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Bixlenvo™ (bictegravir/lenacapavir) Metabolic and Lipid Safety

This document is in response to your request for information regarding Bixlenvo™ (bictegravir/lenacapavir [BIC/LEN]) and metabolic and lipid safety data.

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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]

Weight increased is an adverse reaction that has been identified during postmarketing experience in patients receiving a BIC-containing regimen. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Clinical Data on BIC/LEN and Metabolic and Lipid Safety Data

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.[2-5]

- In phase 3, from BL 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. After participants switched to BIC/LEN, fasting levels of TC, LDL, and TG and the TC:HDL ratio were observed to improve from BL to Week 48; HDL levels remained stable.[3]
- In an analysis of phase 3 Week 48 metabolic outcomes based on BL PI use, switching from a complex ART regimen to BIC/LEN was associated with greater improvements in fasting lipid parameters, particularly among those who switched from a PI-containing regimen. All other assessed metabolic parameters were stable from BL to Week 48 in both treatment groups, regardless of BL PI use. Low rates of treatment-emergent dyslipidemia AEs were reported across all participants.[4]
- In a subgroup analysis that assessed outcomes among participants with dyslipidemia, HTN, and/or DM at BL, there was no meaningful change in the use of lipid-lowering, antihypertensive, or antidiabetic agents from BL to Week 48. Most AEs were Grade ≤2, and Grade ≥3 or serious TRAEs were reported at low rates.[5]

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.[6,7]

- Changes in body weight from BL to Week 48 remained stable, with a median (IQR) change of -0.2 (-2.5 to 1.8) kg in the BIC/LEN group and 0 (-2.2 to 2.3) kg in the BIC/FTC/TAF group.[6]

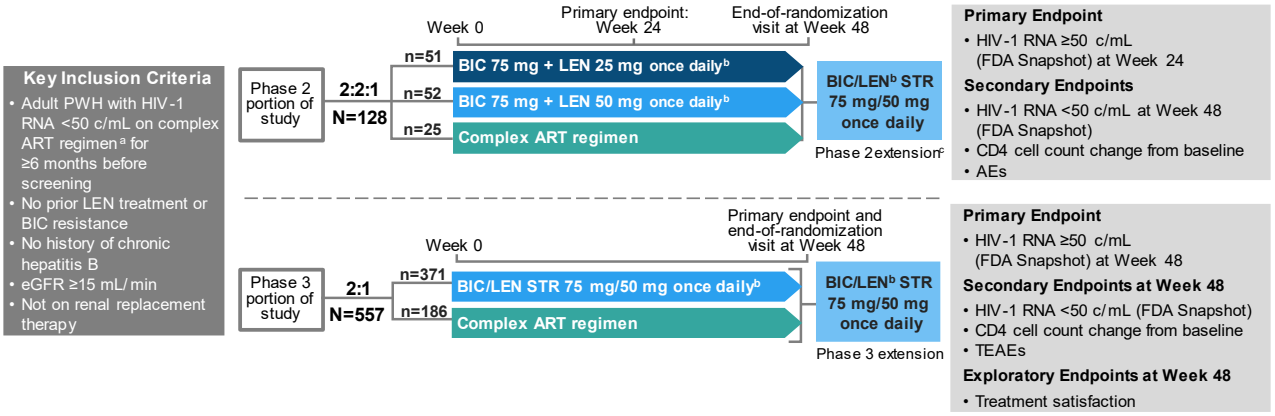
- From BL to Week 48, there were no clinically significant changes in fasting lipid parameters, glucose and HbA1c levels, weight, or BMI overall in participants in either treatment group or in participants with dyslipidemia, hyperglycemia, or DM at BL.[7]

Clinical Data on BIC/LEN and Metabolic and Lipid Safety Data

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.[2,8]

Figure 1. ARTISTRY-1 Phase 2/3: Study Design[3,8,9]



Abbreviations: NNRTI=non-nucleos(t)ide reverse transcriptase; NRTI=nucleos(t)ide reverse transcriptase inhibitor.
[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: BL Demographics, Disease Characteristics, and Historical Resistance Mutations[8]

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)

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)
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/Latine,[a] n (%)	7 (14)	9 (17.6)	4 (16)	20 (15.9)
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)

[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.

