SOLAR 12-Month North American Results: Randomized Switch Trial of CAB + RPV LA vs. Oral BIC/FTC/TAF

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Key Takeaways

- We present Month 12 efficacy, safety, and patient-reported outcomes for North American (NA) participants in SOLAR: a Phase 3b, randomized, active-controlled study comparing outcomes for participants switching to cabotegravir + rilpivirine long-acting (CAB + RPV LA) dosed every 2 months (Q2M) vs. continuing daily oral bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) over 12 months.
- CAB + RPV LA Q2M was efficacious for the maintenance of virologic suppression in NA participants, with one participant (<1%) meeting the confirmed virologic failure (CVF) criterion in the intention-to-treat exposed (ITT-E) population.
- Switching to CAB + RPV LA Q2M was well tolerated and improved treatment satisfaction vs. continuing BIC/FTC/TAF over 12 months, with most participants preferring LA therapy over daily oral therapy.
- A higher proportion of participants reporting a fear of disclosure, reminder of HIV status, or adherence anxiety related to HIV treatment at baseline had improvements in these factors in the CAB + RPV LA Q2M arm vs. the BIC/FTC/TAF arm.

Introduction

- CAB + RPV LA Q2M is the first and only complete LA regimen recommended for the maintenance of virologic suppression in people living with HIV (PWH).[1–3]
- Treatment guidelines recognize the potential of CAB + RPV LA to improve individual quality of life by helping to alleviate privacy and stigma concerns, as well as improving convenience;[1–3] therefore, CAB + RPV LA may be uniquely suited to support the attainment of the proposed UNAIDS' fourth "90" (health-related quality of life).[4]
- The Phase 3b SOLAR study (NCT04542070) demonstrated noninferior efficacy of switching to CAB + RPV LA Q2M vs. continuing daily oral BIC/FTC/TAF at Month 12, with 90% of switch participants preferring LA therapy.[5]
- Clinical outcomes for PWH receiving CAB + RPV LA may be impacted by patient and viral factors, the prevalence of which can vary by geographical location.[6]
- In this *post hoc* descriptive analysis, we present Month 12 efficacy, safety, and patient-reported outcomes for NA participants from the SOLAR study.

Methods

- SOLAR is a Phase 3b, randomized (2:1), open-label, multicenter, noninferiority study assessing switching virologically suppressed adults to CAB + RPV LA Q2M vs. continuing BIC/FTC/TAF.[5]
- The primary analysis was based on the modified intention-to-treat exposed (mITT-E) population (exclusion of one trial site in the NA region for non-compliance to protocol entry criteria).*
- In this *post hoc* analysis, outcomes for SOLAR participants in the NA region, comprising the United States (US) and Canada (CAN), were assessed.
- Endpoints assessed at Month 12:†
  - Proportion of participants with plasma HIV-1 RNA ≥50 copies/mL and <50 copies/mL (FDA Snapshot algorithm).
  - Incidence of CVF (two consecutive HIV-1 RNA ≥200 copies/mL).
  - Safety and tolerability.
  - Treatment satisfaction (12-item HIV Treatment Satisfaction Questionnaire status version [HIVTSQs]) and treatment preference (preference questionnaire [single question]).
  - Three single-item questions exploring how often an individual: feared disclosure of their HIV status; felt that taking HIV medication was an uncomfortable reminder of their HIV status; had anxiety related to adherence requirements.

*After consultation with a blinded external expert, 11 participants were excluded from the ITT-E population (n=681) due to critical findings related to significant and persistent non-compliance to protocol entry criteria at one study site.

†Assessed at Month 11 for CAB + RPV LA Q2M participants starting with injections and Month 12 for CAB + RPV LA Q2M participants who started with an oral lead-in and BIC/FTC/TAF participants (referred to as Month 12 throughout).

