GILEAD | Medical Information

Bixlenvo™ (bictegravir/lenacapavir) Clinical Study Overview

This document is in response to your request for information regarding Bixlenvo™ (bictegravir/lenacapavir [BIC/LEN]) and its use in clinical trials as HIV-1 treatment.

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The full indication, important safety information, and boxed warnings are available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/BIXLENVO/BIXLENVO_pi.

Summary

Product Labeling[1]

BIC/LEN is indicated as a complete regimen for the treatment of HIV-1 in adults to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen with no known or suspected resistance to the individual components of BIC/LEN.

Clinical Data on BIC/LEN Use in HIV-1 Treatment

ARTISTRY-1: An ongoing phase 2/3 study is evaluating the efficacy and safety of switching to BIC + LEN vs continuing a complex ART regimen in VS PWH.[2]

Results from phase 2 through Week 96 have been reported.[2-4]

- Through Week 48, high rates of virologic suppression were maintained in each group: BIC 75 mg + LEN 25 mg, 92.2%; BIC 75 mg + LEN 50 mg, 90.4%; and complex ART regimen, 100%.[2]
- Through Week 48, all commonly reported TEAEs (≥5% in any group) were Grade 1 or 2 in severity, except for 1 case of Grade 3 diarrhea unrelated to study drug. TEAEs led to treatment DC in 2% of participants in the BIC 75 mg + LEN 25 mg group, 1.9% in the BIC 75 mg + LEN 50 mg group, and 0% in the complex ART regimen group.[2]
- Among participants initially randomized to the BIC 75 mg + LEN 50 mg group, virologic suppression was maintained through Week 96 (96%; 45/47). Within this group, 25% reported Grade ≥3 AEs, and 17.3% reported SAEs.[4]

Results from phase 3 through Week 48 have been reported.[5]

- High rates of virologic suppression were maintained in each group: BIC/LEN STR 75 mg/50 mg, 96%, and complex ART regimen, 94%. BIC/LEN was non-inferior to complex ART regimens in the maintenance of virologic suppression.[5]
- In the BIC/LEN and complex ART regimen groups, the rates of Grade ≥3 AEs (each, 14%) and DCs due to AEs (2% vs 1%) were similar.[5]
- Virologic suppression rates were similar between the complex ART regimen group and both BIC + LEN groups and between participants with and those without RAMs at baseline.[6]

ARTISTRY-2: An ongoing phase 3 study is evaluating the efficacy and safety of switching from BIC/FTC/TAF to BIC/LEN STR 75 mg/50 mg vs continuing BIC/FTC/TAF in VS PWH.[7]

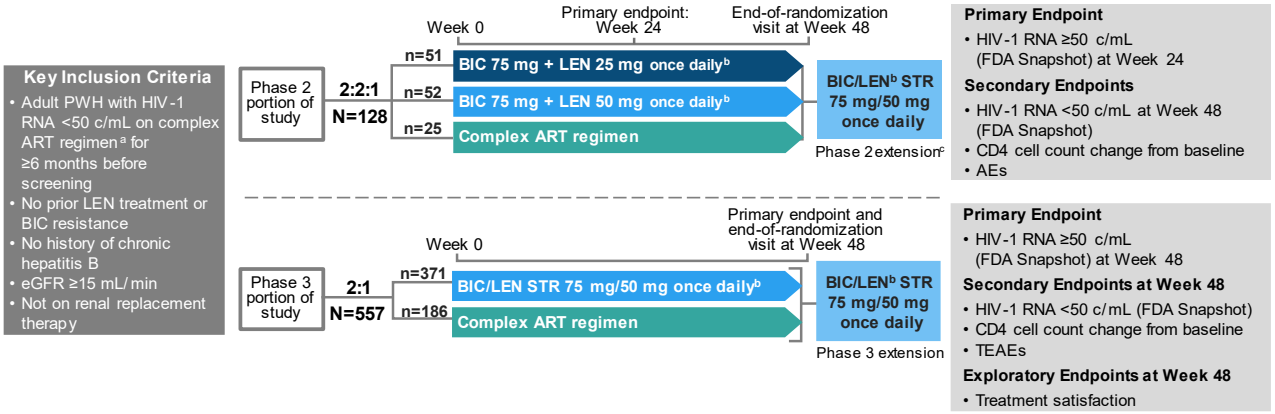
- Through Week 48, virologic suppression rates were high in both groups: BIC/LEN 75 mg/50 mg, 93%; BIC/FTC/TAF, 91%. BIC/LEN was non-inferior to BIC/FTC/TAF in maintaining virologic suppression.[7]
- Through Week 48, in the BIC/LEN and BIC/FTC/TAF groups, the rates of Grade ≥3 AEs (10% vs 8%, respectively) and DCs due to AEs (each, 2%) were similar.[7]
- Across various subgroups, BIC/LEN was associated with high levels of sustained virologic suppression at Week 48. The incidence of TRAEs was similar across assessed subgroups and treatment groups.[8]

Clinical Data on BIC/LEN Use in HIV-1 Treatment

ARTISTRY-1: Switching to BIC/LEN vs Complex ART

An ongoing, randomized, multicenter, open-label, phase 2/3 study (NCT05502341) is evaluating the efficacy and safety of switching to BIC/LEN vs continuing their ART regimen in PWH who were receiving a complex ART regimen.[2,3]

Figure 1. ARTISTRY-1 Phase 2/3: Study Design[3,5,9]



[a]Due to viral resistance, intolerance, or contraindication to existing STRs. Regimens contained the following: a boosted PI or NNRTI + ≥1 other third agent from a class other than NRTIs, or ≥2 pills/day or a dosing frequency >once daily, or parenteral ART (excluding a complete long-acting injectable regimen) plus oral ART.
[b]Oral loading doses of LEN (600 mg for 2 days) were given after participants switched from their complex ART regimen.
[c]All participants reached the Week 48 timepoint and completed the end-of-randomization visit before entering the OLE phase.

