SOLAR (Switch Onto Long-Acting Regimen) 12-Month Results – Randomized Switch Trial of CAB + RPV LA vs. Oral BIC/FTC/TAF

Moti N. Ramgopal[1], Antonella Castagna[2], Charles Cazanave[3], Vicens Diaz-Brito[4], Robin Dretler[5], Shinichi Oka[6], Olayemi Osiyemi[7], Kenneth Sutton[8], Denise Sutherland-Phillips[8], Alessandro Berni[9], Christine Latham[8], Feifan Zhang[10], Ronald D'Amico[8], Kimberly Smith[8], Jean van Wyk[11]

[1]Midway Immunology and Research Center, Fort Pierce, FL, United States; [2]Vita-Salute University San Raffaele Scientific Institute, Milan, Italy; [3]Department of Infectious Diseases, Pellegrin Hospital, University Hospital of Bordeaux, Bordeaux, France; [4]Department of Infectious Diseases, Parc Sanitari Sant Joan de Deu, Sant Boi de Llobregat, Spain; [5]Infectious Disease Specialists of Atlanta, Decatur, GA, United States; [6]AIDS Clinical Center, National Center for Global Health and Medicine, Tokyo, Japan; [7]Triple O Research Institute PA, West Palm Beach, FL, United States; [8]ViiV Healthcare, Durham, NC, United States; [9]GSK, Brentford, United Kingdom; [10]GSK, Collegeville, PA, United States; [11]ViiV Healthcare, Brentford, United Kingdom

Moti Ramgopal, MD, FACP, FIDSA, has received speaking and/or consulting fees from AbbVie, Gilead Sciences, Janssen, Merck, and ViiV Healthcare

Conference on Retroviruses and Opportunistic Infections; February 19-22, 2023; Virtual and Seattle, WA

Disclosures

- The SOLAR study was funded by ViiV Healthcare
- Moti Ramgopal, MD, FACP, FIDSA, has received speaking and/or consulting fees from AbbVie, Gilead Sciences, Janssen, Merck, and ViiV Healthcare

Editorial assistance was provided by Poppy Mashilo of Scimentum (Nucleus Global), with funding provided by ViiV Healthcare.

Background

- Cabotegravir (CAB), an INSTI, 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, large, head-to-head 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

*NCT04542070. INSTI, integrase strand transfer inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor.

1. U.S. Department of Health and Human Services. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. 2021. Available from: https://clinicalinfo.hiv.gov/en/guidelines. Accessed November 2022.
2. Saag MS, et al. *JAMA*. 2020;324(16):1651–1669. 3. European AIDS Clinical Society. Guidelines Version 11.0. 2021. Available from: https://www.eacsociety.org/media/final2021eacsguidelinesv11.0_oct2021.pdf. Accessed November 2022.
4. Ghandi RT, et al. *JAMA*. 2022;E1–E22. 5. De Los Rios P, et al. *OFID*. 2019;6(Suppl 2):S481. 6. United Nations Programme on HIV and AIDS. 90-90-90 An ambitious treatment target to help end the AIDS epidemic. Available from: https://files.unaids.org/en/media/unaids/contentassets/documents/unaidspublication/2014/90-90-90_en.pdf. Accessed December 2022.

