GILEAD | Medical Information

Yeztugo® (lenacapavir) Time to Protection

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

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

Summary

PK Data on YTG and Time to Protection

- The time from initiation of LEN to maximal protection against HIV-1 is unknown.[1]
- The complete initiation dosing schedule, consisting of 2 SUBQ injections and 2 oral tablets on Day 1 and 2 oral tablets on Day 2 is required; the efficacy of LEN has only been established with this dosing schedule.[1]
- The complete oral LEN loading dose on Days 1 and 2 must be taken to achieve adequate LEN concentrations in a timely manner.[2]
- PK data are available from a small phase 1 study in healthy participants that were used as the basis for dosing in the PURPOSE 1 and PURPOSE 2 studies. In this study, 14 healthy individuals who completed the full initiation dosing had a mean plasma LEN concentration thought to be associated with ARV activity 2 hours after the second oral LEN dose on Day 2. These PK data are not correlative of efficacy.[3]

PK Data on YTG and Time to Protection

PK Surrogates

Since direct measurement of time to protection is infeasible, estimates of time to protection come from PK surrogates (ie, how long it takes for relevant drug concentrations to reach target levels thought to be protective). The target IQ4 concentration is thought to be a threshold trough for HIV treatment, but the levels required for HIV prevention remain unknown.[4]

The time for LEN to reach target IQ4 for ARV activity is based on PK surrogates reported from the dose-response relationship of LEN and the mean concentrations predicted to provide near maximal ARV activity.[4] In the case of LEN, the target drug concentration of IQ4 (15.5 ng/mL) is based on the observation that this concentration conferred potent ARV activity as monotherapy in PWH in a phase 1b study and that high rates of virologic

suppression in phase 2/3 studies in PWH when LEN was dosed targeting trough concentrations ≥IQ4.[3]

Please note: While IQ4 is considered a measure associated with ARV activity, it is not a validated threshold, and it is not the only factor in determining ARV or prophylactic activity.[4]

Phase 1 PK Study in Healthy Volunteers[3]

A phase 1, single-center, open-label study evaluated the PK of the following LEN regimen: SUBQ LEN 927 mg and oral LEN 600 mg on Day 1, oral LEN 600 mg on Day 2, and SUBQ LEN every 6 months thereafter. Among 14 healthy individuals, mean plasma LEN concentration and the lower bound of its 90% CI exceeded the target IQ4 (15.5 ng/mL) at 2 hours post-dose on Day 2 and was consistently maintained above the target IQ4 during the dosing interval. These PK data are not correlative of efficacy. Overall, LEN was well tolerated, and there were no serious AEs. Injection site reactions were the most common AEs, and no deaths were reported.

References

1. Enclosed, Gilead Sciences Inc. YEZTUGO® (lenacapavir) tablets, for oral use. YEZTUGO® (lenacapavir) injection, for subcutaneous use. U.S. Prescribing Information. Foster City, CA.
2. Begley R, Lutz J, Rhee M, et al. Lenacapavir Sustained Delivery Formulation Supports 6-Month Dosing Interval [Poster PEB0265]. Paper presented at: AIDS 2020: 23rd International AIDS Conference Virtual; 06-10 July, 2020.
3. Jogiraju V, Graham H, West S, et al. Pharmacokinetics of a Simplified Subcutaneous Lenacapavir Regimen Versus Phase 2/3 Regimen [Poster PESUB22]. Paper presented at: AIDS 2022; 29 July-2 August, 2022; Montreal, Quebec, Canada.
4. Daar E, McDonald C, Crofoot G, et al. Dose-response Relationship of Subcutaneous Long-Acting HIV Capsid Inhibitor GS-6207 [Presentation]. Paper presented at: Conference on Retroviruses and Opportunistic Infections (CROI); 08-11 March, 2020; Boston, MA.

Abbreviations

AE=adverse event
ARV=antiretroviral
IQ=inhibitory quotient
LEN=lenacapavir
PK=pharmacokinetic(s)
PWH=people with HIV
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

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