Similar Virologic Outcomes and Frequency of Isolated Viraemic Events (Blips, Low-Level Viraemia and Suspected Virologic Failure) between Oral and Long-Acting Antiretroviral Therapy: A Pooled Analysis of Phase 3/3b Cabotegravir + Rilpivirine Long-Acting Studies

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**Presenting on behalf of the authors.*

Key Takeaways

- This *post hoc* analysis describes the low frequency of predefined viral events (viral blips, low-level viremia [LLV], and isolated suspected virologic failure [SVF]) and examines subsequent virologic outcomes through 1 year in cabotegravir + rilpivirine long-acting (CAB + RPV LA) Phase 3/3b studies.
- The proportion of participants with confirmed virologic failure (CVF) was low (<1%) and comparable between CAB + RPV LA and oral antiretroviral therapy (ART); viral blips and LLV were not associated with CVF.
- Isolated SVF events were rare, with similar rates of subsequent CVF with CAB + RPV LA and comparator oral ART.
- These data suggest similar CVF outcomes after isolated viremic events with both CAB + RPV LA and oral ART, supporting the noninferior efficacy of CAB + RPV LA vs. oral ART for the maintenance of virologic suppression in people with HIV-1 (PWH).

Introduction

- CAB + RPV LA administered intramuscularly is the first and only complete LA regimen recommended by treatment guidelines for virologically suppressed PWH.[1-3]
- The definition and management of viremia, viral rebound, and virologic failure varies across clinical studies and guidelines[1,2,4,5]; therefore, clearly defining the various types of viremic events occurring in clinical trials may help healthcare providers in their management of PWH.
- In Phase 3/3b clinical studies, low and comparable numbers of viral blips were experienced by participants receiving CAB + RPV LA or daily oral ART; viral blips were not associated with virologic failure.[6-8]
- In this expanded analysis, we present virologic outcomes following predefined viral rebounds ≥50 copies/mL (viral blips or LLV) and ≥200 copies/mL (SVF) through 1 year in CAB + RPV LA Phase 3/3b studies.

Methods

- FLAIR (NCT02938520), ATLAS (NCT02951052), ATLAS-2M (NCT03299049), and SOLAR (NCT04542070) were Phase 3/3b, randomized, open-label, multicenter studies assessing the efficacy and safety of CAB + RPV LA.
- Participants were virologically suppressed (HIV-1 RNA <50 copies/mL) at randomization.
- Viral load assessments were done at the following visits:
  - FLAIR and ATLAS: screening, Day 1, and every month thereafter (Week [W] 4, W8, W12, W16, W20, W24, W28, W32, W36, W40, W44, and W48).
  - ATLAS-2M: screening, Day 1, and every two months thereafter (W4 [oral lead-in only], W8, W16, W24, W32, W40, and W48).
  - SOLAR: screening, Day 1, and every two months thereafter (Month [M] 2, M4, M6, M8, and M12 for oral lead-in and oral ART participants; M1, M3, M5, M7, M9, and M11 for participants starting with injection).
- In this pooled post hoc analysis, we describe the frequency of predefined viral events (**Table 1**) through Week 48 in FLAIR, ATLAS, and ATLAS-2M, and through Month 12 in SOLAR.

Table 1. Predefined Viral Events Assessed *Post Hoc*

Viral event	Definition
Viral blips	A single viral load between 50 and <200 copies/mL, with adjacent values <50 copies/mL.
LLV	≥2 consecutive viral loads between 50 and <200 copies/mL.
Isolated SVF	A single plasma viral load ≥200 copies/mL, with the subsequent value <200 copies/mL. Further divided into:* • A single viral load ≥200–<500 copies/mL • A single viral load ≥500–<1000 copies/mL • A single viral load ≥1000 copies/mL
CVF	Two consecutive HIV-1 RNA values ≥200 copies/mL.

*All with the subsequent adjacent viral load <200 copies/mL.

Results

- Overall, 2506 participants were included in the analysis (CAB + RPV LA, n=1692; comparator oral ART, n=814).
- Baseline characteristics were similar between treatment groups (**Table 2**).
- Overall, CVF occurred in <1% of participants (CAB + RPV LA, n=16/1692; oral ART; n=7/814).

