GILEAD | Medical Information

Yeztugo® (lenacapavir) Use in People Who Inject Drugs

This document is in response to your request for information regarding the use of Yeztugo® (lenacapavir [LEN]) in people who inject drugs (PWID).

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 full indication, important safety information, and boxed warning are available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/yeztugo/yeztugo_pi.

Product Labeling[1]

LEN is indicated for PrEP to reduce the risk of sexually acquired HIV-1 in adults and adolescents weighing at least 35 kg who are at risk for HIV-1 acquisition. Individuals must have a negative HIV-1 test prior to initiating LEN.

Available Data on LEN Use in PWID

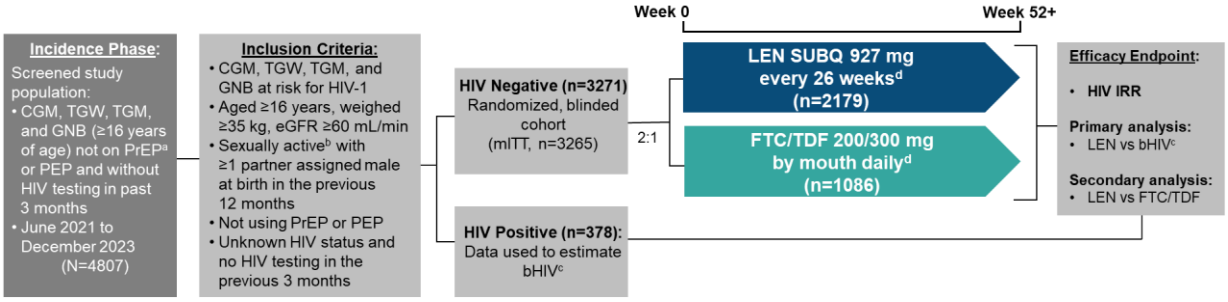
PURPOSE 2 Study

Study design and demographics

PURPOSE 2 (NCT04925752) 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; Figure 1). 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]

The primary efficacy endpoint was the incidence of HIV among randomized participants.[2] A subanalysis was conducted among participants who reported binge drinking at baseline (ie, monthly or more frequent consumption of ≥6 drinks on one occasion) or drug use (ie, oral, injection, or inhalation of cocaine, amphetamine-type stimulants, inhalants, sedative or sleeping pills, hallucinogens, opioids, or prescription drugs for nonprescription purposes; cannabis was excluded) in the past 12 weeks to assess LEN adherence and rates of AEs.[3]

Figure 1. PURPOSE 2: Study Design[2,4]



Abbreviations: IRR=incidence rate ratio; PEP=post-exposure prophylaxis.
[a]Included oral PrEP use within the last 12 weeks or any prior use of long-acting injectable forms of PrEP.
[b]Had condomless receptive anal sex with ≥1 partner in the previous 12 months and met ≥1 of the following criteria: condomless receptive anal sex with ≥2 partners in the previous 12 weeks; history of syphilis, rectal gonorrhea, or rectal chlamydia in the previous 24 weeks; self-reported use of stimulants with sex in the previous 12 weeks.
[c]The bHIV was the incidence of HIV without PrEP that would be anticipated in a placebo group. A total of 45 participants (11.9%) were classified as having recently acquiring HIV.
[d]All participants received an oral initiation dose of LEN (600 mg) or matching oral placebo on Days 1 and 2. Participants randomly assigned to the SUBQ LEN group received oral placebo FTC/TDF, and participants in the FTC/TDF group received SUBQ LEN placebo.

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).[2] Among the LEN participants, 40.5% reported binge drinking, and 37.2% reported drug use (Table 1).[3]

Table 1. PURPOSE 2: Baseline Demographics and Disease Characteristics of Participants Randomly Assigned to LEN[3]

Key Demographics and Characteristics		LEN (n=2183)
Age, median (range), years		28 (17–74)
Age 16 to ≤25 years, n (%)		752 (34.4)
Race, n/N (%)	Black[a]	811/2175 (37.3)
	White	722/2175 (33.2)
	Asian	269/2175 (12.4)
	Other[b]	373/2175 (17.1)
Hispanic/Latinx ethnicity, n/N (%)		1378/2182 (63.2)
Gender identity, n (%)	CGM	1697 (77.7)
	TGW	315 (14.4)
	TGM	29 (1.3)
	GNB[c] and other[d]	142 (6.5)
Self-reported binge drinking,[e] n/N (%)		841/2074 (40.5)

