

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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Background

- Once-daily STRs are the global standard for HIV treatment¹
- However, many PWH take complex antiretroviral treatment regimens for reasons including drug resistance, intolerance, toxicity, drug-drug interactions, or contraindications to existing STRs¹⁻⁴
- 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 exposure⁸

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

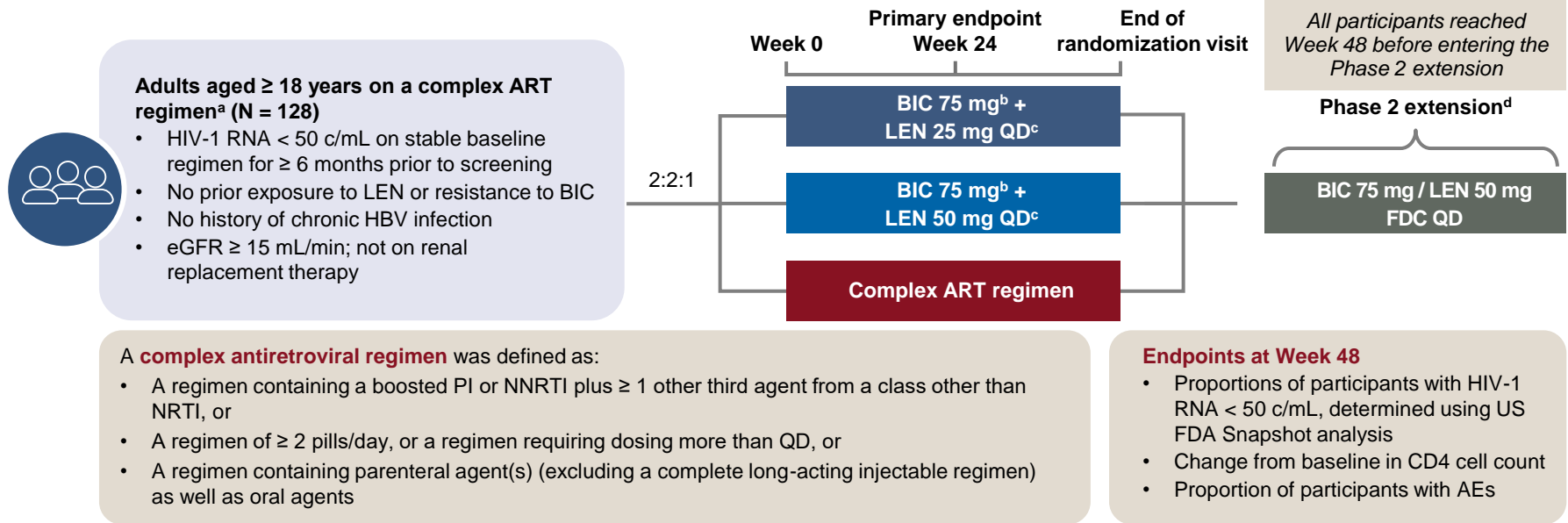
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Objective

- 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 regimen¹
- Here we report longer-term efficacy and safety data from ARTISTRY-1 through 48 weeks of treatment

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

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



^aDue to viral resistance, intolerance, or contraindication to existing STRs. ^bBIC 75 mg single agent provides exposure consistent with BIC 50 mg as part of B/F/TAF. ^cAll participants receiving BIC + LEN received an oral loading dose of LEN 600 mg on Days 1 and 2 of treatment. ^dParticipants who switch from a complex antiretroviral regimen in the extension phase will receive the oral loading doses of LEN.

Demographic and Disease Characteristics

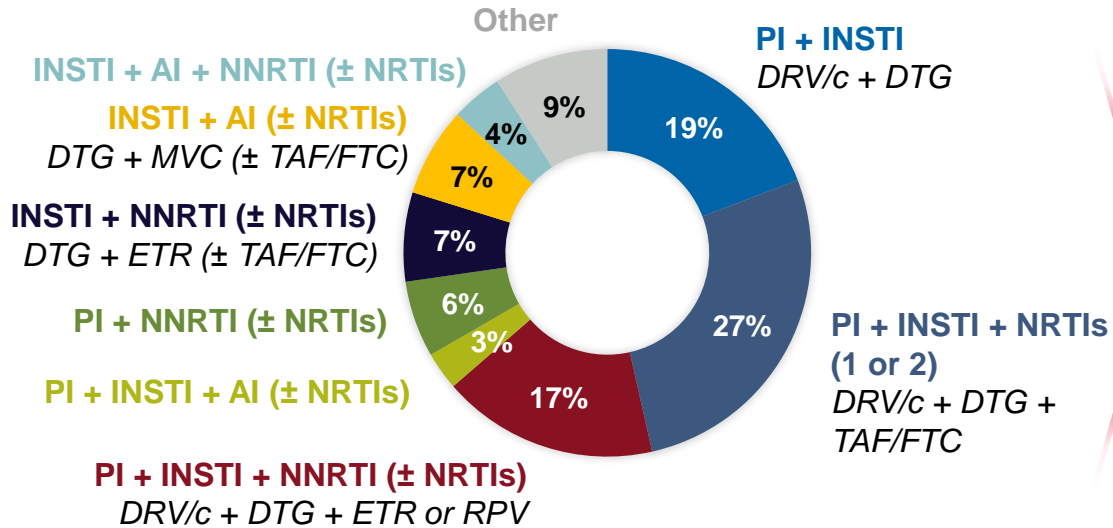
| | BIC 75 mg + LEN 25 mg n = 51 | BIC 75 mg + LEN 50 mg n = 52 | Complex ART Regimen n = 25 | Total N = 128 |
|--|---------------------------------|---------------------------------|-------------------------------|-------------------|
| Age, years, median (range) | 62 (26, 79) | 62 (34, 76) | 58 (41, 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) |

