Baseline and Week 48 Resistance Analyses in the Phase 3 ARTISTRY-1 Study Evaluating the Bictegravir/Lenacapavir Single-Tablet Regimen

THPEB101

ARTISTRY-1

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Conclusions

- At Week 48 in ARTISTRY-1, bictegravir/lenacapavir (BIC/LEN) single-tablet regimen (STR) maintained high rates of virologic suppression despite a high frequency of resistance-associated mutations (RAMs) at baseline
  - Overall, 96% treatment success was observed, regardless of baseline RAMs, including baseline integrase strand-transfer inhibitor (INSTI) RAMs
- No treatment-emergent resistance occurred in either treatment group at Week 48
- These data underscore the potential for the use of once-daily BIC/LEN to optimize therapy in people receiving a complex antiretroviral therapy regimen (CR)

Plain Language Summary

- People with human immunodeficiency virus (HIV) need at least two medicines (called antiretroviral drugs) to control the virus. However, some medicines may not work well for everyone. This can happen because of side effects or because the virus becomes resistant (the medicines no longer kill the virus). As a result, some people need to take several pills each day, which can be difficult
- Bictegravir (BIC) and lenacapavir (LEN) are approved HIV medicines that are usually taken with other drugs. Combining them into one pill taken once a day may reduce the number of pills and make treatment easier
- This study looked at people with HIV who were already taking about three pills per day and who had no HIV in their blood at the start of the study. After 48 weeks, people who switched to BIC and LEN had similar results to those who continued their previous treatments. This shows that the combination works well
- Many people had changes (mutations) in their HIV at the start of the study. Even so, BIC and LEN together controlled the virus and stopped it from making copies of itself

Introduction

- Once-daily STRs are standard of care for HIV treatment[1]
- However, many people with HIV (PWH) take complex regimens (CRs) for reasons including drug resistance, intolerance, toxicity, drug-drug interactions, or contraindications to existing STRs[1-4]
- The STR of BIC, an INSTI, combined with LEN, a first-in-class capsid inhibitor, demonstrated noninferior efficacy in virologically suppressed PWH switching from CRs in the Phase 3 ARTISTRY-1 trial (NCT05502341)[5]
  - The most common reason for receiving CRs was a history of resistance (81% of participants), followed by intolerance to components of STRs (23%)
  - Participants were receiving a median of three pills per day at baseline (range: 2-11)
  - At Week 48, 96% of participants receiving BIC/LEN and 94% of those receiving a CR had virological suppression (HIV-1 RNA < 50 copies [c]/mL)

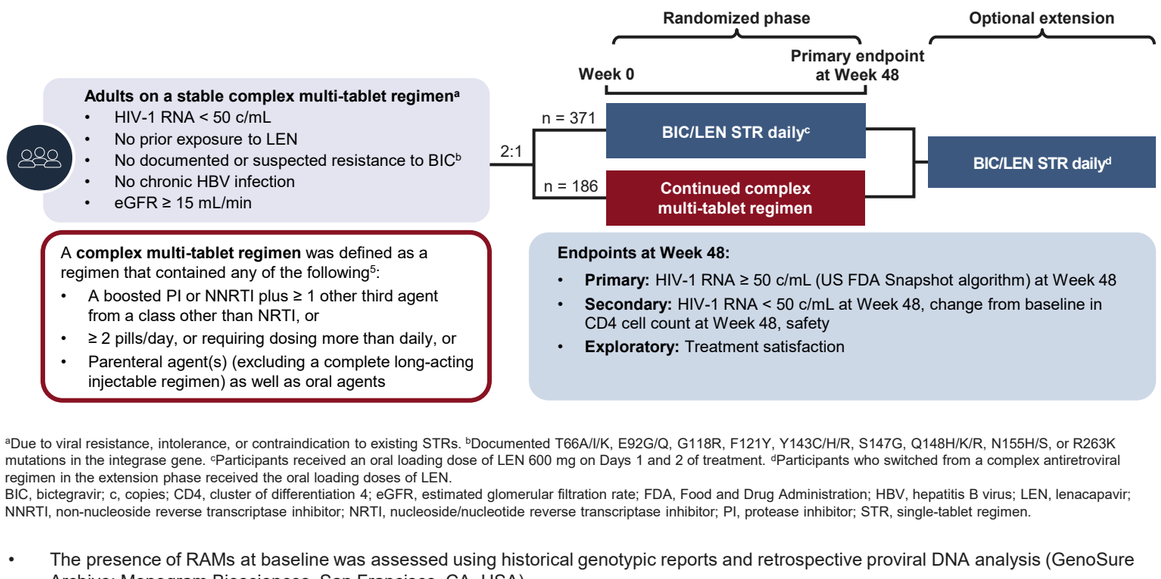
Objective

- To characterize the baseline resistance profile of participants in the Phase 3 ARTISTRY-1 trial, and to analyze the potential emergence of resistance to study drugs after 48 weeks of treatment

