SOLAR 12-Month Results – Randomized Switch Trial of CAB+RPV LA vs Oral B/FTC/TAF

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*Presenting on behalf of the authors.

Key Takeaways

- **Switching to CAB+RPV LA treatment was well-tolerated and demonstrated non-inferior virologic efficacy vs continuing BIC/FTC/TAF at Month 11/12**
- **Participants reported significant improvements in treatment satisfaction after switch to CAB+RPV LA, and a high majority preferred LA treatment over daily oral therapy**
- **These data demonstrate that CAB+RPV LA addresses important unmet needs for people living with HIV who are virologically suppressed on oral daily therapy**

Introduction

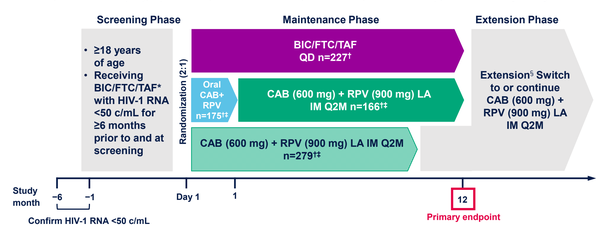
- Cabotegravir (CAB), an INI, plus rilpivirine (RPV), an NNRTI, is the first and only complete long-acting (LA) regimen administered monthly or every 2 months (Q2M) recommended by HIV-1 treatment guidelines for the maintenance of virologic suppression[1-4]
- The less frequent dosing offered by CAB+RPV LA may help address some concerns associated with daily oral therapy, including fear of disclosure, stigma, anxiety around medication adherence, and the daily reminder of HIV status[5]
  - These challenges may impact health-related quality of life for people living with HIV; therefore, CAB+RPV LA may be uniquely suited to support the attainment of UNAIDS's fourth "90"[6]
- SOLAR is the first randomized comparison of CAB+RPV LA dosed Q2M vs daily oral bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF)
- We report Month 12 efficacy, safety, and patient-reported outcomes following switching to CAB+RPV LA Q2M from BIC/FTC/TAF administered orally once daily, compared with continuing BIC/FTC/TAF

Methods

- SOLAR (ClinicalTrials.gov identifier, NCT04542070) is a phase IIIb, randomized (2:1), open-label, multicenter, non-inferiority (NI) study assessing switching virologically suppressed adults to CAB+RPV LA Q2M vs continuing BIC/FTC/TAF (Figure 1)
  - In consultation with their provider, participants randomized to CAB+RPV LA could select to either start with injections (SWI) or use an oral lead-in (OLI) first
- The primary analysis was based on the modified intention-to-treat exposed (mITT-E) population
  - After consultation with a blinded external expert, 11 participants from one trial site were excluded from the intention-to-treat exposed (ITT-E) population (n=681) for site-related non-compliance to protocol entry criteria
- Endpoints assessed at Month 11 (SWI)/12 (OLI / BIC/FTC/TAF; hereafter referred to as Month 12):
  - Proportion with plasma HIV-1 RNA ≥50 c/mL (FDA Snapshot, 4% NI margin; primary endpoint)
  - Proportion with plasma HIV-1 RNA <50 c/mL (FDA Snapshot, −12% NI margin)
  - Incidence of confirmed virologic failure (CVF; 2 consecutive HIV-1 RNA ≥200 c/mL)
  - Safety and tolerability
  - Treatment satisfaction (HIV Treatment Satisfaction Questionnaire status version [HIVTSQs]) and patient preference

Figure 1. SOLAR Study Design

Phase 3b, Randomized (2:1), Open-Label, Active-Controlled, Multicenter, Parallel-Group, Non-Inferiority Study



IM, intramuscular; LA, long-acting; OLI, oral lead-in; Q2M, every 2 months. *A single prior INI regimen is allowed if BIC/FTC/TAF is a second-line regimen 6 months before screening. Any prior change in regimen, defined as a change of a single drug or multiple drugs simultaneously, must have occurred due to tolerability/safety, access to medications, or convenience/simplification, and must not have been done for treatment failure (HIV-1 RNA ≥400 c/mL). †n values are based on the safety population. ‡Participants randomized to the LA arm were offered an optional OLI; the decision was determined by the participants following informed consent discussions with the investigator. §The extension phase will continue study treatment until CAB LA and RPV LA are either locally approved and commercially available, the participant no longer derives clinical benefit, the participant meets a protocol-defined reason for discontinuation, or until development of either CAB LA or RPV LA is terminated.

