Metabolic Changes at 48 Weeks in People With HIV and Virologic Suppression Switching to Single-Tablet Bictegravir/Lenacapavir From Complex Antiretroviral Regimens: Results From the Phase 3 ARTISTRY-1 Trial

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ARTISTRY-1

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Conclusions

- In this analysis of participants enrolled in Phase 3 of the ARTISTRY-1 study, fasting lipid parameters improved at Week 48 after switching to bictegravir/lenacapavir (BIC/LEN) from complex regimens (CRs), particularly those containing a protease inhibitor (PI)
- Treatment-emergent dyslipidemia was reported in 3% of participants in both treatment groups
- Fasting glucose, hemoglobin A_{1c} (HbA_{1c}), body weight, body mass index (BMI), and systolic/diastolic blood pressure all remained stable in both BIC/LEN and CR groups at Week 48
  - Results were similar in participants taking PI-containing and non–PI-containing regimens at baseline
- These results further support the use of BIC/LEN single-tablet regimen (STR) as a new option for treatment optimization for people with HIV with virologic suppression on a CR, including for those with multiple comorbidities, including dyslipidemia

Plain Language Summary

- Some people with human immunodeficiency virus (HIV) need to take several tablets each day (called a complex regimen) because simpler treatments do not work for them or cause side effects
- Bictegravir (BIC) and lenacapavir (LEN) are two HIV medicines that can be taken together as one tablet once a day
- The ARTISTRY-1 study looked at how well BIC/LEN worked in people with HIV who switched from complex regimens
  - BIC/LEN worked equally well at treating HIV and had similar rates of side effects compared with continuing complex regimens over 48 weeks of treatment
- In this analysis from the study, researchers wanted to see whether switching to BIC/LEN affected fat in the blood (cholesterol), how the body breaks down food (metabolism), or body weight, compared with staying on a complex regimen
- After 48 weeks of treatment, researchers found that switching to BIC/LEN lowered levels of cholesterol and other fats in the blood. This effect was greater in participants who were previously taking a type of HIV medicine called a protease inhibitor
  - There were no changes in blood sugar levels, body weight, or blood pressure in people who switched to BIC/LEN or those who stayed on complex regimens

Introduction

- Growing recognition of metabolic complications associated with long-term antiretroviral therapy (ART) has highlighted the need for newer regimens that minimize metabolic effects[1,2]
- The novel BIC/LEN STR could help to optimize treatment for people with HIV and reduce the risk of metabolic complications
  - BIC is a guideline-recommended integrase strand transfer inhibitor (INSTI) with a high barrier to resistance[3-6]
  - LEN is a first-in-class capsid inhibitor with no documented *de novo* resistance in the absence of prior exposure[7]
- ARTISTRY-1 was a randomized, open-label, Phase 2/3 trial (NCT05502341) to evaluate the efficacy and safety of switching to BIC/LEN STR in people with HIV who were virologically suppressed on CRs[8,9]
  - At Week 48, switching to BIC/LEN demonstrated noninferior efficacy and comparable safety versus continuing CRs[8,9]
  - Total cholesterol (TC), low-density lipoprotein cholesterol (LDL), triglycerides, and TC:high-density lipoprotein cholesterol (HDL) ratio improved following switch to BIC/LEN[8,9]
  - Body weight remained stable in both the BIC/LEN and CR groups[8]

Objective

- To evaluate 48-week metabolic outcomes stratified by baseline PI use in people with HIV and virologic suppression switching to BIC/LEN versus those remaining on CRs in Phase 3 of ARTISTRY-1

Methods

Phase 3 ARTISTRY-1 Study Design

For patient-reported outcome (PRO) data, please scan the QR code

[a]Due to antiretroviral resistance, intolerance, drug-drug interactions, or contraindication to existing STRs. [b]BIC/LEN 75/50 mg, with oral loading dose of LEN 600 mg on Days 1 and 2 of treatment. [c]BIC/LEN 75/50 mg.
BIC, bictegravir; BMI, body mass index; c, copies; CD4, cluster of differentiation 4; eGFR, estimated glomerular filtration rate; FDA, Food and Drug Administration; HBV, hepatitis B virus; LEN, lenacapavir; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; PI, protease inhibitor; STR, single-tablet regimen.

