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GILEAD | Medical Information

Yeztugo® (lenacapavir) Adherence

This document is in response to your request for information regarding Yeztugo® (lenacapavir [LEN]) and adherence data.

Some data may be outside of the US FDA-approved prescribing information. In providing this data, Gilead Sciences, Inc. is not making any representation as to its clinical relevance or to the use of any Gilead product(s). For information about the approved conditions of use of any Gilead drug product, please consult the FDA-approved prescribing information.

The use of FTC/TAF for prevention of HIV-1 in individuals at risk of HIV-1 from receptive vaginal sex is investigational and has not been approved by any regulatory authority. The full indication, important safety information, and boxed warning(s) are available at:
www.gilead.com/-/media/files/pdfs/medicines/hiv/yeztugo/yeztugo_pi;
www.gilead.com/-/media/files/pdfs/medicines/hiv/descovy/descovy_pi;
www.gilead.com/-/media/files/pdfs/medicines/hiv/truvada/truvada_pi.

Summary

Adherence Data from PURPOSE 1

Results published in July 2024 from PURPOSE 1 showed high adherence to injections (LEN and placebo LEN), defined as on-time injections at Week 26 and Week 52.[1]

- Most participants received on-time injections at Week 26 (91.5%; 4545/4967) and Week 52 (92.8%; 2025/2181).
- Adherence to LEN therapy was defined as on-time injections within 28 weeks after the last injection.

Adherence Data from PURPOSE 2

Results published in November 2024 from PURPOSE 2 showed high adherence to injections (LEN and placebo LEN), defined as on-time injections at Week 26 and Week 52.[2]

- Adherence to LEN or placebo LEN was similar, and most participants received on-time injections at Week 26 (91%; 2606/2864) and Week 52 (92.8%; 1016/1095).

Product Labeling[3]

Adherence

Prior to starting LEN, healthcare providers should select individuals who agree to the required testing and every 6-month injection dosing schedule, and counsel individuals about the importance of adherence to scheduled LEN dosing visits to help reduce the chance of acquiring HIV-1 and development of resistance.

It is important to select individuals who agree to the required injection dosing schedule because non-adherence to every-6-month injections or missed doses could lead to HIV-1 acquisition and development of resistance. In the event of a missed injection, please refer to Section 2.4 of the Prescribing Information for the appropriate dosing schedule.

Adherence Data from PURPOSE 1 Study

Study Design and Demographics[1]

PURPOSE 1 is a phase 3 ongoing, double-blind, randomized study evaluating the efficacy and safety of twice-yearly, SUBQ LEN and once-daily oral FTC/TAF for HIV-1 PrEP in more than 5,300 cisgender women and adolescent girls across South Africa and Uganda. Additionally, a third group was assigned once-daily oral FTC/TDF, which served as the active control. Study participants were randomized in a 2:2:1 ratio to LEN, FTC/TAF, and FTC/TDF, respectively. Randomly assigned participants were seen for follow-up at Weeks 4, 8, and 13 and every 13 weeks thereafter. A planned interim analysis occurred when 50% of the randomly assigned participants had completed at least 52 weeks of follow-up.

Key inclusion criteria in the randomized phase of the study included: negative fourth generation HIV-1 Ab/Ag test confirmed with central HIV-1 testing, eGFR ≥60 mL/min at screening, and body weight ≥35 kg. Individuals were excluded if they had prior use of long-acting systemic HIV PrEP or HIV PEP.[4]

Table 1. PUPOSE 1: Select Baseline Demographics and Clinical Characteristics[1]

Select Baseline Demographics and Risk Factors		LEN (n=2138)	FTC/TAF (n=2137)	FTC/TDF (n=1070)
Age, median (range), years		21 (16–25)	21 (16–26)	21 (16–25)
Back, n (%)[a]		2135 (99.9)	2136 (>99.9)	1068 (99.8)
Education, n/N (%)	No primary school	17/2136 (0.8)	19/2134 (0.9)	3/1069 (0.3)
	Primary school	235/2136 (11.0)	223/2134 (10.4)	106/1069 (9.9)
	Secondary school	1701/2136 (79.6)	1694/2134 (79.4)	851/1069 (79.6)
	College or university	183/2136 (8.6)	198/2134 (9.3)	109/1069 (10.2)
Living with primary partner, n/N (%)		148/2136 (6.9)	132/2134 (6.2)	73/1069 (6.8)
Any previous use of PrEP, n (%)		143 (6.7)	121 (5.7)	71 (6.6)

[a] Race was reported by the participants. All non-Black participants were multiracial.

Adherence Results[1]

Adherence to LEN was defined as on-time injections (within 28 weeks after the last injection). Most participants received their injections (LEN and placebo LEN) on time at Weeks 26 (91.5%; 4545/4967) and 52 (92.8%; 2025/2181), and adherence to injections was similar across all groups receiving injections.