Results

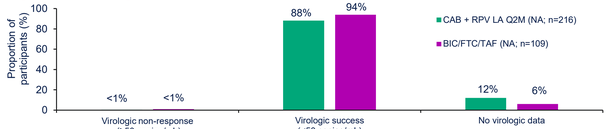
Table 1. Baseline Characteristics

mITT-E population	CAB + RPV LA Q2M (n=216)	BIC/FTC/TAF (n=109)
Age, median (range), years	34 (18–74)	35 (20–66)
≥50 years, n (%)	34 (16)	15 (14)
Sex at birth, n (%)		
Female	31 (14)	17 (16)
Male	185 (86)	92 (84)
Race, n (%)		
White	120 (56)	65 (60)
Black/African American	82 (38)	38 (35)
Asian	3 (1)	2 (2)
Other races*	11 (5)	4 (4)
Ethnicity, n (%)		
Hispanic or Latinx	62 (29)	28 (26)
Weight, median (IQR), kg	83.9 (73.3–97.1)	83.6 (72.1–98.5)
BMI, median (IQR), kg/m^2	27.2 (24.1–31.5)	27.3 (24.2–32.6)
≥30 kg/m^2, n (%)	67 (31)	38 (35)

*Other race participants: American Indian or Alaska Native, n=4 (CAB + RPV LA Q2M); multiple, n=7 (CAB + RPV LA Q2M), n=4 (BIC/FTC/TAF).
BIC/FTC/TAF, bictegravir/emtricitabine/tenofovir alafenamide; BMI, body mass index; CAB, cabotegravir; IQR, interquartile range; LA, long-acting; mITT-E, modified intention-to-treat exposed; Q2M, every 2 months; RPV, rilpivirine.

- Of 325 NA participants (49% [n=325/670] of the global population), 216 (66%) switched to LA and 109 (34%) continued BIC/FTC/TAF (**Table 1**); 273 were from the US (LA arm, n=181; BIC/FTC/TAF arm, n=92) and 52 were from CAN (LA arm, n=35; BIC/FTC/TAF arm, n=17).
- Baseline characteristics were comparable between the NA participants and the global population,[5] although a higher proportion of NA participants were Black/African American (37% vs. 21%) or Hispanic or Latinx (28% vs. 20%) and had a body mass index (BMI) ≥30 kg/m^2 (32% vs. 22%).

Figure 1. Virologic Response at Month 12



BIC/FTC/TAF, bictegravir/emtricitabine/tenofovir alafenamide; CAB, cabotegravir; LA, long-acting; NA, North American; Q2M, every 2 months; RPV, rilpivirine.

- At Month 12, the proportion of NA participants (mITT-E population) with HIV-1 RNA <50 copies/mL was 88% (n=189/216) in the LA arm vs. 94% (n=102/109) in the BIC/FTC/TAF arm (**Figure 1**).

Table 2. Month 12 Snapshot Outcomes

mITT-E population Outcomes, n (%)	CAB + RPV LA Q2M (n=216)	BIC/FTC/TAF (n=109)
HIV-1 RNA <50 copies/mL	189 (88)	102 (94)
HIV-1 RNA ≥50 copies/mL	1 (<1)	1 (<1)
Data in window not below 50 copies/mL	1 (<1)	1 (<1)
Discontinued for lack of efficacy	0	0
Discontinued for other reason while not below 50 copies/mL	0	0
No virologic data	26 (12)	6 (6)
Discontinued due to AE or death*	8 (4)	1 (<1)
Discontinued for other reason	17 (8)	5 (5)
On study but missing data in window	1 (<1)	0

*One death was reported during the maintenance phase (brain injury and encephalopathy following a completed suicide by hanging), which occurred in the BIC/FTC/TAF arm; it was not considered related to study treatment. AE, adverse event; BIC/FTC/TAF, bictegravir/emtricitabine/tenofovir alafenamide; CAB, cabotegravir; LA, long-acting; mITT-E, modified intention-to-treat exposed; Q2M, every 2 months; RPV, rilpivirine.

- Snapshot outcomes at Month 12 were comparable between arms (**Table 2**).
  - Rates of virologic suppression were also similar between participants in CAN and the US across both treatment arms (LA arm: CAN, 89%; US, 87%; BIC/FTC/TAF arm: CAN, 100%; US, 92%).

