EPB183

Week 96 Weight and Lipid Changes From Baseline Among Participants Receiving Cabotegravir + Rilpivirine Long-Acting or Comparator Therapy in the ATLAS-2M and FLAIR Studies

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Key Takeaways

- **We present longer-term weight and lipid changes for participants receiving cabotegravir + rilpivirine long-acting (CAB + RPV LA) or daily oral therapy (abacavir/dolutegravir/lamivudine [ABC/DTG/3TC]) through Week 96 of the Phase 3/3b ATLAS-2M and FLAIR studies.**
- **Longer-term weight, body mass index (BMI), and lipid changes were minor and comparable between participants receiving CAB + RPV LA and daily oral therapy, supporting the use of CAB + RPV LA dosed monthly or every 2 months as a complete regimen for the maintenance of HIV-1 virologic suppression in adults.**

Introduction

- Weight gain and metabolic alterations have been reported with integrase strand transfer inhibitor (INSTI)- and tenofovir alafenamide (TAF)-based antiretroviral regimens.[1–3]
- Multiple associations with weight gain have been described, including immune status, TAF use, female sex, Black race, and pre-existing comorbidities.[1,4]
- CAB, an INSTI, plus RPV, a non-nucleoside reverse transcriptase inhibitor (NNRTI), is a complete LA regimen recommended by treatment guidelines for the maintenance of HIV-1 virologic suppression.[5–7]
- In pooled Phase 3/3b studies, weight and lipid changes were modest in participants receiving CAB + RPV LA or daily oral therapy through Week 48.[8]
- Here, we present weight and lipid changes from baseline to Week 96 in the FLAIR* and ATLAS-2M† studies.

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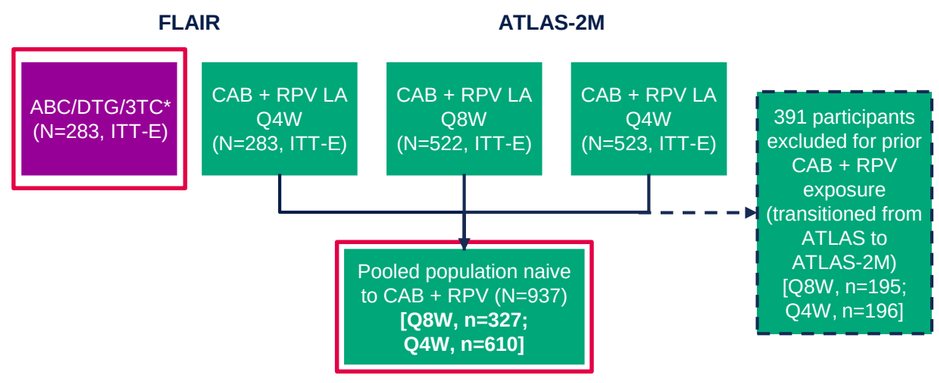
Methods

- Data were pooled for participants receiving CAB + RPV LA every 4 or 8 weeks (Q4W or Q8W, n=937) or daily oral therapy (ABC/DTG/3TC, n=283) through 96 weeks in the FLAIR and ATLAS-2M studies (**Figure 1**).
  - FLAIR participants were antiretroviral naive at study entry and underwent induction with ABC/DTG/3TC for 20 weeks, and were subsequently randomized to receive either CAB + RPV LA Q4W or continue daily oral therapy if their HIV-1 RNA was <50 copies/mL.
  - ATLAS-2M participants were antiretroviral experienced and virologically suppressed on comparator oral therapy before being randomized to receive either CAB + RPV LA Q4W or Q8W.
    - ATLAS-2M participants who transitioned from the Phase 3 ATLAS study with prior exposure to CAB + RPV were excluded to ensure all participants had only 96 weeks of follow-up.
- The following parameters were assessed at baseline, Week 48, and Week 96:
  - Change in weight and BMI.
  - Lipids, including total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides.
  - Proportion with ≥10% weight increase from baseline, overall and by baseline subgroup.