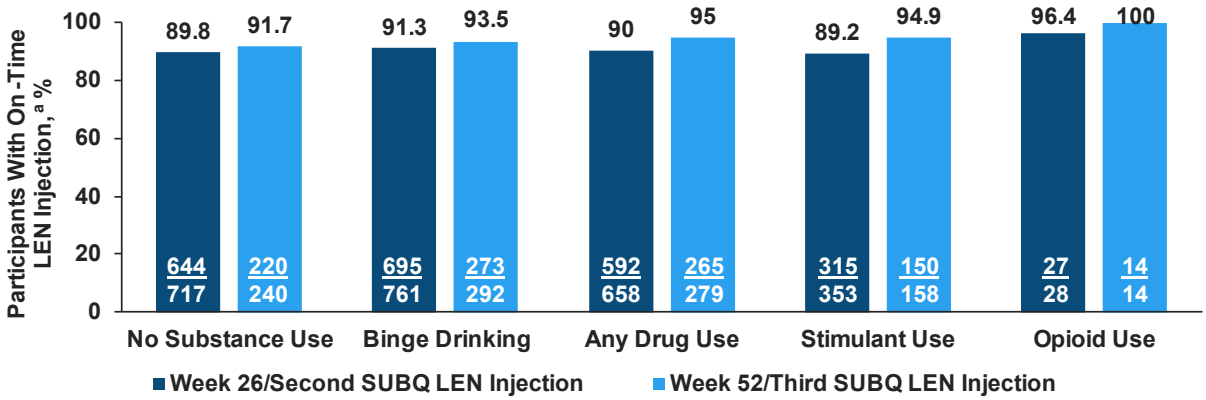
Key Demographics and Characteristics	LEN (n=2183)
Self-reported use of any drug,[f] n/N (%)	767/2061 (37.2)
Cocaine or amphetamine-type stimulant use	409/2058 (19.9)
Opioid use	33/2086 (1.6)
Injection drug use	17/2092 (0.8)

[a]Included all participants who identified as being Black or of Black ancestry, including those who used the terms "Black", "Black/White", "Black/Pardo" (Brazilian term), "Black/Brown" (Brazil), "Black/Colored" (South African term), "Black/American Indian or Alaska Native", "Black/Asian", and "Black/Native Hawaiian or Pacific Islander".
[b]Included "American Indian or Alaska Native", "Native Hawaiian or Pacific Islander", "Asian/Native Hawaiian or Pacific Islander", "White/Native Hawaiian or Pacific Islander", "White/American Indian or Alaskan Native", "Asian/White", "Colored" (South Africa), "Pardo" (Brazil), "White/Brown" (Brazil), "multiracial any other", and "not multiracial other".
[c]In the LEN group, 122/136 GNB participants (89.7%) were assigned male at birth.
[d]Included 3 participants who identified as "Travesti" and 3 participants who identified as "other" gender.
[e]Defined as monthly or more frequent consumption of ≥6 drinks on one occasion.
[f]Within 12 weeks prior to baseline; included cocaine, amphetamine-type stimulants, inhalants, sedatives or sleeping pills, hallucinogens, opioids, and prescription drugs for nonprescription purposes; excluded cannabis use.

Results[3]

Adherence rates, defined as on-time injections ≤28 weeks from the last injection, were high and were similar among participants who reported substance use (89.2–100%) and those who reported no substance use (89.8–91.7%; Figure 2).

Figure 2. PURPOSE 2: SUBQ LEN Adherence Rates Among Participants With and Without Substance Use[3]



[a]On-time LEN injection was defined as ≤28 weeks since last injection.

The frequency of AEs, including rates of ISRs, were similar among participants with and without substance use (Table 2). Excluding ISRs, the most common AEs were gonococcal, chlamydia, and upper respiratory tract infections. No study drug-related serious AEs or substance use-related overdoses were reported.

Table 2. PURPOSE 2: Rates of AEs in LEN Participants With and Without Substance Use[3]

Parameter, n (%)	LEN Participants				
	No Substance Use (n=822)	Binge Drinking (n=841)	Any Drug Use (n=767)	Stimulant Use (n=409)	Opioid Use (n=33)
AEs, excluding ISRs	581 (70.7)	626 (74.4)	599 (78.1)	322 (78.7)	24 (72.7)
Grade ≥2	416 (50.6)	466 (55.4)	469 (61.1)	259 (63.3)	21 (63.6)
Grade ≥3	34 (4.1)	31 (3.7)	33 (4.3)	20 (4.9)	1 (3)
Serious AEs	28 (3.4)	22 (2.6)	24 (3.1)	16 (3.9)	1 (3)
SUBQ LEN ISRs	684 (83.2)	715 (85)	641 (83.6)	341 (83.4)	30 (90.9)
Death	1 (0.1)[a]	1 (0.1)[b]	3 (0.4)[c]	1 (0.2)[d]	0

[a]Due to completed suicide. [b]Due to road traffic accident. [c]Due to road traffic accident, cerebrovascular accident and pulmonary embolism, and unknown cause (each, n=1). [d]Due to unknown cause.
Note: Substance use categories were not mutually exclusive.

