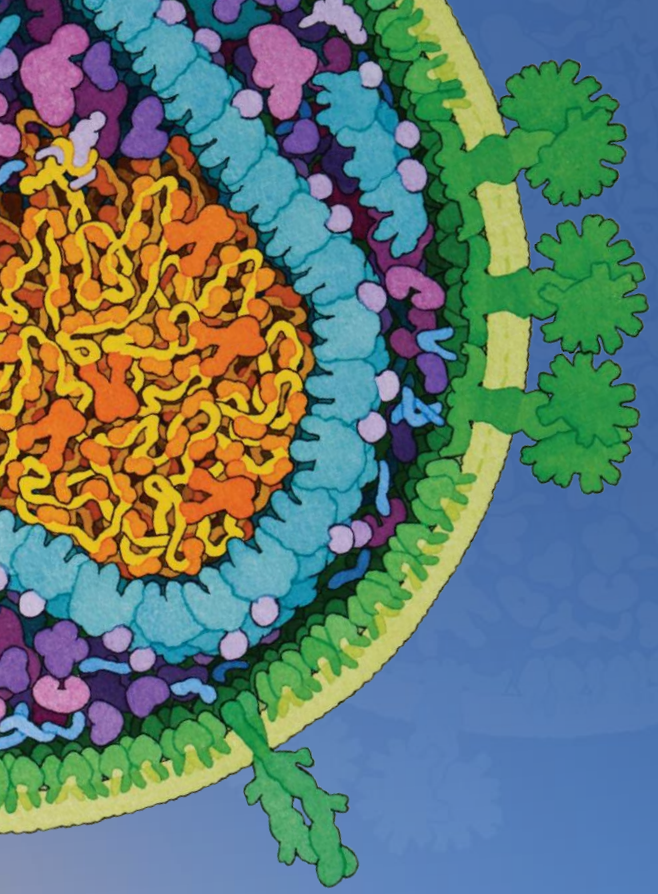

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WEIGHT AND LIPID CHANGES IN PHASE 3 CABOTEGRAVIR AND RILPIVIRINE LONG-ACTING TRIALS

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Introduction

- Weight gain and metabolic alterations have been reported with INSTI- and TAF-based antiretroviral regimens[1–3]
- Cabotegravir (CAB), an INSTI, and rilpivirine (RPV), an NNRTI, have been approved in the US, Canada, and Europe as the first complete long-acting (LA) injectable regimen indicated for the maintenance of virologic suppression in people living with HIV-1[4–6]
- The Phase 3/3b development program demonstrated noninferiority of CAB + RPV LA dosed Q4W vs. daily oral ART (ATLAS and FLAIR studies)[7,8] and Q8W vs. Q4W dosing (ATLAS-2M study)[9] for the maintenance of virologic suppression
- Weight and lipid changes over 48 weeks in adults with virologic suppression receiving CAB + RPV LA within the Phase 3/3b program are presented herein

ART, antiretroviral therapy; INSTI, integrase strand transfer inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; Q4W, every 4 weeks; Q8W, every 8 weeks; TAF, tenofovir alafenamide.

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Methods

- Data for participants randomized to CAB + RPV LA Q4W or Q8W or to oral comparator ART (CAR) through 48 weeks were pooled from the FLAIR, ATLAS, and ATLAS-2M studies
  - For ATLAS-2M participants who transitioned from ATLAS with prior exposure to CAB + RPV, only data from ATLAS were included
- Baseline demographics and participant characteristics were summarized for each treatment group
- Changes in weight, BMI, and lipids from baseline to Week 48 were described
  - Across the CAB development program, weight data were collected as per routine clinical practice across study sites; limited metabolic data were collected

