

Weight and Metabolic Changes With Cabotegravir+Rilpivirine Long-Acting or Bictegravir

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Key Takeaways

Median changes in weight, body mass index, and body composition measurements w between virologically suppressed adults who switched to CAB+RPV LA dosed twice n (Q2M) and who continued daily oral BIC/FTC/TAF through Month 11/Month 12, with no relevant changes

Introduction

- Cabotegravir (CAB), an integrase strand transfer inhibitor (INSTI), plus rilpivirine (RPV), a non-nu transcriptase inhibitor, administered monthly or every 2 months (Q2M) is the first complete long-a recommended by treatment guidelines for the maintenance of HIV-1 virologic suppression¹⁻⁴
- Bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) is an oral, once-daily, 3-drug regin treatment guidelines as one of the choices for therapy for people living with HIV-1 (PLWH)²⁻⁴
- Body weight and lipid changes have been observed in participants receiving INSTI-based regime CAB+RPV LA, and TAF-based regimens including BIC/FTC/TAF⁵⁻¹¹
- Weight and metabolic changes from baseline to Month 12 were assessed in a standardized man switching to CAB+RPV LA Q2M vs continuing BIC/FTC/TAF in the phase IIIb SOLAR study

Methods

- SOLAR (ClinicalTrials.gov identifier, NCT04542070) is the first randomized, large, head-to-head CAB+RPV LA dosed Q2M vs daily oral BIC/FTC/TAF (Figure 1)
- Evaluating weight and metabolic changes from baseline to Month 11/12 were additional endpoints
- Among 687 participants randomized (2:1; n=6 not dosed), 454 switched to CAB+RPV LA Q2M (1 lead-in [OLI] and 279 elected to start with injections [SWI]) and 227 continued on BIC/FTC/TAF

Metabolic Objectives

- Changes in body weight, body mass index (BMI) category, waist and hip circumferences, waist-to hip ratios, and the proportion of participants with insulin resistance or metabolic syndrome (as det clinical criteria) were assessed from baseline (Day 1) to Month 11 (starting with injection)/12 (OLI) (hereafter referred to as Month 12)
- Standardized weight and anthropometric measurements were performed using circumference tapes and Tanita scales

Figure 1. SOLAR Study Design

Phase IIIb, Randomized (2:1), Open-Label, Active-Controlled, Multicenter, Parallel-Group, Noninferiority Study **Screening Phase Maintenance Phase**



Confirm HIV-1 RNA <50 c/mL

M, intramuscular; LA, long-acting; OLI, oral lead-in; Q2M, every 2 months; SWI, starting with injection. *A single prior integrase inhibitor 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). [†]Participants randomized to the LA arm were offered an optional OLI: the decision to dose SWI or with OLI was determined by the participants following informed consent discussions with the investigator

Results

Participants

- Among study participants, 12 transgender females, 1 transgender male, and 1 gender non-conforming individual were included (Table 1)
- In total, 59% (n=401/681) of participants were in the overweight or obesity category at baseline

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	Parameter	CAB+RPV LA Q2M (n=454)	BIC/FTC/TAF (n=227)
	Age, median (range), years	37 (18-74)	37 (18-69)
re similar	≥50 years, n (%)	89 (20)	45 (20)
onthly clinically	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)
cleoside reverse cting (LA) regimen	CD4+ cell count, median (IQR), cells/mm ³	662 (487-853)	645 (489-823)
	Duration of prior ART, median (IQR), years [†]	2.6 (1.6-4.9)	2.5 (1.5-4.7)
	Weight, median (IQR), kg	81.3 (70.7-91.8)	79.0 (69.4-91.7)
	BMI, median (IQR), kg/m ²	26.0 (23.2-29.3)	25.4 (23.6-29.6)
	≥30 kg/m², n (%)	97 (21)	52 (23)
	BMI category, n (%)		
en recommended by	Underweight (<18.5 kg/m ²)	8 (2)	3 (1)
-	Normal (18.5 to <25 kg/m ²	175 (39)	94 (41)
	Overweight (25 to <30 kg/m ²)	174 (38)	78 (34)
sincluaing	Obesity (≥30 kg/m²)	97 (21)	52 (23)
	Baseline lipids, median (range)		
ner among PLWH	TG, mmol/L	1.07 (0.32-20.42)	1.06 (0.38-4.01)
	TC, mmol/L	4.58 (2.25-9.66)	4.77 (2.72-8.94)
	LDL, mmol/L	2.74 (0.55-5.41)	2.77 (1.01-6.97)
	HDL, mmol/L	1.22 (0.47-2.38)	1.26 (0.60-3.06)
	TC/HDL ratio	3.71 (1.45-20.55)	3.56 (1.82-8.25)
comparison of 75 elected for oral	Relevant medical history, n (%)		
	Hypertension	48 (11)	26 (12)
	Diabetes	19 (4)	7 (3)
	Relevant co-medications, n (%)		
	Lipid-lowering therapy [‡]	40 (9)	21 (9)
	BMI, body mass index; HDL, high-density lipoproteins; IQR, interquartile range; LDL, low-density lipoproteins; Q2M, every 2 months; TC, total cholesterol; TG, triglycerides. *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 hav been the participant's first or second regimen. If BIC/FTC/TAF was the second regimen, the first regimen must have been an integrase inhibitor. ‡Started lipid-lowering medication during maintenance phase: CAB+RP LA Q2M, n=17 (4%); BIC/FTC/TAF, n=8 (4%).		
eight and waist-to-	Weight Outcomes		
ad by atomdard	• At Month 12 median (interguartile range: IOR) change in weight in the CAR+RP\/ LA O	2M aroup was -0.40
ed by standard	(2.05, 10.10) km and $(0.05, (2.02, 14.05)$ km	() on ange in weight in the criticity (E) in the DIC/ETC/TAE areas up (E) areas (C)	