Phase 2 of ARTISTRY-1

During the phase 2 portion of the study, participants were randomly assigned to switch to BIC 75 mg + LEN (25 or 50 mg; oral) or to continue their complex ART regimen. After the randomized period, participants could continue on to the extension period and receive BIC/LEN STR (Figure 1).[2]

Table 1. Phase 2 of ARTISTRY-1: Baseline Demographics, Disease Characteristics, and Historical Resistance Mutations[3]

Key Demographics and 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, median (range), years		62 (26–79)	62 (34–76)	58 (41–70)	60 (26–79)
Female sex assigned at birth, n (%)		13 (25.5)	7 (13.5)	4 (16)	24 (19)
Race, White/Black/Asian/other, %		56.9/35.3/3.9/3.9	65.4/30.8/3.8/0	80/20/0/0	64.8/30.5/3.1/1.6
Hispanic/Latinx,[a] n (%)		7 (14)	9 (17.6)	4 (16)	20 (15.9)
CD4 count, median (IQR), cells/mcL		583 (460–764)	624 (517–791)	585 (285–733)	610 (435–766)
<200 cells/mcL, n (%)		1 (2)	1 (1.9)	2 (8)	4 (3.1)
Duration of HIV treatment,[b] median (IQR), years		27.8 (22.7–32.4)[c]	27 (18.9–31.5)	26.9 (19.8–31.9)	27 (19.9–32)
Prior ARTs,[d] median (IQR), n		4 (2–9)	7 (3–11)	8 (3–13)	6 (3–11)
Reasons for complex regimen,[e] n (%)	History of resistance	44 (86.3)	40 (76.9)	20 (80)	104 (81.3)
	Intolerance of STR components	20 (39.2)	11 (21.2)	7 (28)	38 (29.7)
	Contraindications to STRs	7 (13.7)	4 (7.7)	1 (4)	12 (9.4)
ARTs,[d] median (range), n		2 (2–5)	2.5 (2–5)	3 (2–5)	2 (1–5)
Pills/day, median (range)		2 (2–8)	3 (2–9)	3 (2–8)	3 (2–9)
Historical resistance mutations,[e] n (%) INSTI/NNRTI/NRTI/PI		0/49/60.8/ 35.3	0/53.8/67.3/ 32.7	0/56/64/44	0/52.3/64.1/ 35.9

[a]Ethnicity data were not permitted to be collected for 1 patient each in the BIC 75 mg +LEN 25 mg and BIC 75 mg + LEN 50 mg arms.
[b]Calculated with the following equation: (date of first dose – start date of first HIV treatment + 1 day)/365.25.
[c]n=50.
[d]Defined as ARTs taken on Day 1 or up to 14 days before Day 1. If participants received multiple ARTs, they were counted once per participant for each drug name and ART class.
[e]Categories were not mutually exclusive. An alternative response was “no” or “not available.”

In the overall population, 53 participants (41.4%) were taking twice-daily ART, and 43%, 18.8%, 10.9%, and 27.3% were taking 2, 3, 4, or ≥5 pills/day, respectively.[3]

A separate analysis assessed the presence of RAMs at baseline with historical genotypic reports and retrospective proviral DNA analysis, which identified a high level of resistance to NRTI, NNRTI, and PI classes and a high prevalence of M184V/I and TAMs at baseline.[10]

Efficacy, immunological, and resistance outcomes through Week 48

At Week 24, 1 participant (1.9%) in the BIC 75 mg + LEN 50 mg group and no participants in the BIC 75 mg + LEN 25 mg group or complex ART regimen group had HIV-1 RNA ≥50 c/mL (primary endpoint; FDA Snapshot algorithm).[3] At Week 48, similarly high rates of virologic suppression were maintained in each group (Table 2).[2]

Table 2. Phase 2 of ARTISTRY-1: Rates of HIV RNA <50 c/mL (FDA Snapshot) and HIV RNA ≥50 c/mL at Week 48[2]

Efficacy Endpoints	BIC 75 mg + LEN 25 mg	BIC 75 mg + LEN 50 mg	Complex ART Regimen
HIV-1 RNA ≥50 c/mL, % (n/N)	3.9 (2/51)	1.9 (1/52)	0 (0/25)
Difference, % (95% CI); *P*-value	3.9 (−10.7, 13.9); 1	1.9 (−12.2, 10.7); 1	–
HIV-1 RNA <50 c/mL, % (n/N)	92.2 (47/51[a])	90.4 (47/52[b])	100 (25/25)
Difference, % (95% CI); *P*−value	−7.8 (−19.2, 7); 0.3	−9.6 (−21, 5.3); 0.17	–

[a]Reasons for DC before Week 48: AE and participant decision (each, n=1).
[b]Reasons for DC before Week 48: AE, death, participant decision, and investigator decision (each, n=1).
Note: *P*-values were for comparisons vs the complex ART regimen and are reported for descriptive purposes.

