Pharmacokinetic Data Supporting the Safety and Efficacy of BIC/LEN in Phase 3 Studies

TUPEB094
ARTISTRY-1
ARTISTRY-2

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Conclusions

- Bictegravir (BIC) and lenacapavir (LEN) concentrations from ARTISTRY-1 and ARTISTRY-2 exceeded established therapeutic thresholds for efficacy and were within expected historical ranges
- BIC/LEN single-tablet regimen (STR) was shown to be highly efficacious and safe at these exposures in the ARTISTRY studies

Plain Language Summary

- BIC/LEN is a treatment for human immunodeficiency virus (HIV) that combines two medicines – bictegravir (BIC) and lenacapavir (LEN) – into one pill taken once a day
- In the ARTISTRY-1 and ARTISTRY-2 studies, BIC/LEN was safe and worked well for people with HIV
- Researchers looked at how much of each medicine was present in participants' bodies during these studies
- At these levels, both BIC and LEN were safe and worked well to control HIV

Introduction

- An STR of BIC 75 mg/LEN 50 mg (BIC/LEN) is being developed as a complete regimen for the treatment of HIV-1
  - BIC is an integrase strand transfer inhibitor with a high barrier to resistance[1,2]
  - LEN is a first-in-class capsid inhibitor with no cross-resistance to currently available antiretrovirals[3]
- BIC is a substrate of CYP3A and UGT1A1[1] and LEN is a substrate of P-gp, UGT1A1, and CYP3A and a moderate inhibitor of CYP3A[3]
  - LEN could potentially increase BIC concentrations in combination, but no clinically meaningful interaction is expected between BIC and LEN
- BIC/LEN STR demonstrated efficacy and safety in Phase 3 studies in people with HIV-1 (PWH) with virologic suppression
  - In ARTISTRY-1, BIC/LEN STR was noninferior to a treatment arm of a stable baseline complex regimen (CR) and 96.0% of participants who switched to BIC/LEN had HIV-1 RNA < 50 copies/mL at 48 weeks[4]
  - In ARTISTRY-2, BIC/LEN STR was noninferior to a treatment arm of bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) and 93.5% of participants who switched to BIC/LEN had HIV-1 RNA < 50 copies/mL at 48 weeks[5]

Objective

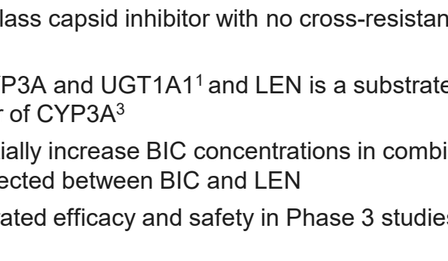
- To characterize and contextualize the pharmacokinetic (PK) data for BIC and LEN that support the safety and efficacy observed for BIC/LEN in the ARTISTRY studies

Methods

Design of ARTISTRY-1 and ARTISTRY-2 Studies

ARTISTRY-1 Phase 3 open-label study

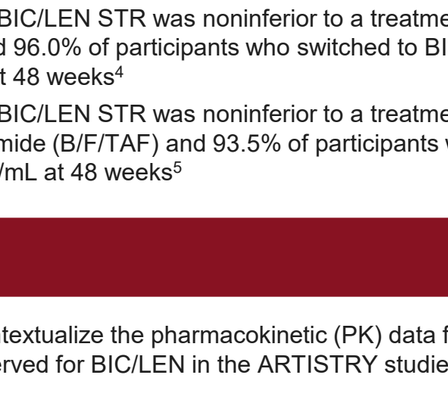
Adults aged ≥ 18 years on a stable complex multi-tablet regimen[a]
- HIV-1 RNA < 50 copies/mL
- No prior exposure to LEN or resistance to BIC
- No chronic HBV infection
- eGFR ≥ 15 mL/min



A **complex multi-tablet regimen** was defined as a regimen which contained any of the following:
- A boosted PI or NNRTI plus ≥ 1 other third agent from a class other than NRTI, or
- ≥ 2 pills/day, or requiring dosing more than daily, or
- Parenteral agent(s) (excluding a complete long-acting injectable regimen) as well as oral agents