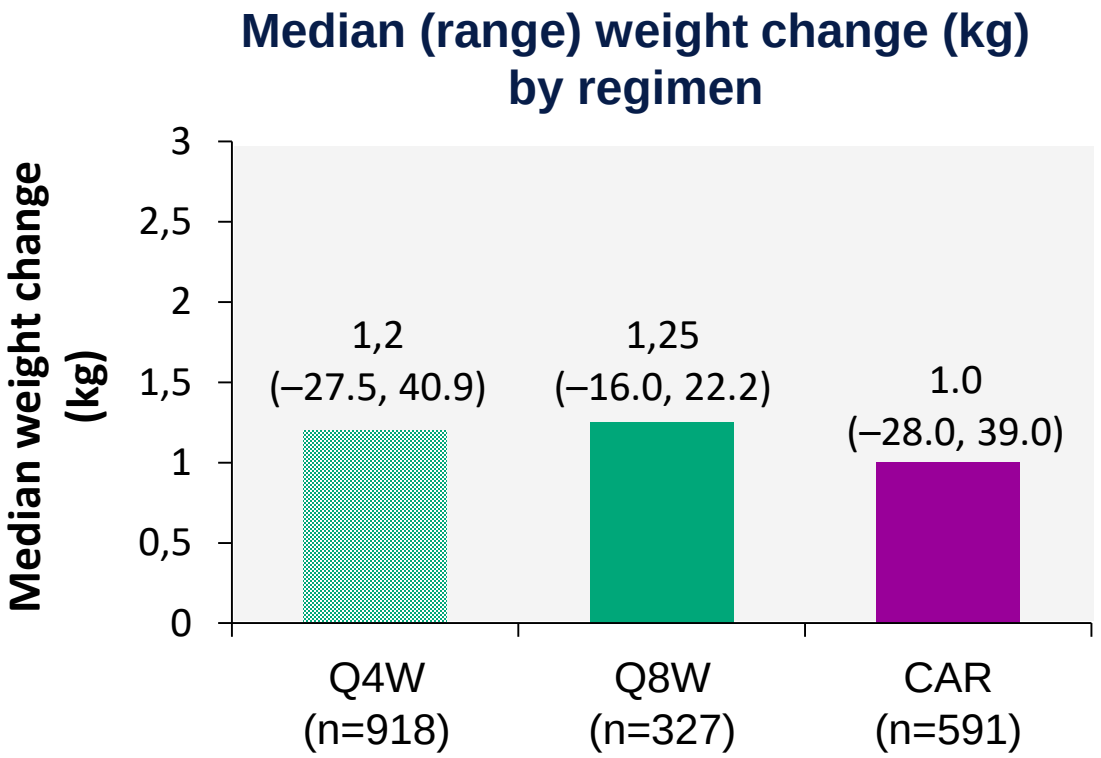
ART, antiretroviral therapy; BMI, body mass index; CAB, cabotegravir; CAR, current antiretroviral regimen; LA, long-acting; Q4W, every 4 weeks; Q8W, every 8 weeks; RPV, rilpivirine.