Metabolic and lipid safety data

In general, with BIC + LEN treatment, most fasting lipid parameters decreased at Week 48, whereas increases in fasting glucose levels, body weight, and BMI were observed (Table 2). Rates of treatment-emergent metabolic disorders are summarized in Table 2.[10]

Table 2. Phase 2 of ARTISTRY-1: Median Changes in Metabolic Parameters at Week 48 and Treatment-Emergent Metabolic Disorders[2,10]

		BIC 75 mg + LEN 25 mg	BIC 75 mg + LEN 50 mg	Complex ART Regimen
Metabolic parameter, median change from BL[a]	TC, mg/dL	−21[b]	−14[b]	+4[c]
	LDL, mg/dL	−10[b]	−11[b]	+5[c]
	HDL, mg/dL	−2[b]	0[b]	-3[c]
	TG, mg/dL	−18[b]	−9[b]	+6[c]
	TC:HDL	−0.3[b]	−0.4[b]	+0.2[c]
	Fasting glucose, mg/dL	+3[b]	+2[d]	-6[c]
	Body weight,[e] kg	+0.6 (−0.6 to +1.9)[f]	+0.9 (−2.1 to +3.3)[g]	-0.7 (-2.4 to +0.2)[h]
	BMI, kg/m^2	+0.2[f]	+0.3[g]	-0.2[h]
	Systolic/diastolic BP, mm Hg	−5/−1[f]	+2/+2[g]	0/+1[h]
Treatment-emergent metabolic disorders,[i] CKD/DM/HTN/dyslipidemia, n (%)		3 (6)/2 (4)/ 1 (2)/ 0	1 (2)/2 (4)/ 6 (12)[j]/0	1 (4)/1 (4)/ 1 (4)/ 0

[a]Results shown from participants with available data at both BL and Week 48.
[b]n=42. [c]n=20. [d]n=43
[e]IQR was reported for the change from BL to Week 48.
[f]n=49. [g]n=48. [h]n=25.
[i]Referred to grouped Standardized MedDRA Query. Disorders began at the beginning of the study and up to 60 days after stopping BIC or LEN (BIC + LEN groups) or at the beginning of the study and up to 30 days after stopping the complex ART regimen. Multiple AEs were counted once per participant.
[j]Included HTN (n=5) and hypertensive crisis (n=1). All cases were reported among participants who had abnormal BP (systolic/diastolic BP, >120/>80 mm Hg), and none were deemed to be drug related.

Laboratory abnormalities were not reported at Week 48.[2,11]

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).[3]

Table 3. Phase 3 of ARTISTRY-1: BL Demographics and Disease Characteristics[3]

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/Latine,[b] n (%)		80 (22)	42 (23)	122 (22)
Duration of HIV treatment, median (IQR), years		28.3 (21.6–32.3)[c]	28.3 (21.4–31.8)[d]	28.3 (21.6–32.1)[e]
History of select comorbidities,[f] dyslipidemia/HTN/DM or hyperglycemia/CKD, %		66/51/25/13	72/48/23/16	68/50/24/14
Select concomitant medications,[g] n (%)	Antidiabetic agents	84 (23)	44 (24)	128 (23)
	Antihypertensive agents	203 (55)	101 (54)	304 (55)
	Lipid-lowering agents	262 (71)	134 (72)	396 (71)
	Antidiabetic and antihypertensive agents	58 (16)	36 (19)	94 (17)
	Antidiabetic, antihypertensive, and lipid-lowering agents	50 (13)	32 (17)	82 (15)
Select concomitant medications, 1/≥2, n (%)		62 (17)/237 (64)	50 (27)/102 (55)	112 (20)/339 (61)

[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=358. [d]n=183. [e]n=541.
[f]Not mutually exclusive. Grouped terms per MedDRA.
[g]Antidiabetic drugs included drugs with WHO ATC2 "drugs used in diabetics"; antihypertensive agents included drugs with WHO ATC2 "agents acting on the renin-angiotensin system", "antihypertensives" (excluding ATC3 "other antihypertensives"), "beta-blocking agents", "calcium channel blockers", or "diuretics"; lipid-lowering agents included drugs with WHO ATC2 "drugs used in diabetes".

Metabolic and lipid safety data

From BL 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.[3]

After participants switched to BIC/LEN, fasting levels of TC, LDL, and TG and the TC:HDL ratio were observed to improve from BL to Week 48; HDL levels remained stable (Table 4).[3]

Table 4. Phase 3 of ARTISTRY-1: Changes in Fasting Lipids From BL to Week 48[3,12]

	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	

[a]Median value; presented as mg/dL. [b]Median change from BL; presented as mg/dL.
[c]BL, n=316. [d]BL, 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).