Methods

Study Design of the Phase 3 Portion of ARTISTRY-1 (NCT05502341)

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



[a]Due to viral resistance, intolerance, or contraindication to existing STRs. [b]Documented T66A/I/K, E92G/Q, G118R, F121Y, Y143C/H/R, S147G, Q148H/K/R, N155H/S, or R263K mutations in the integrase gene. [c]Participants received an oral loading dose of LEN 600 mg on Days 1 and 2 of treatment. [d]Participants who switched from a complex antiretroviral regimen in the extension phase received the oral loading doses of LEN.
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; STR, single-tablet regimen.

- The presence of RAMs at baseline was assessed using historical genotypic reports and retrospective proviral DNA analysis (GenoSure Archive; Monogram Biosciences, San Francisco, CA, USA)
- RAMs are as follows[6,7]:

	Mutation
NRTI	M41L, K65R/E/N, D67N, T69 insertion, K70E/R, L74V/I, Y115F, Q151M, M184V/I, L210W, T215Y/F, K219E/Q/N/R in reverse transcriptase
NNRTI	L100I, K101E/P, K103N/S, V106M/A, V108I, E138A/G/K/Q/R, V179L, Y181C/I/V, Y188C/H/L, G190A/Q/S, H221Y, P225H, F227C/L, M230L/I in reverse transcriptase
PI	D30N, V32I, M46I/L, I47V/A, G48V, I50V/L, I54M/L/V, Q58E, T74P, L76V, V82A/F/L/S/T, N83D, I84V, N88S, L90M in protease
INSTI	T66I/A/K, E92Q/G/V, G118R, F121C/Y, G140R, Y143R/H/C, S147G, Q148H/K/R, N155H/S, R263K in integrase

INSTI, integrase strand-transfer inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; PI, protease inhibitor.

- The impact of baseline RAMs on treatment response at Week 48 was evaluated using the Fisher exact test
- Post-baseline resistance analysis was conducted for participants experiencing virologic rebound (VR)
  - VR: Confirmed HIV-1 RNA ≥ 50 c/mL or last visit HIV-1 RNA ≥ 50 c/mL (participants with VR who resuppressed by Week 48 were excluded from the final resistance analysis population)
  - Samples were analyzed if HIV-1 RNA ≥ 200 c/mL (Monogram Biosciences, USA or Institute of Immunology and Genetics [Seq-IT], Kaiserslautern, Germany)

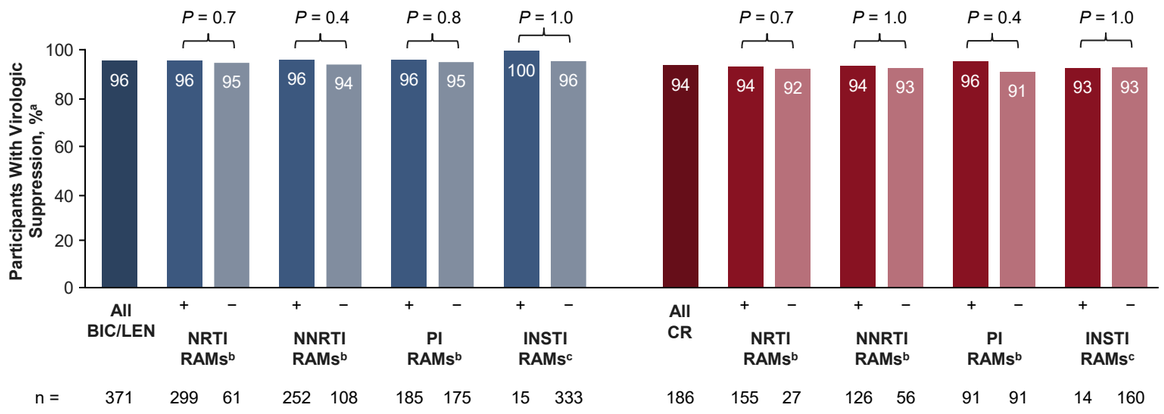
Results

Baseline Pre-Existing Resistance Mutations per Treatment Group

[a]From historical genotypic reports and retrospective proviral DNA analysis, n with data = 542/557 (97%). [b]From historical genotypic reports and retrospective proviral DNA analysis, n with data = 522/557 (94%).
BIC/LEN, bictegravir/lenacapavir; INSTI, integrase strand-transfer inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; PI, protease inhibitor; STR, single-tablet regimen.

