Efficacy and Safety of Bictegravir Plus Lenacapavir: 48-Week Outcomes in Virologically Suppressed People With HIV-1 on Complex Antiretroviral Regimens at Baseline

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Disclosures

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Summary Slide

What is your main question?

We investigated whether the combination of BIC plus LEN could maintain viral suppression in people with HIV who currently take complex antiretroviral regimens.

What did you find?

Our results demonstrated that coadministration of BIC 75 mg and LEN 25 mg or 50 mg effectively maintained viral suppression over 48 weeks in participants switching from a complex regimen, and was well tolerated.

Why is it important?

This study has laid the foundations for the development of the BIC/LEN single-tablet regimen. For people with HIV who are unable to take a once daily single-tablet regimen, the combination of BIC and LEN may offer a way to optimize their treatment regimen.

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BIC, bictegravir; **LEN**, lenacapavir; **QR**, quick response.

Background

- Once-daily STRs are the global standard for HIV treatment[1]
- However, many PWH take complex antiretroviral treatment regimens for reasons including drug resistance, intolerance, toxicity, drug-drug interactions, or contraindications to existing STRs[1-4]
- An STR of BIC and LEN could optimize treatment in VS PWH who are unable to take currently available STRs
  - BIC is a global guideline-recommended INSTI with a high barrier to resistance[1,5-7]
  - LEN is a first-in-class capsid inhibitor without documented *de novo* resistance in the absence of prior exposure[8]

BIC, bictegravir; **INSTI**, integrase strand transfer inhibitor; **LEN**, lenacapavir; **PWH**, people with HIV; **STR**, single-tablet regimen; **VS**, virologically suppressed.

1. DHHS. https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/guidelines-adult-adolescent-arv.pdf (accessed April 23, 2024). 2. Chang HM, et al. *BMC Infect Dis.* 2022;22:2. 3. Rolle C-P, et al. *J Virus Erad*. 2020;6:100021. 4. Colloty J, et al. *Br J Hosp Med (Lond)*. 2023;84:1-9. 5. Acosta RK, et al. *Antimicrob Agents Chemother.* 2019;63:e02533-18. 6. EACS. https://www.eacsociety.org/media/guidelines-12.0.pdf (accessed July 10, 2024). 7. Gandhi RT, et al. *JAMA*. 2023;329(1):63-84. 8. Dvory-Sobol H, et al. *Curr Opin HIV AIDS*. 2022;17:15-21.

Objective

- ARTISTRY-1 is a Phase 2/3, randomized, open-label, multicenter study investigating the efficacy and safety of switching to oral daily BIC 75 mg plus either LEN 25 mg or LEN 50 mg versus continuing on a complex antiretroviral regimen
  - Primary 24-week outcome data, presented at CROI 2024, showed that BIC + LEN was highly effective in maintaining virologic suppression and was well tolerated in participants switching from a complex antiretroviral regimen[1]
- Here we report longer-term efficacy and safety data from ARTISTRY-1 through 48 weeks of treatment

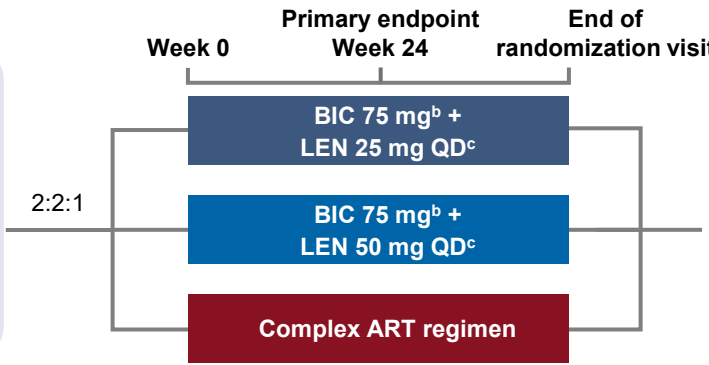
BIC, bictegravir; **CROI**, Conference on Retroviruses and Opportunistic Infections; **LEN**, lenacapavir.
1. Mounzer K, et al. Poster 642 presented at: CROI; March 3-6, 2024; Denver, CO, USA.

