Inflammatory Markers After Switching to Cabotegravir + Rilpivirine Long-Acting vs. Continuing Bictegravir/Emtricitabine/Tenofovir Alafenamide: Data From the Phase 3b SOLAR Study

TUPEB04

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Key Takeaways

- **We present changes in key inflammatory markers in people living with HIV-1 receiving either cabotegravir + rilpivirine long-acting (CAB + RPV LA) dosed every 2 months (Q2M) or daily oral bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) in the Phase 3b SOLAR study.**
- **No clinical differences in key inflammatory marker changes were seen in stably suppressed participants switching to CAB + RPV LA vs. continuing BIC/FTC/TAF.**
- **Analyses by key subgroups (sex at birth, body mass index [BMI], and age) showed similar changes in inflammatory markers, with no meaningful differences between treatment arms.**
- **The lack of clinical differences in inflammatory markers is consistent with the high virologic suppression rates maintained in both arms.**

Background

- CAB + RPV administered monthly or Q2M is the first complete LA regimen recommended by treatment guidelines for the maintenance of HIV-1 virologic suppression.[1–3]
- Effective antiretroviral therapy (ART) has been shown to reduce systemic inflammation caused by HIV infection.[4]
  - Large randomized Phase 3 trials have demonstrated that differences in inflammatory mediators are minimal and comparable between arms when switching from a three/four-drug regimen to an INSTI-based two-drug regimen.[4,5]
- SOLAR (NCT04542070) is a Phase 3b, randomized (2:1), open-label, controlled study that demonstrated noninferior efficacy of switching to CAB + RPV LA Q2M vs. continuing daily oral BIC/FTC/TAF over 12 months.[6]
- Here, we present a *post hoc* analysis of the changes from baseline over 12 months in key inflammatory markers when switching to LA therapy in the SOLAR study, overall and by subgroup (sex at birth, BMI, and age).

Methods

- Data were stratified by sex at birth (male or female), BMI (≥30, <30 kg/m^2), and age (<35, 35–<50, and ≥50 years).
- Key inflammatory markers (serum interleukin-6 [IL-6], C-reactive protein [CRP], platelet-poor plasma D-dimer, CD4/CD8 ratio, and soluble [s] sCD14 and sCD163) were measured at baseline and Month 12 and were compared between treatment arms and subgroups.
  - IL-6 and CRP are potential biomarkers of HIV-related inflammation.[4]
  - D-dimer is a marker of atherogenesis and hypercoagulation.[4]
  - CD4/CD8 ratio is an established marker of immune reconstitution.[4]
  - sCD14 and sCD163 are biomarkers of monocyte and macrophage activation, used for research purposes.[4] They are potential surrogate indicators of ongoing HIV replication below typical limits of viral load quantification.
- Comparisons between CAB + RPV LA Q2M and BIC/FTC/TAF for the overall population were analyzed based on a mixed model for repeated measures with visit as the repeated factor and adjustment for demographic parameters.*

*Adjusted for age (continuous), race, baseline BMI, sex at birth, smoking status, and hepatitis C co-infection.