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Adherence Data from PURPOSE 2 Study

Study Design and Demographics

PURPOSE 2 is an ongoing, phase 3, double-blind, randomized study evaluating the efficacy and safety of twice-yearly SUBQ LEN and once-daily oral FTC/TDF for HIV-1 PrEP in cisgender gay, bisexual, and other men, TGW, TGM, and GNB individuals aged ≥16 years in Argentina, Brazil, Mexico, Peru, South Africa, Thailand, and the US who have condomless receptive anal sex with partners assigned male at birth (N=3265). Eligible participants were tested for HIV at screening, and those who tested negative were randomly assigned in a 2:1 ratio to SUBQ LEN every 26 weeks plus daily oral FTC/TDF placebo (n=2179) or SUBQ LEN placebo every 26 weeks plus daily oral FTC/TDF (n=1086). Additional testing was performed with samples from participants who tested positive for HIV at screening to determine the recency of the HIV infection, and these data were used to estimate the bHIV that would be expected without PrEP.[2]

Key inclusion criteria in the randomized phase of the study included the following: negative results on point-of-care fourth-generation Ag/Ab test and central laboratory fourth-generation Ag/Ab test (if positive, was confirmed by an HIV-1/2 Ab differentiation assay), qualitative HIV-1 RNA test (lower limit of quantification, 20 c/mL), eGFR ≥60 mL/min, and body weight ≥35 kg at screening. Individuals were excluded if they had prior use of HIV PrEP (including FTC/TDF or FTC/TAF) or HIV PEP in the past 3 months, or any prior use of long-acting injectable HIV PrEP.[2,5]

The primary efficacy endpoint was the incidence of HIV among randomized participants. A total of 3271 participants were randomly assigned and received ≥1 dose of study drug; 6 participants were diagnosed with HIV on Day 1 and were excluded from the efficacy analysis (mITT, n=3265). Baseline demographics were balanced between randomized groups (Table 2).[2]

Table 2. PURPOSE 2: Select Baseline Demographics and Disease Characteristics[2]

Key Demographics and Characteristics		LEN (n=2183)	FTC/TDF (n=1088)
Age	Median (range), years	28 (17–74)	29 (17–73)
	16 to ≤25 years, n (%)	752 (34.4)	344 (31.6)
Country, n (%)	Brazil	769 (35.2)	396 (36.4)
	United States	440 (20.2)	235 (21.6)
	Peru	309 (14.2)	138 (12.7)
	Thailand	250 (11.5)	139 (12.8)
	South Africa	246 (11.3)	112 (10.3)
	Argentina	161 (7.4)	64 (5.9)
	Mexico	8 (0.4)	4 (0.4)
Race or ethnicity, n/N (%)	Hispanic or Latine	1378/2182 (63.2)	675/1088 (62)
	Black[a]	811/2175 (37.3)	420/1086 (38.7)
	White	722/2175 (33.2)	344/1086 (31.7)
	Indigenous or Indigenous ancestry[b]	341/2175 (15.7)	156/1086 (14.4)
	Asian	269/2175 (12.4)	144/1086 (13.3)
	Other and other multiracial[c]	32/2175 (1.5)	22/1086 (2)
Gender identity, n (%)	Cisgender man	1697 (77.7)	846 (77.8)
	Transgender woman	315 (14.4)	161 (14.8)
	Gender nonbinary[d]	136 (6.2)	63 (5.8)

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Key Demographics and Characteristics		LEN (n=2183)	FTC/TDF (n=1088)
	Transgender man	29 (1.3)	14 (1.3)
	Other[e]	6 (0.3)	4 (0.4)
Sexually transmitted infections,[f] n (%)	*Chlamydia trachomatis*	253 (11.6)	126 (11.6)
	Neisseria gonorrhea	193 (8.8)	115 (10.6)
	Syphilis	84 (3.8)	43 (4)
No history of HIV test, n (%)		597 (27.3)	306 (28.1)
Any history of PrEP use, n (%)		515 (23.6)	249 (22.9)
Self-reported use of stimulants with sex in last 12 weeks, n (%)		491 (22.5)	271 (24.9)

[a] Included all participants who identified as Black/of Black ancestry: Black, Back/White, Black/Pardo (a specific racial category in Brazil), Black/Brown (Brazil), Black/Colored (a specific racial category in South Africa), Black/American Indian or Alaskan Native, Black/Asian, and Black/Native Hawaiian or Pacific Islander.
[b] Included all participants who identified as American Indian or Alaskan Native, Native Hawaiian or Pacific Islander, Asian/Native Hawaiian or Pacific Islander, White/Native Hawaiian or Pacific Islander, and White/American Indian or Alaskan Native.
[c] Included all participants who identified as Asian/White, Colored (South Africa), Pardo (Brazil), White/Brown (Brazil), multiracial any other, and not multiracial other.
[d] Included 122 participants (89.7%) in the LEN group and 53 participants (84.1%) in the FTC/TDF group assigned male at birth.
[e] Included individuals who identified as Travesti (LEN, n=3; FTC/TDF, n=3) or as an "Other" gender (LEN, n=3; FTC/TDF, n=1).
[f] *Chlamydia trachomatis* and *Neisseria gonorrhea* were diagnosed based on testing pharyngeal, rectal, and urethral (urine) samples by central and local laboratories. Syphilis was diagnosed by testing blood and was performed locally by local testing protocols.