Analysis of metabolic outcomes at Week 48 by BL PI use[4]

Changes from BL to Week 48 in fasting lipid levels, glucose parameters, body weight, BMI, and BP were assessed in each treatment group by BL PI use. BL demographics are presented in Table 5.

Table 5. Phase 3 of ARTISTRY-1:
BL Demographics and Disease Characteristics by BL PI Use[4]

Key Demographics and Characteristics		BIC/LEN		Complex ART Regimen	
		PI (n=279)	No PI (n=92)	PI (n=148)	No PI (n=38)
Age, median (range), years		60 (22–81)	62 (36–84)	60 (24–75)	61 (49–75)
Female sex at birth, n (%)		43 (15.4)	21 (22.8)	30 (20.3)	6 (15.8)
Race, White/Black/Asian/other,[a]		70.6/19/4.7/2.2	68.5/12/3.3/6.5	66.9/19.6/5.4/2	65.8/10.5/2.6/0
Hispanic/Latinx ethnicity,[b] n (%)		69 (24.7)	11 (12)	35 (23.6)	7 (18.4)
History of select comorbidities, dyslipidemia/HTN/DM or hyperglycemia/CKD, %		68.8/48/ 21.9/13.3	56.5/60.9/ 32.6/13	68.9/44.6/ 17.6/14.2	81.6/63.2/ 42.1/21.1
HbA1c, median (IQR), %	Overall	5.4 (5.2–5.7)	5.5 (5.3–6)	5.4 (5.1–5.7)	5.7 (5.2–6.1)
	In participants with hyperglycemia or DM	6 (5.4–6.8)	6.4 (5.8–7.2)	6.2 (5.7–6.7)	6.4 (5.8–7.2)
Select concomitant non-ARV medications, n (%)	1	49 (17.6)	13 (14.1)	43 (29.1)	7 (18.4)
	≥2	180 (64.5)	57 (62)	76 (51.4)	26 (68.4)
	Antidiabetics	62 (22.2)	22 (23.9)	31 (20.9)	13 (34.2)
	Antihypertensives	147 (52.7)	56 (60.9)	74 (50)	27 (71.1)
	Lipid-lowering agents	205 (73.5)	57 (62)	106 (71.6)	28 (73.7)

Abbreviation: ARV=antiretroviral.
[a]Local regulators did not allow the collection of race data for 19 participants in the BIC/LEN group (PI, n=10; no PI, n=9) and 17 in the complex ART regimen group (PI, n=9; no PI, n=8). "Other" included American Indian or Alaska Native, Native Hawaiian or Pacific Islander, and other.
[b]Local regulators did not allow the collection of ethnicity data for 21 participants in the BIC/LEN group (PI, n=12; no PI, n=9) and 16 in the complex ART regimen group (PI, n=8; no PI, n=8).

From BL to Week 48, switching from a complex ART regimen to BIC/LEN was associated with greater improvements in fasting lipid parameters, particularly among those who switched from a PI-containing regimen (Table 6).

Table 6. Phase 3 of ARTISTRY-1:
Change From BL to Week 48 in Fasting Lipid Parameters by BL PI Use[4]

Parameter, Median		BIC/LEN		Complex ART Regimen	
		PI (n=233)	No PI (n=83)	PI (n=115)	No PI (n=32)
TC, mg/dL	BL	181	163	191	158
	Change from BL to Wk 48	-21	-5	+2	+3
LDL, mg/dL	BL	101	88	110	79
	Change from BL to Wk 48	-12	-1	+2	+2
HDL, mg/dL	BL	48	45	49	45
	Change from BL to Wk 48	-1	-1	0	-1
TG, mg/dL	BL	133	121	127	114
	Change from BL to Wk 48	-19	-5	+4	+4
TC:HDL ratio	BL	3.7	3.5	3.7	3.7
	Change from BL to Wk 48	-0.4	-0.1	0	0

From BL to Week 48, fasting glucose, HbA1c levels, body weight, BMI, and systolic and diastolic BP remained stable across treatment groups, regardless of BL PI use. A weight

gain of >10% in the BIC/LEN group was reported in 3.2% of participants (n/N=9/279) who were receiving a PI-containing regimen and in no participants who were not receiving a PI-containing regimen at BL. Among those in the complex ART regimen group, 0.7% of participants (n/N=1/148) who were on a PI-containing regimen at BL and no participants who were not on a PI-containing regimen at BL experienced a weight gain of >10% from BL.