Study Design of Phase 2 of ARTISTRY-1 (NCT05502341)

- ARTISTRY-1 is a Phase 2/3, randomized, open-label, multicenter study

Adults aged ≥ 18 years on a complex ART regimen[a] (N = 128)

- HIV-1 RNA < 50 c/mL on stable baseline regimen for ≥ 6 months prior to screening
- No prior exposure to LEN or resistance to BIC
- No history of chronic HBV infection
- eGFR ≥ 15 mL/min; not on renal replacement therapy



All participants reached Week 48 before entering the Phase 2 extension

Phase 2 extension[d]

BIC 75 mg / LEN 50 mg FDC QD

A **complex antiretroviral 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 dosing more 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, determined using US FDA Snapshot analysis
- Change from baseline in CD4 cell count
- Proportion of participants with AEs

[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 antiretroviral regimen in the extension phase will receive the oral loading doses of LEN.

AE, adverse event; **ART**, antiretroviral therapy; **BIC**, bictegravir; **c**, copies; **CD**, cluster of differentiation; **eGFR**, estimated glomerular filtration rate; **FDA**, Food and Drug Administration; **FDC**, fixed-dose combination; **HBV**, hepatitis B virus; **LEN**, lenacapavir; **NNRTI**, non-nucleoside reverse transcriptase inhibitor; **NRTI**, nucleos(t)ide reverse transcriptase inhibitor; **PI**, protease inhibitor; **QD**, once daily; **STR**, single-tablet regimen.