Table 3. NA Participant With CVF (ITT-E)*

Sex at birth, country	Baseline BMI (kg/m^2)	HIV-1 subtype at baseline	Viral load at SVF/CVF (copies/mL)	RPV RAMs observed at baseline (proviral DNA)	INI RAMs observed at baseline (proviral DNA)	RPV RAMs observed at failure (viral RNA)	INI RAMs observed at failure (viral RNA)	Phenotypic resistance (fold-change) to RPV/CAB	SVF timepoint (month)
Male, US†	30.5	C‡	3797/928	Assay failed	Assay failed	E138E/K + Y181Y/C	None	4.2/assay failed	3

*Two non-NA participants receiving CAB + RPV LA Q2M in the mITT-E population met the CVF criterion through Month 12. †Prior to enrolling in the study, the participant had received prohibited prior ART with at least three prior INI regimens; he resuppressed on BIC/FTC/TAF during long-term follow-up. ‡Participant had HIV-1 subtype C at Month 3. Baseline analysis failed.
ART, antiretroviral therapy; BIC/FTC/TAF, bictegravir/emtricitabine/tenofovir alafenamide; BMI, body mass index; CAB, cabotegravir; CVF, confirmed virologic failure; INI, integrase inhibitor; ITT-E, intention-to-treat exposed; LA, long-acting; mITT-E, modified intention-to-treat exposed; NA, North American; Q2M, every 2 months; RAM, resistance-associated mutation; RPV, rilpivirine; SVF, suspected virologic failure.

- In the mITT-E population, no NA participants in either arm met the CVF criterion through Month 12.
- One NA participant receiving CAB + RPV LA in the ITT-E population met the CVF criterion through Month 12.
  - Genotyping for this participant failed at baseline; the participant had RPV resistance-associated mutations (RAMs) E138E/K + Y181Y/C and no integrase inhibitor RAMs detected at failure (**Table 3**).

Table 4. Safety Summary Through Month 12 Excluding Injection Site Reactions (ISRs)

ITT-E population Parameter, n (%)	CAB + RPV LA Q2M (n=223)	BIC/FTC/TAF (n=113)
Any AE	164 (74)	83 (73)
Drug-related	32 (14)	1 (<1)
Any Grade ≥3 AE	22 (10)	13 (12)
Drug-related	3 (1)	0
Leading to withdrawal	10 (4)	1 (<1)
Drug-related	5 (2)*	0
Any serious AE	9 (4)	7 (6)
Drug-related	1 (<1)‡	0

*Dysesthesia/limb discomfort/paresthesia/peripheral swelling, n=1; dizziness, n=1; fatigue, n=1; deafness/ear congestion/fatigue, n=1; myocardial infarction, n=1.
‡Acute myocardial infarction (non-fatal), n=1.
AE, adverse event; BIC/FTC/TAF, bictegravir/emtricitabine/tenofovir alafenamide; CAB, cabotegravir; ITT-E, intention-to-treat exposed; LA, long-acting; Q2M, every 2 months; RPV, rilpivirine.

- The number of NA participants with adverse events (AEs) was similar between the LA (74% [n=164/223]) and BIC/FTC/TAF arms (73% [n=83/113]) (**Table 4**).
- Drug-related AEs were higher in the LA vs. BIC/FTC/TAF arm (14% vs. <1%); however, drug-related AEs leading to withdrawal were low in both arms.

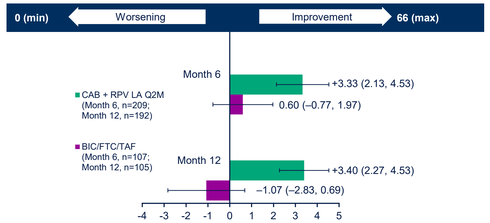
Table 5. ISR Summary (Event-Level) Through Month 12

ITT-E population Parameter, n (%)	CAB + RPV LA Q2M (n=223)
Participants receiving ≥1 injection	217 (97)
Number of injections, n	2840
ISR events, n*	792
Pain, n (% of injections)	603 (21)
Nodule, n (% of injections)	41 (1)
Swelling, n (% of injections)	36 (1)
Grade 3, n (% of ISR events)†	13 (2)
Median duration (IQR), days	3 (2–5)
Participant withdrawal due to injection-related reasons, n (% of participants with injections)	8 (4)

*A single injection could result in more than one ISR. †There were no Grade 4 or Grade 5 ISRs.
CAB, cabotegravir; IQR, interquartile range; ISR, injection site reaction; ITT-E, intention-to-treat exposed; LA, long-acting; Q2M, every 2 months; RPV, rilpivirine.