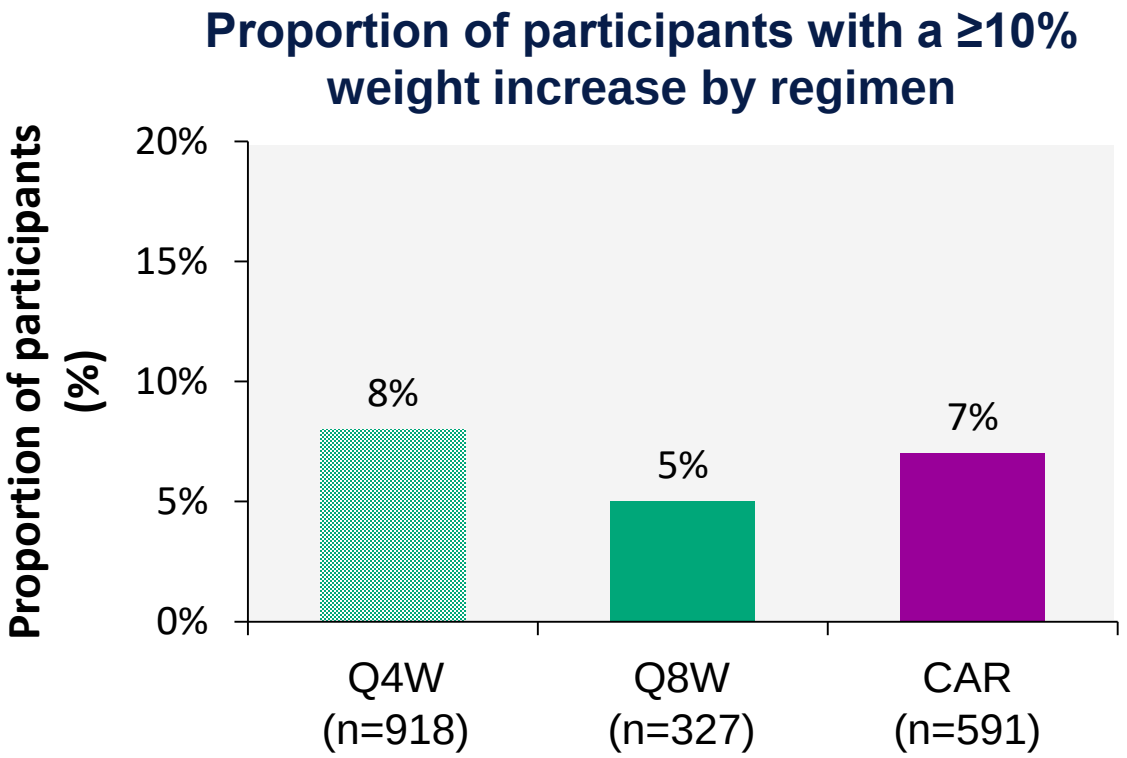
Results: Baseline Characteristics

Baseline demographics/characteristics (ITT-E population)	Pooled Q4W arm ATLAS, FLAIR,* and ATLAS-2M (n=918)†	Q8W arm ATLAS-2M (n=327)‡	Pooled CAR arm ATLAS and FLAIR* (n=591)
Median age (range), years	39 (19–74)	41 (20–83)	38 (18–82)
Female (sex at birth), n (%)	237 (26)	73 (22)	168 (28)
Black or African American race, n (%)	154 (17)	57 (17)	133 (23)
Median CD4 count at baseline (cells/mm^3)	661	643	641
BMI category, n (%)			
Underweight (<18.5 kg/m^2)	20 (2)	4 (1)	12 (2)
Normal (18.5–25 kg/m^2)	440 (48)	151 (46)	298 (50)
Overweight (25–30 kg/m^2)	306 (33)	113 (35)	178 (30)
Obese (≥30 kg/m^2)	152 (17)	59 (18)	103 (17)
Weight (kg), median (IQR)	76.0 (67.0, 85.9)	77.0 (68.0, 77.0)	75.2 (65.4, 85.7)
Baseline lipids, mean (SD)			
TG (mmol/L)	1.43 (1.014)	1.46 (0.954)	1.43 (1.051)
TC (mmol/L)	4.73 (1.014)	4.82 (1.052)	4.72 (1.055)
LDL (mmol/L)	2.74 (0.855)	2.78 (0.899)	2.71 (0.835)
HDL (mmol/L)	1.34 (0.420)	1.39 (0.421)	1.36 (0.428)
TC/HDL ratio	3.82 (1.538)	3.73 (1.276)	3.72 (1.197)
Medical history, n (%)			
Hypertension	92 (10)	51 (16)	76 (13)
Diabetes	22 (2)	11 (3)	22 (4)
Select co-medications, n (%)			
Anti-hypertensives	11 (1.2)	6 (1.8)	3 (0.5)
Anti-diabetes	16 (1.7)	10 (3.1)	17 (2.9)
Anti-lipids	90 (9.8)	39 (11.9)	30 (5.1)
SSRIs	54 (5.9)	14 (4.3)	28 (4.7)
Antipsychotics	13 (1.4)	9 (2.8)	7 (1.2)
Pre-switch ART regimen, n (%)§			
IN-based	526 (57)	136 (42)	382 (65)
PI-based	81 (9)	40 (12)	54 (9)
NNRTI-based	311 (34)	151 (46)	155 (26)