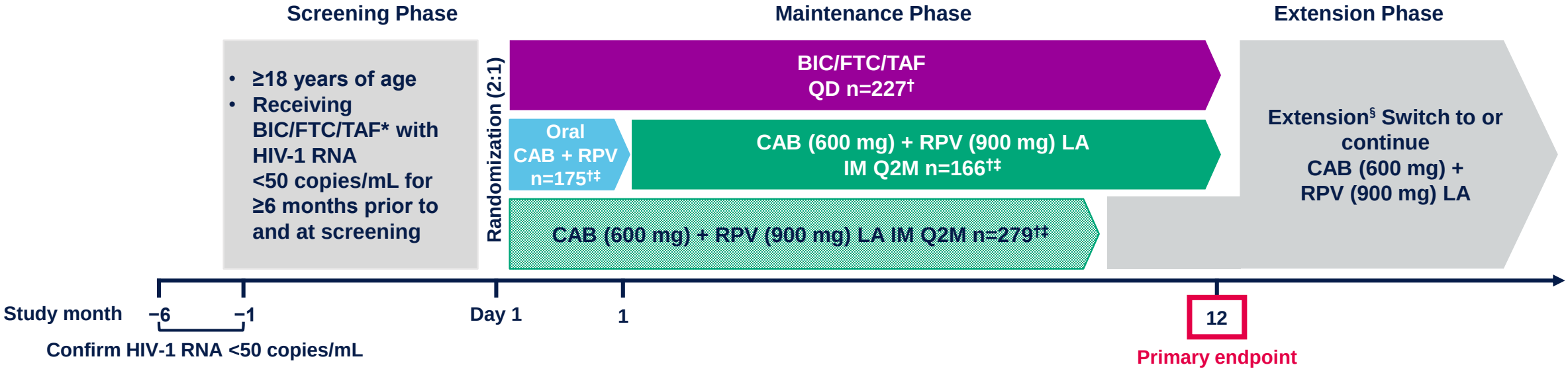
Methods

- SOLAR is a Phase 3b, randomized (2:1), open-label, multicenter, noninferiority (NI) study assessing switching virologically suppressed adults to CAB + RPV LA Q2M vs. continuing on BIC/FTC/TAF
  - 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 (exclusion of one trial site for non-compliance to protocol entry criteria)*
- Endpoints assessed at Month 11 (SWI)/12 (OLI / BIC/FTC/TAF) (hereafter referred to as Month 12):
  - Proportion of participants with plasma HIV-1 RNA ≥50 copies/mL (FDA Snapshot, 4% NI margin) (**Primary endpoint**)
  - Proportion of participants with plasma HIV-1 RNA <50 copies/mL (FDA Snapshot, –12% NI margin)
  - Incidence of confirmed virologic failure (CVF; two consecutive HIV-1 RNA ≥200 copies/mL)
  - Safety and tolerability
  - Treatment satisfaction (HIV Treatment Satisfaction Questionnaire status version [HIVTSQs]) and patient preference

*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.
FDA, U.S. Food and Drug Administration; LA, long-acting; Q2M, every 2 months.

SOLAR Study Design

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



*A single prior INI regimen is allowed if BIC/FTC/TAF is a second-line regimen 6 months prior to 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 copies/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. Visits will continue to occur Q2M.
IM, intramuscular; LA, long-acting; OD, once daily; OLI, oral lead-in; Q2M, every 2 months.

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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 (kg/m^2), median (IQR)	26.0 (23.2–29.4)	25.4 (23.4–29.6)
Prior duration of ART, median, years	2.58	2.47

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

*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).
BMI, body mass index; IQR, interquartile range; LA, long-acting; mITT-E, modified intention-to-treat exposed; OLI, oral lead-in; Q2M, every 2 months; SWI, starting with injections.

Psychosocial Challenges With Daily Oral BIC/FTC/TAF at Baseline

- 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*"