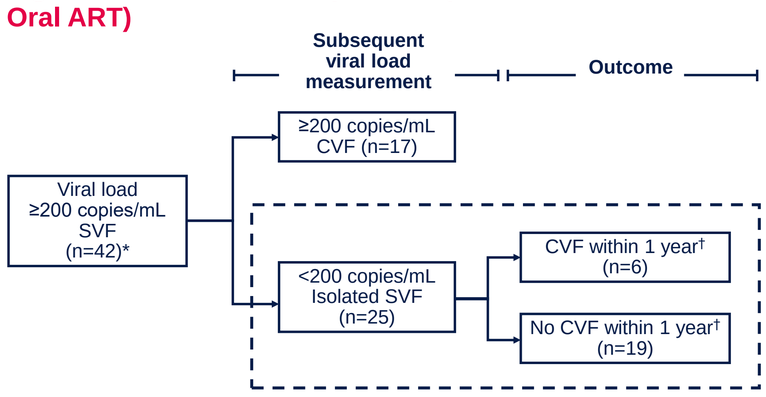
Table 2. Baseline Characteristics

Parameter	CAB + RPV LA (n=1692)	Oral ART (n=814)*
Age, median (range), years	39 (18–83)	38 (18–82)
≥50 years, n (%)	360 (21)	167 (21)
Sex at birth, n (%)		
Female	387 (23)	209 (26)
Male	1305 (77)	605 (74)
Gender identity,† n (%)		
Female	392 (23)	209 (26)
Male	1288 (76)	601 (74)
Transgender female	9 (<1)	3 (<1)
Transgender male	1 (<1)	0
Gender variant or gender non-conforming	1 (<1)	0
Other gender identities	1 (<1)	1 (<1)
Race, n (%)		
White	1232 (73)	566 (70)
Black/African American	306 (18)	181 (22)
Asian	86 (5)	40 (5)
Other races	68 (4)	27 (3)
Ethnicity, n (%)		
Hispanic or Latinx	250 (15)	112 (14)
Median BMI, kg/m^2 (range)	25.4 (15–65)	25.0 (16–68)
≥30 kg/m^2, n (%)	306 (18)	155 (19)

*Oral regimens were: DTG/ABC/3TC (n=283; FLAIR [participants with side effects to this therapy, or who were positive for HLAB*5701, received DTG + 2 non-ABC NRTIs]), BIC/FTC/TAF (n=223; SOLAR), and various standard oral therapies (n=308; ATLAS). †Self-reported gender. ART, antiretroviral therapy; BIC/FTC/TAF, bictegravir/emtricitabine/tenofovir alafenamide; BMI, body mass index; CAB, cabotegravir; DTG/ABC/3TC, dolutegravir/abacavir/lamivudine; LA, long-acting; NRTI, nucleoside reverse transcriptase inhibitor; RPV, rilpivirine.

- Overall, 6% (n=97/1692) and 7% (n=61/814) of participants experienced viral blips with CAB + RPV LA and oral ART, respectively (**Table 3**).
- The proportion of participants with LLV was similar between treatment arms (CAB + RPV LA, 1% [n=18/1692]; oral ART, 1% [n=10/814]).
- There were few isolated SVF events (**Figure 1**), occurring in ≤2% of participants in both arms (**Table 3**).

Figure 1. Isolated SVF Population (CAB + RPV LA and Oral ART)



The dashed box shows analysis of isolated SVF data for CAB + RPV LA (n=12/1692) and oral ART (n=13/814) combined.
*Viral loads ranged from 202 copies/mL to 737,830 copies/mL. †Within 1 year from the start of maintenance treatment. ART, antiretroviral therapy; CAB, cabotegravir; CVF, confirmed virologic failure; LA, long-acting; RPV, rilpivirine; SVF, suspected virologic failure.

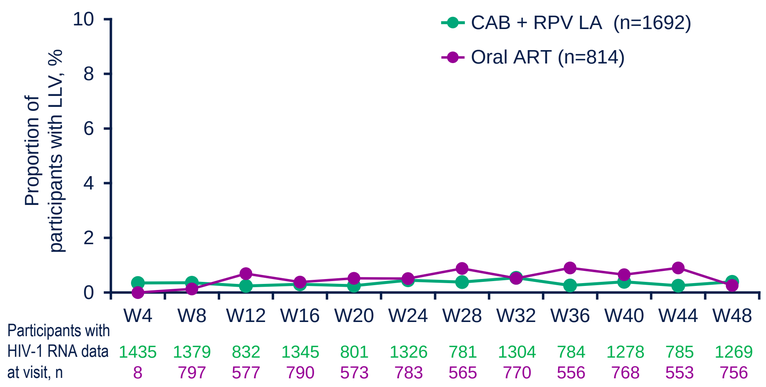
Table 3. Proportion of Participants With Blips, LLV, and Isolated SVF Through 1 Year*

n (%)	CAB + RPV LA (n=1692)	Oral ART (n=814)
Blips	97/1692 (6)	61/814 (7)
LLV†	18/1692 (1)	10/814 (1)
Isolated SVF‡	12/1692 (<1)	13/814 (2)
Isolated SVF 200–<500 copies/mL	9/1692 (<1)	4/814 (<1)
Isolated SVF 500–<1000 copies/mL	3/1692 (<1)	5/814 (<1)
Isolated SVF >1000 copies/mL	0/1692	4/814 (<1)

*Participants with vaccination within a month prior – Blips: CAB + RPV LA, n=11; oral ART, n=8; LLV: CAB + RPV LA, n=2; oral ART, n=1. †≥2 consecutive viral loads 50–<200 copies/mL. ‡A single plasma HIV-1 RNA value ≥200 copies/mL, with the subsequent value <200 copies/mL. ART, antiretroviral therapy; CAB, cabotegravir; LA, long-acting; LLV, low-level viremia; RPV, rilpivirine; SVF, suspected virologic failure.