*FLAIR study baseline was at maintenance baseline (study Week 0), at which point DTG/ABC/3TC or DTG + TDF/3TC was switched to CAB + RPV LA. †Includes all participants who received CAB + RPV LA Q4W in the ATLAS, FLAIR, and ATLAS-2M studies. For participants in ATLAS-2M who transitioned from ATLAS with prior CAB + RPV LA exposure, only ATLAS data were included. ‡Includes all participants who received CAB + RPV LA Q8W in ATLAS-2M excluding those who transitioned from ATLAS-2M with prior exposure to CAB + RPV. §Participants on TAF regimen at baseline: Q4W, n=162; Q8W, n=99; CAR, n=56.
3TC, lamivudine; ABC, abacavir; ART, antiretroviral therapy; BMI, body mass index; CAB, cabotegravir; CAR, current antiretroviral regimen; DTG, dolutegravir; HDL, high-density lipoproteins; ITT-E, intention-to-treat exposed; IN, integrase; IQR, interquartile range; LA, long-acting; LDL, low-density lipoproteins; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; Q4W, every 4 weeks; Q8W, every 8 weeks; RPV, rilpivirine; SD, standard deviation; SSRI, selective serotonin reuptake inhibitor; TAF, tenofovir alafenamide; TC, total cholesterol; TDF, tenofovir disoproxil fumarate; TG, triglycerides.