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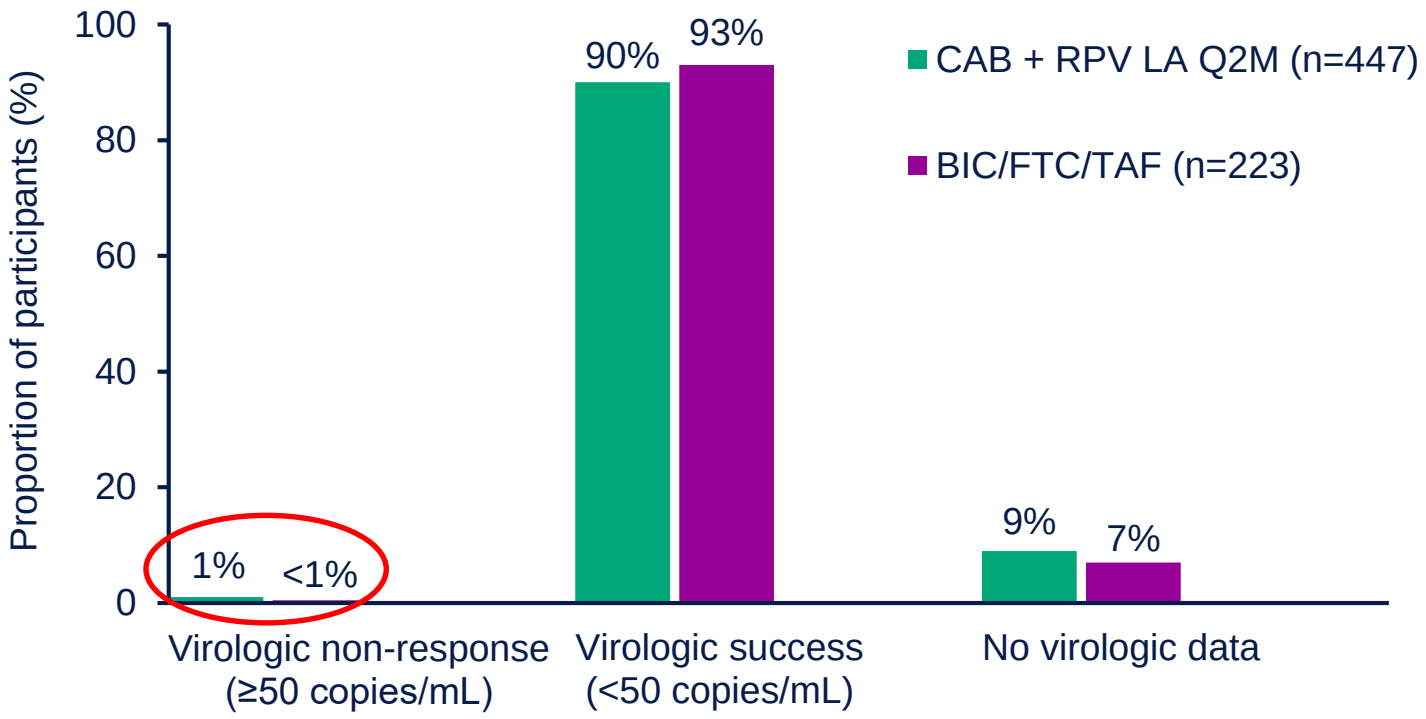
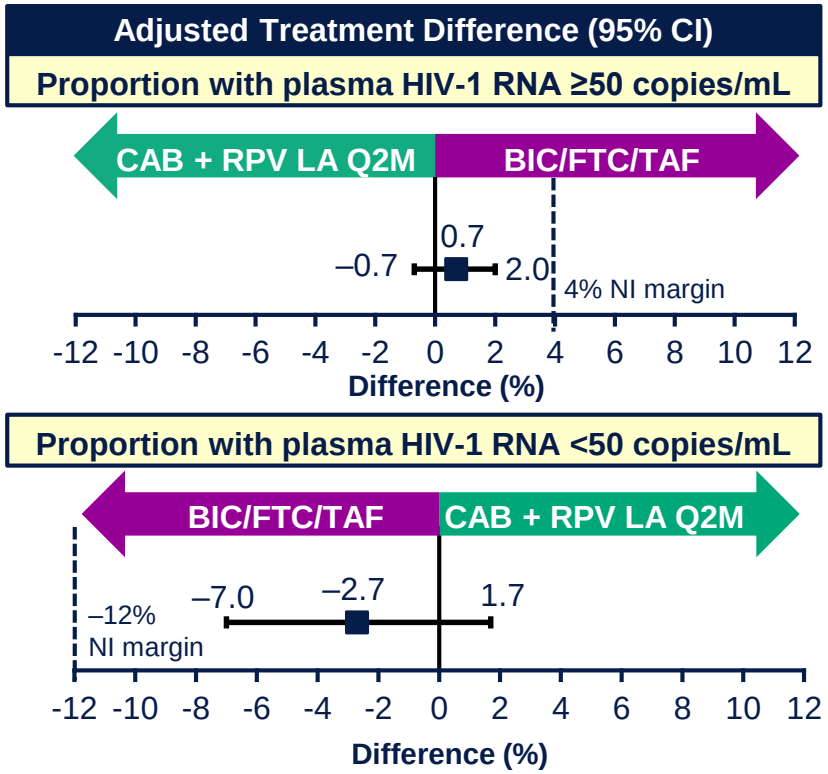
Virologic Outcomes at Month 12 (mITT-E Population)





