Metabolic Changes at 48 Weeks in Virologically Suppressed People With HIV Switching From Complex Antiretroviral Regimens to Bictegravir Plus Lenacapavir: ARTISTRY-1 Trial

P050

ARTISTRY-1

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Conclusions

- In this analysis of participants enrolled in the ARTISTRY-1 trial (including data through 48 weeks), fasting lipid parameters generally improved after switching from baseline complex ART regimens to BIC + LEN
- None of the studied treatments had a clinically significant impact on body weight or BMI
- A small proportion of participants in all three treatment groups experienced treatment-emergent metabolic disorders
- Phase 3 studies are underway to confirm the efficacy and safety of BIC and LEN combination therapy in PWH

Plain Language Summary

- BIC + LEN is a human immunodeficiency virus (HIV) treatment where the medicines bictegravir (BIC) and lenacapavir (LEN) are taken together once a day
- Some people need complex treatments for their HIV that involve taking multiple pills, taking pills more than once a day, or taking a combination of pills and injections
  - They may need a complex treatment because their HIV is resistant to other treatments, or because they have side effects to other treatments
- BIC + LEN may be another option instead of complex treatments
- The ARTISTRY-1 study looks at how well BIC + LEN works, and if it is safe for people switching from complex treatments
- Previously, this study showed that BIC + LEN stopped HIV from showing in the blood in people with HIV during 48 weeks of treatment
- In this analysis from the study, researchers wanted to compare BIC + LEN and complex treatment to see if there were any effects on fat in the blood (cholesterol), body weight, or changes in the way the body breaks down food into energy (metabolism)
- 48 weeks after switching from a complex treatment to BIC + LEN, researchers found that BIC + LEN:
  - Lowered levels of cholesterol and other fats in the blood
  - Did not affect body weight or the way the body breaks down food into energy

Introduction

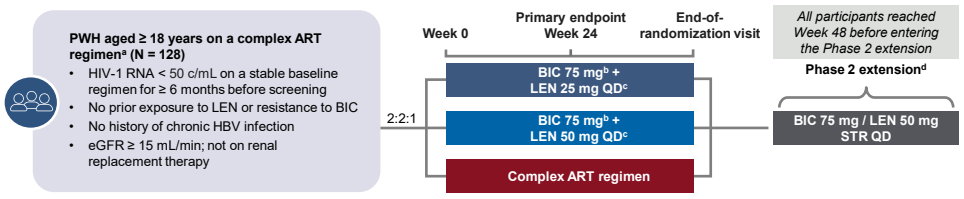
- Bictegravir (BIC) and lenacapavir (LEN) combination therapy is being developed as an alternative to complex antiretroviral therapy (ART) regimens for people with HIV (PWH) who are unable to use single tablet regimens (eg, due to drug resistance, intolerance, toxicity, drug-drug interactions, or contraindications)
  - BIC is an integrase strand transfer inhibitor (INSTI) with a high barrier to resistance[1]
  - LEN is a first-in-class capsid inhibitor, expected to have an absence of resistance mutations in unexposed PWH[2]
- BIC + LEN could help optimize treatment in PWH and reduce the risk of metabolic complications
- ARTISTRY-1 (NCT05502341) is an ongoing, randomized, open-label, multicenter, Phase 2/3 trial evaluating the efficacy and safety of switching from complex ART regimens to BIC + LEN in virologically suppressed PWH[3,4]
- The Phase 2 portion of ARTISTRY-1 demonstrated that BIC + LEN was highly effective in maintaining virologic suppression and well tolerated over 48 weeks in participants switching from a complex ART regimen
  - At Week 48, 92% and 90% of participants had HIV-1 RNA < 50 copies/mL with BIC 75 mg + LEN 25 mg and with BIC 75 mg + LEN 50 mg, respectively[3]
  - Similar safety profiles were observed regardless of LEN dose
- Metabolic outcomes with BIC + LEN have not yet been reported

Objective

- To evaluate Week 48 metabolic outcomes for BIC + LEN versus complex ART regimens in virologically suppressed PWH participating in Phase 2 of the ARTISTRY-1 trial