- All participants who took ≥ 1 dose of the study drug (BIC/LEN or CR) were included in the metabolic outcomes analysis (full analysis set)
- This analysis reports changes from baseline in fasting lipid and glucose parameters, body weight, BMI, and blood pressure at Week 48
- Treatment-emergent dyslipidemia adverse events are also summarized
- Results are presented according to whether participants were receiving a PI-containing or a non–PI-containing ART regimen at baseline
- Changes in fasting lipid parameters are also presented according to use of lipid-lowering treatments (LLTs) at baseline

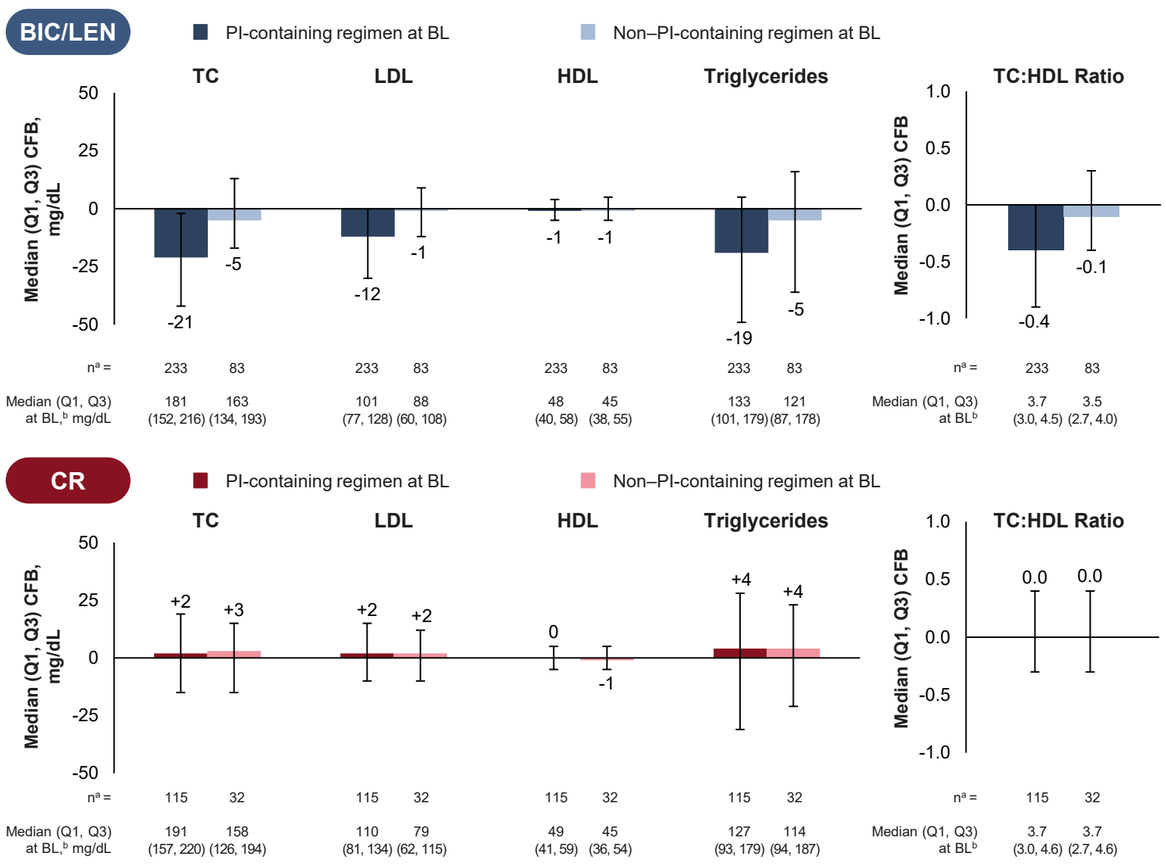
Results

Baseline Demographics and Clinical Characteristics

	BIC/LEN[a]		Complex Regimen	
	PI-Containing Regimen at Baseline n = 279	Non–PI-Containing Regimen at Baseline n = 92	PI-Containing Regimen at Baseline n = 148	Non–PI-Containing Regimen at Baseline n = 38
Age, years, median (range)	60 (22-81)	62 (36-84)	60 (24-75)	61 (49-75)
Female sex at birth, n (%)	43 (15.4)	21 (22.8)	30 (20.3)	6 (15.8)
Race, n (%)[b]				
White	197 (70.6)	63 (68.5)	99 (66.9)	25 (65.8)
Black	53 (19.0)	11 (12.0)	29 (19.6)	4 (10.5)
Asian	13 (4.7)	3 (3.3)	8 (5.4)	1 (2.6)
Other[c]	6 (2.2)	6 (6.5)	3 (2.0)	0
Hispanic or Latine, n (%)[d]	69 (24.7)	11 (12.0)	35 (23.6)	7 (18.4)
Select comorbidities, n (%)[e,f]				
Dyslipidemia	192 (68.8)	52 (56.5)	102 (68.9)	31 (81.6)
Hypertension	134 (48.0)	56 (60.9)	66 (44.6)	24 (63.2)
Hyperglycemia/diabetes mellitus	61 (21.9)	30 (32.6)	26 (17.6)	16 (42.1)
Chronic kidney disease	37 (13.3)	12 (13.0)	21 (14.2)	8 (21.1)
HbA_{1c} at baseline, %, median (Q1, Q3)	5.4 (5.2, 5.7) [n = 271]	5.5 (5.3, 6.0) [n = 90]	5.4 (5.1, 5.7) [n = 139]	5.7 (5.2, 6.1) [n = 38]
In participants with hyperglycemia/diabetes mellitus	6.0 (5.4, 6.8) [n = 59]	6.4 (5.8, 7.2) [n = 29]	6.2 (5.7, 6.7) [n = 26]	6.4 (5.8, 7.2) [n = 16]
Select concomitant non-antiretroviral medications, n (%)[g]				
1	49 (17.6)	13 (14.1)	43 (29.1)	7 (18.4)
≥ 2	180 (64.5)	57 (62.0)	76 (51.4)	26 (68.4)
