Early Switch to CAB+RPV LA in Treatment-Naive Adults With HIV-1: Month 11 Outcomes From VOLITION

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Plain Language Summary

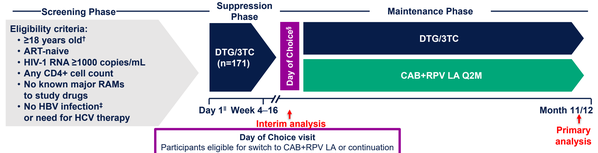
- Most people new to HIV treatment chose to switch to cabotegravir plus rilpivirine long-acting (CAB+RPV LA) injections after quickly getting the virus under control on daily pills.
- Those who chose to switch to CAB+RPV LA did very well. They kept their virus under control, felt satisfied with their care, and had no new safety issues with CAB+RPV LA, with most wanting to continue the CAB+RPV LA after the study.

Introduction

- CAB+RPV LA is the first and only complete LA injectable regimen dosed every 2 months (Q2M), and is recommended for the treatment of virologically suppressed people with HIV.[1,2]
- In real-world and clinical studies, CAB+RPV LA has demonstrated durable efficacy and a low virologic failure rate,[3–10] with greater treatment satisfaction and preference over daily oral therapy.[11–13]
- CAB+RPV LA and dolutegravir and lamivudine (DTG/3TC) are integrase strand transfer inhibitor-based, HIV antiretroviral therapy (ART) regimens with different modalities and dosing frequencies, allowing for greater patient choice and selection of regimens according to lifestyle considerations.
- VOLITION (NCT05917509) is the first study to evaluate optional early switch to CAB+RPV LA, through shared decision-making, immediately after attaining virologic suppression with DTG/3TC in ART-naive adults with HIV-1.
  - Time to virologic suppression (HIV-1 RNA <50 copies/mL) from Day 1 was a co-primary endpoint; DTG/3TC enabled rapid virologic suppression with median time to suppression of 4.1 weeks (95% CI: 4.1–4.3).[14]
  - On Day 1, 85% (n=101/119) of participants who had considered what treatment they would choose at Day of Choice (DoC) expressed an interest in switching to CAB+RPV LA therapy.[14]
- Here, we present VOLITION Month 11 outcomes for participants choosing to switch to CAB+RPV LA.

Methods

Figure 1. VOLITION Study Design*



*VOLITION was conducted at 45 sites across the United States (n=15), Spain (n=6), France (n=5), Italy (n=4), Argentina (n=4), Chile (n=4), Germany (n=3), and Canada (n=2). †≥18 years (or older, if required by local regulations). ‡Participants positive for HBsAg were excluded. Participants negative for anti-HBs but positive for anti-HBc were excluded only if HBV DNA was detected. §Participants proceeded to DoC at their next study visit following the first plasma HIV-1 RNA result <50 copies/mL (Week 4 at the earliest but no later than Week 16). Participants had to be suppressed <50 copies/mL in order to qualify for option switch to CAB+RPV LA. Exclusion criteria for switch included: treatment-emergent ALT >5×ULN; or ALT ≥3×ULN and bilirubin ≥1.5×ULN (with >35% direct bilirubin) and pregnancy. DoC is used as baseline for CAB+RPV LA switch participants in the Maintenance Phase. ¶Day 1 is used as baseline for full study population at Suppression Phase and for participants continuing DTG/3TC into the Maintenance Phase.
3TC, lamivudine; ALT, alanine aminotransferase; anti-HBc, hepatitis B core antigen antibody; anti-HBs, hepatitis B surface antibody; ART, antiretroviral therapy; CAB, cabotegravir; DoC, Day of Choice; DTG, dolutegravir; HBV, hepatitis B virus; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; LA, long-acting; Q2M, every 2 months; RAM, resistance-associated mutation; RPV, rilpivirine; ULN, upper limit of normal.