Adherence Results[2]

Adherence to LEN was defined as on-time injections (within 28 weeks after the last injection). Overall adherence to LEN or placebo injection was similar in the two groups at Week 26 (91%; 2606/2864) and 52 (92.8%; 1016/1095; Table 3).

Table 3. PURPOSE 2: Adherence to Injections for LEN and Placebo LEN[6]

Category	LEN	Placebo LEN
Number of participants expected to receive Week 26 / SUBQ injection 2, n[a]	1912	952
On-time SUBQ injection, n (%)	1729 (90.4)	877 (92.1)
< -14 days	2 (0.1)	4 (0.4)
-14 to -8 days	12 (0.6)	9 (0.9)
-7 to 7 days	1643 (85.9)	826 (86.8)
8 to 14 days	72 (3.8)	38 (4.0)
>14 days (late injection)	81 (4.2)	40 (4.2)
Did not receive injection	102 (5.3)	35 (3.7)
Number of participants expected to receive Week 52 / SUBQ injection 3, n	727	368
On-time SUBQ injection, n (%)	678 (93.3)	338 (91.8)
< -14 days	4 (0.6)	4 (1.1)
-14 to -8 days	13 (1.8)	4 (1.1)
-7 to 7 days	615 (84.6)	305 (82.9)
8 to 14 days	46 (6.3)	25 (6.8)
>14 days (late injection)	32 (4.4)	16 (4.3)
Did not receive injection	17 (2.3)	14 (3.8)

[a] Projected SUBQ LEN or placebo injection visit date is the previous injection visit date plus 26 weeks (182 days). Expected to receive an SUBQ injection includes participants with the potential to be followed up on or

beyond the upper limit of the clinical injection visit window (previous SUBQ injection date +189 days [26+1 weeks]) and didn't permanently discontinue randomized blinded phase prior to upper limit of the protocol clinical injection visit window. Participants with an SUBQ injection at a visit also counted as expected at the visit. Injections are considered received if any injection dose is administered, including partial or incomplete injections.

References

1. Bekker LG, Das M, Abdool Karim Q, et al. Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women. *N Engl J Med.* 2024;391(13):1179-1192.
2. Kelley CF, Acevedo-Quinones M, Agwu AL, et al. Twice-Yearly Lenacapavir for HIV Prevention in Men and Gender-Diverse Persons. *N Engl J Med.* 2024.
3. Enclosed, Gilead Sciences Inc. YEZTUGO® (lenacapavir) tablets, for oral use. YEZTUGO® (lenacapavir) injection, for subcutaneous use. U.S. Prescribing Information. Foster City, CA.
4. ClinicalTrials.gov. Study to Assess Safety and Efficacy of Lenacapavir and Emtricitabine/Tenofovir Alafenamide for Pre-Exposure Prophylaxis in Adolescent Girls and Young Women at Risk of HIV Infection (PURPOSE 1). ClinicalTrials.gov Identifier: NCT04994509. Available at: https://clinicaltrials.gov/ct2/show/NCT04994509. Accessed: 22 December. Last Updated: 19 December. 2022.
5. ClinicalTrials.gov. Study to Assess the Effectiveness and Safety of Lenacapavir for Human Immunodeficiency Virus (HIV) Pre-Exposure Prophylaxis (PURPOSE 2). ClinicalTrials.gov Identifier: NCT04925752. Available at: https://clinicaltrials.gov/ct2/show/NCT04925752. Accessed: 22 December. Last Updated: 21 December. 2022.
6. Kelley CF, Acevedo-Quinones M, Agwu AL, et al. Twice-Yearly Lenacapavir for HIV Prevention in Men and Gender-Diverse Persons [Supplementary Appendix]. *N Engl J Med.* 2024.

Abbreviations

Ab=antibody
Ag=antigen
bHIV=background HIV incidence
FTC=emtricitabine
GNB=gender non-binary
LEN=lenacapavir
mITT=modified intent-to-treat
MSM=men who have sex with men
PEP=post-exposure prophylaxis
PrEP=pre-exposure prophylaxis
SUBQ=subcutaneous(ly)
TAF=tenofovir alafenamide
TDF=tenofovir disoproxil fumarate
TGM=transgender men
TGW=transgender women

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Yeztugo, Descovy, and Truvada US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/yeztugo/yeztugo_pi; www.gilead.com/-/media/files/pdfs/medicines/hiv/descovy/descovy_pi; www.gilead.com/-/media/files/pdfs/medicines/hiv/truvada/truvada_pi.

Follow-Up

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FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or 🖱 www.accessdata.fda.gov/scripts/medwatch

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