Antidiabetics	62 (22.2)	22 (23.9)	31 (20.9)	13 (34.2)
Antihypertensives	147 (52.7)	56 (60.9)	74 (50.0)	27 (71.1)
Lipid-lowering agents	205 (73.5)	57 (62.0)	106 (71.6)	28 (73.7)

[a]Two (< 1%) participants in the BIC/LEN group were on an efavirenz-containing regimen at baseline. [b]Local regulators did not allow the collection of race information for 36 participants (BIC/LEN PI-containing regimen at baseline, n = 10; BIC/LEN non–PI-containing regimen at baseline, n = 9; CR PI-containing regimen at baseline, n = 9; CR non–PI-containing regimen at baseline, n = 8); percentages were calculated using total number of participants as the denominator. [c]Category includes American Indian or Alaska Native, Native Hawaiian or Pacific Islander, and Other. [d]Local regulators did not allow the collection of ethnicity information for 37 participants (BIC/LEN PI-containing regimen at baseline, n =12; BIC/LEN non–PI-containing regimen at baseline, n = 9; CR PI-containing regimen at baseline, n = 8; CR non–PI-containing regimen at baseline, n = 8); percentages were calculated using total number of participants as the denominator. [e]Categories are not mutually exclusive. [f]Grouped terms on standardized MedDRA query narrow search. [g]Concomitant medications were those taken while on study drug or complex regimen. Medications collected were coded using WHO Drug Dictionary BMAR25. Select concomitant medications include antidiabetic agents (including drugs with WHO ATC2 "drugs used in diabetes") antihypertensive agents (including drugs with WHO ATC2 "agents acting on the renin-angiotensin system", "antihypertensives" [excluding ATC3 "other antihypertensives"], "beta-blocking agents", "calcium channel blockers", or "diuretics"), and lipid-lowering agents (including drugs with WHO ATC2 "lipid-modifying agents").
ATC, Anatomical Therapeutic Chemical [level]; BIC, bictegravir; HbA_{1c}, hemoglobin A_{1c}; LEN, lenacapavir; MedDRA, Medical Dictionary for Regulatory Activities; PI, protease inhibitor; Q, quartile; WHO, World Health Organization.