PURPOSE 4 Study[5]

PURPOSE 4 (NCT06101342) is an ongoing phase 2, open-label, multicenter, randomized controlled trial evaluating the PK and safety of twice-yearly SUBQ LEN in PWID. Approximately 180 PWID age ≥18 years without HIV in the US will be included and randomly assigned to either twice-yearly SUBQ LEN or once-daily oral FTC/TDF. Eligible participants are negative for hepatitis B surface antigen; have a positive urine test for any drug misuse including, but not limited to, opioids (eg, fentanyl, heroin), stimulants (eg, cocaine, amphetamines), psychoactive drugs (eg, benzodiazepines), or a combination of these drugs; show evidence of recent injection (eg, track marks); and self-report sharing of injection paraphernalia within the past 30 days. Exclusion criteria include prior use of long-acting PrEP, history or evidence of a positive HIV test, or acute viral hepatitis A or acute or chronic HBV or HCV. The study began in December 2023, and the estimated completion date is January 2028.

References

1. YEZTUGO®, Gilead Sciences Inc. YEZTUGO® (lenacapavir) tablets, for oral use. YEZTUGO® (lenacapavir) injection, for subcutaneous use. U.S. Prescribing Information. Foster City, CA.
2. Kelley CF, Acevedo-Quinones M, et al. Use Endnote No. 76142. Twice-Yearly Lenacapavir for HIV Prevention in Men and Gender-Diverse Persons. *N Engl J Med.* 2024.
3. Clark J, Agwu AL, Buchbinder S, et al. Favorable Adherence and Safety of Twice-Yearly Subcutaneous Lenacapavir for PrEP Among PURPOSE 2 Participants Who Used Substances. [Presentation]. Paper presented at: IDWeek; October 19–22, 2025; Atlanta, GA.
4. 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?term=purpose-2&draw=2&rank=1.
5. Gilead Sciences. Study of Lenacapavir and Emtricitabine/Tenofovir Disoproxil Fumarate (F/TDF) for Prevention of HIV in People Who Inject Drugs (HPTN-103) (PURPOSE-4) Available at: https://clinicaltrials.gov/study/NCT06101342?intr=lenacapavir&rank=5.

Abbreviations

AE=adverse event
bHIV=background HIV
CGM=cisgender man
FTC=emtricitabine
GNB=gender nonbinary
ISR=injection site reaction
LEN=lenacapavir
mITT=modified intent-to-treat
PK=pharmacokinetic(s)
PrEP=pre-exposure prophylaxis
PWID=people who inject drugs
TDF=tenofovir disoproxil fumarate
TGM=transgender man
TGW=transgender woman
SUBQ=subcutaneous(ly)

Product Label

For the full indication, important safety information, and boxed warning, please refer to the Yeztugo US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/yeztugo/yeztugo_pi.

Follow-Up

For any additional questions, please contact Gilead Medical Information at:

☎1-866-MEDI-GSI (1-866-633-4474) or 🖱 www.askgileadmedical.com

Adverse Event Reporting

Please report all adverse events to:

Gilead Global Patient Safety ☎ 1-800-445-3235, option 3 or
🖱 www.gilead.com/utility/contact/report-an-adverse-event

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

Data Privacy

The Medical Information service at Gilead Sciences may collect, store, and use your personal information to provide a response to your medical request. We may share your information with other Gilead Sciences colleagues to ensure that your request is addressed appropriately. If you report an adverse event or concern about the quality of a Gilead or Kite product, we will need to use the information you have given us in order to meet our regulatory requirements in relation to the safety of our medicines.

It may be necessary for us to share your information with Gilead's affiliates, business partners, service providers, and regulatory authorities located in countries besides your own. Gilead Sciences has implemented measures to protect the personal information you provide. Please see the Gilead Privacy Statement (www.gilead.com/privacy-statements) for more information about how Gilead handles your personal information and your rights. If you have any further questions about the use of your personal information, please contact privacy@gilead.com.