Three participants had HIV RNA levels ≥50 c/mL[2]:

- 2 participants (3.9%) in the BIC 75 mg + LEN 25 mg group were resuppressed at their next study visit without a change in ART (HIV-1 RNA at Week 48: 50 c/mL and 98 c/mL, respectively)[2];
- 1 participant (1.9%) in the BIC 75 mg + LEN 50 mg group (HIV-1 RNA at Week 48: 305 c/mL) was resuppressed by Day 368 after switching treatment to DTG + MVC + LEN SUBQ. This participant underwent a resistance analysis, and the N74T capsid mutation was noted with PhenoSense assay failure; this novel capsid polymorphism did not confer resistance to LEN and no change in BIC sensitivity occurred.[2,10]

At Week 48, the median (Q1, Q3) change in CD4 cell counts from baseline to Week 48 were as follows: BIC 75 mg + LEN 25 mg, +29 (−45, +96) cells/mcL; BIC 75 mg + LEN 50 mg, +48 (−59, +150) cells/mcL; complex ART regimen, +31 (−46, +111) cells/mcL.[2]

Safety results through Week 48

Through Week 48, the safety profile of BIC + LEN was similar regardless of LEN dose. Common TEAEs (≥5% in any group) were Grade 1 or 2 in severity, except for 1 case of Grade 3 diarrhea, which was deemed unrelated to study drug (Table 3).[2]

Table 3. Phase 2 of ARTISTRY-1: TEAEs Through Week 48[9]

Safety Outcomes, n (%)		BIC 75 mg + LEN 25 mg (n=51)	BIC 75 mg + LEN 50 mg (n=52)	Complex ART Regimen (n=25)
Any TEAE		42 (82.4)	41 (78.8)	19 (76)
Grade ≥3 TEAEs		7 (13.7)	4 (7.7)	1 (4)
Treatment-related TEAEs		9 (17.6)	3 (5.8)	0
Serious TEAEs		4 (7.8)[a]	3 (5.8)[a]	3 (12)[a]
TEAEs that led to treatment DC		1 (2)[b]	1 (1.9)[c]	0
TEAEs (≥5% in either LEN group)	COVID-19	8 (15.7)	5 (9.6)	4 (16)
	Diarrhea	5 (9.8)	2 (3.8)	1 (4)
	Nasopharyngitis	5 (9.8)	0	1 (4)
	Cough	4 (7.8)	3 (5.8)	0
	URTI	3 (5.9)	4 (7.7)	2 (8)
	Arthralgia	3 (5.9)	4 (7.7)	0
	Constipation	3 (5.9)	2 (3.8)	0
	Nausea	3 (5.9)	2 (3.8)	0
	Vertigo	3 (5.9)	0	0
	HTN	1 (2)	5 (9.6)	1 (4)
	Pain in extremity	1 (2)	3 (5.8)	1 (4)
Death		0	1 (1.9)[d]	0

[a]Deemed unrelated to study treatment. [b]Grade 1 nausea was reported on Day 1.
[c]Grade 3 worsening of vomiting was reported in a participant with prior history of nausea and vomiting.
[d]Death was due to coronary artery disease and was deemed unrelated to study drug.

At Week 24, Grade 3 and 4 treatment-emergent laboratory abnormalities were experienced by 9.8% and 2% of participants, respectively, in the BIC 75 mg + LEN 25 mg group; by 17.3% and 5.8% in the BIC 75 mg + LEN 50 mg group; and by 32% and 0% in the complex ART regimen group.[11] Laboratory abnormalities were not reported at Week 48.[2,12]

Efficacy and safety through Week 96: participants initially randomized to the BIC 75 mg + LEN 50 mg group[4]

Efficacy and safety outcomes through Week 96 were analyzed for participants who were initially randomized to the BIC 75 mg + LEN 50 mg group (n=52). Of these participants, 5 discontinued from the study during the randomized phase and 47 continued in the OLE.

Virologic suppression was maintained in 96% of participants (45/47; missing=excluded) through Week 96. The 2 participants with HIV-1 RNA ≥50 c/mL had low-level viremia (defined as HIV-1 RNA <500 c/mL) and were later resuppressed without requiring a change in their ART regimen. One of these participants met criteria for resistance testing and had assay failures for all genes. The median (Q1, Q3) change from baseline to Week 96 in CD4 count was -6 (-118, 123) cells/mcL.

Through Week 96, 46 participants (88.5%) reported an AE, including 13 (25%) with a Grade ≥3 AE. Nine participants (17.3%) reported SAEs, 3 (5.8%) TRAEs were reported (atrial conduction time prolongation, decreased blood pressure, and nausea and vomiting), and no serious TRAEs were reported. No new AEs led to treatment DCs and no deaths were reported between Week 48 and Week 96.