Figure 1. Participants Analyzed



*Participants with HLA-B*5701 positivity or tolerability issues with ABC received FTC + TDF, FTC + TAF, or 3TC/TDF.
3TC, lamivudine; ABC, abacavir; CAB, cabotegravir; DTG, dolutegravir; FTC, emtricitabine; ITT-E, intention-to-treat exposed; LA, long-acting; Q4W, every 4 weeks; Q8W, every 8 weeks; RPV, rilpivirine; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.

Results

Table 1. Baseline Demographics and Characteristics*

ITT-E population	Pooled Q8W arm (ATLAS-2M only) (n=327)	Pooled Q4W arm (FLAIR and ATLAS-2M) (n=610)	ABC/DTG/3TC† (FLAIR only) (n=283)
Median age (range), years	41 (20–83)	37 (19–68)	34 (18–68)
Female sex at birth, n (%)	73 (22)	138 (23)	64 (23)
Transgender female, n (%)	2 (<1)	4 (<1)	0
Race, n (%)			
Black or African American	57 (17)	92 (15)	56 (20)
White	239 (73)	472 (77)	203 (72)
Asian	17 (5)	24 (4)	15 (5)
Other	14 (4)	22 (4)	9 (3)
BMI (kg/m^2), median (IQR)	25.3 (22.7–28.6)	24.8 (22.5–27.7)	24.0 (21.8–27.1)
Weight (kg), median (IQR)	77.0 (68.0–87.0)	76.0 (67.0–85.4)	74.0 (64.5–83.7)
Pre-switch ART regimen, n (%)			
INI-based	136 (42)	424 (70)	283 (100)
NNRTI-based	151 (46)	156 (26)	N/A
PI-based	40 (12)	30 (5)	N/A
Pre-switch TAF, n (%)	99 (3)	113 (19)	3 (1)
Pre-switch TDF, n (%)	151 (46)	148 (24)	11 (4)
CD4 count at baseline (cells/mm^3), median (IQR)	643 (496–849)	572 (411–778)	453 (323–604)

*Participants in FLAIR were ART naive and underwent induction with ABC/DTG/3TC for 20 weeks. Baseline for FLAIR refers to induction phase baseline (Week –20), prior to participants receiving ABC/DTG/3TC for 20 weeks; participants in ATLAS-2M were ART experienced and virologically suppressed prior to entering the study.
†14 participants received DTG + two non-ABC nucleoside reverse transcriptase inhibitors due to HLA-B*5701 positivity or tolerability issues with ABC.
3TC, lamivudine; ABC, abacavir; ART, antiretroviral therapy; BMI, body mass index; DTG, dolutegravir; INI, integrase inhibitor; IQR, interquartile range; ITT-E, intention-to-treat exposed; N/A, not applicable; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; Q4W, every 4 weeks; Q8W, every 8 weeks; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.

- In participants receiving CAB + RPV LA, the median age was 39 years, 23% were female (sex at birth), and 16% were of Black or African American race (**Table 1**), comparable to participants receiving daily oral therapy.

Table 2. Pertinent Baseline Metabolic Parameters, Medical History, and Co-medications History

ITT-E population	Pooled Q8W arm (ATLAS-2M only) (n=327)	Pooled Q4W arm (FLAIR and ATLAS-2M) (n=610)	ABC/DTG/3TC (FLAIR only) (n=283)
BMI category, n (%)*			
Underweight (<18.5 kg/m^2)	4 (1)	11 (2)	10 (4)
Normal (18.5–<25 kg/m^2)	151 (46)	309 (51)	160 (57)
Overweight (≥25–<30 kg/m^2)	113 (35)	198 (32)	76 (27)
Obese (≥30 kg/m^2)	59 (18)	92 (15)	37 (13)
Baseline lipids, median (range)†			
TG (mmol/L)	1.23 (0.21–8.30)	1.14 (0.36–10.60)	1.12 (0.30–4.88)
TC (mmol/L)	4.75 (2.00–8.45)	4.60 (2.30–8.50)	4.40 (2.05–9.50)
LDL (mmol/L)	2.75 (0.98–5.77)	2.64 (0.67–5.60)	2.45 (0.60–5.86)
HDL (mmol/L)	1.30 (0.50–2.90)	1.25 (0.10–3.30)	1.25 (0.60–3.00)
TC/HDL ratio	3.45 (1.21–10.73)	3.48 (1.45–26.00)	3.50 (1.66–9.50)
Relevant medical history, n (%)*			
Hypertension	51 (16)	56 (9)	22 (8)
Diabetes	11 (3)	15 (2)	5 (2)
Relevant co-medications, n (%)†			
Anti-hypertensives	6 (12)	13 (13)	3 (13)
Anti-diabetes	8 (16)	11 (11)	4 (17)
Anti-lipids	31 (63)	53 (54)	8 (35)
SSRIs	9 (18)	30 (31)	8 (35)
Anti-psychotics	4 (8)	5 (5)	3 (13)