- High level of resistance to nucleoside/nucleotide reverse transcriptase inhibitor, non-nucleoside reverse transcriptase inhibitor, and protease inhibitor classes at baseline

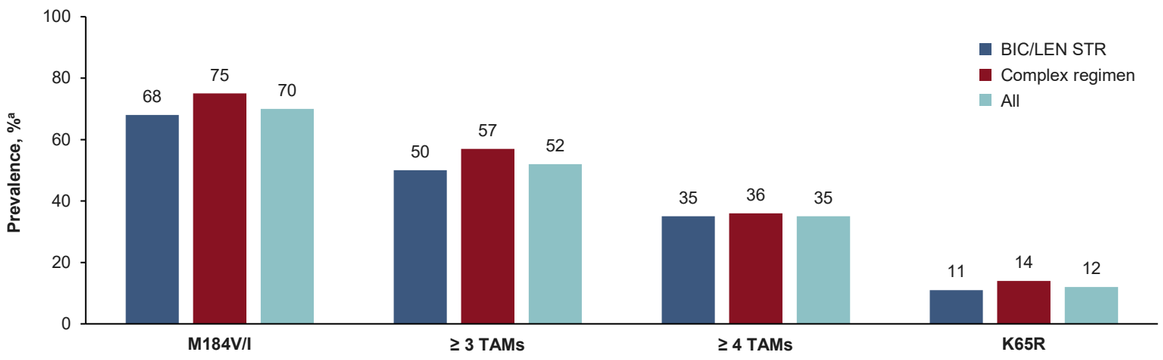
Response to Treatment per Baseline RAM Category



P values calculated using the Fisher exact test. + and – symbols indicate the group of participants with/without RAMs at baseline. [a]HIV-1 RNA < 50 c/mL by US FDA–defined Snapshot algorithm. [b]Protease and reverse transcriptase genotypic data were available for 360/371 and 182/186 participants in the BIC/LEN and CR groups, respectively. [c]Integrase genotypic data were available for 348/371 and 174/186 participants in the BIC/LEN and CR groups, respectively.
BIC/LEN, bictegravir/lenacapavir; c, copies; CR, complex regimen; FDA, Food and Drug Administration; INSTI, integrase strand-transfer inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; PI, protease inhibitor; RAM, resistance-associated mutation.

- Similarly high virologic suppression rates across groups
- Presence of baseline RAMs did not affect treatment response at Week 48

Baseline Pre-Existing NRTI Mutations per Treatment Group



[a]From historical genotypic reports and retrospective proviral DNA analysis, n with data = 542/557 (97%).
BIC/LEN, bictegravir/lenacapavir; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; STR, single-tablet regimen; TAM, thymidine analog mutation (M41L, D67N, K70R, L210W, T215Y/F, and K219E/N/Q/R in reverse transcriptase).

- High prevalence of M184V/I and thymidine analog mutations at baseline
  - Only 6.5% of participants had M184V/I alone

Details of Participants With Baseline INSTI RAMs

Pretreatment INSTI RAMs	BIC/LEN STR n = 371	Complex Regimen n = 186	All N = 557
Participants with data, n (%)	348 (93.8)	174 (93.5)	522 (93.7)
Participants with primary INSTI RAMs, n (%)	15 (4.3)	14 (8.0)	29 (5.6)
Mean number of primary INSTI RAMs per participant	1.1	1.1	1.1
Primary INSTI RAMs, n (%)			
T66A/I/K	5 (1.4)	2 (1.1)	7 (1.3)
E92G/Q/V	1 (0.3)	2 (1.1)	3 (0.6)
G118R	0	0	0
F121C/Y	1 (0.3)	0	1 (0.2)
G140R	1 (0.3)	2 (1.1)	3 (0.6)
Y143C/H/R	0	1 (0.6)	1 (0.2)
S147G	1 (0.3)	0	1 (0.2)
Q148H/K/R	5 (1.4)	6 (3.4)	11 (2.1)
N155H/S	1 (0.3)	1 (0.6)	2 (0.4)
R263K	1 (0.3)	1 (0.6)	2 (0.4)

BIC/LEN, bictegravir/lenacapavir; INSTI, integrase strand-transfer inhibitor; RAM, resistance-associated mutation; STR, single-tablet regimen.