Phase 3 of ARTISTRY-1

For the phase 3 portion of the study, participants were randomly assigned (2:1) to receive an STR of BIC/LEN 75 mg/50 mg (n=371) or continue their stable complex ART regimen (n=186) for 48 weeks (Figure 1). At baseline, participants had a history of resistance to multiple drug classes (Table 4).[5]

Table 4. Phase 3 of ARTISTRY-1: Baseline Demographics, Disease Characteristics, and Preexisting Resistance Mutations[5]

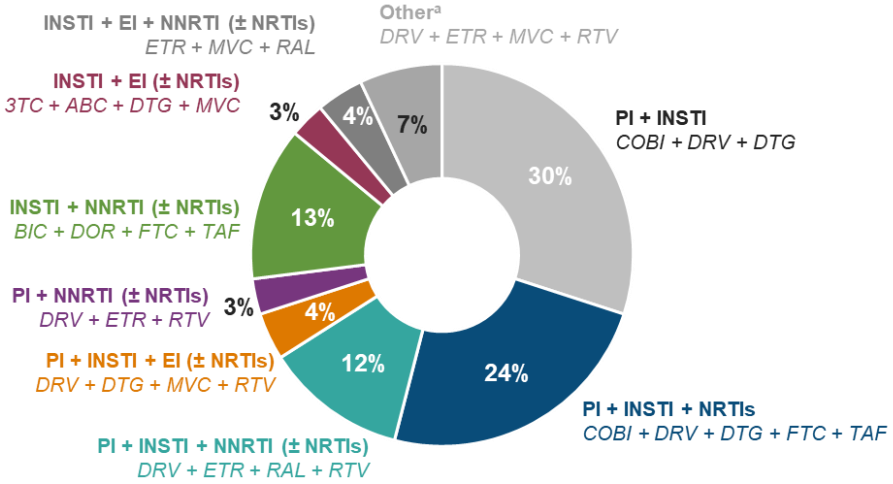
Key Demographics and Characteristics		BIC/LEN 75 mg/50 mg (n=371)	Complex ART Regimen (n=186)	Overall (N=557)
Age, median (range), years		60 (22–84)	60 (24–75)	60 (22–84)
Female sex assigned at birth, n (%)		64 (17)	36 (19)	100 (18)
Race, White/Black/Asian/other,[a] %		70/17/4/3	67/18/5/2	69/17/4/3
Hispanic/Latinx,[b] n (%)		80 (22)	42 (23)	122 (22)
CD4 count, median (IQR), cells/mcL		626 (457–836)[c]	579 (450–747)[d]	612 (456–809)[e]
Duration of HIV treatment, median (IQR), years		28.3 (21.6–32.3)[f]	28.3 (21.4–31.8)[g]	28.3 (21.6–32.1)[h]
ARV pills/day, median (range), n		3 (2–11)	3 (2–9)	3 (2–11)
Reasons for taking complex regimen,[i] n (%)	History of resistance	297 (80)	153 (82)	450 (81)
	Intolerance to STR components	89 (24)	39 (21)	128 (23)
	Contraindications to STR components	23 (6)	10 (5)	33 (6)
History of selected comorbidities,[i,j] dyslipidemia/HTN/DM or hyperglycemia/CKD, %		66/51/25/13	72/48/23/16	68/50/24/14
Historical drug class resistance,[i,k] n (%)	NRTI	247 (67)	128 (69)	375 (67)
	NNRTI	203 (55)	104 (56)	307 (55)
	PI	151 (41)	77 (41)	228 (41)
	INSTI	1 (<1)	2 (1)	3 (1)

[a]Local regulations did not permit the collection of race data for 19 participants in the BIC/LEN group and 17 in the complex ART regimen group. The "other" category included participants who were American Indian or Alaska Native, Native Hawaiian, Pacific Islander, or other.
[b]Local regulations did not permit the collection of ethnicity data for 21 participants in the BIC/LEN group and 16 in the complex ART regimen group.
[c]n=366. [d]n=185. [e]n=551.

[f]n=358. [g]n=183. [h]n=541.
[i]Not mutually exclusive.
[j]Grouped terms per MedDRA.
[k]NRTI, NNRTI, PI, and INSTI data were not available for 75, 79, 78, and 197 participants in the BIC/LEN group, respectively, and 44, 46, 50, and 100 participants in the complex ART regimen group. The denominator used for percentage calculations was the total number of participants.

Refer to Figure 2 for a summary of complex ART regimens; 77% of participants (n=427) were receiving a PI at baseline, and 75% of those participants (n=419) received a boosted PI-based regimen. At baseline, 39% of overall participants were receiving twice-daily ART, and 41%, 26%, 11%, and 22% were taking 2, 3, 4, or ≥5 pills/day, respectively.[4,13]

Figure 2. Phase 3 of ARTISTRY-1: Complex ART Regimens at Baseline[5]



Abbreviations: 3TC=lamivudine; ABC=abacavir; DOR=doravirine; EI=entry inhibitor; ETR=etravirine.
[a]Other regimens could have contained a PI.
Note: Regimens in italics were the most common regimen in each category.

Efficacy outcomes through Week 48

The median (Q1, Q3) exposure in the BIC/LEN group was 65.9 (56.6, 74) weeks and 65.9 (55.6, 73.9) weeks in the complex ART group. BIC/LEN was non-inferior to complex ART regimens in maintaining virologic suppression at Week 48 (Table 5).[5] Each of the participants in the BIC/LEN group with HIV-1 RNA ≥50 c/mL at Week 48 achieved virologic resuppression or had low-level viremia without changes in their ART regimen.[13]

Table 5. Phase 3 of ARTISTRY-1: Rates of HIV RNA ≥50 c/mL and HIV RNA <50 c/mL (FDA Snapshot) at Week 48 in the Full Analysis Set[5]