*Participants in FLAIR were ART naive and underwent induction with ABC/DTG/3TC for 20 weeks. Baseline BMI category and relevant medical history for FLAIR refers to induction phase baseline (Week –20), prior to participants receiving ABC/DTG/3TC for 20 weeks; participants in ATLAS-2M were ART experienced and virologically suppressed prior to entering the study.
†Baseline lipid and co-medication values for participants from FLAIR represent maintenance baseline, after the 20-week induction period on ABC/DTG/3TC. Participants in ATLAS-2M were ART experienced and virologically suppressed prior to entering the study.
3TC, lamivudine; ABC, abacavir; ART, antiretroviral therapy; BMI, body mass index; DTG, dolutegravir; HDL, high-density lipoproteins; ITT-E, intention-to-treat exposed; LDL, low-density lipoproteins; Q4W, every 4 weeks; Q8W, every 8 weeks; SSRI, selective serotonin reuptake inhibitor; TC, total cholesterol; TG, triglycerides.

- Overall, 33% of participants receiving CAB + RPV LA were overweight and 16% were obese at baseline (**Table 2**); this was generally comparable between arms.
- Lipid-lowering agents and SSRIs were the most common reported co-medications across treatment arms at baseline.
  - SSRI use was higher in the daily oral therapy arm vs. the CAB + RPV LA arms (29% vs. 24%, respectively).

