HIV-1 RNA Blips and Low-Level Viral Replication: SOLAR (CAB + RPV LA vs. BIC/FTC/TAF)

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Introduction

- Cabotegravir + rilpivirine long-acting (CAB + RPV LA) administered intramuscularly monthly or every 2 months (Q2M) is the first and only complete LA regimen recommended by treatment guidelines for virologically suppressed people living with HIV-1 (PWH).[1–3]
- The Phase 3b SOLAR study (NCT04542070) demonstrated the noninferior efficacy of switching to CAB + RPV LA Q2M vs. continuing daily oral bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) at Month 12, with 90% of switch participants preferring CAB + RPV LA.[4]
- Low and comparable numbers of viral load blips were experienced by participants receiving CAB + RPV LA every 4 weeks (FLAIR [NCT02938520] and ATLAS [NCT02951052]) or every 8 weeks (ATLAS-2M [NCT03299049]) across study visits in Phase 3/3b clinical studies; viral blips were not associated with virologic failure.[5,6]
  - Similar proportions of participants receiving CAB + RPV LA and daily oral therapy experienced viral blips.[5,6]
- Here, we report HIV-1 RNA viral blips, target not detected (TND), and the impact of HIV-1 RNA viral blips on confirmed virologic failure (CVF) and viral load measurements in participants switching to CAB + RPV LA vs. continuing daily oral BIC/FTC/TAF through Month 12 in the SOLAR study.

Methods

- SOLAR (NCT04542070) 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.[4]
  - In consultation with their provider, participants randomized to CAB + RPV LA could select to either use an oral lead-in (OLI) for up to 4 weeks or start with injections (SWI).
- In this exploratory analysis, we analyzed participant plasma HIV-1 RNA samples from baseline through Month 12* in the SOLAR study.
  - The 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).†
  - HIV-1 RNA viral blips were defined as a single HIV-1 RNA value between 50 and <200 copies/mL with adjacent values <50 copies/mL.
  - HIV-1 RNA values <40 copies/mL were delineated into qualitative target detected (TD) or TND.
  - CVF was defined as two consecutive HIV-1 RNA values ≥200 copies/mL.
  - Plasma samples were analyzed for HIV-1 RNA viral load using the Abbott RealTime HIV-1 assay, and TD/TND outcomes were provided for HIV-1 RNA <40 copies/mL.

*Participants receiving CAB + RPV LA with an OLI were assessed at Month 1/Month 2/Month 4/Month 6/Month 8/Month 10/Month 12, whereas participants receiving CAB + RPV LA SWI were assessed at Month 1/Month 3/Month 5/Month 7/Month 9/Month 11 (henceforth referred to as Month 1/Month 2/Month 4/Month 6/Month 8/Month 10/Month 12). Participants receiving BIC/FTC/TAF were assessed at Month 2/Month 4/Month 6/Month 8/Month 10/Month 12.
†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 study site.

In the SOLAR study, HIV-1 viral blips were not associated with confirmed virologic failure, consistent with prior Phase 3 clinical study data.

Results

Study Population

- Of 670 randomized participants (mITT-E), 447 (67%) switched to CAB + RPV LA (OLI, n=173 [39%]; SWI, n=274 [61%]) and 223 (33%) continued BIC/FTC/TAF.
- Baseline characteristics were similar between arms; the median age was 37 years (range: 18–74), 18% were female (sex at birth), and the median body mass index was 25.9 kg/m^2 (interquartile range: 23.3–29.5).

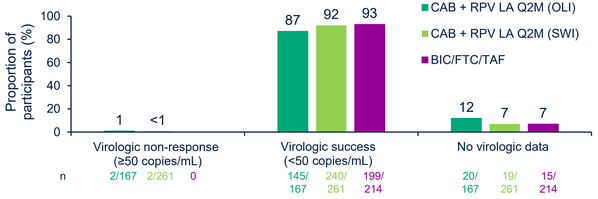
Table 1. Participants With HIV-1 Blips and/or CVF

Outcome at Month 12 (mITT-E), n (%)	CAB + RPV LA Q2M (OLI)	CAB + RPV LA Q2M (SWI)	BIC/FTC/TAF
Participants with HIV-1 blip* at any study visit	6/173 (3)	13/274 (5)	9/223 (4)
Participants with CVF†	1/173 (<1)	1/274 (<1)	0/223
With HIV-1 blip*	0/6	0/13	0/9
Without HIV-1 blip*	1/167 (<1)	1/261 (<1)	0/214

*A single HIV-1 RNA value between 50 and <200 copies/mL with adjacent values <50 copies/mL.
†Two consecutive HIV-1 RNA values ≥200 copies/mL.
BIC/FTC/TAF, bictegravir/emtricitabine/tenofovir alafenamide; CAB, cabotegravir; CVF, confirmed virologic failure; LA, long-acting; mITT-E, modified intention-to-treat exposed; OLI, oral lead-in; Q2M, every 2 months; RPV, rilpivirine; SWI, starting with injection.