Treatment-emergent dyslipidemia occurred at low rates across all treatment groups regardless of BL PI use (Table 7).

Table 7. Phase 3 of ARTISTRY-1: Treatment-Emergent Dyslipidemia AEs[4]

AE, n (%)	BIC/LEN		Complex ART Regimen	
	PI (n=279)	No PI (n=92)	PI (n=148)	No PI (n=38)
Participants with treatment-emergent dyslipidemia AEs[a]	8 (2.9)	2 (2.2)	4 (2.7)	0
Hypertriglyceridemia	2 (0.7)	1 (1.1)	0	0
Dyslipidemia	2 (0.7)	0	1 (0.7)	0
Hyperlipidemia	2 (0.7)	0	1 (0.7)	0
Hypercholesterolemia	1 (0.4)	1 (1.1)	2 (1.4)	0
Type V hyperlipidemia	1 (0.4)	0	0	0
Low-density lipoprotein increased	0	0	1 (0.7)	0

[a]Grouped terms in a standardized MedDRA narrow search were used. Data included treatment-emergent metabolic disorders that began on or after study drug initiation and up to 60 days after permanent study drug discontinuation in the BIC/LEN group and on/after Day 1 and up to 30 days after permanent discontinuation of a complex regimen in the complex ART regimen group. Multiple AEs were counted only once per participant.

Subgroup analysis in participants with dyslipidemia, HTN, and/or DM at BL[5]

A subgroup analysis assessed the safety outcomes at Week 48 of VS PWH with dyslipidemia, HTN, and/or DM at BL who switched to BIC/LEN or continued their complex ART regimen. Of the participants with dyslipidemia, HTN, and/or DM at BL, most were taking ≥2 concomitant medications during the study (Table 8).

Table 8. ARTISTRY-1: Select Concomitant Medications by BL Comorbidity[5]

Participants, n (%)	Dyslipidemia		HTN		DM	
	BIC/LEN (n=244)	CAR (n=133)	BIC/LEN (n=190)	CAR (n=90)	BIC/LEN (n=91)	CAR (n=42)
Select concomitant medications						
1	43 (18)	34 (26)	16 (8)	9 (10)	10 (11)	1 (2)
≥2	190 (78)	93 (70)	168 (88)	79 (88)	79 (87)	41 (98)
Types of select concomitant medications						
Lipid-lowering agents	225 (92)	119 (89)	156 (82)	75 (83)	76 (84)	39 (93)
Antihypertensive agents	154 (63)	86 (65)	170 (89)	84 (93)	62 (68)	36 (86)
Antidiabetic agents	67 (27)	38 (29)	56 (29)	33 (37)	66 (73)	32 (76)
Antidiabetic and antihypertensive agents	46 (19)	32 (24)	49 (26)	32 (36)	48 (53)	28 (67)
Antidiabetic, antihypertensive, and lipid-lowering agents	44 (18)	28 (21)	42 (22)	28 (31)	40 (44)	26 (62)
Any GLP-1 agents	26 (11)	15 (11)	24 (13)	14 (16)	22 (24)	9 (21)

Note: Select comorbidities were categorized by MedDRA v28.0 with a standardized MedDRA query narrow search. The full search term for DM was “hyperglycemia/new onset DM.” Comorbidities were not mutually exclusive, and participants with >1 select comorbidity were included in the other group(s). The WHODrug dictionary was used to code concomitant medications and included antidiabetic, antihypertensive, GLP-1 agents (liraglutide, semaglutide, or tirzepatide), and lipid-lowering agents.

From BL to Week 48, there was no meaningful change in the use of lipid-lowering, antihypertensive, or antidiabetic agents (Table 9).