Results

Participants

- At baseline, 47% (n=315/670) of participants who were virologically suppressed on BIC/FTC/TAF "always/often" reported at least one of the following psychosocial challenges with daily oral therapy:
  - *"Worried about people unintentionally discovering their HIV status"*
  - *"Worried about forgetting to take their HIV medication"*
  - *"Felt that taking their HIV medication was an uncomfortable reminder of their HIV status"*

Table 1. Participant Demographics and Baseline Characteristics

mITT-E population	CAB+RPV LA Q2M (n=447)	BIC/FTC/TAF (n=223)
Median age (range), years	37 (18-74)	37 (18-66)
≥50 years, n (%)	86 (19)	42 (19)
Female (sex at birth), n (%)	77 (17)	41 (18)
Race, n (%)		
Black	95 (21)	49 (22)
White	307 (69)	156 (70)
Asian	23 (5)	11 (5)
Other races*	22 (5)	7 (3)
BMI, median (IQR), kg/m^2	26.0 (23.2-29.4)	25.4 (23.4-29.6)

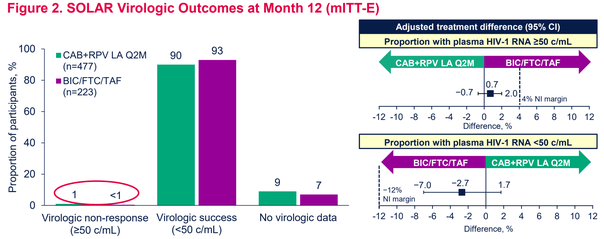
IQR, interquartile range; LA, long-acting; mITT-E, modified intention-to-treat exposed; Q2M, every 2 months. *Other race participants: American Indian or Alaska Native, n=14 (CAB+RPV LA Q2M) and n=2 (BIC/FTC/TAF); Native Hawaiian or other Pacific Islander, n=1 (BIC/FTC/TAF); multiple, n=8 (CAB+RPV LA Q2M) and n=4 (BIC/FTC/TAF).

- Among study participants, 12 transgender females, 1 transgender male, and 1 gender non-conforming individual were included (Table 1)

SOLAR Virologic Outcomes at Month 12 (mITT-E)

- At Month 12, CAB+RPV LA demonstrated non-inferior efficacy compared with BIC/FTC/TAF for the proportion of participants with HIV-1 RNA ≥50 c/mL and <50 c/mL in the mITT-E and ITT-E populations (Figure 2)
  - In the ITT-E population, 406/454 (89%) and 211/227 (93%) participants receiving CAB+RPV LA and BIC/FTC/TAF had HIV-1 RNA <50 c/mL; 6/454 (1%) and 1/227 (<1%) had HIV-1 RNA ≥50 c/mL; 42/454 (9%) and 15/227 (7%) had no virologic data, respectively

Figure 2. SOLAR Virologic Outcomes at Month 12 (mITT-E)



LA, long-acting; mITT-E, modified intention-to-treat exposed; NI, non-inferiority; Q2M, every 2 months.

- Among participants with no virologic data, the incidence of adverse events (AEs) leading to withdrawal was low, and discontinuations for other reasons were similar between the LA and BIC/FTC/TAF arms (Table 2)

Table 2. SOLAR Snapshot Outcomes at Month 12 (mITT-E)

Parameter, n (%)	CAB+RPV LA Q2M (n=447)	BIC/FTC/TAF (n=223)
HIV-1 RNA <50 c/mL	403 (90)	207 (93)
HIV-1 RNA ≥50 c/mL	5 (1)	1 (<1)
Data in window not below threshold	3 (<1)	1 (<1)
Discontinued for lack of efficacy	1 (<1)	0
Discontinued for other reason while not below 50 c/mL	1 (<1)	0
No virologic data	39 (9)	15 (7)
Discontinued due to AE	13 (3)*	0
Discontinued due to death	0	1 (<1)†
Discontinued for other reason	24 (5)‡	13 (6)§
On study but missing data in window	2 (<1)	1 (<1)

AE, adverse event; LA, long-acting; mITT-E, modified intention-to-treat exposed; Q2M, every 2 months. *n=2 injection site pain; n=1 each: acute myocardial infarction; dysesthesia/limb discomfort/paresthesia/peripheral swelling; dizziness; fatigue; deafness/ear congestion/fatigue; blood pressure fluctuation (participant reported)/depression; alanine aminotransferase increase; diarrhea/joint stiffness; acute hepatitis B; fatigue/pyrexia; injection site discharge. †Fatal SAE of brain injury and encephalopathy. ‡Withdrawal by participant, n=12; lost to follow-up, n=6; protocol deviation, n=5; investigator decision, n=1. §Physician decision (pregnancy), n=1; withdrawal by participant, n=9; protocol deviation, n=1; lost to follow-up, n=2.