Weight Change by Treatment Regimen From Baseline to Week 48

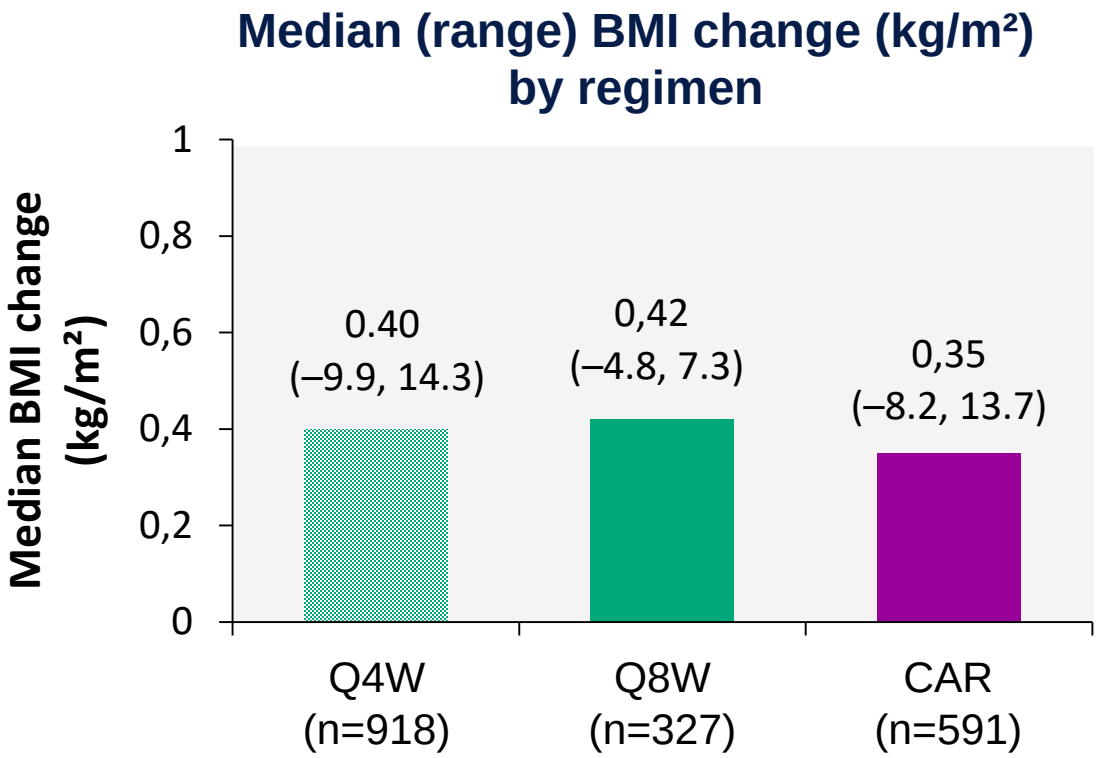


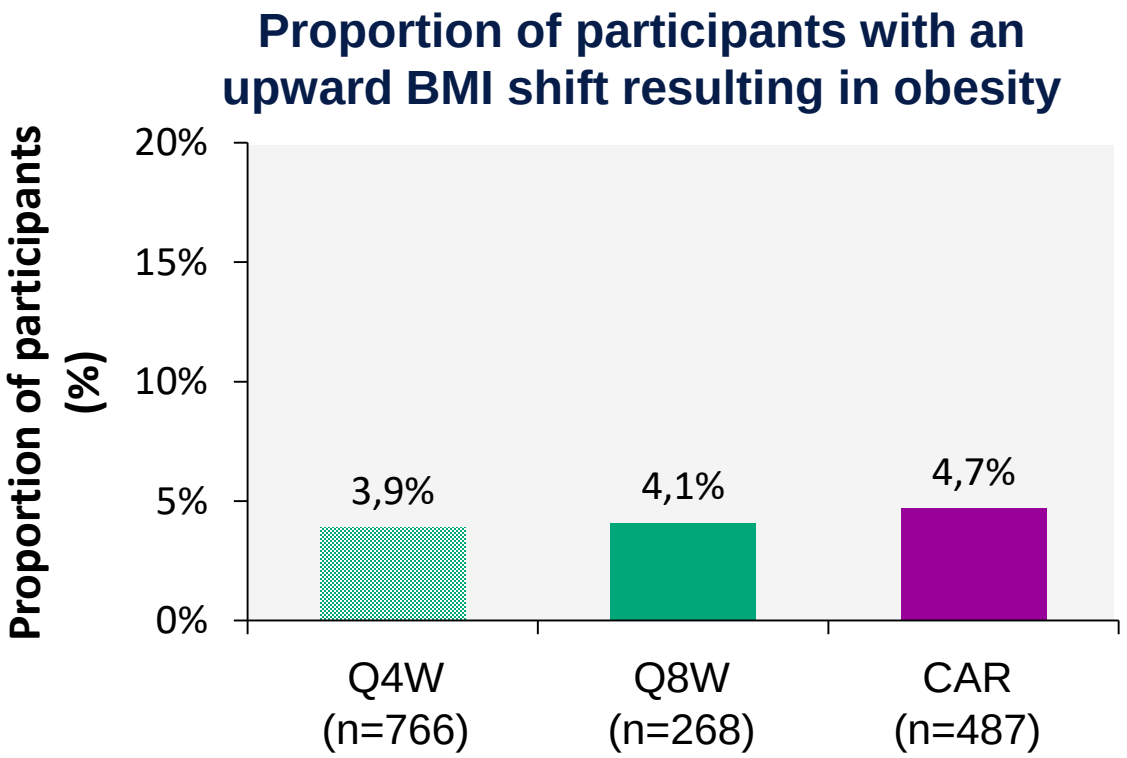


- Median weight increased from baseline* across all regimens, with slightly higher increases observed in participants receiving CAB + RPV LA vs. those receiving CAR
- The proportion of participants with a ≥10% weight increase was similar for the CAB + RPV LA regimens and CAR

*Median (IQR) weight (kg) at baseline: Q4W, 76.0 (67.0, 85.9); Q8W, 77.0 (68.0, 87.0); CAR, 75.2 (65.4, 85.7).
CAB, cabotegravir; CAR, current antiretroviral regimen; IQR, interquartile range; LA, long-acting; Q4W, every 4 weeks; Q8W, every 8 weeks; RPV, rilpivirine.