Table 9. ARTISTRY-1: Select Concomitant Medication Use at BL and Week 48[5]

Participants, n (%)	Dyslipidemia		HTN		DM	
	BIC/LEN (n=244)	CAR (n=133)	BIC/LEN (n=190)	CAR (n=90)	BIC/LEN (n=91)	CAR (n=42)
Lipid-lowering agents						
Use at BL	215 (88)	113 (85)	146 (77)	70 (78)	73 (80)	38 (90)
Use at Week 48	217 (89)	119 (89)	151 (79)	74 (82)	73 (80)	39 (93)
Initiated during the study	10 (4)	6 (5)	10 (5)	5 (6)	3 (3)	1 (2)
Stopped during the study	5 (2)	0	4 (2)	0	2 (2)	0
Antihypertensive agents						
Use at BL	143 (59)	81 (61)	165 (87)	82 (91)	61 (67)	36 (86)
Use at Week 48	151 (62)	83 (62)	166 (87)	82 (91)	61 (67)	36 (86)
Initiated during the study	11 (5)	5 (4)	5 (3)	2 (2)	1 (1)	0
Stopped during the study	4 (2)	3 (2)	3 (2)	3 (3)	2 (2)	1 (2)
Antidiabetic agents						
Use at BL	53 (22)	29 (22)	46 (24)	25 (28)	59 (65)	29 (69)
Use at Week 48	61 (25)	37 (28)	52 (27)	32 (36)	65 (71)	31 (74)
Initiated during the study	14 (6)	9 (7)	10 (5)	8 (9)	7 (8)	3 (7)
Stopped during the study	1 (<1)	0	2 (1)	0	0	0
GLP-1 agents						
Use at BL	20 (8)	8 (6)	20 (11)	8 (9)	19 (21)	6 (14)
Use at Week 48	22 (9)	15 (11)	20 (11)	14 (16)	21 (23)	9 (21)
Initiated during the study	6 (2)	7 (5)	4 (2)	6 (7)	3 (3)	3 (7)
Stopped during the study	3 (1)	0	3 (2)	0	2 (2)	0

Most AEs were Grade ≤2 in severity, and Grade ≥3 and serious TRAEs were reported at low rates (Table 10).

Table 10. ARTISTRY 1:
Safety Outcomes at Week 48 Overall and by BL Comorbidities[5]

Participants, n (%)	Overall		Dyslipidemia		HTN		DM	
	BIC/LEN (n=371)	CAR (n=186)	BIC/LEN (n=244)	CAR (n=133)	BIC/LEN (n=190)	CAR (n=90)	BIC/LEN (n=91)	CAR (n=42)
AEs	305 (82)	157 (84)	198 (81)	117 (88)	156 (82)	78 (87)	72 (79)	40 (95)
Grade ≥3	51 (14)	26 (14)	36 (15)	22 (17)	28 (15)	16 (18)	17 (19)	8 (19)
SAEs	52 (14)	22 (12)	38 (16)	21 (16)	31 (16)	13 (14)	17 (19)	9 (21)
AEs that occurred in ≥2 participants with dyslipidemia, HTN, and/or DM at BL								
CVA	3 (1)	0	3 (1)	0	3 (2)	0	0	0
CAD	2 (1)	1 (1)	2 (1)	1 (1)	1 (1)	0	1 (1)	0
AKI	2 (1)	0	2 (1)	0	2 (1)	0	0	0
Unstable angina	2 (1)	0	2 (1)	0	1 (1)	0	1 (1)	0
COVID-19	2 (1)	0	1 (<1)	0	2 (1)	0	1(1)	0
AMI	0	2 (1)	0	2 (2)	0	2 (2)	0	1 (2)
TRAEs	53 (14)	3 (2)	28 (11)	3 (2)	26 (14)	1 (1)	15 (16)	0
Grade ≥3	2 (1)	0	2 (1)	0	0	0	0	0
Serious	1 (<1)	0	1 (<1)	0	0	0	0	0

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Participants, n (%)	Overall		Dyslipidemia		HTN		DM	
	BIC/LEN (n=371)	CAR (n=186)	BIC/LEN (n=244)	CAR (n=133)	BIC/LEN (n=190)	CAR (n=90)	BIC/LEN (n=91)	CAR (n=42)
Occurred in any participant with dyslipidemia, HTN, and/or DM at BL								
CVA	1 (<1)	0	1 (<1)	0	1 (1)	0	0	0
HBV reactivation	1 (<1)	0	1 (<1)	0	1 (1)	0	1 (1)	0
New DM diagnosis	1 (<1)	0	1 (<1)	0	0	0	0	0
Erectile dysfunction	1 (<1)	0	0	0	1 (<1)	0	0	0
Worsening HTN	1 (<1)	0	0	0	1 (1)	0	0	0
PE	0	1 (1)	0	1 (1)	0	1 (1)	0	0
AEs that led to treatment DC[a]	6 (2)	1 (1)	3 (1)	1 (1)	3 (2)	1 (1)	1 (1)	0
Deaths[b]	5 (1)	0	2 (1)	0	3 (2)	0	2 (2)	0

