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

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Key Takeaways

- **We present the Month 12 efficacy, safety, and patient-reported outcomes for European 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 HIV-1 virologic suppression in European participants, with two participants (1%) meeting the confirmed virologic failure (CVF) criterion.**
- **Switching to CAB + RPV LA Q2M was well tolerated and improved treatment satisfaction vs. continuing BIC/FTC/TAF over 12 months, with most switch 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 virologically suppressed people living with HIV.[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 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]
  - Participants reporting a fear of disclosure, reminder of HIV status, or adherence anxiety related to HIV treatment at baseline experienced statistically and clinically significant improvements in treatment satisfaction after switching to CAB + RPV LA Q2M vs. remaining on BIC/FTC/TAF.[6]
- In this *post hoc* descriptive analysis, we present the Month 12 efficacy, safety, and patient-reported outcomes for European 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 population (exclusion of one non-European trial site for non-compliance to protocol entry criteria).*
- In this *post hoc* analysis, outcomes for SOLAR participants in the European region were assessed.
- Endpoints assessed at Month 12:†
  - The proportion of participants with plasma HIV-1 RNA ≥50 copies/mL and <50 copies/mL (FDA Snapshot algorithm).
  - The 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 intention-to-treat exposed population (n=681) due to critical findings related to significant and persistent non-compliance to protocol entry criteria at one non-European study site.
†Assessed at Month 11 for CAB + RPV LA Q2M participants starting with injections, and at 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).

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Results

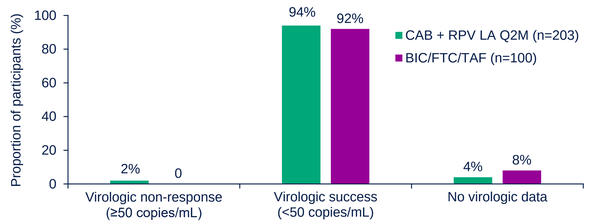
Table 1. Baseline Characteristics

mITT-E population*	CAB + RPV LA Q2M (n=203)	BIC/FTC/TAF (n=100)
Age, median (IQR), years	39 (31–49)	37 (30–49)
≥50 years, n (%)	43 (21)	22 (22)
Sex at birth, n (%)		
Female	42 (21)	22 (22)
Male	161 (79)	78 (78)
Race, n (%)		
White	176 (87)	83 (83)
Black or African heritage	13 (6)	11 (11)
Asian	4 (2)	3 (3)
Other races†	10 (5)	3 (3)
Country, n (%)		
Austria	3 (1)	6 (6)
Belgium	7 (3)	8 (8)
France	22 (11)	11 (11)
Germany	25 (12)	13 (13)
Ireland	4 (2)	1 (1)
Italy	60 (30)	24 (24)
The Netherlands	6 (3)	2 (2)
Spain	53 (26)	25 (25)
Switzerland	10 (5)	6 (6)
United Kingdom	13 (6)	4 (4)
Weight, median (IQR), kg	79.1 (68.0–86.8)	75.6 (65.9–84.5)
BMI, median (IQR), kg/m^2	25.2 (22.8–27.6)	24.9 (22.9–27.4)
≥30 kg/m^2, n (%)	23 (11)	11 (11)

*No European participants were excluded from the ITT-E population. †Other race participants: American Indian or Alaska Native, n=10 (CAB + RPV LA Q2M) and n=2 (BIC/FTC/TAF); Native Hawaiian or Other Pacific Islander, n=1 (BIC/FTC/TAF).
BIC/FTC/TAF, bictegravir/emtricitabine/tenofovir alafenamide; BMI, body mass index; CAB, cabotegravir; IQR, interquartile range; ITT-E, intention-to-treat exposed; LA, long-acting; mITT-E, modified intention-to-treat exposed; Q2M, every 2 months; RPV, rilpivirine.

- Of 303 European participants, 203 (67%) switched to LA and 100 (33%) continued BIC/FTC/TAF (**Table 1**).

Figure 1. Virologic Response at Month 12



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

- At Month 12, the proportion of European participants with HIV-1 RNA <50 copies/mL was 94% (n=191/203) in the LA arm vs. 92% (n=92/100) in the BIC/FTC/TAF arm (**Figure 1**); four participants (2%) in the LA arm and no participants in the BIC/FTC/TAF arm had HIV-1 RNA ≥50 copies/mL.

Table 2. Snapshot Outcomes at Month 12

Outcomes, n (%)	CAB + RPV LA Q2M (n=203)	BIC/FTC/TAF (n=100)
HIV-1 RNA <50 copies/mL	191 (94)	92 (92)
HIV-1 RNA ≥50 copies/mL	4 (2)	0
Data in window not below 50 copies/mL	2 (<1)	0
Discontinued for lack of efficacy	1 (<1)	0
Discontinued for other reason while not below 50 copies/mL	1 (<1)	0
No virologic data	8 (4)	8 (8)
Discontinued due to AE or death	4 (2)	0
Discontinued for other reason	3 (1)	7 (7)
On study but missing data in window	1 (<1)	1 (1)

AE, adverse event; BIC/FTC/TAF, bictegravir/emtricitabine/tenofovir alafenamide; CAB, cabotegravir; LA, long-acting; Q2M, every 2 months; RPV, rilpivirine.