ARTISTRY-2 Phase 3 double-blind study

Adults aged ≥ 18 years on B/F/TAF
- HIV-1 RNA < 50 copies/mL
- No prior exposure to LEN
- No resistance to BIC or TAF
- No chronic HBV infection
- eGFR > 30 mL/min



Sparse PK sampling timepoint
Optional intensive PK sampling timepoint

[a]Due to ARV 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]Placebo-to-match B/F/TAF. [d]Participants received placebo-to-match oral LEN on Days 1 and 2 of treatment. [e]Placebo-to-match BIC/LEN.
ARV, antiretroviral; BIC, bictegravir; eGFR, estimated glomerular filtration rate; F, emtricitabine; HBV, hepatitis B virus; LEN, lenacapavir; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; PI, protease inhibitor; PK, pharmacokinetic; STR, single-tablet regimen; TAF, tenofovir alafenamide

- Sparse PK blood samples were collected at on-treatment study visits up to Week 48 from all participants in the BIC/LEN groups of both studies
  - Day 1 predose and 4 hours post-dose
  - ARTISTRY-1: Week 4, 12, 24, 36, 48 predose and 2 hours post-dose
  - ARTISTRY-2: Week 4, 12, 24, 36, 48 predose and Week 24 and 36 at 2 hours post-dose
- An intensive PK (iPK) substudy was performed in a subset of participants in the BIC/LEN group of ARTISTRY-1 at a steady-state visit at either Week 24, 36, or 48
  - Blood samples collected at trough, and 0.5, 1, 2, 3, 4, 6, and 8 hours post-dose
- Concentrations of BIC and LEN were determined using validated bioanalytical assays

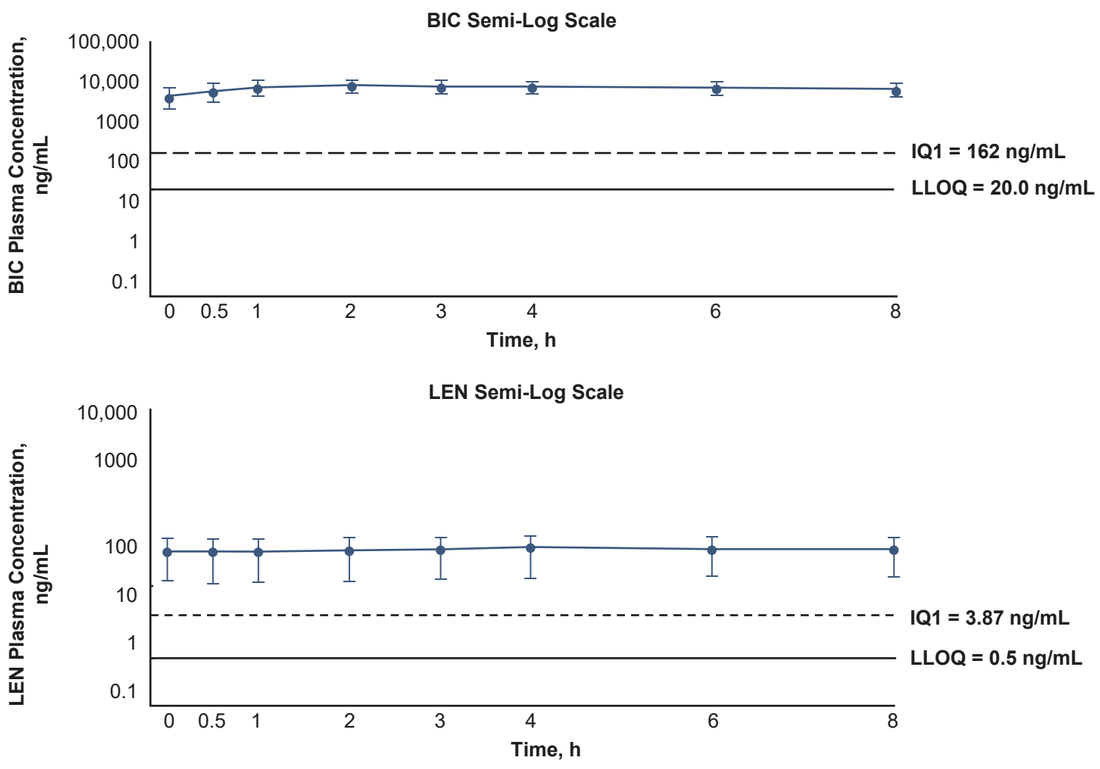
Results

Demographics and Baseline Characteristics for Participants on BIC/LEN Contributing Sparse PK Data