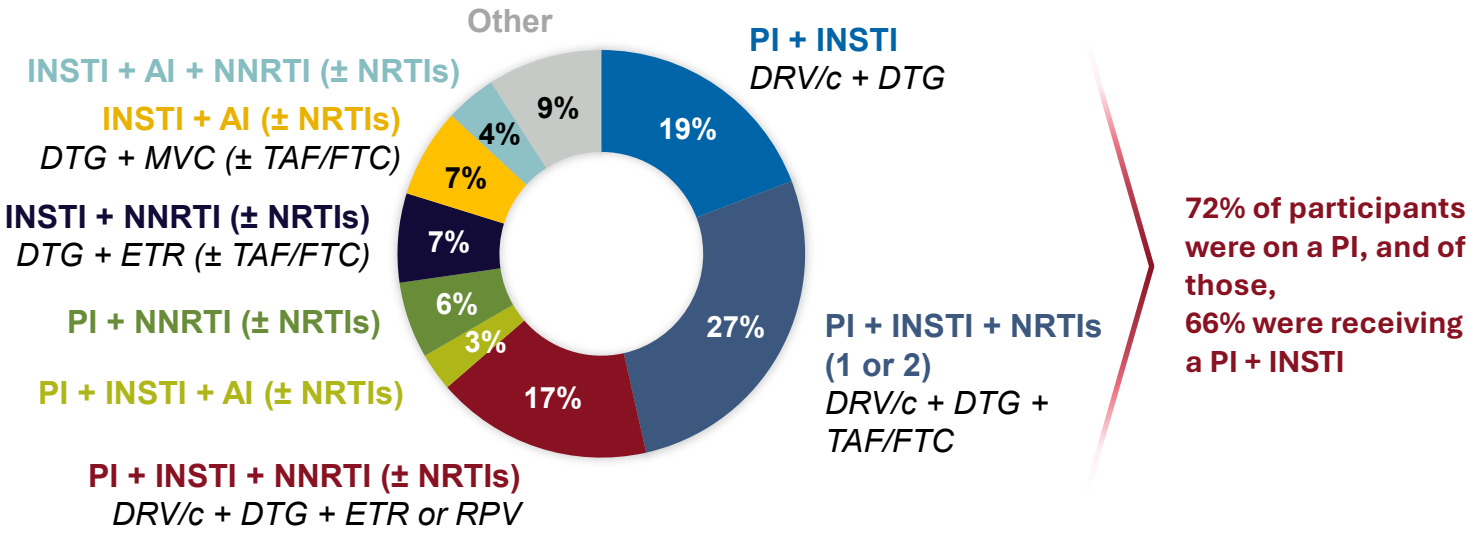
Demographic and Disease Characteristics

	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)
Female at birth, n (%)	13 (25.5)	7 (13.5)	4 (16.0)	24 (18.8)
Race, n (%)				
Asian	2 (3.9)	2 (3.8)	0	4 (3.1)
White	29 (56.9)	34 (65.4)	20 (80.0)	83 (64.8)
Black	18 (35.3)	16 (30.8)	5 (20.0)	39 (30.5)
Other	2 (3.9)	0	0	2 (1.6)
Hispanic or Latinx,[a] n (%)	7 (14.0)	9 (17.6)	4 (16.0)	20 (15.9)
CD4 count, cells/μL, median (Q1, Q3)	583 (460, 764)	624 (517, 791)	585 (285, 733)	610 (435, 766)
Past medical history of AIDS, n (%)	14 (27.5)	10 (19.2)	2 (8.0)	26 (20.3)
Duration of HIV treatment, years,[b,c] median (Q1, Q3)	27.8 (22.7, 32.4)	27.0 (18.9, 31.5)	26.9 (19.8, 31.9)	27.0 (19.9, 32.0)
Number of prior ARTs, median (Q1, Q3)	4.0 (2.0, 9.0)	7.0 (3.0, 11.0)	8.0 (3.0, 13.0)	6.0 (3.0, 11.0)
Reasons for taking a complex regimen,[d] n (%)				
History of resistance	44 (86.3)	40 (76.9)	20 (80.0)	104 (81.3)
Intolerance to components of STRs	20 (39.2)	11 (21.2)	7 (28.0)	38 (29.7)
Contraindication to STRs	7 (13.7)	4 (7.7)	1 (4.0)	12 (9.4)
Historical resistance mutations,[e] n (%)				
INSTI	0	0	0	0
NNRTI	25 (49.0)	28 (53.8)	14 (56.0)	67 (52.3)
NRTI	31 (60.8)	35 (67.3)	16 (64.0)	82 (64.1)
PI	18 (35.3)	17 (32.7)	11 (44.0)	46 (35.9)

[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]Duration of HIV treatment = (first dose date - start date of the first HIV treatment + 1 day)/365.25. [c]n = 50 for BIC 75 mg + LEN 25 mg group as this information was not available for one participant. [d]Categories are not mutually exclusive. [e]Alternative response was no or not available; historical resistance mutations were available for 39% (INSTI), 73% (NNRTI), 75% (NRTI) and 73% (PI) participants

ART, antiretroviral therapy; **BIC**, bictegravir; **CD**, cluster of differentiation; **INSTI**, integrase strand transfer inhibitor; **LEN**, lenacapavir; **NNRTI**, non-nucleoside reverse transcriptase inhibitor; **NRTI**, nucleos(t)ide reverse transcriptase inhibitor; **PI**, protease inhibitor; **Q**, quartile; **STR**, single-tablet regimen.