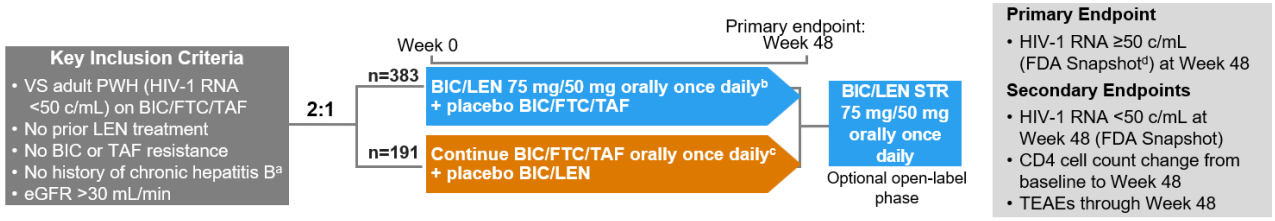
Abbreviations: AKI=acute kidney injury; AMI=acute myocardial infarction; CAD=coronary artery disease; CVA=cerebrovascular accident; DC=discontinuation; PE=pulmonary embolism.
[a]Participants could have ≥1 AE that led to treatment DC.
[b]Due to unknown cause (n=2); and liver failure secondary to metastatic cancer, oropharyngeal cell carcinoma, and sudden cardiac arrest (each, n=1). All deaths were considered unrelated to BIC/LEN treatment.
Note: Select comorbidities were categorized by MedDRA, Version 28.0 with a standardized MedDRA query narrow search. The full search term for DM was "hyperglycemia/new onset DM." Comorbidities were not mutually exclusive, and participants with >1 select comorbidity were included in the other group(s). Multiple events experienced by any given participant were counted only once.

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

Study design and demographics[6]

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 2. ARTISTRY-2: Study Design[6]



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%.

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Table 11. ARTISTRY-2: BL Demographics and Disease Characteristics[6]

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/Latine,[a] n (%)	106 (28)	49 (26)	155 (27)
BMI, median (IQR), kg/m^2	26.8 (24.2–30.3)	27.1 (24.1–31.2)	26.8 (24.1–30.5)
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.

Metabolic and lipid safety

Changes in body weight from BL to Week 48 remained stable, with a median (IQR) change of -0.2 (-2.5 to 1.8) kg in the BIC/LEN group and 0 (-2.2 to 2.3) kg in the BIC/FTC/TAF group.[6]

Grade ≥3 laboratory abnormalities occurred in 24% of participants in the BIC/LEN group and in 23% of participants in the BIC/FTC/TAF group (Table 12).[13]

Table 12. ARTISTRY-2: Metabolic and Lipid-Related Laboratory Abnormalities (Safety Analysis Set)[6,13]

Metabolic and Lipid-Related Laboratory Abnormality, n/N (%)		BIC/LEN 75 mg/50 mg	BIC/FTC/TAF
Grade ≥3 that occurred in ≥2% of participants in either treatment group	Increased fasting serum glucose	10/381 (3)	2/189 (1)
	Glycosuria	7/379 (2)	4/181 (2)
	Increased fasting TG	5/377 (1)	4/180 (2)
	Increased non-fasting serum glucose	3/235 (1)	3/126 (2)

Subgroup analysis in participants with dyslipidemia, HTN, and/or hyperglycemia or DM at BL[7]

A subgroup analysis assessed Week 48 outcomes in participants with dyslipidemia, HTN, and/or hyperglycemia or DM at BL who switched to BIC/LEN or continued BIC/FTC/TAF. Key outcome measures included metabolic parameters (ie, fasting lipid and glucose levels, HbA1c levels, weight, and BMI); concomitant lipid-lowering, antihypertensive, and antidiabetic agent use; and TEAEs.

From BL to Week 48, there were no clinically significant changes in fasting lipid levels in either treatment group overall or by dyslipidemia status at BL (Table 13).