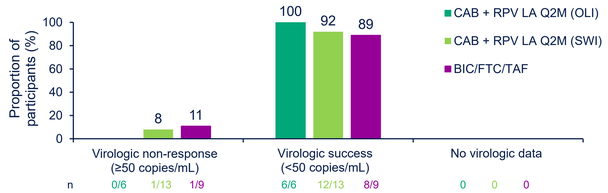
- The proportion of participants with HIV-1 viral blips through Month 12 was 4% (n=19/447) in the CAB + RPV LA arm (OLI and SWI) and 4% (n=9/223) in the BIC/FTC/TAF arm (**Table 1**).
- Two (<1%) participants in the CAB + RPV LA arm (OLI, n=1; SWI, n=1) had CVF through Month 12, neither of whom experienced a viral blip at any previous study visit.

Figure 1. Snapshot Outcomes for Participants Without Blips (mITT-E)



BIC/FTC/TAF, bictegravir/emtricitabine/tenofovir alafenamide; CAB, cabotegravir; LA, long-acting; mITT-E, modified intention-to-treat exposed; OLI, oral lead-in; Q2M, every 2 months; RPV, rilpivirine; SWI, starting with injection.

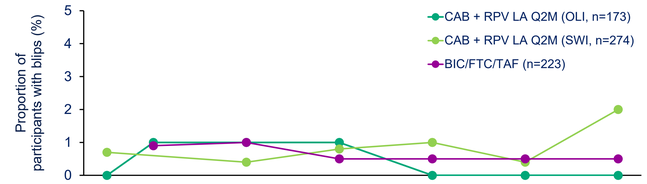
Figure 2. Snapshot Outcomes for Participants With Blips (mITT-E)



BIC/FTC/TAF, bictegravir/emtricitabine/tenofovir alafenamide; CAB, cabotegravir; LA, long-acting; mITT-E, modified intention-to-treat exposed; OLI, oral lead-in; Q2M, every 2 months; RPV, rilpivirine; SWI, starting with injection.

- Of participants with viral blips, 5% (n=1/19) in the CAB + RPV LA arm (OLI and SWI) and 11% (n=1/9) in the BIC/FTC/TAF arm had HIV-1 RNA ≥50 copies/mL at Month 12 (**Figure 2**).

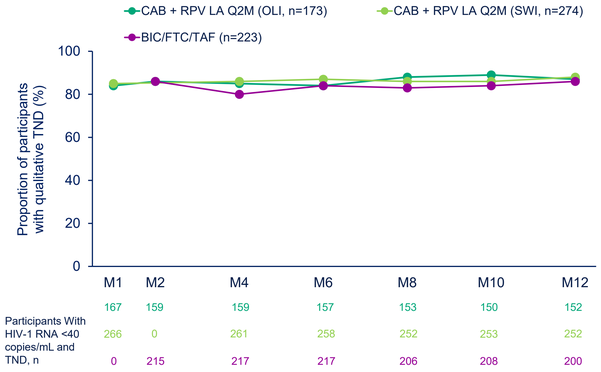
Figure 3. Proportion of Participants With Blips by Visit (mITT-E)



BIC/FTC/TAF, bictegravir/emtricitabine/tenofovir alafenamide; CAB, cabotegravir; LA, long-acting; M, month; mITT-E, modified intention-to-treat exposed; OLI, oral lead-in; Q2M, every 2 months; RPV, rilpivirine; SWI, starting with injection.

- The proportions of participants with viral blips were comparable between treatment arms through Month 12 (**Figure 3**).

Figure 4. Proportions of Participants With HIV-1 RNA <40 Copies/mL and TND by Visit (mITT-E)



BIC/FTC/TAF, bictegravir/emtricitabine/tenofovir alafenamide; CAB, cabotegravir; LA, long-acting; M, month; mITT-E, modified intention-to-treat exposed; OLI, oral lead-in; Q2M, every 2 months; RPV, rilpivirine; SWI, starting with injection; TND, target not detected.

- TND outcomes at individual study visits were similar between study arms (CAB + RPV LA OLI, 84–89%; CAB + RPV LA SWI, 85–88%; BIC/FTC/TAF, 80–86%) through Month 12 (**Figure 4**).

Conclusions

- The proportions of study participants with HIV-1 RNA viral blips, TND, and HIV-1 RNA <40 copies/mL were similar between CAB + RPV LA Q2M (whether OLI or SWI) and BIC/FTC/TAF through Month 12.
- HIV-1 viral blips with CAB + RPV LA were not associated with CVF, consistent with prior CAB + RPV LA Phase 3/3b clinical study data.[5,6]
- Neither of the two (<1%) participants with CVF in the CAB + RPV LA arm experienced a viral blip at any previous study visit.
- Overall, 4% of participants in each arm experienced viral blips through Month 12, two of whom (CAB + RPV LA, n=1; BIC/FTC/TAF, n=1) had viral loads ≥50 copies/mL at Month 12.
- These data support the robustness of CAB + RPV LA for the maintenance of virologic suppression in PWH.

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