^aLocal 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.

^bDuration of HIV treatment = (first dose date - start date of the first HIV treatment + 1 day)/365.25. ^cn = 50 for BIC 75 mg + LEN 25 mg group as this information was not available for one participant.

^dCategories are not mutually exclusive. ^eAlternative response was no or not available; historical resistance mutations were available for 39% (INSTI), 73% (NNRTI), 75% (NRTI) and 73% (PI) participants

Complexity of ART Regimens in Phase 2

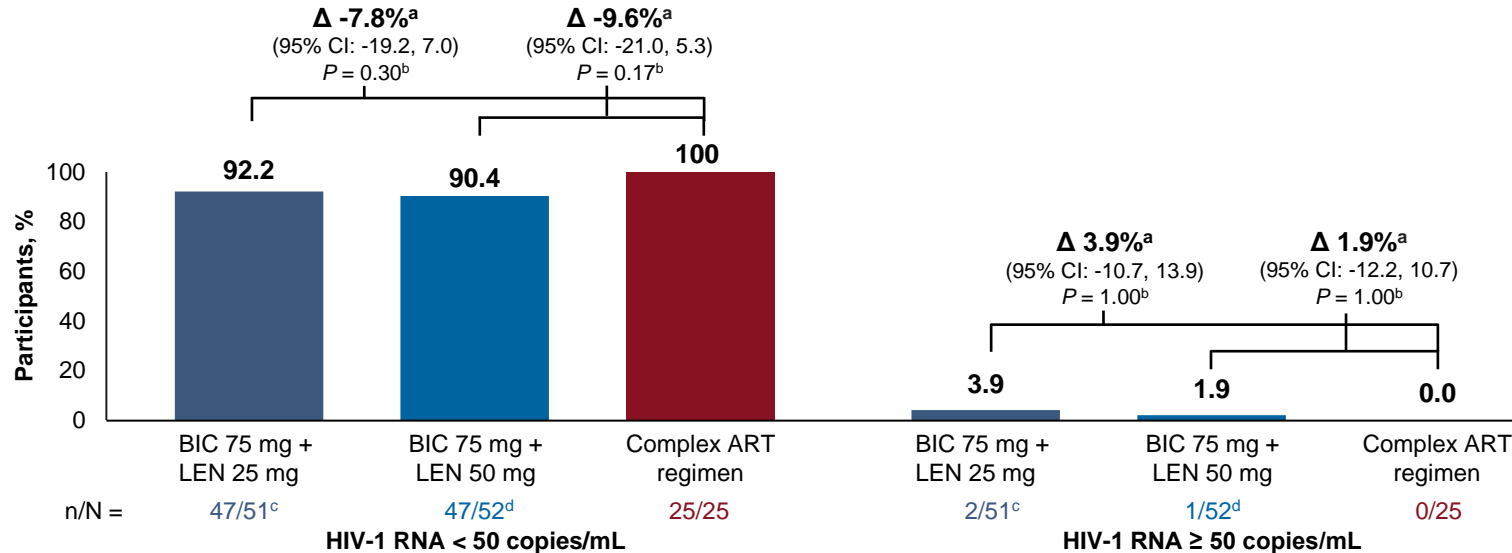


72% of participants were on a PI, and of those, 66% were receiving a PI + INSTI

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

Virologic Suppression at Week 48 (US FDA Snapshot Analysis)



^aDifference in % (95% CI): BIC + LEN - complex ART regimen calculated based on an unconditional exact method using two inverted one-sided tests. ^bBased on Fisher exact test.

^cTwo 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.

^dFour 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

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.

^aTwo 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. ^bFour 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).

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.

^aGrade 1 nausea on Day 1. ^bGrade 3 worsening of vomiting in a participant with preexisting episodes of nausea and vomiting. ^cUnrelated to study treatment.

^dCause of death: coronary artery disease.

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

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

| | BIC 75 mg + LEN 25 mg n = 51 | BIC 75 mg + LEN 50 mg n = 52 | Complex ART Regimen n = 25 |
|-----------------------------------|------------------------------------|------------------------------------|----------------------------------|
| \geq 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 \geq 5% of participants in \geq 1 of the treatment groups are shown.

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

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

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