- Snapshot outcomes at Month 12 were comparable between arms, with a small number of participants having no virologic data due to withdrawals from AEs (**Table 2**).

Table 3. Participants With CVF*

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 time point (month)
Male, Italy†	21.5	B	1327/1409	None	None	M230L	Q148R	3.2/3.1	6
Male, Spain‡	22.9	AE	6348/419	None	G140G/R	K101E	G118R	1.9/8.4	11

*One additional non-European participant receiving CAB + RPV LA in the ITT-E population met the CVF criterion through Month 12; this participant was excluded from the mITT-E population due to significant and persistent non-compliance to protocol entry requirements at the study site. †Prior to enrolling in the study, the participant received BIC/FTC/TAF, and after discontinuation re-suppressed on darunavir/cobicistat/emtricitabine/tenofovir alafenamide during long-term follow-up. ‡Prior to enrolling in the study, the participant received abacavir/dolutegravir/lamivudine and BIC/FTC/TAF; they re-suppressed on BIC/FTC/TAF followed by darunavir/cobicistat/emtricitabine/tenofovir alafenamide during long-term follow-up. The participant did not continue in the long-term follow-up phase.
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; RAM, resistance-associated mutation; RPV, rilpivirine; SVF, suspected virologic failure.

- Two European participants in the LA arm met the CVF criterion through Month 12.
  - Neither participant had injections outside of the dosing window (±7 days), and their plasma drug concentrations were above Phase 3 benchmarks (CAB, 0.65 µg/mL; RPV, 17.3 ng/mL) at suspected virologic failure time points.
  - One participant had no RPV or integrase inhibitor (INI) resistance-associated mutations (RAMs) detected at baseline, with the RPV RAM M230L and INI RAM Q148R detected at failure; the second participant had the INI RAM G140G/R at baseline, with the RPV RAM K101E and INI RAM G118R detected at failure (**Table 3**).
- No participants in the BIC/FTC/TAF arm met the CVF criterion through Month 12.

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

Parameter, n (%)	CAB + RPV LA Q2M (n=203)	BIC/FTC/TAF (n=100)
Any AE	160 (79)	77 (77)
Drug related	47 (23)	0
Any Grade ≥3 AE	17 (8)	11 (11)
Drug related	4 (2)	0
Leading to withdrawal	3 (1)	1 (1)
Drug related	3 (1)*	0
Any serious AE	9 (4)	7 (7)
Drug related	2 (<1)†	0

*Blood pressure fluctuation (participant reported) and depression, n=1; alanine aminotransferase increase, n=1; diarrhea and joint stiffness, n=1. †Alanine aminotransferase increase, n=2; AE, adverse event; BIC/FTC/TAF, bictegravir/emtricitabine/tenofovir alafenamide; CAB, cabotegravir; ISR, injection site reaction; LA, long-acting; Q2M, every 2 months; RPV, rilpivirine.

- Excluding ISRs, the incidence of AEs was similar between the LA (79% [n=160/203]) and BIC/FTC/TAF arms (77% [n=77/100])(**Table 4**).
- Of participants reporting AEs, most reported AEs were of a maximum Grade 1 or 2 (LA, 89% [n=143/160]; BIC/FTC/TAF, 86% [n=66/77]).

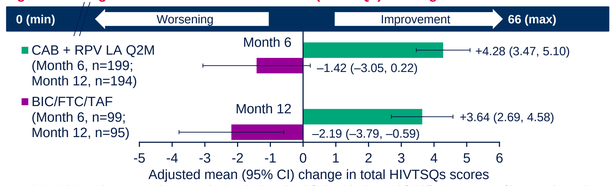
Table 5. ISR Summary (Event-Level) Through Month 12

Parameter	CAB + RPV LA Q2M (n=203)
Participants with injections, n	201 (99)
Number of injections, n	2766
ISR events, n*	1027
Pain, n (% of injections)	708 (26)
Discomfort, n (% of injections)	95 (3)
Induration, n (% of injections)	63 (2)
Grade 3, n (% of ISR events)†	14 (1)
Median duration (IQR), days	3 (2–5)
Participant withdrawal due to injection-related reasons, n (% of participants with injections)	3 (1)

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

- Most ISRs were Grade 1 or 2 (99%) and short-lived (median 3 days; **Table 5**).
- Pain was the most common ISR reported among European participants, with few participants (1%) discontinuing due to injection-related reasons.