Efficacy Endpoints	BIC/LEN 75 mg/50 mg	Complex ART Regimen
HIV-1 RNA ≥50 c/mL, % (n/N)	1 (3/371)	1 (2/186)
Difference,[a] % (95.002% CI)	−0.3 (−2.3, 1.8)	
HIV-1 RNA <50 c/mL, % (n/N)	96 (356/371)	94 (174/186)
Difference, % (95.002% CI)	2.4 (-1.8 to 6.6)	
No virologic data, % (n/N)	3 (12/371)[b]	5 (10/186)[c]

[a]Two-sided CI was based on Mantel-Haenszel stratum weights and Koch variance estimator and was adjusted by geographic region (US vs non-US).
[b]Reasons for DC before Week 48: AE or death, n=7 (AEs, n=5; deaths, n=2); other reasons and last HIV-1 RNA <50 c/mL, n=5.
[c]Reasons for DC before Week 48: other reasons and last HIV-1 RNA <50 c/mL, n=8; AE or death, n=1; and missing data but still on study drug, n=1.

CD4 counts remained stable in both groups, with a median (IQR) change in CD4 count from baseline to Week 48 of +18 (-72 to 98) cells/mcL in the BIC/LEN group and -12 (-82 to 93) cells/mcL in the complex ART group (difference in change: +19 cells/mcL; 95% CI: -11.6 to 49.5; *P*=0.22).[5]

Baseline and Week 48 resistance analysis

A separate analysis assessed the presence of RAMs at baseline using historical genotypic reports and retrospective proviral DNA analysis. Reports identified a high level of resistance to NRTI, NNRTI, and PI classes and a high prevalence of M184V/I and TAMs at baseline (Table 6).[6]

Table 6. Phase 3 of ARTISTRY-1: Baseline Preexisting Resistance Mutations by ARV Class, NRTI Mutations, and INSTI RAMs by Treatment Group[6]

Baseline Resistance Mutations		BIC/LEN 75 mg/50 mg (n=371)	Complex ART Regimen (n=186)	Total (N=557)
Preexisting resistance mutations by ARV class, NRTI/NNRTI/PI/INSTI,[a] %		83/70/51/4	85/69/50/8	84/70/51/6
Preexisting NRTI mutations,[b] %	M184V/I	68	75	70
	K65R	11	14	12
	≥3/≥4 TAMs	50/35	57/36	52/35
Preexisting INSTI RAMs, n (%)		15 (4.3)	14 (8)	29 (5.6)
Primary INSTI RAMs, n (%)	Q148H/K/R	5 (1.4)	6 (3.4)	11 (2.1)
	T66A/I/K	5 (1.4)	2 (1.1)	7 (1.3)
	E92G/Q/V	1 (0.3)	2 (1.1)	3 (0.6)
	G140R	1 (0.3)	2 (1.1)	3 (0.6)
	N155H/S	1 (0.3)	1 (0.6)	2 (0.4)
	R263K	1 (0.3)	1 (0.6)	2 (0.4)
	F121C/Y	1 (0.3)	0	1 (0.2)
	S147G	1 (0.3)	0	1 (0.2)
	Y143C/H/R	0	1 (0.6)	1 (0.2)
	G118R	0	0	0

[a]NRTI, NNRTI, and PI data were available in 542 participants, INSTI data were available in 522 participants, and NRTI mutation data were available in 542 participants. Baseline RAM data were evaluated using historical genotypes and retrospective proviral DNA analysis.
[b]TAMs included M41L, D67N, K70R, L210W, T215Y/F, and K219E/N/Q/R in RT; 6.5% had M184V/I alone.

Through Week 48, participants with and without baseline NRTI, NNRTI, PI, and INSTI RAMs had high rates of virologic suppression, and there were no significant differences in the rates of virologic suppression between participants with and those without baseline RAMs within each treatment group (Table 7).[10]

Table 7. Rates of HIV RNA <50 c/mL at Week 48 Overall and by Baseline Resistance Category (FDA Snapshot)[6]

HIV-1 RNA <50 c/mL, %		BIC/LEN 75 mg/50 mg (n=371)	Complex ART Regimen (n=186)
Overall		96	94
NRTI RAMs[a]	Yes	96	94
	No	95	92
NNRTI RAMs[a]	Yes	96	94
	No	94	93
PI RAMs[a]	Yes	96	96
	No	95	91

HIV-1 RNA <50 c/mL, %		BIC/LEN 75 mg/50 mg (n=371)	Complex ART Regimen (n=186)
INSTI RAMs[b]	Yes	100	93
	No	96	93

[a]Data were available for 360/371 participants in the BIC/LEN group and 182/186 participants in the complex ART regimen group.
[b]Data were available for 348/371 participants in the BIC/LEN group and 174/186 participants in the complex ART regimen group.
Note: Within each treatment group, comparisons between participants with and those without each class of RAMs were nonsignificant (*P*>0.05).