- Most participants in this group had only one INSTI RAM at baseline
  - One participant had T66T/A + S147S/G, and one participant had Y143Y/H + Q148Q/H

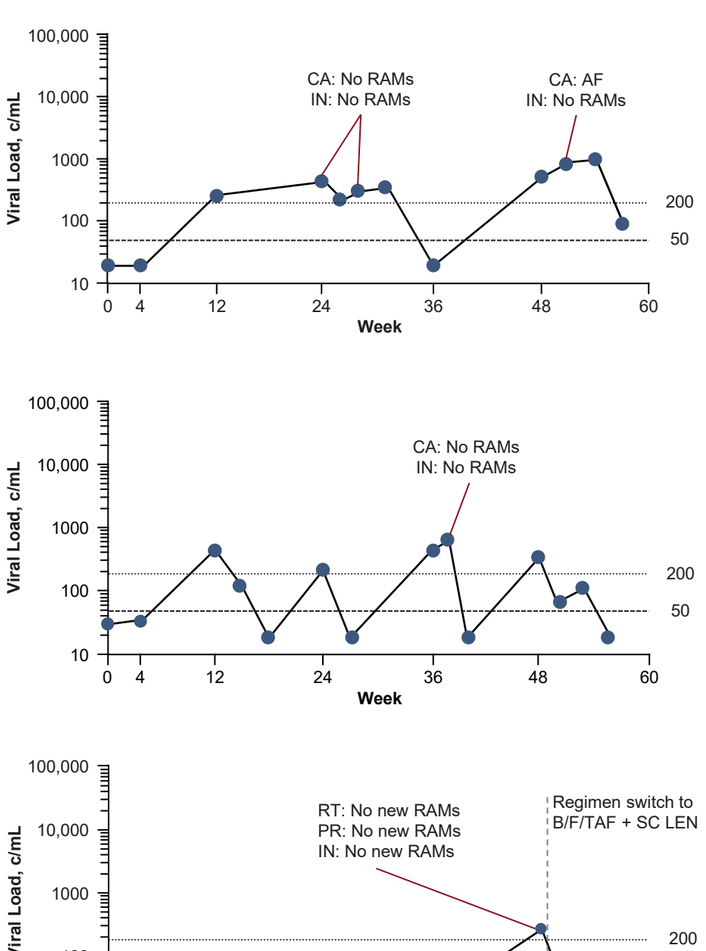
Resistance Analysis Population by Week 48

Resistance Categories	BIC/LEN STR n = 371	Complex Regimen n = 186	All N = 557
Final resistance analysis population, n (%)	2 (0.5)	1 (0.5)	3 (0.5)
With data, n (%)	2 (0.5)	1 (0.5)	3 (0.5)
NRTI/NNRTI RAMs	NA	0	0
PI RAMs	NA	0	0
INSTI RAMs	0	0	0
CAI RAMs	0	NA	0

Resistance emergence is shown for drug classes that were part of the regimens, ie, only CAI and INSTI for BIC/LEN; and INSTI, PI, and RTIs for the CR group.
BIC/LEN, bictegravir/lenacapavir; CAI, capsid inhibitor; CR, complex regimen; INSTI, integrase strand-transfer inhibitor; NA, not applicable; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; PI, protease inhibitor; RAM, resistance-associated mutation; RTI, reverse transcriptase inhibitor; STR, single-tablet regimen.

- Of three participants in the BIC/LEN group and two in the CR group with HIV-1 RNA ≥ 50 c/mL at Week 48, two had a viral load < 200 c/mL and did not qualify for resistance testing (one in each group)[5]
- No participants had emerging RAMs by Week 48

Details of Participants With HIV-1 RNA ≥ 50 c/mL at Week 48



Participant 1 (BIC/LEN STR)

Baseline RAMs:
- RT: M41L, K65R, L74I, K103N, M184V, Y188L, T210W, T215Y, K219N, H221Y
- PR: M46I/L, I54V, I84V, L90M
- IN: none
- CA: none

No resistance detected in CA or IN at multiple visits

Participant 2 (BIC/LEN STR)

Baseline RAMs:
- RT: D67N, K70R, K103N, V108I, M184V, L210W, T215Y, K219E
- PR: none
- IN: none
- CA: none

No resistance detected in CA or IN at virologic rebound

Participant 3 (Complex regimen: B/F/TAF + DRV/r)

Baseline RAMs:
- RT: M41L, M184V, T215Y
- PR: D30N
- IN: E92M/V

No resistance detected at last visit on complex regimen prior to resuppression after switch

AF, assay failure; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; BIC/LEN, bictegravir/lenacapavir; c, copies; CA, capsid; DRV/r, darunavir boosted with ritonavir; IN, integrase; PR, protease; RAM, resistance-associated mutation; RT, reverse transcriptase; SC, subcutaneous; STR, single-tablet regimen.

References: **1.** Department of Health and Human Services. https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/guidelines-adult-adolescent-arv.pdf (accessed April 30, 2025). **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.** Orkin et al. *Lancet*. 2026;407:1249-58. **6.** Wensing AM, et al. *Top Antivir Med*. 2025;33:457-73. **7.** Margot NA, et al. *J Infect Dis*. 2017;215:920-7.

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Disclosures: All authors are employees of, and own stock in, Gilead Sciences, Inc.

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