BMI Change by Treatment Regimen From Baseline to Week 48



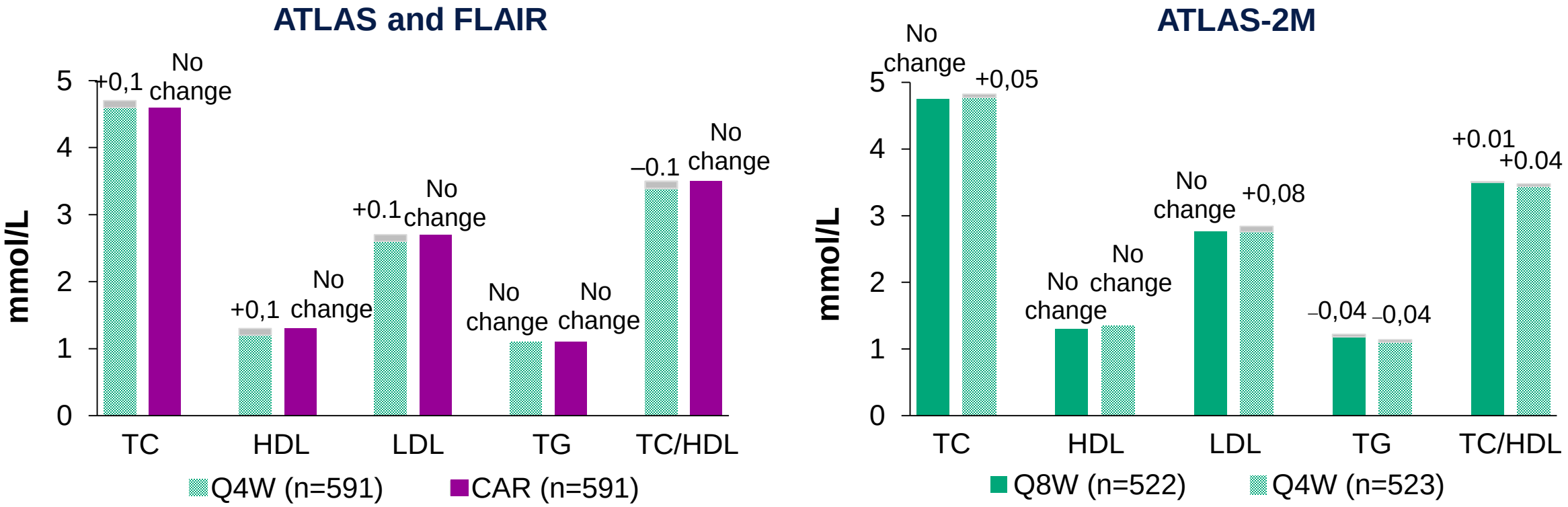


- Median BMI increased modestly and similarly from baseline across all regimens
- BMI shifts were similar across the three regimens, with 13.2% and 0.6% of participants overall experiencing an upward change in BMI category from normal to overweight or normal to obese, respectively
- Across the three regimens, ~4% of participants had an upward BMI shift resulting in obesity (BMI ≥30 kg/m^2)

*Median (min, max) BMI at baseline: Q4W, 24.95 (15.3, 54.0); Q8W, 25.26 (17.8, 46.0); CAR, 24.80 (12.6, 57.7).
BMI, body mass index; CAR, current antiretroviral regimen; Q4W, every 4 weeks; Q8W, every 8 weeks.

Baseline and Change From Baseline at Week 48 in Lipid Parameters

Median lipid parameters at BL (solid bars) and median change (mmol/L) from BL (grey bars) at Week 48



- Changes in lipid parameters were similar between regimens, with no clinically significant changes in triglycerides; total, HDL, and LDL cholesterols; and TC/HDL ratios across the three treatment groups

CAR, current antiretroviral regimen; BL, baseline; HDL, high-density lipoproteins; LDL, low-density lipoproteins; Q4W, every 4 weeks; Q8W, every 8 weeks; TC, total cholesterol; TG, triglycerides.

Conclusions

- At Week 48, minimal changes in weight gain were observed across treatment arms, with no meaningful changes in lipid parameters
- The potential for weight gain and metabolic perturbations with contemporary ART regimens is the subject of ongoing investigation; future and ongoing studies will further characterize this relationship
- These data demonstrate an overall favorable metabolic profile of CAB + RPV LA dosed monthly or every 2 months, and support the therapeutic potential of this novel long-acting regimen for HIV treatment

ART, antiretroviral therapy; CAB, cabotegravir; CAR, current antiretroviral regimen; LA, long-acting; RPV, rilpivirine.

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