- At Month 12, CAB + RPV LA demonstrated noninferior efficacy compared with BIC/FTC/TAF for the proportion of participants with HIV-1 RNA ≥50 copies/mL and <50 copies/mL in the mITT-E, ITT-E, and per-protocol populations*

*In the ITT-E population, 89% (n=406/454) and 93% (n=211/227) of participants receiving LA and BIC/FTC/TAF demonstrated virologic success (HIV-1 RNA <50 copies/mL; adjusted treatment difference [95% CI], –3.5% [–7.9, 0.9]), 1% (n=6/454) and <1% (n=1/227) of participants receiving LA and BIC/FTC/TAF demonstrated virologic non-response (HIV-1 RNA ≥50 copies/mL; adjusted treatment difference [95% CI], 0.9% [–0.5, 2.2]), and 9% (n=42/454) and 7% (n=15/227) of participants receiving LA and BIC/FTC/TAF had no virologic data, respectively. In the per protocol population, 91% (n=394/433) and 93% (n=203/218) of participants receiving LA and BIC/FTC/TAF demonstrated virologic success (HIV-1 RNA <50 copies/mL; adjusted treatment difference [95% CI], –2.1% [–6.4, 2.2]), <1% (n=4/433) and <1% (n=1/218) of participants receiving LA and BIC/FTC/TAF demonstrated virologic non-response (HIV ≥50 copies/mL; adjusted treatment difference [95% CI], 0.5 [–0.8, 1.7]). ITT-E, intention-to-treat exposed; mITT-E, modified intention-to-treat exposed; NI, noninferiority.

Month 12 Snapshot Outcomes (mITT-E Population)

Parameter	CAB + RPV LA Q2M (n=447)	BIC/FTC/TAF (n=223)
HIV-1 RNA ≥50 copies/mL	5 (1)	1 (<1)
Data in window not below 50 copies/mL	3 (<1)	1 (<1)
Discontinued for lack of efficacy	1 (<1)	0
Discontinued for other reason while not below 50 copies/mL	1 (<1)	0
HIV-1 RNA <50 copies/mL	403 (90)	207 (93)
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)

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

*Injection site pain, n=2; acute myocardial infarction, n=1; dysesthesia/limb discomfort/paresthesia/peripheral swelling, n=1; dizziness, n=1; fatigue, n=1; deafness/ear congestion/fatigue, n=1; blood pressure fluctuation (participant reported)/depression, n=1; alanine aminotransferase increase, n=1; diarrhea/joint stiffness, n=1; acute hepatitis B, n=1; fatigue/pyrexia, n=1; injection site discharge, n=1. †Participant had a 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.
AE, adverse event; mITT-E, modified intention-to-treat exposed; Q2M, every 2 months; SAE, serious adverse event.