- Most ISRs were Grade 1 or 2 (98%) and short-lived (median 3 days) (**Table 5**).
- Pain was the most common ISR reported in both the US (19%) and CAN (36%) participants, with few (4%, all from the US) discontinuing due to injection-related reasons.

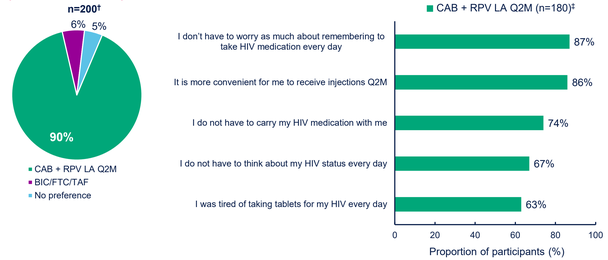
Figure 2. Change in Total Treatment Satisfaction (HIVTSQs)* Through Month 12



*HIVTSQs: 12-item version; range per item was 0–6, where 0 = "very dissatisfied" and 6 = "very satisfied." Total score = sum of items 1–11; item 12 is not included in summary scores. Baseline mean (standard deviation) scores were 58.06 (8.61) and 59.64 (7.16) for the CAB + RPV LA Q2M arm (n=216) and BIC/FTC/TAF arm (n=109), respectively. BIC/FTC/TAF, bictegravir/emtricitabine/tenofovir alafenamide; CAB, cabotegravir; CI, confidence interval; HIVTSQs, HIV Treatment Satisfaction Questionnaire status version; LA, long-acting; Q2M, every 2 months; RPV, rilpivirine.

- Mean adjusted HIVTSQs scores improved to a greater magnitude from baseline to Month 6 and Month 12 for LA vs. BIC/FTC/TAF NA participants (**Figure 2**).
  - Mean adjusted HIVTSQs scores improved across both US and CAN from baseline to Month 6 (US: +4.05 vs. –0.36; CAN: +2.29 vs. +0.29) and Month 12 (US: +4.59 vs. –2.35; CAN: +5.81 vs. +0.94) for LA vs. BIC/FTC/TAF participants.
- At Month 12, mean (standard deviation) scores were 62.70 (6.11) vs. 57.58 (10.68) and 62.63 (7.39) vs. 60.29 (5.44) for LA vs. BIC/FTC/TAF participants in the US and CAN, respectively.

Figure 3. Treatment Preference and Reason for Preference* at Month 12 (or Withdrawal)

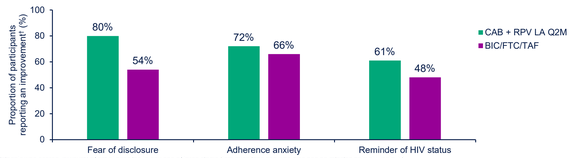


*Top five most frequently reported reasons for preference. †n is the total number of responders to the preference questionnaire. Percentages are rounded to the nearest whole number and therefore may not equal 100%. ‡n is the total number of participants who indicated a preference for CAB + RPV LA Q2M.
BIC/FTC/TAF, bictegravir/emtricitabine/tenofovir alafenamide; CAB, cabotegravir; LA, long-acting; Q2M, every 2 months; RPV, rilpivirine.

- At the time of study withdrawal or at Month 12, 90% (n=180/200) of participants in the LA arm preferred CAB + RPV LA compared with 6% (n=11/200) who preferred daily oral BIC/FTC/TAF; 5% (n=9/200) reported no preference (**Figure 3**).
- Supporting reasons for LA therapy preference included not having to worry about remembering to take HIV medicine, convenience, and not having to carry HIV medication; reasons for LA preference were similar between US and CAN.
- Supporting reasons for participants preferring BIC/FTC/TAF (US, 4% [n=7/167]; CAN, 12% [n=4/33]) included aversion to injection, convenience of oral therapy, the inconvenience of LA clinic appointments, the reliability of oral medication to keep viral load undetectable, and other reasons.*

*Aversion to injection (US, 100% [n=7/7]; CAN, 25% [n=1/4]); other reasons (US, 43% [n=3/7]; CAN, 50% [n=2/4]); convenience of oral therapy (US, 29% [n=2/7]; CAN, 50% [n=2/4]); inconvenience of LA clinic appointments (US, 43% [n=3/7]; CAN, 0%); reliability of oral medication to keep viral load undetectable (US, 43% [n=3/7]; CAN, 0%).