Post-baseline resistance testing was conducted in participants with virologic rebound with HIV-1 RNA ≥200 c/mL. The resistance analysis population at Week 48 included 2 participants (0.5%) in the BIC/LEN group and 1 participant (0.5%) in the complex ART regimen group; no treatment-emergent resistance was detected in any participants.[6]

Safety outcomes through Week 48

Between groups, similar rates of AEs and SAEs were reported, most AEs were mild to moderate in severity, and the incidence of treatment DC due to AEs was low (Table 8). The incidence of renal-related AEs was low and the safety profile was similar between treatment groups regardless of the level of renal function.[4]

Table 8. Phase 3 of ARTISTRY-1: Safety Outcomes Through Week 48[5,14]

Safety Outcomes, n (%)		BIC/LEN 75 mg/50 mg (n=371)	Complex ART Regimen (n=186)
AE		305 (82)	157 (84)
TRAE		53 (14)	3 (2)
Grade ≥3 AE		51 (14)	26 (14)
Grade ≥3 TRAE		2 (1)[a]	0
SAE		52 (14)	22 (12)
Treatment-related SAE		1 (<1)[b]	0
AE that led to study drug DC		6 (2)[c]	1 (1)[d]
AEs with ≥5% frequency in the BIC/LEN group	URTI	34 (9)	24 (13)
	Headache	28 (8)	4 (2)
	Nasopharyngitis	26 (7)	17 (9)
	Diarrhea	22 (6)	11 (6)
	HTN	21 (6)	6 (3)
	COVID-19	20 (5)	6 (3)
	Arthralgia	19 (5)	8 (4)
	Cough	18 (5)	11 (6)
Death		5 (1)[e]	0
Any-grade laboratory abnormality		341 (92)	178 (97)[f]
Grade ≥3 laboratory abnormality		124 (33)	64 (35)[f]

Abbreviation: EFV=efavirenz.
[a]DM and maculopapular rash. [b]DM was newly diagnosed in a participant who had a high fasting glucose level at baseline. This resolved on Day 173 after a switch in ARV regimen to EFV + DRV/RTV on Day 103.
[c]Cerebrovascular accident; DM; erectile dysfunction and worsened HTN; headache and hypoesthesia; HBV viremia; and alopecia, dizziness, worsened fatigue, headache, and nausea (each, n=1). All AEs except for hypoesthesia, HBV viremia, and cerebrovascular accident were related to BIC/LEN.
[d]Pulmonary embolism; unrelated to study drug.
[e]None of the deaths were deemed related to BIC/LEN: unknown cause (n=2), metastatic neoplasm (n=1), cardiac arrest (n=1), and respiratory failure (n=1). [f]n=183.

From baseline to Week 48, body weight remained stable in both groups, with a median (IQR) change of +0.6 (-1.1 to 2.6) kg in the BIC/LEN group and 0 (-2 to 2.4) kg in the complex ART regimen group.[4]

After switching to BIC/LEN, fasting levels of TC, LDL, and TG, and the TC:HDL ratio was observed to improve from baseline to Week 48; HDL levels remained stable (Table 9).[4]

Table 9. Phase 3 of ARTISTRY-1: Changes in Fasting Lipids From Baseline to Week 48[4,14]

	TC		LDL		HDL		TG		TC:HDL	
	BL[a]	Change From BL to Week 48[b]	BL[a]	Change From BL to Week 48[b]	BL[a]	Change From BL to Week 48[b]	BL[a]	Change From BL to Week 48[b]	BL[a]	Change From BL to Week 48[b]
BIC/LEN[c]	176	-15	97	-9	47	-1	130	-15	3.6	-0.3
Complex ART Regimen[d]	188	+2	105	+2	48	0	123	+4	3.7	0
P-Value[e]	<0.0001		<0.0001		0.46		0.0008		<0.0001	

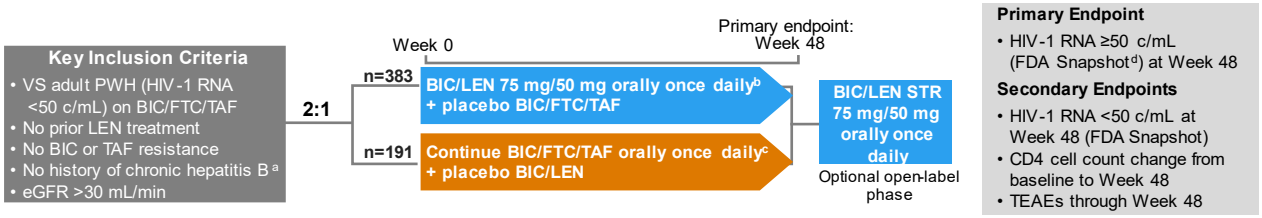
Abbreviation: BL=baseline.
[a]Median value; presented as mg/dL. [b]Median change from baseline; presented as mg/dL.
[c]Baseline, n=316. [d]Baseline, n=147.
[e]Nominal *P*-values for comparison between treatment groups were estimated using the mixed model with repeated measures of the change from BL (fixed effects: treatment, visit, treatment by visit, BL value, and geographic region [US vs non-US]; random effect: participant).

ARTISTRY-2: Switching to BIC/LEN vs BIC/FTC/TAF

Study design and demographics[7]

An ongoing, randomized, multicenter, double-blind, active-controlled, phase 3 study (NCT06333808) is evaluating the efficacy and safety of switching from BIC/FTC/TAF to STR BIC/LEN 75 mg/50 mg vs continuing BIC/FTC/TAF in VS PWH. After the randomized period, participants could continue in the OLE phase and receive BIC/LEN.

Figure 3. ARTISTRY-2: Study Design[7]



Abbreviations: HBcAb=HBV core antibody; HBsAb=HBV surface antibody; HBsAg=HBV surface antigen.
[a]Determined by the following at the screening visit: either HBsAg+ status or HBcAb+ and HBsAb status.
[b]Oral loading doses of LEN 600 mg on Days 1 and 2 were given.
[c]Participants were given placebo to match LEN on Days 1 and 2 of treatment.
[d]Non-inferiority margin: 4%.