- The VOLITION study evaluated initial virologic suppression with DTG/3TC followed by participant-determined optional switch to CAB+RPV LA dosed Q2M or continuation of DTG/3TC through Month 11/12.
- A co-primary endpoint was the proportion of participants with HIV-1 RNA <50 copies/mL per Snapshot algorithm at Month 11 with CAB+RPV LA.
  - Observed data, comprising only participants with available virologic data in-window, are also presented.
- Secondary outcomes assessed included:
  - The proportion of participants with confirmed virologic failure (CVF; defined as two consecutive plasma HIV-1 RNA values ≥200 copies/mL after prior suppression to <50 copies/mL).
  - Safety and tolerability.
  - Patient experience outcomes: Reasons for switch; advantages of having the option to switch to CAB+RPV LA; treatment satisfaction (12-item HIV Treatment Satisfaction Questionnaire status version [HIVTSQs]); treatment preference (preference questionnaire [single question]).
- HIV-1 RNA was measured using the Roche cobas 6800 assay (F. Hoffmann-La Roche) for participant virologic management. Prior studies in the clinical development program have used the RealTime HIV-1 assay (Abbott).
- During the study, it was noted in contemporaneous trials, including VOLITION, that central lab viral load results were inconsistent with local lab findings, prompting additional testing using the RealTime assay.
- Virologic efficacy analyses presented here are based on the results from the RealTime assay (modified Snapshot algorithm).

Empowering people with the option for early switch to CAB+RPV LA immediately following virologic suppression through shared decision-making can enable treatment success, as shown by high rates of virologic suppression, low rates of CVF with resistance, and high treatment satisfaction and preference at Month 11.

Results

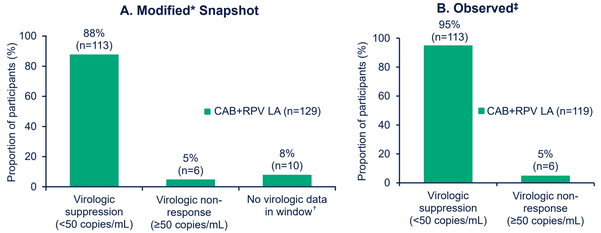
Table 1. A Diverse Population of Participants Chose to Switch to CAB+RPV LA at DoC

Parameter	CAB+RPV LA (n=129)
Median years (range)	31 (18–67)
<35 years, n (%)	79 (61)
35–<50 years, n (%)	37 (29)
≥50 years, n (%)	13 (10)
Women (self-reported gender), n (%)	34 (26)
Race, n (%)	
Black or African American	42 (33)
White	77 (60)
Other races*	5 (4)
Not reported or unknown	5 (4)
Hispanic/Latinx ethnicity, n (%)	66 (51)
Region, n† (%)	
North America	63 (49)
Europe	30 (23)
South America	36 (28)
Median (IQR) weight (kg)	77.7 (65.3, 86.0)
Median (IQR) BMI (kg/m²)	25.5 (22.4, 29.4)
BMI (kg/m²) category, n (%)	
Overweight (25 to <30)	47 (36)
Obesity (≥30)	27 (21)
Median (IQR) CD4+ cell (cells/mm³)	555 (427, 668)
CD4+ cell (cells/mm³) category, n (%)‡	
<100	1 (<1)
100 to <200	7 (6)
200 to <350	20 (16)
≥350	98 (78)

- Overall, 171 participants enrolled in the study and initiated DTG/3TC, 151 (88%) of whom were eligible and were offered the choice to switch to CAB+RPV LA at DoC§.
- Of those offered the choice, 129 (85%) participants chose to switch to CAB+RPV LA.
- A diverse population of participants was represented, comprising 51% Hispanic/Latinx, 33% Black or African American, and 26% women (**Table 1**).

*Other race participants: Multiple, n=3; Asian, n=2. †North America includes United States (including Puerto Rico; n=54) and Canada (n=9); Europe includes France (n=6), Germany (n=4), Italy (n=9), and Spain (n=11); South America includes Argentina (n=20) and Chile (n=16). ‡n=126. §Four participants withdrew during the suppression phase; reasons for ineligibility for switch were: did not achieve virologic suppression (defined as HIV-1 RNA <50 copies/mL; n=15); and baseline resistance to NNRTI [E138A] (n=1).
3TC, lamivudine; BMI, body mass index; CAB, cabotegravir; DoC, Day of Choice; DTG, dolutegravir; IQR, interquartile range; LA, long-acting; NNRTI, non-nucleoside reverse transcriptase inhibitor; RPV, rilpivirine.