Figure 4. Improvement in Fear of Disclosure, Reminder of HIV Status, and Adherence Anxiety Related to HIV treatment in Participants Reporting Challenges at Baseline*



*Participants who scored "always"/"often" at baseline to any one of three single-item questions and who also had no missing data at Month 12.
†Moving from "always" at baseline to "sometimes"/"rarely"/"never"/"often" or "often" at baseline to "sometimes"/"rarely"/"never." Fear of HIV status disclosure: LA, 80% (n=35/44); BIC/FTC/TAF, 54% (n=13/24). Adherence anxiety: LA, 72% (n=38/53); BIC/FTC/TAF, 66% (n=19/29). Reminder of HIV status: LA, 61% (n=31/51); BIC/FTC/TAF, 48% (n=13/27).
BIC/FTC/TAF, bictegravir/emtricitabine/tenofovir alafenamide; CAB, cabotegravir; LA, long-acting; Q2M, every 2 months; RPV, rilpivirine.

- The proportion of NA participants reporting either a fear of disclosure, reminder of HIV status, or adherence anxiety related to HIV treatment at study entry was similar across arms (LA, 47% [n=101/216]; BIC/FTC/TAF, 48% [n=52/109]).
- At Month 12, there was a decrease in the proportion of participants reporting any one of these challenges across both treatment groups (LA, 35% [n=66/191]; BIC/FTC/TAF, 36% [n=38/105]), with greater decreases observed in the LA arm regarding challenges around fear of HIV status disclosure and adherence anxiety.
  - Fear of HIV status disclosure: LA (baseline, 23% [n=49/216]; Month 12, 9% [n=17/191]); BIC/FTC/TAF (baseline, 24% [n=26/109]; Month 12, 17% [n=18/105]). Adherence anxiety: LA (baseline, 27% [n=59/216]; Month 12, 18% [n=34/191]); BIC/FTC/TAF (baseline, 28% [n=30/109]; Month 12, 21% [n=22/105]). Reminder of HIV status: LA (baseline, 25% [n=54/216]; Month 12, 25% [n=48/191]); BIC/FTC/TAF (baseline, 27% [n=29/109]; Month 12, 25% [n=26/105]).
- Of those participants reporting challenges at baseline, a higher proportion of participants in the CAB + RPV LA Q2M arm reported improvements across each of the three questions compared with participants receiving BIC/FTC/TAF (**Figure 4**).

Conclusions

- Switching to CAB + RPV LA Q2M from BIC/FTC/TAF was efficacious for the maintenance of virologic suppression and was well tolerated in NA participants, consistent with results for the global population.[5]
- The overall CVF rate was low (<1%), with one NA participant in the ITT-E population having CVF in the CAB + RPV LA arm.
- CAB + RPV LA was well tolerated, with most (98%) ISRs being mild to moderate in severity, short in duration (median 3 days), and rarely leading to withdrawal (4%), comparable with the ISR profile for the global population.[5]
- Treatment satisfaction improved to a greater magnitude in NA participants who switched to CAB + RPV LA vs. continuing BIC/FTC/TAF; most participants (90%) preferred LA therapy over daily oral therapy at Month 12.
- Of participants who reported either a fear of disclosure, reminder of HIV status, or adherence anxiety related to HIV treatment at study entry, a higher proportion of participants in the CAB + RPV LA Q2M arm reported improvements across each of the three questions compared with participants receiving BIC/FTC/TAF.
- These data reinforce the ability of CAB + RPV LA to potentially address important unmet needs for some PWH in NA who are virologically suppressed on oral daily ART.

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