Table 10. ARTISTRY-2: Baseline Demographics and Disease Characteristics[7]

Key Demographics and Characteristics	BIC/LEN 75 mg/50 mg (n=383)	BIC/FTC/TAF (n=191)	Total (N=574)
Age, median (range), years	47 (23–77)	51 (26–77)	49 (23–77)
Male sex assigned at birth, n (%)	314 (82)	149 (78)	463 (81)
Race, White/Black/Asian/American Indian or Alaska Native/Native Hawaiian or Pacific Islander/other, %	52/30/13/<1/<1/5	58/23/14/1/0/5	54/27/13/<1/<1/5
Hispanic/Latinx,[a] n (%)	106 (28)	49 (26)	155 (27)

Key Demographics and Characteristics	BIC/LEN 75 mg/50 mg (n=383)	BIC/FTC/TAF (n=191)	Total (N=574)
CD4 count, median (IQR), cells/mcL	711 (547–914)	663 (522–873)	695 (541–902)
History of select comorbidities,[b] dyslipidemia/HTN/DM or hyperglycemia/CKD, %	41/37/18/5	41/33/16/6	41/36/17/6
Number of select comorbidities, 1/≥2, n (%)	94 (25)/ 121 (32)	57 (30)/ 52 (27)	151 (26)/ 173 (30)

[a]Local regulations did not permit the collection of ethnicity data for 1 participant in the BIC/FTC/TAF group.
[b]Grouped terms per MedDRA; not mutually exclusive.

Efficacy outcomes through Week 48[7]

The median (IQR) exposure was 60.6 (53–69) weeks for BIC/LEN and 59.9 (52–67.9) weeks for BIC/FTC/TAF. BIC/LEN was non-inferior to BIC/FTC/TAF in maintaining virologic suppression at Week 48 (Table 11).

Table 11. ARTISTRY-2: Rates of HIV RNA ≥50 c/mL and HIV RNA <50 c/mL (FDA Snapshot) at Week 48[7]

Efficacy Endpoints	BIC/LEN 75 mg/50 mg	BIC/FTC/TAF
HIV-1 RNA ≥50 c/mL, n/N (%)	5/383 (1)[a]	2/191 (1)
Difference,[b] % (95.002% CI)	0.3 (-1.9 to 2.4)	
HIV-1 RNA <50 c/mL, n/N (%)	358/383 (93)	173/191 (91)
Difference,[b] % (95.002% CI)	3.1 (-1.8 to 8)	
No virologic data, n/N (%)	20/383 (5)[c]	16/191 (8)[d]

[a]Four of the 5 participants had HIV-1 RNA between 56 and 147 c/mL.
[b]Two-sided CI was based on Mantel-Haenszel stratum weights and the Koch variance estimator and was adjusted by geographic region (US vs non-US).
[c]Reasons for DC before Week 48: other reasons and last HIV-1 RNA was <50 c/mL, n=14; AE or death, n=6; other reasons and last HIV-1 RNA was ≥50 c/mL, n=3.
[d]Reasons for DC before Week 48: other reasons and last HIV-1 RNA was <50 c/mL, n=12; AE or death, n=4; other reasons and last HIV-1 RNA was ≥50 c/mL, n=2.

In the BIC/LEN group, 1 participant had an HIV-1 RNA of 10,700 c/mL at Week 48, was switched to BIC/FTC/TAF, and then was resuppressed on DRV/COBI/FTC/TAF.
Two participants in each group underwent resistance analysis. No treatment-emergent resistance was noted for 1 participant in the BIC/LEN group and for both participants in the BIC/FTC/TAF group. The other participant in the BIC/LEN group had a history of RAL and DTG exposure and had an isolated R263K integrase substitution recorded at Week 36; the R263K isolate was susceptible to BIC, and no capsid mutations were detected.

Through Week 48, CD4 cell counts remained stable in both treatment groups, with a median (IQR) change from baseline of -7 (-111 to 88) cells/mcL in the BIC/LEN group and 6 (-87 to 95) cells/mcL in the BIC/FTC/TAF group.

Safety outcomes through Week 48[7]

Similar rates of AEs and TRAEs were reported in both groups, and the overall incidence of treatment DC due to AEs was low (Table 12).

Table 12. ARTISTRY-2: Safety Outcomes Through Week 48[7]

Safety Outcomes, n (%)		BIC/LEN 75 mg/50 mg (n=383)	BIC/FTC/TAF (n=191)
Any-grade AEs		288 (75)	141 (74)
Grade ≥3 AEs		38 (10)	15 (8)
Any-grade TRAEs		40 (10)	23 (12)
Grade ≥3 TRAE		1 (<1)[a]	0
SAEs		27 (7)	13 (7)
Treatment-related SAEs		0	0
AEs that led to study drug DC		6 (2)[b]	3 (2)[c]
AEs that occurred in ≥5% in either group	Diarrhea	31 (8)	9 (5)
	Nasopharyngitis	30 (8)	13 (7)
	URTI	29 (8)	9 (5)
	Headache	22 (6)	6 (3)
	Nausea	20 (5)	11 (6)
	COVID-19	5 (1)	10 (5)
Death		0	1 (<1)[d]
Grade ≥3 laboratory abnormalities[e]		93 (24)	44 (23)

[a]Grade 3 rhabdomyolysis that was revised to Grade 1 after data cutoff.
[b]The following were deemed unrelated to BIC/LEN (each, n=1): anxiety; colon cancer; decreased libido; and encephalopathy and intracranial mass. The following were deemed related to BIC/LEN (each, n=1): alopecia and fatigue; and rash, restless leg syndrome, and trismus.
[c]The following were deemed unrelated to BIC/FTC/TAF (each, n=1): abdominal discomfort; road traffic accident. Dry mouth was deemed related to BIC/FTC/TAF treatment.
[d]Due to coronary artery disease and was deemed unrelated to study treatment.
[e]The most common were increased direct bilirubin concentration (BIC/LEN, n=36 [9%]; BIC/FTC/TAF, n=7 [4%]) and decreased CrCl (BIC/LEN, n=23 [6%]; BIC/FTC/TAF, n=21 [11%]).