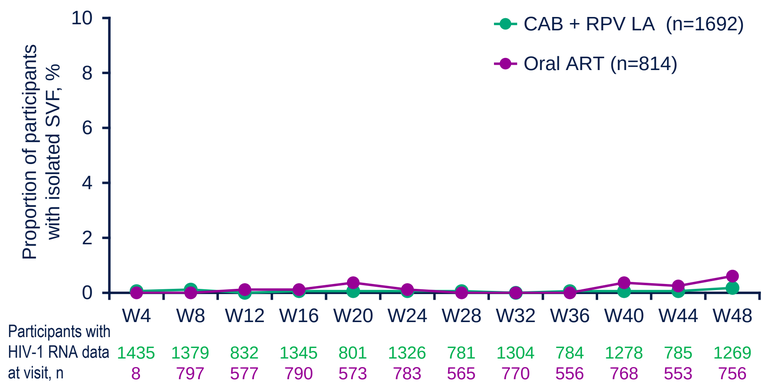
- The proportions of participants with viral blips were consistently ≤2% across both arms at all timepoints.
- The proportions of participants with LLV at each visit were consistently <1% across the treatment arms (**Figure 2**).
- The proportions of participants with isolated SVF at each visit were also consistently <1% across the treatment arms (**Figure 3**).

Figure 2. Proportion of Participants With LLV by Visit



ART, antiretroviral therapy; CAB, cabotegravir; LA, long-acting; LLV, low-level viremia; RPV, rilpivirine; W, week.

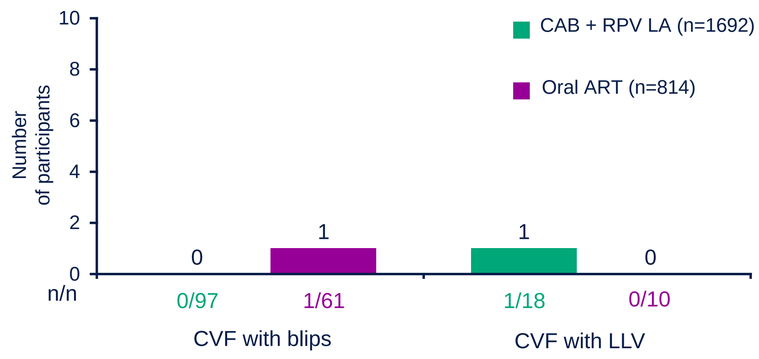
Figure 3. Proportion of Participants With Isolated SVF by Visit



ART, antiretroviral therapy; CAB, cabotegravir; LA, long-acting; RPV, rilpivirine; SVF, suspected virologic failure; W, week.

- The number of participants with previous viral blips or LLV experiencing CVF was low across both arms (**Figure 4**).

Figure 4. Participants Experiencing CVF With Previous Blips and LLV



ART, antiretroviral therapy; CAB, cabotegravir; CVF, confirmed virologic failure; LA, long-acting; LLV, low-level viremia; RPV, rilpivirine.

- Overall, three of 12 participants in the CAB + RPV LA arm with an isolated SVF event had subsequent CVF compared with three of 13 participants in the oral ART arm.
- Participants with CVF according to previous isolated SVF viral load were:
  - A single viral load 200–<500 copies/mL: CAB + RPV LA, n=2/9; oral ART, n=1/4.
  - A single viral load 500–<1000 copies/mL: CAB + RPV LA, n=1/3; oral ART, n=1/5.
  - A single viral load ≥1000 copies/mL: CAB + RPV LA, n=0; oral ART, n=1/4.

Conclusions

- In this expanded pooled analysis across four Phase 3/3b studies, CVF rates were low (<1%) and similar between CAB + RPV LA and oral ART through 1 year.
- The frequency of viral blips was similar with both CAB + RPV LA and oral ART, and viral blips were not associated with CVF, consistent with prior analyses.[6-8]
- The proportion of participants with LLV was low (<1%) at all time points across both arms and was not associated with CVF.
- There were few isolated SVF events, with similar rates of subsequent CVF occurring with CAB + RPV LA and comparator oral ART.
- These data suggest similar outcomes after isolated viremic events with both regimens, supporting the noninferior efficacy of CAB + RPV LA vs. oral ART for the maintenance of virologic suppression in PWH.

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