Figure 2. Change in Weight From Baseline*

Figure 2A. Median Weight Change (kg) by Regimen

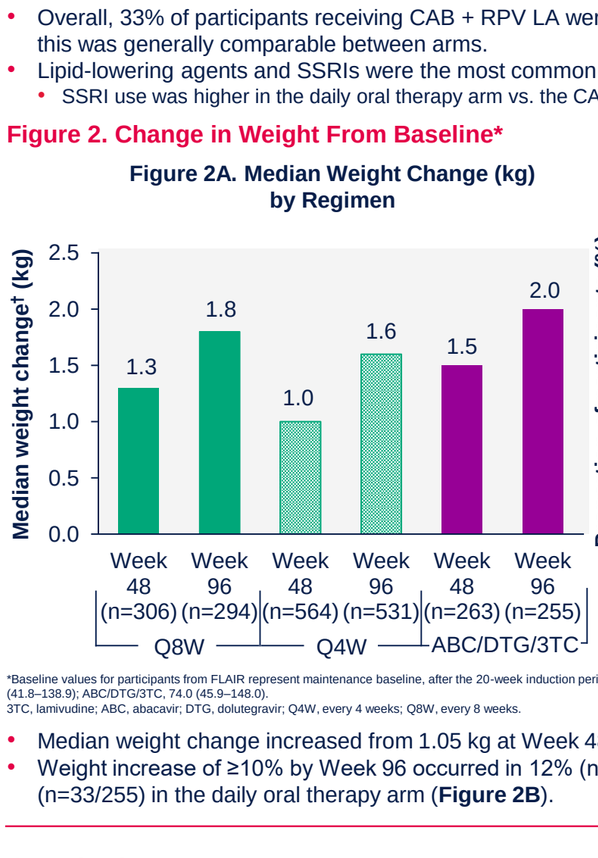
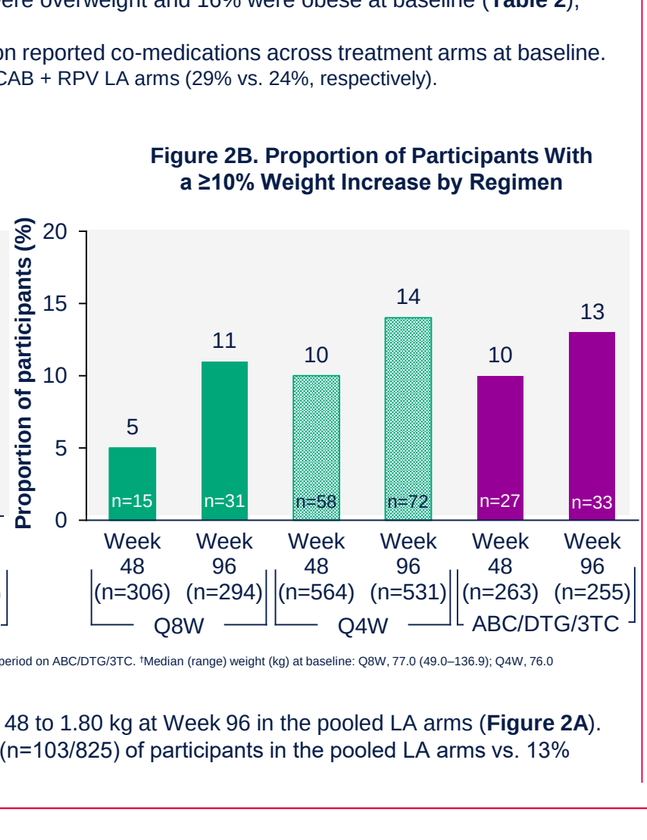


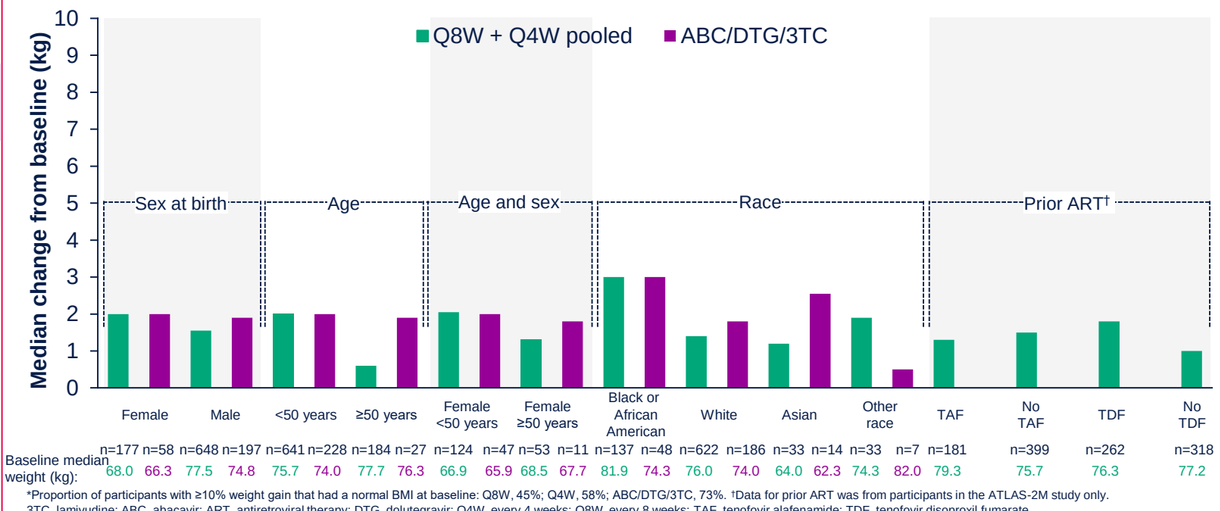
Figure 2B. Proportion of Participants With a ≥10% Weight Increase by Regimen



*Baseline values for participants from FLAIR represent maintenance baseline, after the 20-week induction period on ABC/DTG/3TC. †Median (range) weight (kg) at baseline: Q8W, 77.0 (49.0–136.9); Q4W, 76.0 (41.8–138.9); ABC/DTG/3TC, 74.0 (45.9–148.0).
3TC, lamivudine; ABC, abacavir; DTG, dolutegravir; Q4W, every 4 weeks; Q8W, every 8 weeks.