Bodyweight remained stable from baseline to Week 48, with median changes of -0.2 kg in the BIC/LEN group and 0 kg in the BIC/FTC/TAF group.

Subgroup analyses[8]

The efficacy and safety of switching from BIC/FTC/TAF to BIC/LEN were assessed in the following subgroups: age (<55 years and ≥55 years), sex, race (White and non-White), and geographic region (US and ex-US). Baseline demographics and disease characteristics were similar between treatment groups and subgroups.

At Week 48, participants who received BIC/LEN maintained high rates of virologic suppression across all subgroups, and the proportions of participants with HIV-1 RNA ≥50 c/mL and <50 c/mL were generally similar between treatment groups (Table 13).

Table 13. ARTISTRY-2: Efficacy Outcomes at Week 48 by Subgroup Analyses[8]

Subgroup			BIC/LEN, n/N (%)	BIC/FTC/TAF, n/N (%)	Difference, % (95% CI)
HIV-1 RNA ≥50 c/mL at Week 48	**Overall**		5/383 (1.3)	2/191 (1)	0.3 (-2.6, 2.2)
	Age, years	<55	4/248 (1.6)	0	1.6 (-1.8, 4.2)
		≥55	1/135 (0.7)	2/70 (2.9)	-2.1 (-9.4, 1.9)
	Sex	Male	4/314 (1.3)	1/149 (0.7)	0.6 (-2.7, 2.7)
		Female	1/69 (1.4)	1/42 (2.4)	-0.9 (-11.3, 6)
	Race	White	3/199 (1.5)	2/111 (1.8)	-0.3 (-5.1, 3)
		Non-White	2/184 (1.1)	0	1.1 (-3.9, 4)
	Region	US	3/249 (1.2)	1/115 (0.9)	0.3 (-3.9, 2.9)
		Ex-US	2/134 (1.5)	1/76 (1.3)	0.2 (-5.9, 4.4)

Subgroup			BIC/LEN, n/N (%)	BIC/FTC/TAF, n/N (%)	Difference, % (95% CI)
HIV-1 RNA <50 c/mL at Week 48	**Overall**		358/383 (93.5)	173/191 (90.6)	2.9 (-1.7, 8.4)
	Age, years	<55	228/248 (91.9)	111/121 (91.7)	0.2 (-5.5, 7.2)
		≥55	130/135 (96.3)	62/70 (88.6)	7.7 (0.1, 17.8)
	Sex	Male	299/314 (95.2)	133/149 (89.3)	6 (0.3, 12.4)
		Female	59/69 (85.5)	40/42 (95.2)	-9.7 (-21.1, 3.5)
	Race	White	188/199 (94.5)	99/111 (89.2)	5.3 (-1.1, 13)
		Non-White	170/184 (92.4)	74/80 (92.5)	-0.1 (-6.7, 8.6)
	Region	US	228/249 (91.6)	103/115 (89.6)	2 (-4.2, 9.7)
		Ex-US	130/134 (97)	70/76 (92.1)	4.9 (-1.6, 13.6)

Note: Cells shaded in blue indicate the treatment difference favored BIC/LEN; cells shaded in orange indicate the treatment difference favored BIC/FTC/TAF. Differences in percentages of participants between treatment groups and 95% CIs were calculated based on an unconditional exact method using two inverted one-sided tests.

The incidence of TRAEs was similar with BIC/LEN and BIC/FTC/TAF across assessed subgroups.

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Abbreviations

AE=adverse event
ART=antiretroviral therapy
ARV=antiretroviral
BIC=bictegravir
c/mL=copies per mL
CD4=cluster of differentiation
CKD=chronic kidney disease
COBI=cobicistat
DC=discontinuation
DM=diabetes mellitus
DRV=darunavir
DTG=dolutegravir
FTC=emtricitabine
HTN=hypertension
INSTI=integrase strand transfer inhibitor
LEN=lenacapavir
MedDRA=Medical Dictionary for Regulatory Activities
MVC=maraviroc
NNRTI=non-nucleos(t)ide reverse transcriptase inhibitor
NRTI=nucleos(t)ide reverse transcriptase inhibitor
OLE=open-label extension
PI=protease inhibitor
PWH=people with HIV
Q=quartile
RAL=raltegravir
RAM=resistance-associated mutation
RTV=ritonavir
SAE=serious adverse event
STR=single-tablet regimen
SUBQ=subcutaneous
TAF=tenofovir alafenamide
TAM=thymidine analog mutation
TC=total cholesterol
TEAE=treatment-emergent adverse event
TG=triglycerides
TRAE=treatment-related adverse event
URTI=upper respiratory tract infection
VS=virologically suppressed

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