Absolute Change From Baseline in Fasting Lipid Parameters at Week 48

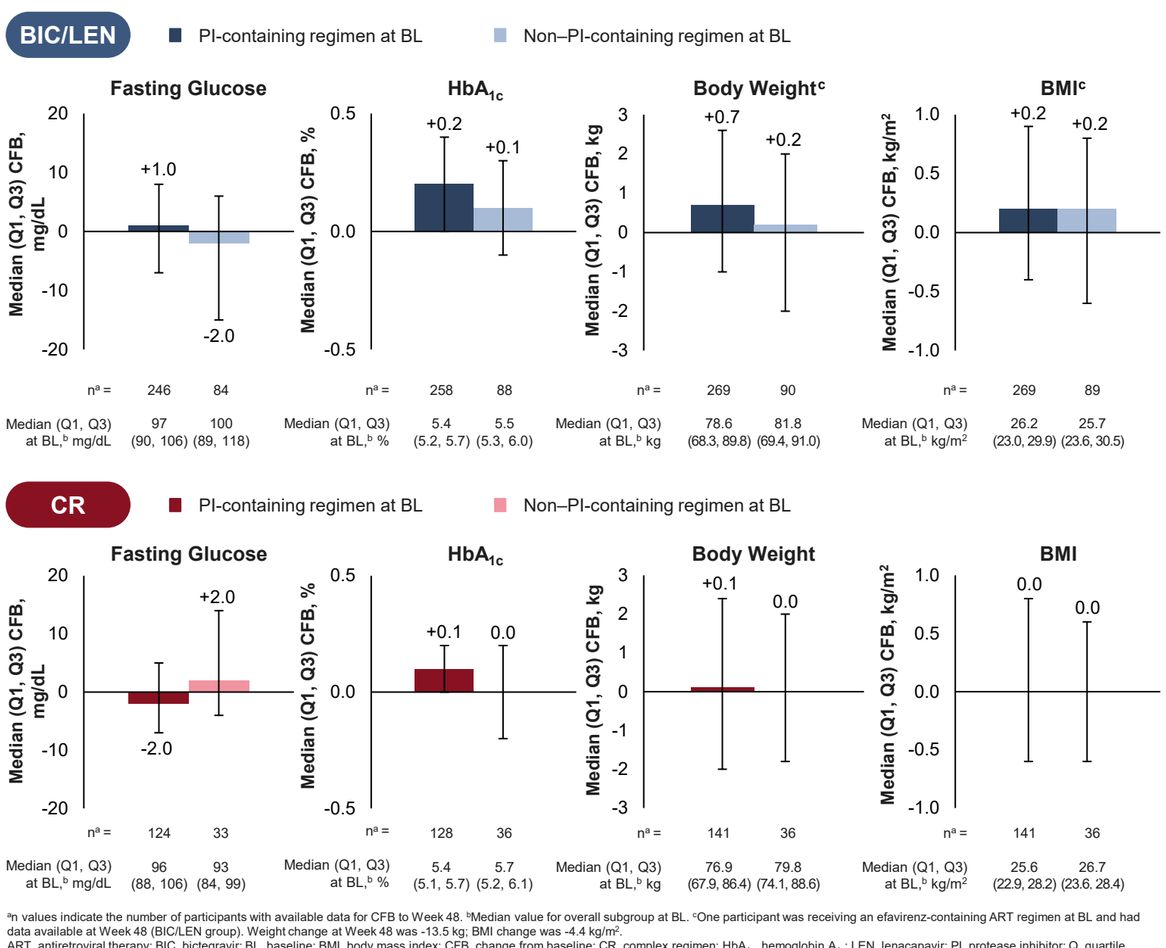


[a]n values indicate the number of participants with available data for CFB to Week 48. [b]Median value for overall subgroup at BL.
BIC, bictegravir; BL, baseline; CFB, change from baseline; CR, complex regimen; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; LEN, lenacapavir; PI, protease inhibitor; Q, quartile; TC, total cholesterol.

- At Week 48, fasting lipid parameters improved from baseline with BIC/LEN versus CR, particularly in participants switching from PI-containing regimens
- Results were similar between participants taking LLTs at baseline and those not taking LLTs