- Median weight change increased from 1.05 kg at Week 48 to 1.80 kg at Week 96 in the pooled LA arms (**Figure 2A**).
- Weight increase of ≥10% by Week 96 occurred in 12% (n=103/825) of participants in the pooled LA arms vs. 13% (n=33/255) in the daily oral therapy arm (**Figure 2B**).

Figure 3. Median Weight Gain at Week 96 by Baseline Subgroup*



*Proportion of participants with ≥10% weight gain that had a normal BMI at baseline: Q8W, 45%; Q4W, 58%; ABC/DTG/3TC, 73%. †Data for prior ART was from participants in the ATLAS-2M study only.
3TC, lamivudine; ABC, abacavir; ART, antiretroviral therapy; DTG, dolutegravir; Q4W, every 4 weeks; Q8W, every 8 weeks; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.

- The median weight increased most for participants of Black or African American race in both the pooled LA and daily oral therapy arm, followed by females, participants <50 years, and female participants <50 years (**Figure 3**).

Figure 4. Change in BMI From Baseline

Figure 4A. Median BMI Change (kg/m^2) by Regimen Through Week 96

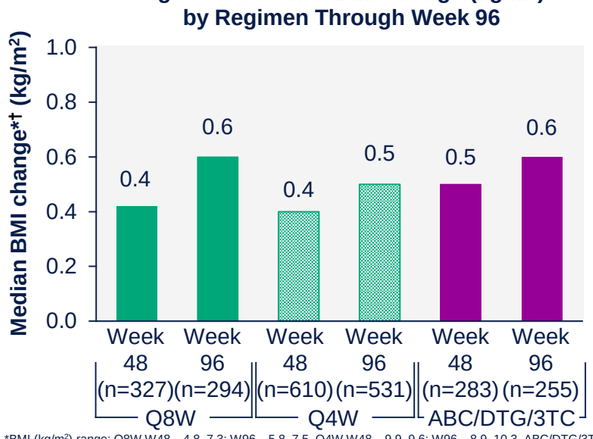
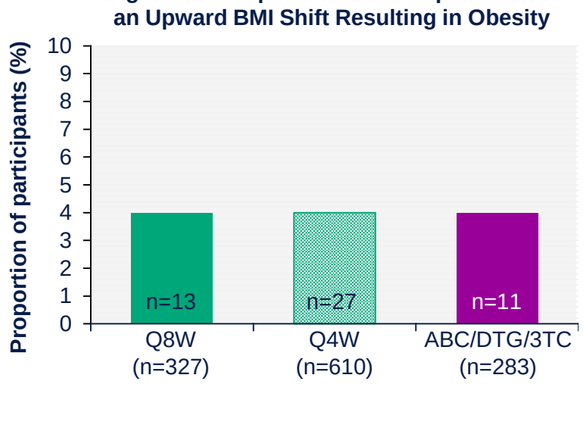


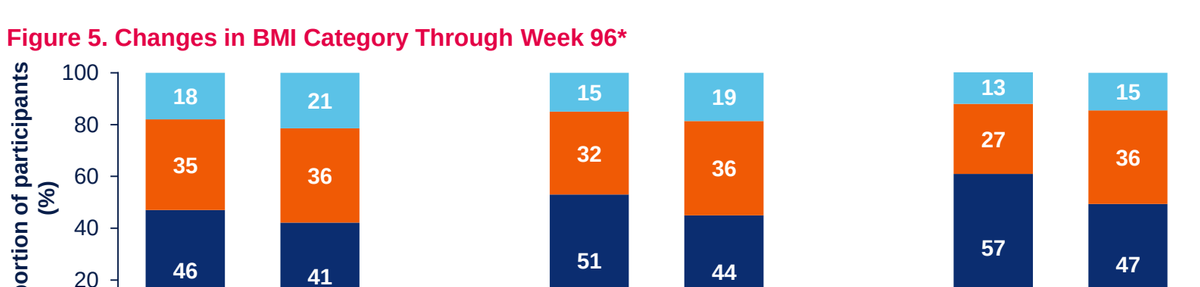
Figure 4B. Proportion of Participants‡ With an Upward BMI Shift Resulting in Obesity



