C virus; RAM, resistance-associated mutation; ULN, upper limit of normal. [a]VOLITION was conducted at 45 sites across the United States (n=15), Spain (n=8), France (n=5), Italy (n=4), Argentina (n=4), Chile (n=4), Germany (n=3), and Canada (n=2). [b]Or older, if required by local regulations. [c]Participants positive for HBsAg were excluded. Participants negative for anti-HBs but positive for anti-HBc were excluded only if HBV DNA was detected. [d]Participants proceeded to DoC at the study visit following their first plasma HIV-1 RNA result <50 copies/mL (Week 4 at the earliest but no later than Week 16). Participants must have had a suppressed viral load <50 copies/mL to qualify for the optional switch to CAB+RPV LA. The exclusion criteria for switching included: treatment-emergent ALT ≥5 × ULN; ALT ≥3 × ULN and bilirubin ≥1.5 × ULN (with >35% direct bilirubin); and pregnancy.

Results

Participant Demographics

- Participants in the adherence categories had demographic and clinical characteristics similar to those of the overall group (Table 1)

Table 1. Baseline Demographic and Clinical Characteristics

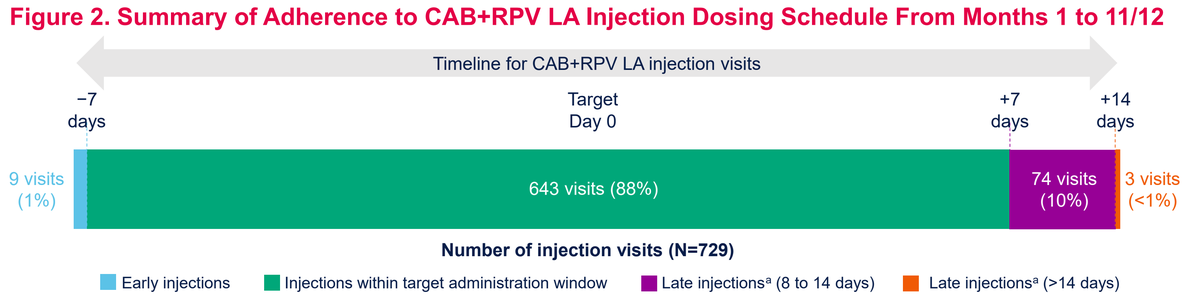
Parameter, n (%)[a]	Overall (N=129)	Adherence: Early/On-Time injections (n=75)	Adherence: Late injections (n=54)
Age, median (IQR), y	31.0 (25.0-40.0)	32.0 (26.0-42.0)	30.0 (24.0-36.0)
Sex reported at birth			
Female	31 (24)	16 (21)	15 (28)
Male	98 (76)	59 (79)	39 (72)
Ethnicity			
Hispanic or Latine	66 (51)	37 (49)	29 (54)
Not Hispanic or Latine	63 (49)	38 (51)	25 (46)
BMI, median (IQR), kg/m^2	25.5 (22.4-29.4)	25.8 (23.0-29.4)	24.2 (22.0-29.4)
BMI category			
Overweight (25 to <30 kg/m^2)	47 (36)	32 (43)	15 (28)
Obese (≥30 kg/m^2)	27 (21)	16 (21)	11 (20)
CD4 counts at baseline, median (IQR), cells/mm^3	415 (262-548)	416 (290-518)	415 (252-568)
Viral load at baseline, median (IQR), c/mL	51,300 (20,500-118,000)	53,400 (20,800-117,000)	48,100 (16,800-124,000)
Received oral bridging therapy with DTG/3TC	1 (1)	0	1 (2)

BMI, body mass index; IQR, interquartile range. [a]Unless otherwise indicated.

Timing of Injections

- Adherence to the injection schedule was high; of 729 injection visits (all participants) from Months 1 to 11/12, 88% (643/729) occurred on time (within the ±7-day window) or earlier (1%, 9/729; Figure 2)

Figure 2. Summary of Adherence to CAB+RPV LA Injection Dosing Schedule From Months 1 to 11/12