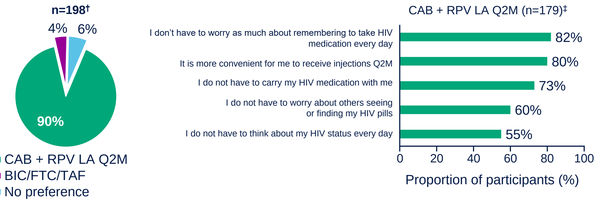
Figure 2. Change in Total Treatment Satisfaction (HIVTSQs)* Through Month 12



*HIVTSQs: 12-item version; range per item was 0–6, where 0 = "very dissatisfied" and 6 = "very satisfied." Total score = sum of item 1–11; item 12 is not included in summary scores. Baseline mean (SD) scores were 58.29 (6.74) and 57.37 (9.13) for the CAB + RPV LA Q2M arm (n=202) and BIC/FTC/TAF arm (n=99), 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; SD, standard deviation.

- There was a greater magnitude of improvement in mean adjusted HIVTSQs scores from baseline to Month 6 and Month 12 for LA vs. BIC/FTC/TAF European participants (**Figure 2**).
- At Month 12, mean (standard deviation) scores were 61.95 (5.81) and 55.67 (9.94) for the LA and BIC/FTC/TAF arms, respectively.

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

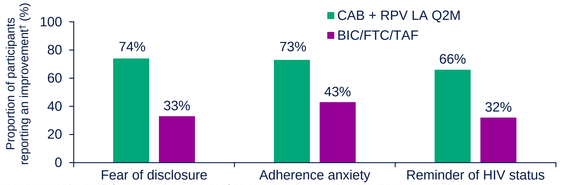


*Top five most frequently reported reasons for preference. †n is the total number of responders to the preference questionnaire. ‡n is the total number of participants who indicated a preference for CAB + RPV LA Q2M.
BIC/FTC/TAF, bictegravir/emtricitabine/tenofovir alafenamide; CAB, cabotegravir; LA, long-acting; Q2M, every 2 months; RPV, rilpivirine.

- At the time of study withdrawal or at Month 12, 90% (n=179/198) of participants in the LA arm preferred CAB + RPV LA compared with 4% (n=8/198) of participants who preferred daily oral BIC/FTC/TAF therapy; 6% (n=11/198) 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.
- Supporting reasons for participants preferring BIC/FTC/TAF (4% [n=8/198]) included aversion to injection, the inconvenience of clinic appointments, other reasons, and the convenience of oral therapy.*

*Aversion to injection, 63% (n=5/8); the inconvenience of clinic appointments, 38% (n=3/8); other reasons, 25% (n=2/8); the convenience of oral therapy, 25% (n=2/8).

Figure 4. Improvement at Month 12 in Fear of Disclosure, Adherence Anxiety Related to HIV Treatment, and Reminder of HIV Status in Participants Reporting Challenges at Baseline*



*Participants who scored "always"/"often" at baseline to any one of the 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 from "often" at baseline to "sometimes"/"rarely"/"never." Fear of HIV status disclosure: LA, 74% (n=37/50); BIC/FTC/TAF, 33% (n=8/24). Adherence anxiety: LA, 73% (n=37/51); BIC/FTC/TAF, 43% (n=9/21). Reminder of HIV status: LA, 66% (n=33/50); BIC/FTC/TAF, 32% (n=6/19). BIC/FTC/TAF, bictegravir/emtricitabine/tenofovir alafenamide; CAB, cabotegravir; LA, long-acting; Q2M, every 2 months; RPV, rilpivirine

- The proportion of European participants reporting either a fear of disclosure, anxiety related to HIV treatment, or reminder of HIV status at study entry was broadly comparable across arms (LA, 51% [n=103/203]; BIC/FTC/TAF, 45% [n=45/100]).
- At Month 12, there was a decrease in the proportion of participants reporting any one of these challenges in the LA arm (33% [n=64/195]) but not in the BIC/FTC/TAF arm (49% [n=47/96]), in which there was an increase.
  - Fear of HIV status disclosure: LA (baseline, 25% [n=51/203]; Month 12, 18% [n=36/195]); BIC/FTC/TAF (baseline, 26% [n=26/100]; Month 12, 28% [n=27/96]). Adherence anxiety: LA (baseline, 26% [n=52/203]; Month 12, 14% [n=28/195]); BIC/FTC/TAF (baseline, 23% [n=23/100]; Month 12, 29% [n=28/96]). Reminder of HIV status: LA (baseline, 25% [n=50/203]; Month 12, 19% [n=37/195]); BIC/FTC/TAF (baseline, 20% [n=20/100]; Month 12, 26% [n=25/96]).
- 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 HIV-1 virologic suppression and was well tolerated in European participants, consistent with results for the global population.[5]
- CVF was infrequent, with two European participants in the CAB + RPV LA Q2M arm meeting the CVF criterion through Month 12.
- CAB + RPV LA was well tolerated, with most (99%) ISRs being mild to moderate in severity, short in duration (median 3 days), and infrequently leading to withdrawal (1%), comparable with the ISR profile for the global population.[5]
- Treatment satisfaction improved to a greater magnitude in European participants who switched to CAB + RPV LA vs. continuing BIC/FTC/TAF; most switch 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.

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