Figure 2. High Rate of Virologic Suppression at Month 11



*In the modified Snapshot algorithm, RealTime HIV-1 RNA results were prioritized over the cobas 6800 assay when available and within the Snapshot window. †n=10 discontinued study for other reasons. ‡Includes only participants with available virologic data in-window.
CAB, cabotegravir; LA, long-acting; RPV, rilpivirine.

- At Month 11, high rates of virologic suppression were observed following early switch to CAB+RPV LA, with 88% (n=113/129) of participants maintaining virologic suppression, per the modified Snapshot (**Figure 2A**). The observed virologic suppression rate at Month 11 was 95% (n=113/119) with available virologic data in-window, **Figure 2B**).
- Of the 729 injection visits in the maintenance phase, 661 (91%) were administered within the dosing window (89% [652/729]) or earlier (1% [9/729]; >7 days before the target injection date); the median (IQR) delay for late injections was 9 (8–10) days.

CD4+ Cell Counts Improved From DoC to Month 11 with CAB+RPV LA

- Median (interquartile range [IQR]) CD4+ cell counts increased from DoC to Month 11 by 78 (–10, 182) cells/mm³ (n=118/129) following early switch to CAB+RPV LA, with an absolute (median [IQR]) CD4+ count of 624 (431, 826) cells/mm³ at Month 11.

Table 2. One Participant Met CVF Criteria With Emergent Resistance

	Participant*
Sex at birth, age range (years)	Male, 20–29
BMI (kg/m²)†	≥30
HIV-1 subtype	B
Viral load at Day 1 (copies/mL; cobas 6800)	55,700
RAMs at DoC (proviral DNA)	None
Time to virologic failure (months)	9
Viral load at SVF/CVF (copies/mL; cobas 6800)	405/1410
Viral load at SVF/CVF (copies/mL; RealTime)	285/1213
RAMs at failure	NNRTI: M230L INSTI: E138K, Q148K
ART following CAB+RPV LA discontinuation	DRV/COBI/FTC/TAF‡

- One (<1%) participant met CVF criteria with emergent INSTI and NNRTI resistance (**Table 2**).
- Three additional participants were withdrawn from the study after meeting CVF criteria with the cobas 6800 assay; these participants did not meet CVF criteria based on retrospective retesting with the RealTime assay.
  - None of these participants had treatment-emergent resistance mutations.

*CAB+RPV LA injections were administered with 1.5-inch needles, and all injections were received on time. †BMI at DoC. ‡Participant resuppressed within ~6 months.
ART, antiretroviral therapy; BMI, body mass index; CAB, cabotegravir; COBI, cobicistat; CVF, confirmed virologic failure; DoC, Day of Choice; DRV, darunavir; FTC, emtricitabine; INSTI, integrase strand transfer inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; RAM, resistance-associated mutation; SVF, suspected virologic failure; TAF, tenofovir alafenamide fumarate.

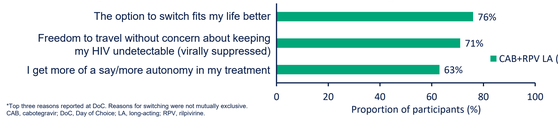
Table 3. CAB+RPV LA Was Well Tolerated Through Month 11

Parameter, n (%)	CAB + RPV LA (n=129)
Any AE	97 (75)
Drug-related AE*	66 (51)
Injection site pain	55 (43)
Injection site discomfort	9 (7)
Injection site nodule	5 (4)
Injection site bruising	4 (3)
Drug-related AEs excluding ISRs	13 (10)†
Grade 3 to 4 AEs	17 (13)
Drug-related Grade 3 to 4 AEs	3 (2)‡
AEs leading to withdrawal	0
Any SAEs	12 (9)§
Drug-related SAEs	0
Fatal AEs	0

*AEs occurring in more than 2% of participants are shown. †Drug-related, non-ISR AEs occurring in >1 participant: pyrexia (n=3), back pain (n=2), myalgia (n=2), pain in extremity (n=2), dizziness (n=2), headache (n=2), and nausea (n=2). ‡Three participants had drug-related Grade 3 events: injection site pain (n=2) and injection pain swelling (n=1 [participant had two instances of this AE]) §SAEs included (all n=1) spontaneous abortion, oral abscess, acute kidney injury, burn infection, cardiac failure, cellulitis, facial paralysis, erosive gastritis, herpes zoster, latent tuberculosis, metastatic malignant melanoma, pancreatitis acute, pneumonia, and suicidal ideation.
AE, adverse event; CAB, cabotegravir; ISR, injection site reaction; LA, long-acting; RPV, rilpivirine; SAE, serious adverse event.