	ARTISTRY-1 n = 371	ARTISTRY-2 n = 383
Age, years	60 (55, 66)	47 (38, 58)
Male sex at birth, %	82.7	82.0
Body weight, kg	79.6 (68.7, 90.0)	81.1 (71.8, 92.8)
BMI, kg/m²	26.1 (23.1, 29.9)	26.8 (24.2, 30.3)
CrCl,[a] mL/min	82.9 (66.4, 103.2)	101.4 (83.9, 117.0)
Number of prior antiretroviral medications	7 (3, 14)	Not available

Values are median (Q1, Q3) unless otherwise noted. [a]CrCl by Cockcroft-Gault.
BIC, bictegravir; BMI, body mass index; CrCl, creatinine clearance; LEN, lenacapavir; PK, pharmacokinetic; Q, quartile.

Mean (SD) Plasma BIC and LEN Concentrations Versus Time at Steady State From ARTISTRY-1 iPK



BLQ values were treated as 0 for predose and post-dose summaries. Predose and trough values were displayed at time 0 in the figure.
Mean concentration values that are less than or equal to LLOQ are not displayed on the figure. For each participant in the intensive PK substudy, intensive serial PK sample collection was performed at either Week 24, 36, or 48.
BIC, bictegravir; BLQ, below lower limit of quantitation; iPK, intensive PK; IQ, inhibitory quotient; LEN, lenacapavir; LLOQ, lower limit of quantitation; PK, pharmacokinetic.

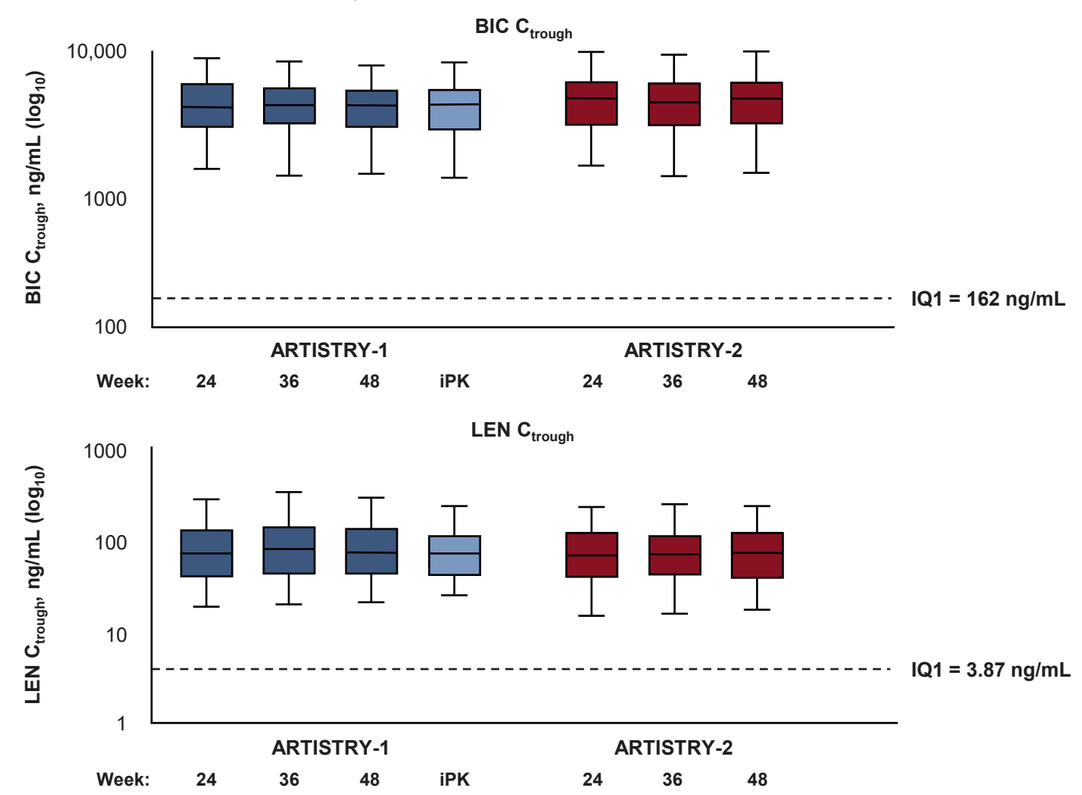
- Observed mean steady-state BIC C_{trough} concentrations were approximately 26- to 30-fold above the inhibitory quotient (IQ)1 (162 ng/mL) for BIC, the threshold above which efficacious exposure against HIV is expected
- Observed mean steady-state LEN C_{trough} concentrations were approximately 21- to 29-fold above the IQ1 (3.87 ng/mL) for LEN