9.000 (1.90

Figure 2. Median Change From Baseline in Weight Through Month 12^{*}



IQR, interquartile range; LA, long-acting; Q2M, every 2 months. *Any participant that started lipid-modifying agents during the study was non-evaluable in anthropometric assessments. †Median (IQR) weight at baseline: CAB+RPV LA Q2M, 81.3 (70.70, 91.80) kg; BIC/FTC/TAF, 79.0 (69.40, 91.70) kg.

• Weight increases of $\geq 10\%$ by Month 12 occurred in 3% (n=11/454) of participants in the LA arm vs 4% (n=9/227) in the BIC/FTC/TAF arm (Figure 3)

Figure 3. Percent Change in Weight Through Month 12*



LA, long-acting; Q2M, every 2 months. *Any participant that started lipid-modifying agents during the study was non-evaluable in anthropometric assessments.

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Extension Phase

Extension Switch

to or continue

CAB (600 mg) +

RPV (900 mg) LA





BMI Outcomes



Waist and Hip Circumference Outcomes

- respectively (Figure 5)

Figure 5. Change From Baseline in Waist and Hip Circumferences Through Month 12



BIC/FTC/TAF (n=180) CAB+RPV LA Q2M (n=352)

IQR, interquartile range; LA, long-acting; Q2M, every 2 months. *Median (IQR) waist circumference at baseline: CAB+RPV LA Q2M, 90.35 (82.20, 100.98) cm; BIC/FTC/TAF, 90.00 (81.30, 101.00) cm. †Median (IQR) hip circumference at baseline: CAB+RPV LA Q2M, 99.00 (92.00, 106.00) cm; BIC/FTC/TAF, 97.0 (90.00, 106.68) cm.

Metabolic Outcomes

syndrome or insulin resistance in either arm (Figure 6)



HDL-C, high-density lipoprotein cholesterol; HOMA-IR, Homeostasis Model of Assessment for Insulin Resistance; LA, long-acting; M, month; Q2M, every 2 months. *Three abnormal findings out of the following five qualifies a person for metabolic syndrome: elevated waist circumference (females: \geq 88 cm [\geq 35 in]; males: \geq 102 cm [\geq 40 in]), elevated triglycerides (\geq 150 mg/dL [1.7 mmol/L]), reduced HDL-C (females: <50 mg/dL [1.3 mmol/L]; males: <40 mg/dL [1.0 mmol/L]), elevated blood pressure (meeting either or both criteria; systolic ≥130 and/or diastolic ≥85 mm Hg), and elevated fasting glucose (≥100 mg/dL). †HOMA-IR ≥2.

Conclusions

- BIC/FTC/TAF through Month 12
- resistance between arms at Month 12
- treatment in adults with HIV-1

Proportion of Participants With an Upward BMI Shift **Resulting in Overweight or Obesity at Month 12*** 15 Underweight Normal Overweight Obesity Normal to Overweight to overweight obesity BIC/FTC/TAF baseline BIC/FTC/TAF Month 12 CAB+RPV LA Q2M BIC/FTC/TAF

• Overall, the proportion of individuals in BMI categories remained similar at Month 12 (Figure 4)

• Mean (SD) change in waist circumference and hip circumference was +0.19 cm (8.01) and +0.26 cm (7.81) in the CAB+RPV LA Q2M arm, respectively, and +1.64 cm (9.19) and +0.51 cm (11.44) in the BIC/FTC/TAF arm at M11/12,

• There were no clinically relevant changes from baseline to Month 12 in the median (IQR) waist-to-height ratio (CAB+RPV LA Q2M, +0.000 [-0.020, 0.020]; BIC/FTC/TAF, +0.010 [-0.020, 0.030]) and median waist-to-hip ratio (CAB+RPV LA Q2M, +0.000 [-0.040, 0.040]; BIC/FTC/TAF, +0.010 [-0.030, 0.040])



There were no clinically relevant changes from baseline to Month 12 in the proportion of participants with metabolic

CAB+RPV LA Q2M (n=454) BIC/FTC/TAF (n=227)

• This is the first randomized phase IIIb study to compare weight, anthropometric, and metabolic changes in a standardized manner among PLWH switching to CAB+RPV LA Q2M or continuing BIC/FTC/TAF • Median changes in weight, BMI, and body composition measurements were similar between CAB+RPV LA Q2M and

There were no clinically relevant changes in the proportion of participants with metabolic syndrome or insulin

• These data on weight and metabolic changes with CAB+RPV LA dosed Q2M support its use for maintenance