Methods

Study Design



A complex ART regimen was defined as:
- A regimen containing a boosted PI or NNRTI plus ≥ 1 other third agent from a class other than NRTI, or
- A regimen of ≥ 2 pills/day, or
- A regimen requiring more frequent dosing than QD, or
- A regimen containing parenteral agent(s) (excluding a complete long-acting injectable regimen) as well as oral agents

Endpoints at Week 48:
- Proportions of participants with HIV-1 RNA < 50 c/mL (US FDA Snapshot analysis)
- Change from baseline in CD4 cell count
- Proportion of participants with adverse events
- Changes from baseline in fasting lipid and glucose parameters, body weight, BMI, and blood pressure

[a]Due to viral resistance, intolerance, or contraindication to existing STRs. [b]BIC 75 mg single agent provides exposure consistent with BIC 50 mg as part of B/F/TAF. [c]All participants receiving BIC + LEN received an oral loading dose of LEN 600 mg on Days 1 and 2 of treatment. [d]Participants who switch from a complex ART regimen in the extension phase will receive the oral loading doses of LEN.
ART, antiretroviral therapy; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; BIC, bictegravir; 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; PWH, people with HIV; QD, once daily; STR, single tablet regimen.

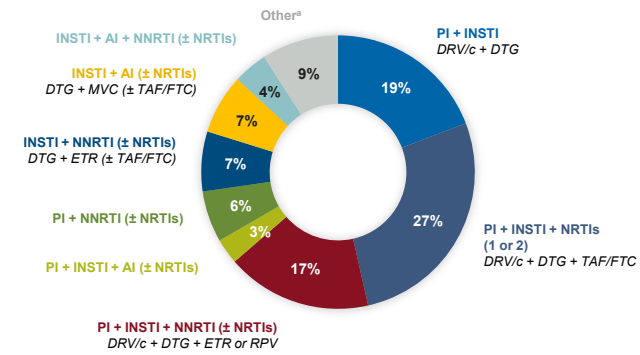
Results

Baseline Demographics and Clinical Characteristics

	BIC 75 mg + LEN 25 mg (n = 51)	BIC 75 mg + LEN 50 mg (n = 52)	Complex ART Regimen (n = 25)	Total (N = 128)
Age, years, median (range)	62 (26-79)	62 (34-76)	58 (41-70)	60 (26-79)
Assigned female at birth, n (%)	13 (25)	7 (13)	4 (16)	24 (19)
Race, n (%)				
Asian	2 (4)	2 (4)	0	4 (3)
Black	18 (35)	16 (31)	5 (20)	39 (30)
White	29 (57)	34 (65)	20 (80)	83 (65)
Other	2 (4)	0	0	2 (2)
Hispanic/Latine ethnicity,[a] n (%)	7 (14)	9 (18)	4 (16)	20 (16)
BMI, kg/m², median (Q1, Q3)	27 (23, 30)	26 (23, 31)	26 (24, 28)	26 (23, 30)
ART pills/day, median (range)	2 (2-8)	3 (2-9)	3 (2-8)	3 (2-9)
Number of prior ARTs, median (range)	4 (2-21)	7 (2-23)	8 (2-18)	6 (2-23)
Reasons for taking a complex regimen,[b] n (%)				
History of resistance	44 (86)	40 (77)	20 (80)	104 (81)
Intolerance to components of STRs	20 (39)	11 (21)	7 (28)	38 (30)
Contraindication to STRs	7 (14)	4 (8)	1 (4)	12 (9)
History of selected medical conditions,[b,c] n (%)				
Dyslipidemia	39 (76)	37 (71)	20 (80)	96 (75)
Diabetes mellitus	36 (71)	36 (69)	16 (64)	88 (69)
Hypertension	34 (67)	29 (56)	15 (60)	78 (61)
Chronic kidney disease	12 (24)	14 (27)	5 (20)	31 (24)

[a]Local regulators did not allow collection of ethnicity information for one participant in the BIC 75 mg + LEN 25 mg group and one participant in the BIC 75 mg + LEN 50 mg group. [b]Categories are not mutually exclusive. [c]Grouped SMQ terms.
ART, antiretroviral therapy; BIC, bictegravir; LEN, lenacapavir; Q, quartile; SMQ, Standardized Medical Dictionary for Regulatory Activities Query; STR, single tablet regimen.