For changes in lipid parameters stratified by LLT use, please scan the QR code

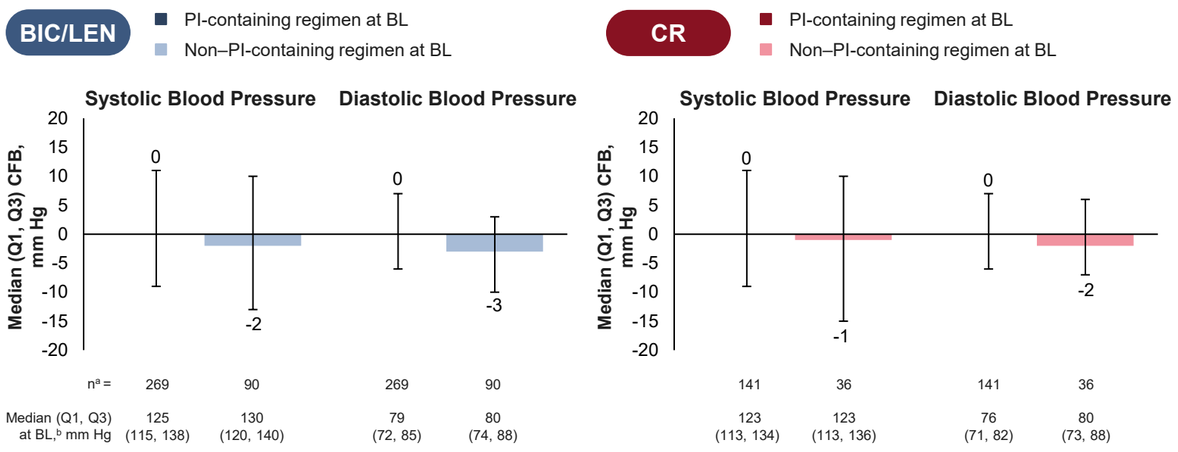
Absolute Change From Baseline in Cardiometabolic Parameters at Week 48



[a]n values indicate the number of participants with available data for CFB to Week 48. [b]Median value for overall subgroup at BL. [c]One participant was receiving an efavirenz-containing ART regimen at BL and had data available at Week 48 (BIC/LEN group). Weight change at Week 48 was -13.5 kg; BMI change was -4.4 kg/m^2.
ART, antiretroviral therapy; BIC, bictegravir; BL, baseline; BMI, body mass index; CFB, change from baseline; CR, complex regimen; HbA_{1c}, hemoglobin A_{1c}; LEN, lenacapavir; PI, protease inhibitor; Q, quartile.

- At Week 48, fasting glucose, HbA_{1c}, body weight, and BMI remained stable in both treatment groups for participants taking PI-containing and non–PI-containing regimens at baseline
- At Week 48, few participants experienced weight gain of > 10% from baseline
  - Among participants in the BIC/LEN group, 3.2% (9/279) of those taking PI-containing regimens and none (0) of those taking non–PI-containing regimens at baseline experienced weight gain of > 10% from baseline
  - Among participants in the CR group, 0.7% (1/148) of those taking PI-containing regimens and none (0) of those taking non–PI-containing regimens at baseline experienced weight gain of > 10% from baseline

Absolute Change From Baseline in Blood Pressure at Week 48



[a]n values indicate the number of participants with available data for CFB to Week 48. [b]Median value for overall subgroup at BL.
BIC, bictegravir; BL, baseline; CFB, change from baseline; CR, complex regimen; LEN, lenacapavir; PI, protease inhibitor; Q, quartile.

- Systolic and diastolic blood pressure remained stable at Week 48 in both treatment groups

Treatment-Emergent Dyslipidemia Adverse Events

	BIC/LEN		Complex Regimen	
	PI-Containing Regimen at Baseline n = 279	Non–PI-Containing Regimen at Baseline n = 92	PI-Containing Regimen at Baseline n = 148	Non–PI-Containing Regimen at Baseline n = 38
Participants with treatment-emergent dyslipidemia adverse events, n (%)[a]	8 (2.9)	2 (2.2)	4 (2.7)	0
Hypercholesterolemia	1 (0.4)	1 (1.1)	2 (1.4)	0
Dyslipidemia	2 (0.7)	0	1 (0.7)	0
Hyperlipidemia	2 (0.7)	0	1 (0.7)	0
Hypertriglyceridemia	2 (0.7)	1 (1.1)	0	0
Low-density lipoprotein increased	0	0	1 (0.7)	0
Type V hyperlipidemia	1 (0.4)	0	0	0

[a]Grouped terms on standardized MedDRA query narrow search. Treatment-emergent metabolic disorders began on or after study drug start date and up to 60 days after permanent discontinuation of study drugs in the BIC/LEN group, or on or after Day 1 and up to 30 days after permanent discontinuation of a CR in the CR group. Multiple adverse events were counted only once per participant.
BIC, bictegravir; CR, complex regimen; LEN, lenacapavir; MedDRA, Medical Dictionary for Regulatory Activities; PI, protease inhibitor.

- Few participants experienced treatment-emergent dyslipidemia across all groups

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