Table 13. ARTISTRY-2: Fasting Lipid Parameters at BL and Changes From BL to Week 48 Overall and in Participants With BL Dyslipidemia[7]

Parameter, Median (Q1, Q3)		Overall		Dyslipidemia at BL	
		BIC/LEN	BIC/FTC/TAF	BIC/LEN	BIC/FTC/TAF
TC, mg/dL	BL	172 (152, 197); n=367	172 (150, 201); n=187	168 (144, 194); n=156	166 (148, 195); n=77
	Change from BL to Week 48	0 (-16, 17); n=343	1 (-11, 18); n=162	-2 (-20, 17); n=145	-1 (-12, 12); n=70
LDL, mg/dL	BL	99 (80, 125); n=367	99 (82, 124); n=187	93 (74, 116); n=156	95 (82, 116); n=77
	Change from BL to Week 48	1 (-12, 15); n=343	3 (-8, 16); n=162	-1 (-13, 18); n=145	1 (-9, 12); n=70
HDL, mg/dL	BL	48 (41, 57); n=366	47 (39, 58); n=187	46 (41, 56); n=155	46 (40, 58); n=77
	Change from BL to Week 48	0 (-4, 5); n=341	0 (-3, 5); n=162	0 (-5, 5); n=144	-1 (-3, 4); n=70
TG, mg/dL	BL	102 (74, 148); n=366	101 (76, 151); n=187	110 (78, 165); n=155	100 (75, 155); n=77
	Change from BL to Wk 48	0 (-29, 25); n=341	-5 (-27, 23); n=162	-3 (-30, 27); n-n=144	-6 (-33, 34); n=70
TC:HDL	BL	3.5 (3, 4.4); n=366	3.7 (3, 4.4); n=187	3.5 (2.9, 4.3); n=155	3.5 (3, 4.1); n=77
	Change from BL to Week 48	-0.1 (-0.4, 0.3); n=341	0 (-0.3, 0.3); n=162	0 (-0.6, 0.5); n=144	0 (-0.3, 0.3); n=70

From BL to Week 48, there were no clinically significant changes in fasting glucose or body weight overall or in participants with hyperglycemia or DM at BL (Table 14).

Table 14. ARTISTRY-2: Metabolic Outcomes at BL and Changes From BL to Week 48 in Participants Overall and in Participants With Hyperglycemia or DM at BL[7]

Parameter, Median (Q1, Q3)		Overall		Hyperglycemia or DM at BL	
		BIC/LEN	BIC/FTC/TAF	BIC/LEN	BIC/FTC/TAF
HbA1c, %	BL	5.3 (5.1, 5.7); n=377	5.3 (5, 5.7); n=188	6.2 (5.6, 6.7); n=67	5.9 (5.6, 6.5); n=31
	Change from BL to Week 48	0.1 (-0.1, 0.3); n=354	0.1 (-0.1, 0.3); n=170	0.1 (-0.2, 0.3); n=66	0 (-0.2, 0.5); n=29
Fasting glucose, mg/dL	BL	93 (86, 102); n=375	94 (78, 102); n=190	108 (94, 126); n=68	109 (95, 124); n=31
	Change from BL to Week 48	0 (-7, 6); n=354	-1 (-7, 7); n=172	1 (-13, 12); n=66	-1 (-7, 11); n=29
Weight, kg	BL	81.1 (71.7, 92.4); n=383	81.1 (72, 94.1); n=191	88.5 (79.4, 111.1); n=68	95.6 (83.5, 108); n=31
	Change from BL to Week 48	-0.2 (-2.5, 1.8); n=361	0 (-2.2, 2.3); n=173	-0.2 (-3.1, 1.9); n=67	0 (-3.8, 2.8); n=29
BMI, kg/m^2	BL	26.8 (24.2, 30.3); n=383	27.1 (24.1, 31.2); n=191	29.8 (27, 38.2); n=68	33.2 (30.4, 36); n=31
	Change from BL to Week 48	-0.1 (-0.8, 0.6); n=361	0 (-0.7, 0.7); n=173	-0.1 (-1.2, 0.6); n=67	0 (-1.4, 1.1); n=29

From BL to Week 48, the use of lipid-lowering, antihypertensive, antidiabetic, and GLP-1 medications was similar between treatment groups (Table 15).