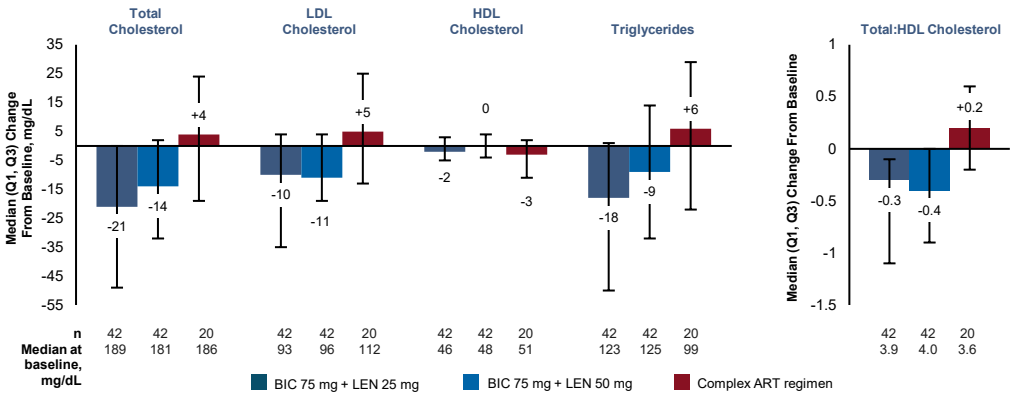
Complexity of ART Regimens in Phase 2



N = 128. The most common regimen(s) are shown in italics in each regimen category box; this is not an exhaustive list. Percentages do not sum to 100% due to rounding.
[a]Can contain PI.
AI, attachment inhibitor; ART, antiretroviral therapy; DRV/c, darunavir/cobicistat; DTG, dolutegravir; ETR, etravirine; FTC, emtricitabine; INSTI, integrase strand transfer inhibitor; MVC, maraviroc; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; PI, protease inhibitor; RPV, rilpivirine; TAF, tenofovir alafenamide.

- Overall, 41% (n = 53) of participants were taking ART dosed twice daily at baseline
- At baseline, 43%, 19%, 11%, and 27% of participants were taking 2, 3, 4, or ≥ 5 pills/day

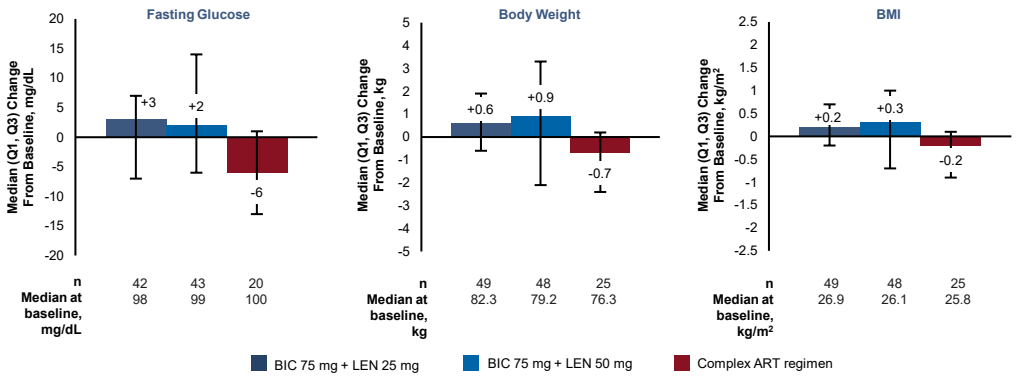
Absolute Change From Baseline in Fasting Lipid Parameters at Week 48



n numbers indicate the number of participants with available data for change from baseline to Week 48.
ART, antiretroviral therapy; BIC, bictegravir; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LEN, lenacapavir; Q, quartile.