Participants With Confirmed Virologic Failure (CVF)

Participants With CVF in the mITT-E Population									
Sex at birth, country	**Baseline BMI (kg/m²)**	**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, 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

- 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
  - Two of the participants had on-treatment RPV and/or INI RAMs (genotyping for third participant failed at baseline)
- No participants in the BIC/FTC/TAF arm met the CVF criterion through Month 12

*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 had received abacavir/dolutegravir/lamivudine and BIC/FTC/TAF; they re-suppressed on BIC/FTC/TAF and darunavir/cobicistat/emtricitabine/tenofovir alafenamide during long-term follow-up. The participant did not continue in the long-term follow-up phase. ‡Prior to 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.
ITT-E, intention-to-treat exposed; LA, long-acting; mITT-E, modified intention-to-treat exposed; NA, not available; RAM, resistance-associated mutation; SVF, suspected virologic failure.

Safety Summary (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	16 (4)	2 (<1)
Drug-related	9 (2)*	0
Any serious AE	21 (5)	15 (7)
Drug-related	3 (<1)†	0

- 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 two drug-related AEs reported were weight gain (<1%) and abnormal hepatic function (<1%)
- More participants in the CAB + RPV LA arm had AEs leading to withdrawal (4% vs. <1%)

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

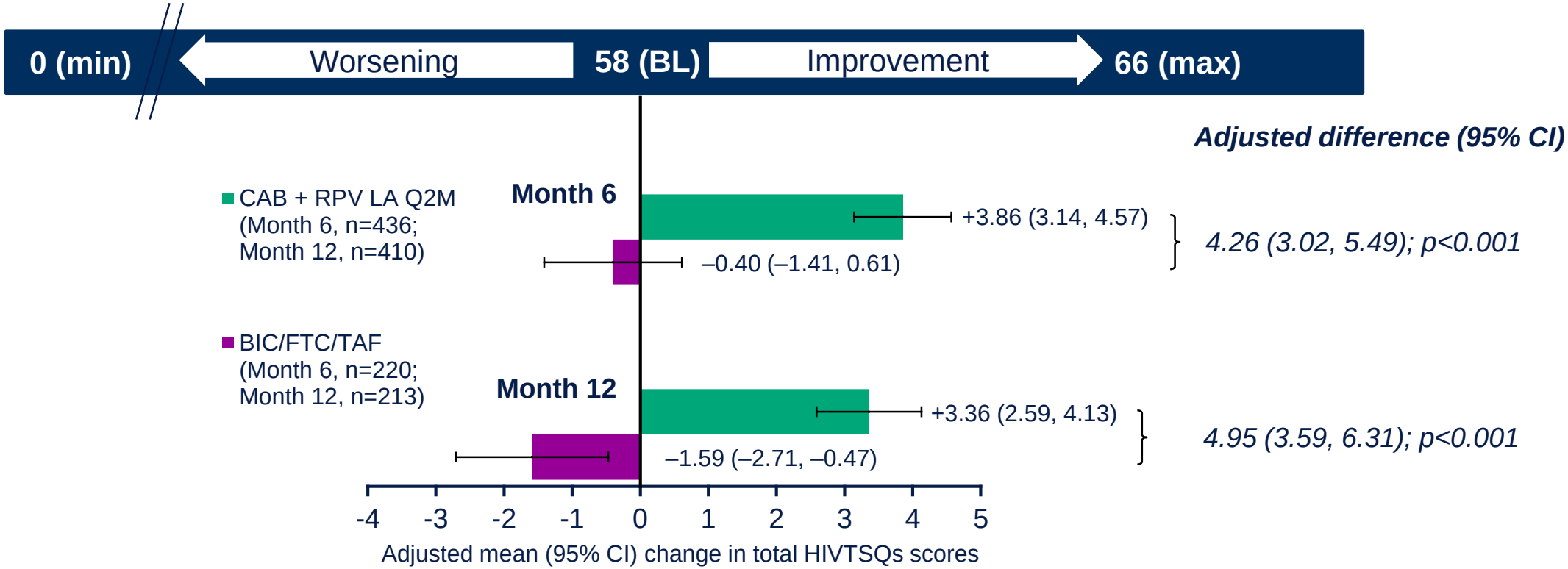
ISR Summary (Event-Level)

Parameter, n (%)	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)

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

*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.
AE, adverse event; CAB, cabotegravir; 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; RPV, rilpivirine; SWI, starting with injections.