*BMI (kg/m^2) range: Q8W W48, –4.8, 7.3; W96, –5.8, 7.5. Q4W W48, –9.9, 9.6; W96, –8.9, 10.3. ABC/DTG/3TC W48, –8.2, 9.7; W96, –5.9, 12.7. †Median (range) BMI (kg/m^2) at baseline: Q8W, 25.26 (17.8–46.0); Q4W, 24.81 (16.6–54.0); ABC/DTG/3TC, 24.00 (16.2–47.4). ‡Includes those classified as normal and overweight. No underweight participants had an upward shift resulting in obesity.
3TC, lamivudine; ABC, abacavir; BMI, body mass index; DTG, dolutegravir; Q4W, every 4 weeks; Q8W, every 8 weeks; W, week.

- Median change in BMI from baseline was 0.5 kg/m^2 vs. 0.6 kg/m^2 in the pooled LA arms vs. the daily oral therapy arm, respectively, through Week 96 (**Figure 4A**).
- At Week 96, 4% (n=40/937) of pooled LA participants and 4% (n=11/283) of participants receiving daily oral therapy had an upward shift in BMI category resulting in obesity (**Figure 4B**).

Figure 5. Changes in BMI Category Through Week 96*



*Participants in FLAIR entered the study naive to ART and underwent a 20-week induction period on ABC/DTG/3TC prior to the start of the maintenance phase.
3TC, lamivudine; ABC, abacavir; ART, antiretroviral therapy; BMI, body mass index; DTG, dolutegravir; Q4W, every 4 weeks; Q8W, every 8 weeks.

- At Week 96, 16% (n=75/460) of pooled LA participants and 20% (n=32/160) of participants receiving daily oral therapy shifted BMI category from normal at baseline to overweight.
- At Week 96, 12% (n=37/311) of pooled LA participants and 11% (n=8/75) of participants receiving daily oral therapy who were overweight at baseline shifted to obesity.

Figure 6. Median Lipid Parameters at Baseline and Median Change From Baseline at Week 96*

*Proportion of participants reporting anti-lipids: Q8W, 63%; Q4W, 54%; ABC/DTG/3TC: 35%. SSRIs: Q8W, 18%; Q4W, 31%; ABC/DTG/3TC, 35%.
3TC, lamivudine; ABC, abacavir; DTG, dolutegravir; HDL, high-density lipoproteins; LDL, low-density lipoproteins; Q4W, every 4 weeks; Q8W, every 8 weeks; SSRI, selective serotonin reuptake inhibitor; TC, total cholesterol; TG, triglycerides.

- Changes in laboratory values for total cholesterol, HDL cholesterol, LDL cholesterol, and TC/HDL ratio were similar between treatment groups, and not clinically relevant (**Figure 6**).

Conclusions

- Median weight changes were minor and comparable between CAB + RPV LA and daily oral therapy participants at Week 96.
- Weight increases of ≥10% and upward BMI shifts were uncommon, with no significant lipid changes observed.
  - The largest median weight gain was observed in participants of Black or African American race, consistent with previously published data,[1] followed by female participants, participants aged under 50 years, and female participants aged under 50 years.
- Across the CAB development program, weight data were collected as per routine clinical practice across study sites, warranting future exploration with comprehensive and standardized weight and metabolic data collection.
- CAB + RPV LA dosed Q8W and Q4W demonstrated an overall favorable weight and lipid profile through 96 weeks, supporting its use for maintenance HIV-1 treatment in adults with HIV.

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