Steady-State Plasma PK Data for BIC and LEN Following Once-Daily Administration of BIC/LEN 75/50 mg Tablets[a]

Parameter	BIC							LEN						
	ARTISTRY-1				ARTISTRY-2			ARTISTRY-1				ARTISTRY-2		
	iPK[b]	Sparse PK			Sparse PK			iPK[b]	Sparse PK			Sparse PK		
		W24	W36	W48	W24	W36	W48		W24	W36	W48	W24	W36	W48
C_{trough}, mean (% CV), ng/mL	4190 (52.6) n=89	4480 (55.4) n=264	4400 (53.4) n=292	4290 (49.6) n=211	4880 (53.7) n=314	4630 (53.4) n=305	4760 (50.4) n=191	81.5 (70.8) n=51	103 (104) n=267	113 (109) n=293	106 (100) n=213	94.8 (109) n=313	89.2 (86.5) n=305	94.8 (106) n=225
C_{max}, mean (% CV), ng/mL	8670 (35.0) n=97	-						107 (76.2) n=97	-					
AUC_{tau}, mean (% CV), h*ng/mL	140,000 (40.6) n=89	-						2130 (69.2) n=51	-					

Phase 3 electronic data capture PK snapshot dates: Sept. 19, 2025 (ARTISTRY-1), Oct. 17, 2025 (ARTISTRY-2). [a]Administered in conjunction with oral loading doses of LEN 600 mg on Days 1 and 2. [b]iPK data were analyzed using standard non-compartmental analysis with Phoenix WinNonlin® to calculate relevant PK parameters including AUC_{tau}, C_{max}, and C_{trough}.
AUC_{tau}, area under the plasma concentration–time curve over the dosing interval; BIC, bictegravir; C_{max}, maximum observed plasma drug concentration; C_{trough}, trough plasma drug concentration; CV, coefficient of variation; iPK, intensive pharmacokinetic; LEN, lenacapavir; PK, pharmacokinetic; W, Week.

Plasma BIC and LEN C_{trough} Concentrations From ARTISTRY-1 and ARTISTRY-2



Box plots depict median (horizontal line), interquartile range (box), and 5th-95th percentiles (whiskers).
BIC, bictegravir; C_{trough}, trough plasma drug concentration; iPK, intensive PK; IQ, inhibitory quotient; LEN, lenacapavir.

- Sparse PK was representative of iPK

References: 1. Biktarvy. Package insert. Gilead Sciences, Inc. 2025. **2.** Acosta RK, et al. *Antimicrob Agents Chemother.* 2019;63:e02533-18. **3.** Sunlenca. Package insert. Gilead Sciences, Inc. 2026. **4.** Orkin C, et al. *Lancet.* 2026;407:1249-58. **5.** Meissner EG, et al. *Lancet HIV.* Published online May 6, 2026. doi: 10.1016/S2352-3018(26)00078-0.

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