Results

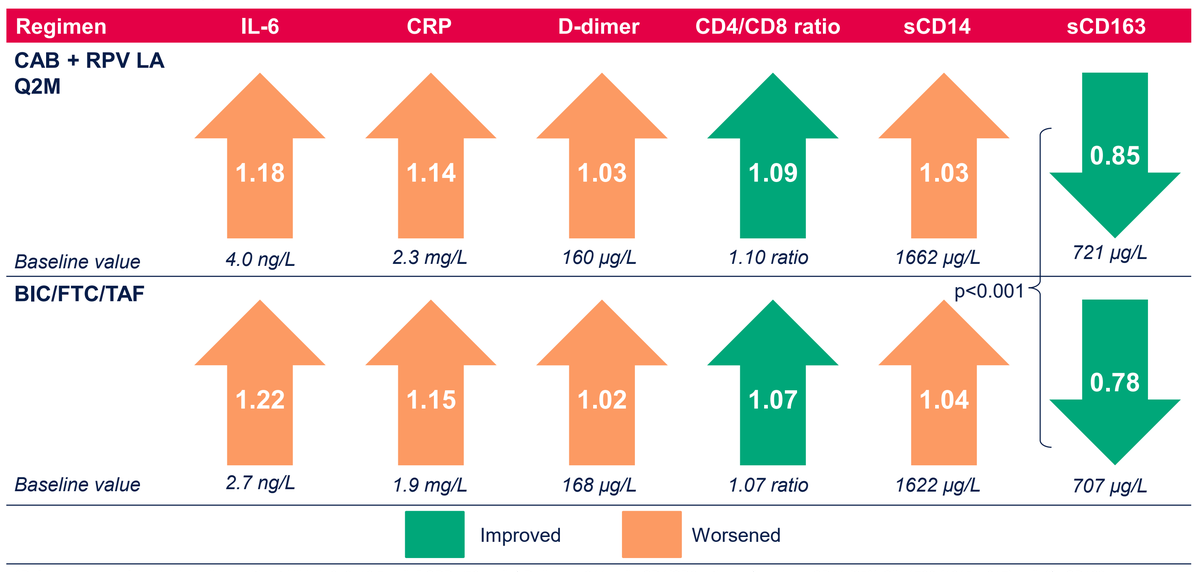
Table 1. Baseline Characteristics

ITT-E population	CAB + RPV LA Q2M (n=454)	BIC/FTC/TAF (n=227)
Median age (range), years	37 (18–74)	37 (18–69)
<35 years, n (%)	192 (42)	99 (44)
35–<50 years, n (%)	173 (38)	83 (37)
≥50 years, n (%)	89 (20)	45 (20)
Female (sex at birth), n (%)	79 (17)	41 (18)
Race, n (%)		
Black	96 (21)	49 (22)
White	313 (69)	160 (70)
Asian	23 (5)	11 (5)
Other races*	22 (5)	7 (3)
BMI (kg/m^2), median (IQR)	26.0 (23.2–29.3)	25.4 (23.6–29.6)
≥30 kg/m^2, n (%)	97 (21)	52 (23)
CD4$^+$ cell count (cells/mm^3), median (IQR)	650 (479–850)	630 (458–842)
Duration of prior ART (years), median (IQR)†	2.6 (1.6–4.9)	2.5 (1.5–4.7)
Duration of prior BIC/FTC/TAF (years), median (IQR)†	1.7 (1.2–2.2)	1.6 (1.2–2.1)

*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).
†BIC/FTC/TAF must have been the participant's first or second regimen. If BIC/FTC/TAF was the second regimen, the first regimen must have been an INSTI-based regimen.
Numbers represent the modified ITT-E population (CAB + RPV LA, n=447; BIC/FTC/TAF, n=223).
ART, antiretroviral therapy; BIC/FTC/TAF, bictegravir/emtricitabine/tenofovir alafenamide; BMI, body mass index; CAB, cabotegravir; IQR, interquartile range; INSTI, integrase strand transfer inhibitor; ITT-E, intention-to-treat exposed; LA, long-acting; Q2M, every 2 months; RPV, rilpivirine.

- Of 681 participants, 454 (67%) switched to LA and 227 (33%) continued BIC/FTC/TAF (**Table 1**).
  - Overall, 18% of the total population were female (sex at birth), 20% were aged ≥50 years, and 22% had a BMI ≥30 kg/m^2.

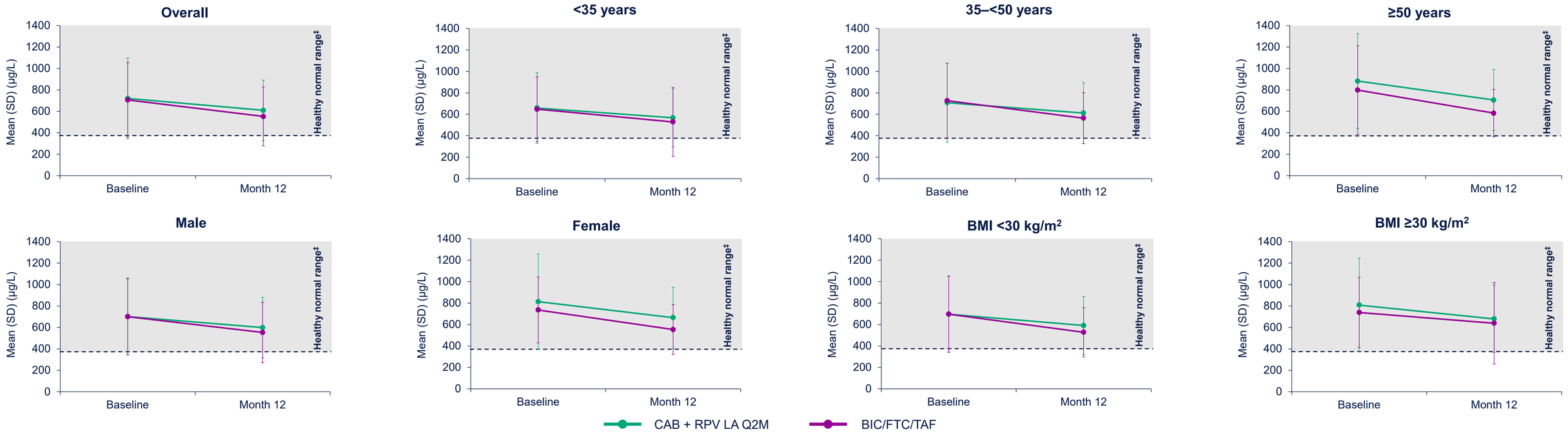
Figure 1. Model-Adjusted Geometric Mean Treatment Ratios for Inflammatory Marker Changes From Baseline to Month 12*