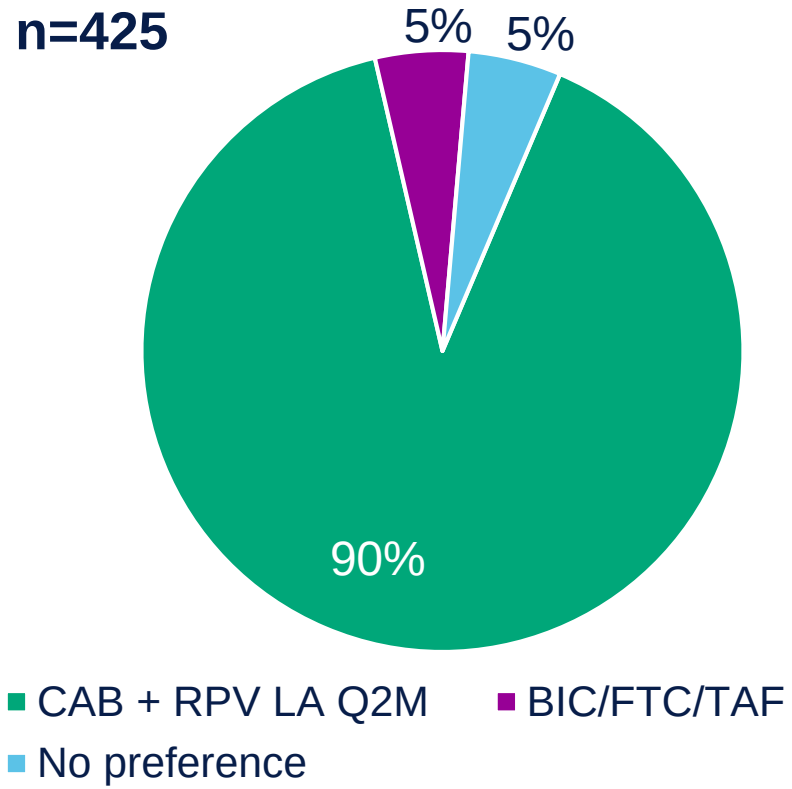
Treatment Satisfaction

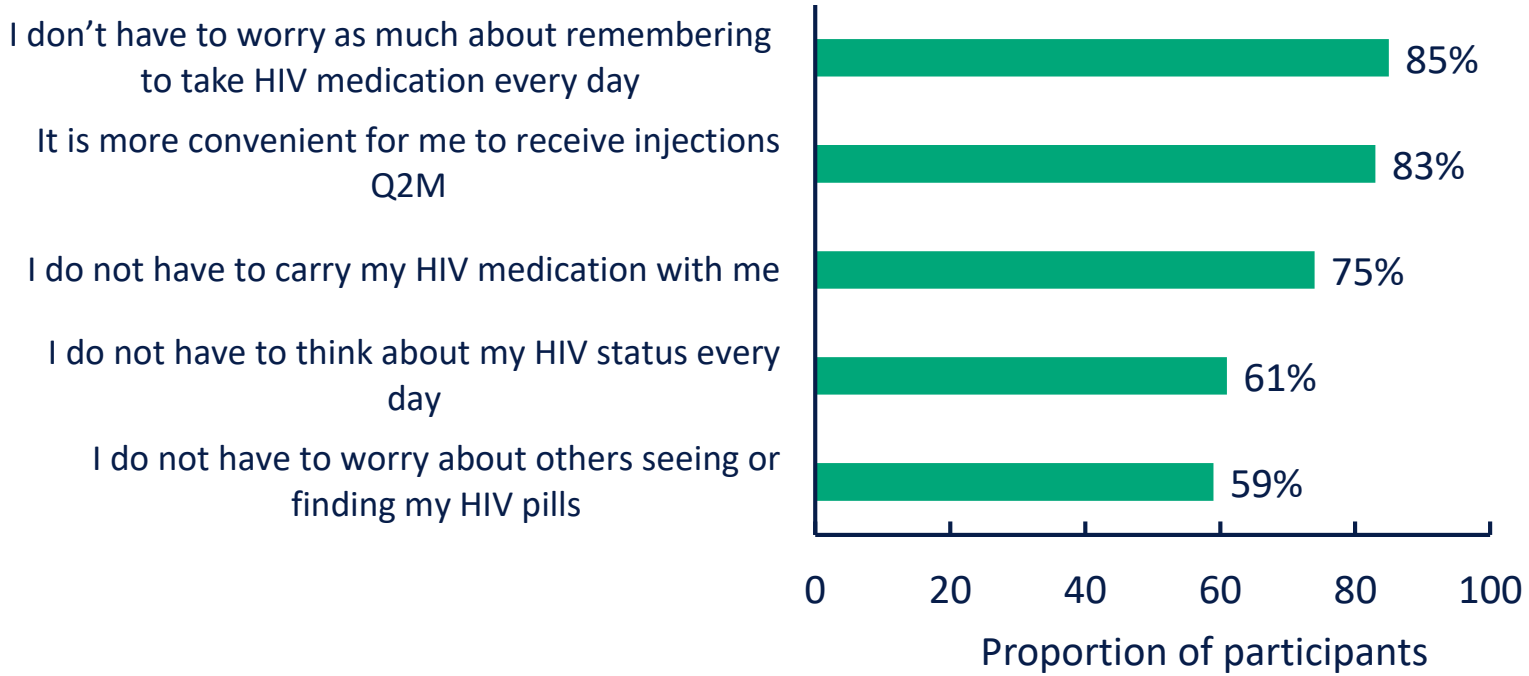


- Mean adjusted HIVTSQs scores improved significantly for CAB + RPV LA vs. BIC/FTC/TAF participants from baseline (LA, 57.88; BIC/FTC/TAF, 58.38) to Month 6 (LA, +3.86; BIC/FTC/TAF, –0.40) and Month 12 (LA, +3.36; BIC/FTC/TAF, –1.59) demonstrating greater improvement from baseline in HIV treatment satisfaction for participants receiving CAB + RPV LA compared with BIC/FTC/TAF

HIVTSQs, HIV Treatment Satisfaction Questionnaire status version.

Treatment Preference and Reason for Preference*





- 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

*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 noninferior 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
- 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 virally suppressed on oral daily therapy

Acknowledgments

- The authors thank everyone who has contributed to the success of the SOLAR study
  - All study participants and their families
  - The SOLAR clinical investigators and their staff in Australia, Austria, Belgium, Canada, France, Germany, Ireland, Italy, Japan, the Netherlands, Spain, Switzerland, the United Kingdom, and the United States

Australia
Bloch
Baker
Shields
Eu

Austria
Rieger
Oellinger Sarcletti

Belgium
Demeester Messiaen
Derdelinckx Moutschen

Canada
Smith
Trottier
Wong
Tan
Kasper
Angel
Szabo
LeBlanc Costiniuk
Walmsley

France
Cua
Jacomet
Gallien
Goujard
Raffi
Meybeck
Bouchaud
Cazanave

Germany
Arasteh
Hartikainen
Degen
Potthoff
Knechten
Postel
Rockstroh
Schellberg
Scholten
Wyen

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Italy
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Oka
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