- At Week 48, fasting lipid parameters generally improved from baseline in both BIC + LEN groups versus the complex ART regimen group

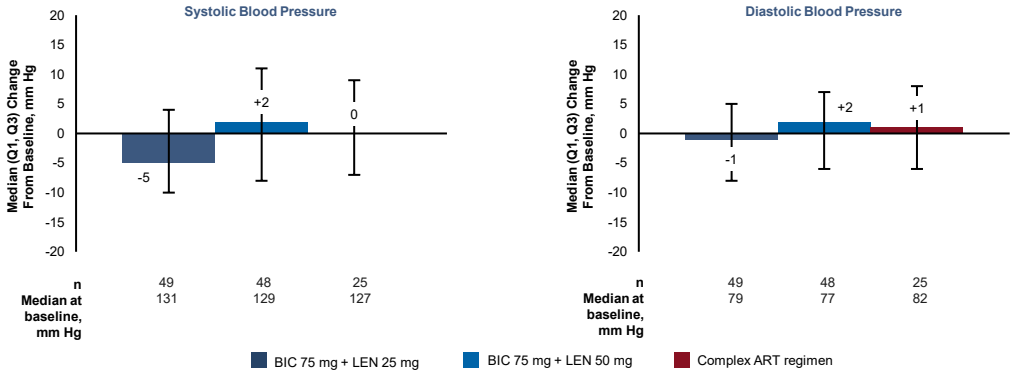
Absolute Change From Baseline in Fasting Glucose, Body Weight, and BMI at Week 48



n numbers indicate the number of participants with available data for change from baseline to Week 48.
ART, antiretroviral therapy; BIC, bictegravir; LEN, lenacapavir; Q, quartile.

- Fasting glucose, body weight and BMI remained stable at Week 48 in all groups

Blood Pressure at Week 48



n numbers indicate the number of participants with available data for change from baseline to Week 48.
ART, antiretroviral therapy; BIC, bictegravir; LEN, lenacapavir; Q, quartile.

- Systolic/diastolic blood pressure was comparable between treatment groups at both baseline and Week 48, and remained stable at Week 48 in all groups

Treatment-Emergent Metabolic Disorders

Treatment-Emergent Metabolic Disorder,[a] n (%)	BIC 75 mg + LEN 25 mg (n = 51)	BIC 75 mg + LEN 50 mg (n = 52)	Complex ART Regimen (n = 25)
Dyslipidemia	0	0	0
Diabetes	2 (4)	2 (4)	1 (4)
Hypertension	1 (2)	6 (12)[b]	1 (4)
Chronic kidney disease	3 (6)	1 (2)	1 (4)

[a]Grouped SMQ terms. Treatment-emergent metabolic disorders began on or after study drug start date and up to 60 days after permanent discontinuation of BIC or LEN in the BIC + LEN groups, or on or after Day 1 and up to 30 days after permanent discontinuation of a complex regimen in the complex ART regimen group. Multiple adverse events were counted only once per participant.
[b]Includes hypertension (n = 5) and hypertensive crisis (n = 1); none of the events were considered drug related; all cases were reported in participants with abnormal blood pressure values at baseline (systolic > 120 mm Hg, diastolic > 80 mm Hg).
ART, antiretroviral therapy; BIC, bictegravir; LEN, lenacapavir; SMQ, Standardized Medical Dictionary for Regulatory Activities Query.

- Treatment-emergent metabolic disorders were generally balanced across treatment groups, with a higher proportion of participants in the BIC 75 mg + LEN 50 mg group experiencing treatment-emergent hypertension

References: **1.** Acosta RK, et al. *Antimicrob Agents Chemother*. 2019;63:e02533-18. **2.** Dvory-Sobol H, et al. *Curr Opin HIV AIDS*. 2022;17:15-21. **3.** Mounzer K, et al. Oral OAB2602 presented at: AIDS; July 22-26, 2024; Munich, Germany. **4.** Mounzer K, et al. Poster 642 presented at: CROI; March 3-6, 2024; Denver, CO, USA.

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