- Overall, 51% of participants had a drug-related AE, the majority of which were ISRs (**Table 3**).
- ISRs were reported in 49% (n=63/129) of participants, most of which were Grade 1 or 2 (98%), with a median (IQR) duration of 3 days (2–6).
- There were no AEs leading to withdrawal and no participants had drug-related SAEs; no deaths occurred.

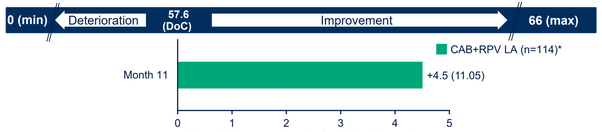
Figure 3. Top Advantages of Having the Option to Switch to CAB+RPV LA Centered Around Lifestyle Fit, Greater Freedom, and More Autonomy*



*Top three reasons reported at DoC. Reasons for switching were not mutually exclusive.
CAB, cabotegravir; DoC, Day of Choice; LA, long-acting; RPV, rilpivirine.

- When asked about the perceived advantages of having the option to switch to CAB+RPV LA at DoC, participants most frequently cited better fit with life (n=96/127, 76%), freedom to travel, (n=90/127, 71%), and more autonomy in their treatment (n=80/127, 63%; **Figure 3**).
- At DoC, the most common reasons for switching to CAB+RPV LA were to avoid worrying about missed daily doses (n=103/129, 80%), travel convenience (n=88/129, 68%) and lifestyle fit (n=82/129, 64%).

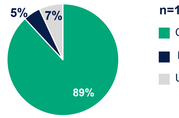
Figure 4. Treatment Satisfaction Improved After DoC and Remained High Through Month 11 With CAB+RPV LA



*DoC, n=127; Month 11; n=114. †HIVTSQs: 12-item version; range per item 0–6, where 0 = "very dissatisfied" and 6 = "very satisfied." Total score = sum of item 1–11.
CAB, cabotegravir; DoC, Day of Choice; HIVTSQs, HIV Treatment Satisfaction Questionnaire status version; LA, long-acting; RPV, rilpivirine; SD, standard deviation.

- Participants reported high levels of treatment satisfaction at DoC (mean [standard deviation; SD] total score, 57.6 [10.36]; n=127) which improved to Month 11 (**Figure 4**).

Figure 5. The Majority of Participants Planned to Continue CAB+RPV LA After the Study



- At Month 11, 89% (n=93/105) of participants receiving CAB+RPV LA who responded to the preference questionnaire stated that they planned to continue CAB+RPV LA after the study (**Figure 5**).

*Includes only participants who received CAB+RPV LA and responded to the questionnaire. The question asked was "'What are your plans for your treatment after the study ends?' Options selected were 'I will continue with CAB+RPV LA (injection)', 'I am currently on CAB+RPV LA (injection) but I am not sure if I will continue with it', and 'I am currently on CAB+RPV LA (injection) but I will switch back to DTG/3TC (pill)'. Where percentages do not sum to 100%, this is due to rounding.
3TC, lamivudine; CAB, cabotegravir; DTG, dolutegravir; LA, long-acting; RPV, rilpivirine.

Conclusions

- In VOLITION, providing ART-naive individuals with the option for early switch to CAB+RPV LA immediately following virologic suppression with daily oral therapy, allowed them to choose a treatment to meet their individualized needs, which is essential for long-term treatment success and optimized quality of life.
- Early switch to CAB+RPV LA demonstrated:
  - High rates of virologic suppression
  - Low rates (<1%) of CVF with resistance
  - High treatment satisfaction with CAB+RPV LA at Month 11
  - High rates of preference for continuing CAB+RPV LA after the study
- CAB+RPV LA was well tolerated, with no new safety signals identified.
- The VOLITION study integrates shared decision-making into treatment selection by empowering people to choose their preferred treatment, which can facilitate better alignment with individual preferences and support treatment success.

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