- Two (0.4%) participants receiving CAB+RPV LA in the mITT-E population, and one additional participant receiving CAB+RPV LA in the ITT-E population, met the CVF criterion through Month 12 (Table 3)
  - Two participants had on-treatment RPV and/or INI resistance-associated mutations (RAMs; genotyping for third participant failed at baseline)
- No participants in the BIC/FTC/TAF arm met the CVF criterion through Month 12

Table 3. SOLAR Participants With Confirmed Virologic Failure

Sex at birth, country	Baseline BMI (kg/m^2)	Baseline HIV-1 subtype	Viral load at SVF/CVF (c/mL)	RAMs at baseline (proviral DNA) RPV	RAMs at baseline (proviral DNA) INI	RAMs at failure (viral RNA) RPV	RAMs at failure (viral RNA) INI	Phenotypic resistance (fold-change) to RPV/CAB	SVF time point (month)
Participants with CVF in the mITT-E population									
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
Participant with CVF in the ITT-E population‡									
Male, United States	30.5	C§	3797/ 928	Assay failed	Assay failed	E138E/K + Y181Y/C	None	4.2/assay failed	3

CVF, confirmed virologic failure; mITT-E, modified intention-to-treat exposed; RAM, resistance-associated mutation; SVF, suspected virologic failure. *Before enrolling in the study, the participant received BIC/FTC/TAF, and after discontinuation re-suppressed on DRV/COBI/FTC/TAF during long-term follow-up. †Before enrolling in the study, the participant had received ABC/DTG/3TC and BIC/FTC/TAF; they re-suppressed on BIC/FTC/TAF and DRV/COBI/FTC/TAF during long-term follow-up. The participant did not continue in the long-term follow-up phase. ‡Before enrolling in the study, the participant had received prohibited prior ART with at least three prior INI regimens; they re-suppressed on BIC/FTC/TAF during long-term follow-up. This participant was excluded from the mITT-E population due to significant and persistent non-compliance to protocol entry requirements at the study site. §Participant had HIV-1 subtype C at Month 3. Baseline analysis failed.

Safety Outcomes at Month 12

- The most commonly reported drug-related AEs in the LA arm were pyrexia (3%), headache (2%), fatigue (2%), and diarrhea (2%); in the BIC/FTC/TAF arm, the 2 drug-related AEs reported were weight gain (<1%) and abnormal hepatic function (<1%; Table 4)
- More participants in the CAB+RPV LA arm had AEs leading to withdrawal (3% vs <1%)

Table 4. Safety Overview (Excluding Injection Site Reactions [ISRs])

Parameter, n (%)	CAB+RPV LA Q2M (n=454)	BIC/FTC/TAF (n=227)
Any AE	349 (77)	172 (76)
Drug-related AEs	90 (20)	2 (<1)
Any grade ≥3 AE	42 (9)	26 (11)
Drug-related	7 (2)	0
Leading to withdrawal	15 (3)	2 (<1)
Drug-related	9 (2)*	0
Any serious AE	21 (5)	15 (7)
Drug-related	3 (<1)†	0

AE, adverse event; LA, long-acting; OLI, oral lead-in; Q2M, every 2 months. *OLI period (n=1 each): dysesthesia/limb discomfort/paresthesia/peripheral swelling; dizziness; fatigue; deafness/ear congestion/fatigue; blood pressure fluctuation (participant reported)/depression; diarrhea/joint stiffness; injection period (n=1 each): myocardial infarction; alanine aminotransferase increase; fatigue/pyrexia. †Increased alanine aminotransferase, n=2; acute myocardial infarction, n=1.