*Reference ranges for individuals living without HIV: IL-6, 0–43.5 ng/L;[7] CRP, ≤50 mg/L;[8] D-dimer, <244 µg/L; CD4/CD8 ratio, ≥1;[9] median sCD14 (95% CI), 1788 (1615–1917) µg/L;[10] sCD163, 387–1785 µg/L.[11] CAB + RPV LA/BIC/FTC/TAF: IL-6, n=397/202; CRP, n=400/205; D-dimer, n=390/201; CD4/CD8 ratio, n=377/193; sCD14, n=399/205; sCD163, n=400/205. Based on a mixed model for repeated measures with visit as the repeated factor: log(value) – log(baseline) = treatment + visit + treatment × visit + log(baseline) + gender at birth (male, female) + baseline BMI (<30, ≥30 kg/m^2) + age (continuous) + race (White, Black/African American, Other) + smoking status (never, former, current) + HCV co-infection (yes, no). Note: p values are not adjusted for presence of cardiometabolic conditions (e.g. cardiovascular disease, diabetes mellitus, or multiple sclerosis), previous ART, CD4, or nadir viral load. ART, antiretroviral therapy; BIC/FTC/TAF, bictegravir/emtricitabine/tenofovir alafenamide; CAB, cabotegravir; CI, confidence interval; HCV, hepatitis C virus; LA, long-acting; Q2M, every 2 months; RPV, rilpivirine.

- There were no significant differences between treatment arms in change from baseline for serum IL-6, CRP, D-dimer, CD4/CD8 ratio, or sCD14 (**Figure 1**).
- sCD163 was within the normal reference range in both treatment arms at baseline and improved (decreased) in both arms over 12 months, with a statistically slightly greater change in the BIC/FTC/TAF group (~50 units).

Figure 2. sCD163 at Baseline* and Month 12† by Key Subgroups and Treatment Arms



*CAB + RPV LA/BIC/FTC/TAF: overall, n=449/226; female, n=79/41; male, n=370/185; BMI <30 kg/m^2, n=353/174; BMI ≥30 kg/m^2, n=96/52; <35 years, n=189/99; 35–<50 years, n=172/83; ≥50 years, n=88/44.
†CAB + RPV LA/BIC/FTC/TAF: overall, n=408/210; female, n=71/34; male, n=337/176; BMI <30 kg/m^2, n=321/162; BMI ≥30 kg/m^2, n=87/48; <35 years, n=174/90; 35–<50 years, n=156/78; ≥50 years, n=78/42.
‡Reference range for individuals living without HIV (387–1785 µg/L).[11]
BIC/FTC/TAF, bictegravir/emtricitabine/tenofovir alafenamide; BMI, body mass index; CAB, cabotegravir; LA, long-acting; Q2M, every 2 months; RPV, rilpivirine; SD, standard deviation.

- Subgroup analyses of IL-6, CRP, D-dimer, CD4/CD8 ratio, sCD14, and sCD163 showed no meaningful differences in changes over 12 months between treatment arms.
- sCD163 subgroup analyses are shown in **Figure 2**.

Conclusions

- Similar changes in key inflammatory markers were observed in stably suppressed participants switching to CAB + RPV LA vs. continuing BIC/FTC/TAF.
- sCD163 was within the normal reference range in both treatment arms at baseline and improved in both arms over 12 months, with a slightly greater change in the BIC/FTC/TAF group.
  - The clinical significance of the difference between treatment groups was deemed negligible and was not driven by any specific subgroup.
- Analyses by key subgroups showed similar changes in inflammatory markers, with no differences between treatment arms.
- The lack of clinical differences in inflammatory markers is consistent with the high virologic suppression rates maintained in both arms and the demonstrated virologic noninferiority of switching to CAB + RPV LA vs. continuing daily oral BIC/FTC/TAF at Month 12.[6]

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