Complexity of ART Regimens in Phase 2

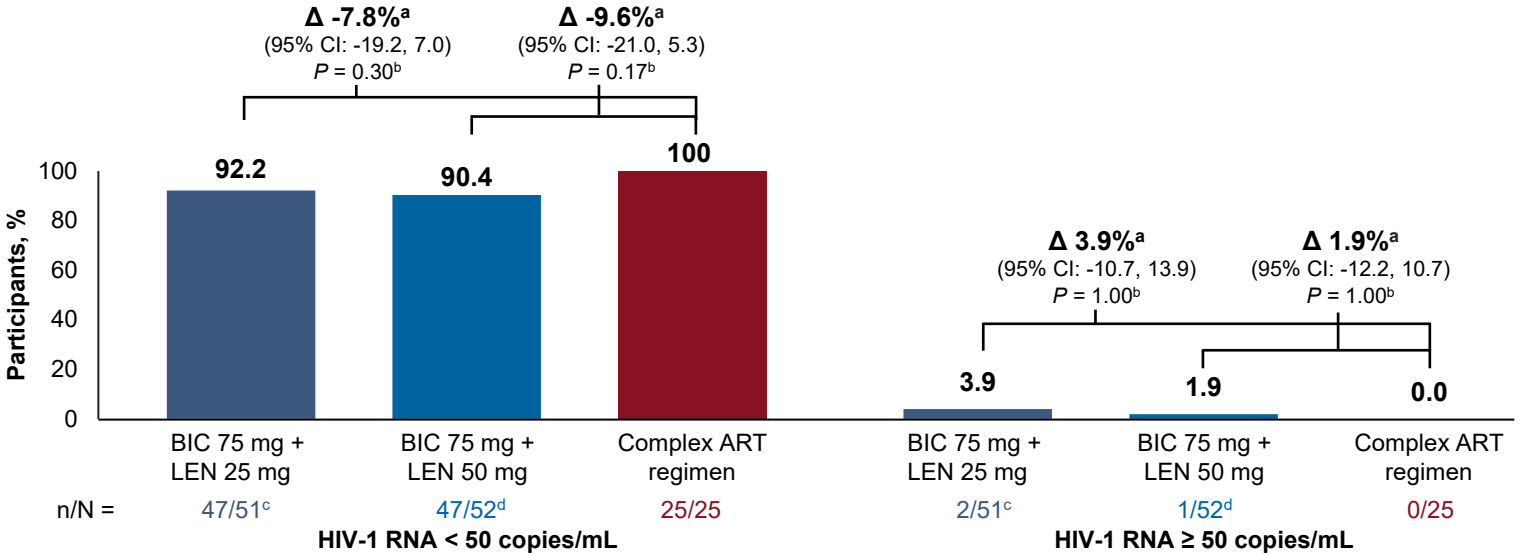


N = 128. The most common regimen(s) are shown in italics in each regimen category box; this is not an exhaustive list.
Percentages do not sum to 100% due to rounding.

- Overall, 41.4% (n = 53) of participants were taking ART dosed twice daily at baseline
- At baseline, 43.0%, 18.8%, 10.9%, and 27.3% of participants were taking 2, 3, 4, or ≥ 5 pills/day

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**, nucleos(t)ide reverse transcriptase inhibitor; **PI**, protease inhibitor; **RPV**, rilpivirine; **TAF**, tenofovir alafenamide.

Virologic Suppression at Week 48 (US FDA Snapshot Analysis)



[a]Difference in % (95% CI): BIC + LEN - complex ART regimen calculated based on an unconditional exact method using two inverted one-sided tests. [b]Based on Fisher exact test.
[c]Two participants had no virologic data in the Week 48 window as they discontinued study drug before Week 48 visit; one participant due to AE and one participant due to participant decision.
[d]Four participants had no virologic data in the Week 48 window as they discontinued study drug before Week 48 visit due to AE, death, participant decision, and investigator decision (n = 1 for each).

- Rates of virologic suppression were high across all treatment groups at Week 48
- Changes in CD4 cell count and percentage were comparable among groups

AE, adverse event; **ART**, antiretroviral therapy; **BIC**, bictegravir; **CD**, cluster of differentiation; **CI**, confidence interval; **FDA**, Food and Drug Administration; **LEN**, lenacapavir.

Virologic Suppression at Week 48 (US FDA Snapshot Analysis)

	BIC 75 mg + LEN 25 mg n = 51	BIC 75 mg + LEN 50 mg n = 52	Complex ART Regimen n = 25
HIV-1 RNA < 50 c/mL	47 (92.2)	47 (90.4)	25 (100)
HIV-1 RNA ≥ 50 c/mL	2 (3.9)	1 (1.9)	0
No virologic data in Week 48 window	2 (3.9)	4 (7.7)	0
Discontinued due to AE/death and last available HIV-1 RNA < 50 c/mL	1 (2.0)[a]	2 (3.8)[b]	0
Discontinued due to other reasons and last available HIV-1 RNA < 50 c/mL	1 (2.0)[a]	2 (3.8)[b]	0

Data shown as n (%). N-values represent numbers of participants.
[a]Two participants had no virologic data in the Week 48 window as they discontinued study drug before Week 48 visit; one participant due to AE and one participant due to participant decision. [b]Four participants had no virologic data in the Week 48 window as they discontinued study drug before Week 48 visit due to AE, death, participant decision, and investigator decision (n = 1 for each).