- Most injection site reactions (ISRs) were Grade 1 or 2 (98%), short-lived (median 3 days), with few participants discontinuing due to injection-related reasons (Table 5)

Table 5. Injection Site Reactions (Event-Level)

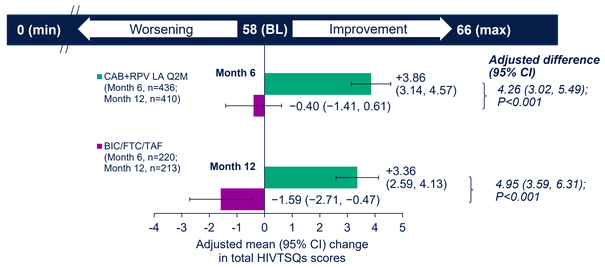
Parameter	CAB+RPV LA Q2M (with OLI; n=166)*	CAB+RPV LA Q2M (SWI; n=279)*	Total (n=445)*
Number of injections, n	2228	3724	5952
ISR events, n†	734	1181	1915
Pain, n (% of injections)	507 (23)	887 (24)	1394 (23)
Discomfort, n (% of injections)	56 (3)	65 (2)	121 (2)
Nodule, n (% of injections)	28 (1)	56 (2)	84 (1)
Grade 3, n (% of ISR events)‡	19 (3)	10 (<1)	29 (2)
Median duration (IQR), days	3 (2, 5)	3 (2, 5)	3 (2, 5)
Participant withdrawal due to injection-related reasons, n (% of participants with injections)§	3 (2)	8 (3)	11 (2)

AE, adverse event; IQR, interquartile range; ISR, injection site reaction; LA, long-acting; mITT-E, modified intention-to-treat exposed; OLI, oral lead-in; Q2M, every 2 months; SWI, starting with injections. *Represents the number of participants who received an injection. †A single injection could result in more than one ISR. Grading was missed for one ISR event in the CAB+RPV LA SWI group. ‡There were no Grade 4 or Grade 5 ISRs. §Includes participants who discontinued due to ISR AEs, and an additional participant who withdrew from the study citing injection intolerability. This also includes one participant who was excluded from the primary analysis (mITT-E) population.

Participant Satisfaction

- Mean adjusted HIVTSQs scores improved significantly for CAB+RPV LA vs BIC/FTC/TAF participants from baseline (LA, 57.88; BIC/FTC/TAF, 58.38) to Months 6 and 12, demonstrating greater improvement from baseline in HIV treatment satisfaction for participants receiving CAB+RPV LA compared with BIC/FTC/TAF (Figure 3)

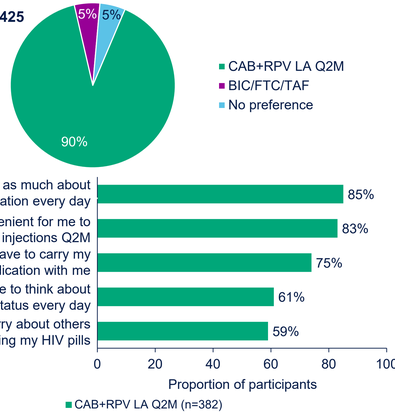
Figure 3. Participant Satisfaction



BL, baseline; HIVTSQs, HIV Treatment Satisfaction Questionnaire status version; LA, long-acting; Q2M, every 2 months.

- Overall, at the time of study withdrawal or at Month 12, 90% (n=382/425) of participants preferred CAB+RPV LA compared with 5% (n=21/425) who preferred daily oral BIC/FTC/TAF therapy (Figure 4)

Figure 4. Treatment Preference and Reason for Preference Among Participants Who Switched to CAB+RPV LA Q2M at Month 12 or at Time of Study Withdrawal*



LA, long-acting; Q2M, every 2 months. *Top five most frequently reported reasons for preference.

Conclusions

- At baseline, 47% of participants on BIC/FTC/TAF reported psychosocial challenges with their daily oral therapy
- At Month 12, CAB+RPV LA Q2M demonstrated non-inferior virologic efficacy vs BIC/FTC/TAF
  - The overall CVF rate was low (<1%) in the population receiving CAB+RPV LA; all re-suppressed on alternative oral ART
- 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 (2%)
- 90% of participants in the LA arm preferred CAB+RPV LA after switch from BIC/FTC/TAF and had significant improvement in treatment satisfaction
- Participants who switched to CAB+RPV LA from BIC/FTC/TAF had significant improvement in treatment satisfaction
- These data demonstrate that CAB+RPV LA addresses important unmet needs for people living with HIV who are virologically suppressed on oral daily therapy

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