Table 15. ARTISTRY-2: Select Concomitant Medication Use at BL and Week 48[7]

Paricipants, n (%)	BIC/LEN (n=383)	BIC/FTC/TAF (n=191)	Total (N=574)
Antihypertensive agents	160 (42)	68 (36)	228 (40)
Used at BL	140 (37)	62 (33)	202 (35)
Used at Week 48	152 (40)	66 (35)	218 (38)
Initiated during the study	20 (5)	6 (3)	26 (5)
Stopped during the study	3 (1)	2 (1)	5 (1)
Lipid-lowering agents	157 (41)	77 (40)	234 (41)
Used at BL	139 (36)	73 (38)	212 (37)
Used at Week 48	155 (41)	76 (40)	231 (40)
Initiated during the study	18 (5)	4 (2)	22 (4)
Stopped during the study	3 (1)	3 (2)	6 (1)
Antidiabetic agents	71 (19)	24 (13)	95 (17)
Used at BL	58 (15)	20 (11)	78 (14)
Used at Week 48	70 (18)	23 (12)	93 (16)
Initiated during the study	13 (3)	4 (2)	17 (3)
Stopped during the study	1 (<1)	3 (2)	4 (1)
GLP-1 agents	45 (12)	13 (7)	58 (10)
Used at BL	27 (7)	10 (5)	37 (6)
Used at Week 48	42 (11)	11 (6)	53 (9)
Initiated during the study	18 (5)	3 (2)	21 (4)
Stopped during the study	4 (1)	3 (2)	7 (1)

The incidences of TRAEs among participants with dyslipidemia, HTN, and/or hyperglycemia or DM at BL were generally low and were similar between treatment groups and compared with the overall population (Table 16).

Table 16. ARTISTRY-2:
Safety Outcomes at Week 48 Overall and by BL Comorbidity[7]

Participants, n (%)	Overall		Dyslipidemia		HTN		Hyperglycemia or DM	
	BIC/LEN (n=383)	BIC/FTC/TAF (n=191)	BIC/LEN (n=158)	BIC/FTC/TAF (n=79)	BIC/LEN (n=141)	BIC/FTC/TAF (n=63)	BIC/LEN (n=68)	BIC/FTC/TAF (n=31)
Any-grade AEs	288 (75)	141(74)	122 (77)	63 (80)	110 (78)	43 (68)	57 (84)	18 (58)
Grade ≥3	38 (10)	15 (8)	16 (10)	7 (9)	15 (11)	6 (10)	8 (12)	3 (10)
SAEs	27 (7)	13 (7)	9 (6)	7 (9)	10 (7)	5 (8)	6 (9)	2 (7)
TRAEs	40 (10)	23 (12)	15 (10)	7 (9)	10 (7)	4 (6)	4 (6)	5 (16)
Grade ≥3	1 (<1)[a]	0	1 (<1)[a]	0	0	0	0	0
AEs that led to treatment DC	6 (2)	3 (2)	3 (2)	0	2 (1)	1 (2)	1 (2)	0
Deaths	0	1 (1)	0	1 (1)	0	1 (2)	0	1 (3)

Abbreviation: DC=discontinuation.
[a]Grade 3 rhabdomyolysis that resolved with continued treatment without a dose interruption or regimen change and was subsequently recategorized as a Grade 1 AE after the cutoff date for this analysis.
Note: Grade severity was defined by the Division of AIDS Toxicology Grading Scale Version 2.1.

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Abbreviations

AE=adverse event
ART=antiretroviral therapy
ATC2/3=Anatomical Therapeutic Chemical 2nd-/3rd-level classification
BIC=bictegravir
BL=baseline
BP=blood pressure
c/mL=copies per mL
CAR=complex ART regimen
CD4=cluster of differentiation 4
CKD=chronic kidney disease
DM=diabetes mellitus
FTC=emtricitabine
GLP-1=glucagon-like peptide-1
HTN=hypertension
LEN=lenacapavir
MedDRA=Medical Dictionary for Regulatory Activities
OLE=open-label extension
PI=protease inhibitor
PWH=people with HIV
Q=quartile
SAE=serious adverse event
STR=single-tablet regimen
TAF=tenofovir alafenamide
TC=total cholesterol
TEAE=treatment-emergent adverse event
TG=triglycerides
TRAE=treatment-related adverse event
VS=virologically suppressed
WHO=World Health Organization

Product Label

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