AE, adverse event; **ART**, antiretroviral therapy; **BIC**, bictegravir; **c**, copies; **FDA**, Food and Drug Administration; **LEN**, lenacapavir.

TEAEs up to Week 48

	BIC 75 mg + LEN 25 mg n = 51	BIC 75 mg + LEN 50 mg n = 52	Complex ART Regimen n = 25
≥ 1 TEAE	42 (82.4)	41 (78.8)	19 (76.0)
≥ 1 TEAE of Grade 3 or higher	7 (13.7)	4 (7.7)	1 (4.0)
≥ 1 TEAE leading to premature treatment discontinuation	1[a] (2.0)	1[b] (1.9)	0
≥ 1 treatment-related TEAE	9 (17.6)	3 (5.8)	0
≥ 1 serious TEAE	4[c] (7.8)	3[c] (5.8)	3[c] (12.0)
Death	0	1[c,d] (1.9)	0

Data shown as n (%). N-values represent numbers of participants. Only AEs with onset date on or before the nominal Week 48 visit date were included in this summary.
[a]Grade 1 nausea on Day 1. [b]Grade 3 worsening of vomiting in a participant with preexisting episodes of nausea and vomiting. [c]Unrelated to study treatment.
[d]Cause of death: coronary artery disease.

- BIC + LEN was well tolerated, with few TEAEs leading to premature treatment discontinuation

AE, adverse event; **ART**, antiretroviral therapy; **BIC,** bictegravir; **LEN**, lenacapavir; **TEAE**, treatment-emergent adverse event.

TEAEs by Preferred Term up to Week 48 (Frequency ≥ 5%)

	BIC 75 mg + LEN 25 mg n = 51	BIC 75 mg + LEN 50 mg n = 52	Complex ART Regimen n = 25
≥ 1 TEAE	42 (82.4)	41 (78.8)	19 (76.0)
COVID-19	8 (15.7)	5 (9.6)	4 (16.0)
Upper respiratory tract infection	3 (5.9)	4 (7.7)	2 (8.0)
Diarrhea	5 (9.8)	2 (3.8)	1 (4.0)
Arthralgia	3 (5.9)	4 (7.7)	0
Cough	4 (7.8)	3 (5.8)	0
Hypertension	1 (2.0)	5 (9.6)	1 (4.0)
Nasopharyngitis	5 (9.8)	0	1 (4.0)
Constipation	3 (5.9)	2 (3.8)	0
Nausea	3 (5.9)	2 (3.8)	0
Pain in extremity	1 (2.0)	3 (5.8)	1 (4.0)
Benign prostatic hyperplasia	1 (2.0)	1 (1.9)	2 (8.0)
Vertigo	3 (5.9)	0	0
Herpes zoster	0	0	2 (8.0)

Data shown as n (%). N-values represent numbers of participants. Only AEs with onset date on or before the nominal Week 48 visit date were included. Preferred Terms of AEs experienced by ≥ 5% of participants in ≥ 1 of the treatment groups are shown.

- All TEAEs with frequency ≥ 5% were Grade 1 or 2 apart from one report of Grade 3 diarrhea, which was unrelated to study drug

AE, adverse event; **ART**, antiretroviral therapy; **BIC**, bictegravir; **LEN**, lenacapavir; **TEAE**, treatment-emergent adverse event.

Conclusions

- BIC + LEN was highly effective in maintaining viral suppression over 48 weeks in participants switching from a complex regimen
- BIC + LEN was well tolerated through 48 weeks, with similar safety profiles observed regardless of LEN dose
- These findings support the continued evaluation of the combination of BIC and LEN to optimize treatment in VS people with HIV who are receiving complex regimens
- A BIC 75 mg/LEN 50 mg STR will be assessed in the Phase 3 part of this study; additional data from Phase 2 and Phase 3 will be presented at future congresses

BIC, bictegravir; **LEN**, lenacapavir; **STR**, single-tablet regimen; **VS**, virologically suppressed.

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