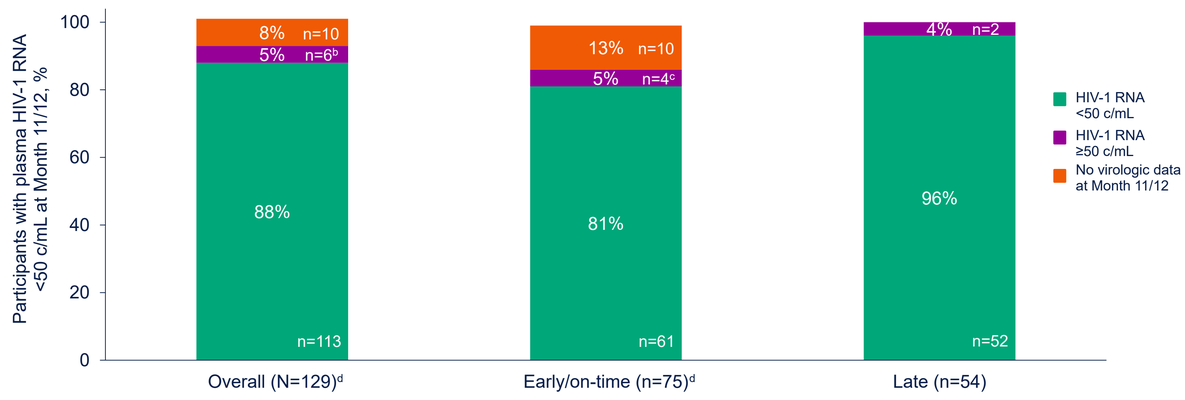


[a]A late injection was defined as ≥1 injection >7 days late OR ≥1 missed injection OR oral bridging therapy required.

Virologic Suppression

- Overall, 42% of participants (54/129) experienced ≥1 "late" injection during the 11/12-month period
  - Delays were infrequent, with a median (range) of 9 (8-18) days after the scheduled injection date
- Despite these delays, 96% (n=52/54) still had suppressed viral loads (<50 copies/mL) at Month 11/12 and 81% (n=61/75) in the "early/on-time" subgroup (Figure 3)
  - The lower proportion with suppressed viral load in the "early/on-time" subgroup is likely due to the absence of virologic data at Month 11/12 for 10 participants
- 1 participant (<1%) in the "late" group required oral DTG/3TC bridging therapy and the remaining 53 participants with late injections received their scheduled injection without bridging

Figure 3. Durable Month 11/12 Virologic Suppression With CAB+RPV LA by Adherence Category[a]



[a]A late injection was defined as ≥1 injection >7 days late OR ≥1 missed injection OR oral bridging therapy required. [b]Of these, 5 participants had data in window not below threshold and 1 participant discontinued due to lack of efficacy. [c]Of these, 3 participants had data in window not below threshold and 1 participant discontinued due to lack of efficacy. [d]Percentages may not equal 100% due to rounding.

Confirmed Virologic Failure

- No CVFs were reported in the "late" group and 4 were reported in the "early/on-time" group

Safety and Tolerability

- Injection site reactions were the most frequently reported adverse event (Table 2)

Table 2. Safety Summary of CAB+RPV LA Through Month 11/12

Event, n (%)	Overall (N=129)	Early/On-Time (n=75)	Late (n=54)
Any AE	97 (75)	59 (79)	38 (70)
Treatment-related AEs	66 (51)	39 (52)	27 (50)
Injection site pain	55 (43)	33 (44)	22 (41)
Injection site discomfort	9 (7)	5 (7)	4 (7)
Injection site nodule	5 (4)	1 (1)	4 (7)
Injection site bruising	4 (3)	3 (4)	1 (2)
Any SAE	12 (9)	9 (12)	3 (6)

AE, adverse event; ISR, injection site reaction; SAE, serious adverse event.

Treatment Discontinuation

- Treatment discontinuation rates were low across groups, and only 1 participant discontinued in the "late" group (Table 3)

Table 3. Reasons for Discontinuing the Study

n (%)	Overall (N=129)	Early/On-Time (n=75)	Late (n=54)
Discontinued from the study	13 (10)	12 (16)	1 (2)
Lost to follow-up	6 (5)	6 (8)	0
Withdrawal by participant	3 (2)	2 (3)	1 (2)[a]
Reached stopping criteria	4 (3)	4 (5)	0

AE, adverse event. [a]Participant withdrew due to burden of the procedure.

Conclusions

- In this post-hoc analysis, short injection delays (>7 days) beyond the ±7-day dosing window were not associated with loss of virologic suppression, supporting good therapeutic forgiveness of CAB+RPV LA
  - No CVFs occurred in the "late" group
- No study discontinuations due to adverse events were reported in either group
- Rates of adverse event profiles and discontinuation rates were low across subgroups
- These findings may provide reassurance to clinicians managing unavoidable scheduling delays and support shared decision-making
- The results from this study are consistent with guidance for the management of late injections[2-4] as well as the known pharmacological profile of CAB+RPV LA
- These findings support the therapeutic forgiveness associated with short scheduling delays[6] while reinforcing that adherence to the injection schedule remains the standard of care

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References: 1. Gandhi et al. *JAMA*. 2025;333:609-628. **2.** Vocabria. [summary of product characteristics]. ViiV Healthcare; 2025. **3.** Cabenuva [prescribing information]. ViiV Healthcare; 2025. **4.** Rekambys. [summary of product characteristics]. ViiV Healthcare; 2025. **5.** Córdova et al. *OFID*. 2026. [Epub ahead of print]. **6.** Hodge et al. *Clin Pharm*. 2021;60:835-853.

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