

Low Incidence of Hepatitis B Infection Among People Receiving Lenacapavir or Tenofovir-Based HIV Pre-exposure Prophylaxis in PURPOSE 1 and PURPOSE 2

Allison L Agwu¹, José Valdez Ramalho Madruga², Javier R Lama³, Moelo Malahleha⁴, Noah Kiwanuka⁵, Christoph C Carter⁶, Sarah B Puryear⁶, Ramin Ebrahimi⁶, Anchalee Avihingsanon⁷

1. The Johns Hopkins University School of Medicine, Baltimore, MD, USA; 2. Centro de Referência e Treinamento DST/AIDS-SP, São Paulo, Brazil; 3. Asociación Civil Impacta Salud y Educación, Lima, Peru; 4. Synergy Biomed Research Institute, East London, South Africa; 5. Makerere University School of Public Health, Kampala, Uganda; 6. Gilead Sciences, Inc., Foster City, CA, USA; 7. HIVNAT, Thai Red Cross AIDS and Infectious Disease Research Centre and Center of Excellence in Tuberculosis, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Copies of this poster obtained through QR (Quick Response) code are for personal use only and may not be reproduced without written permission of the authors



Conclusions

- Lenacapavir (LEN) has no clinically meaningful activity against the hepatitis B virus (HBV)
- Universal HBV screening in PURPOSE 1 and PURPOSE 2 resulted in vaccination of a substantial proportion of participants
- Incident HBV infection was rare in participants receiving either LEN or tenofovir-based HIV pre-exposure prophylaxis (PrEP), indicating that proactive HBV screening and immunization support low HBV incidence, regardless of the anti-HBV activity of the PrEP drug used

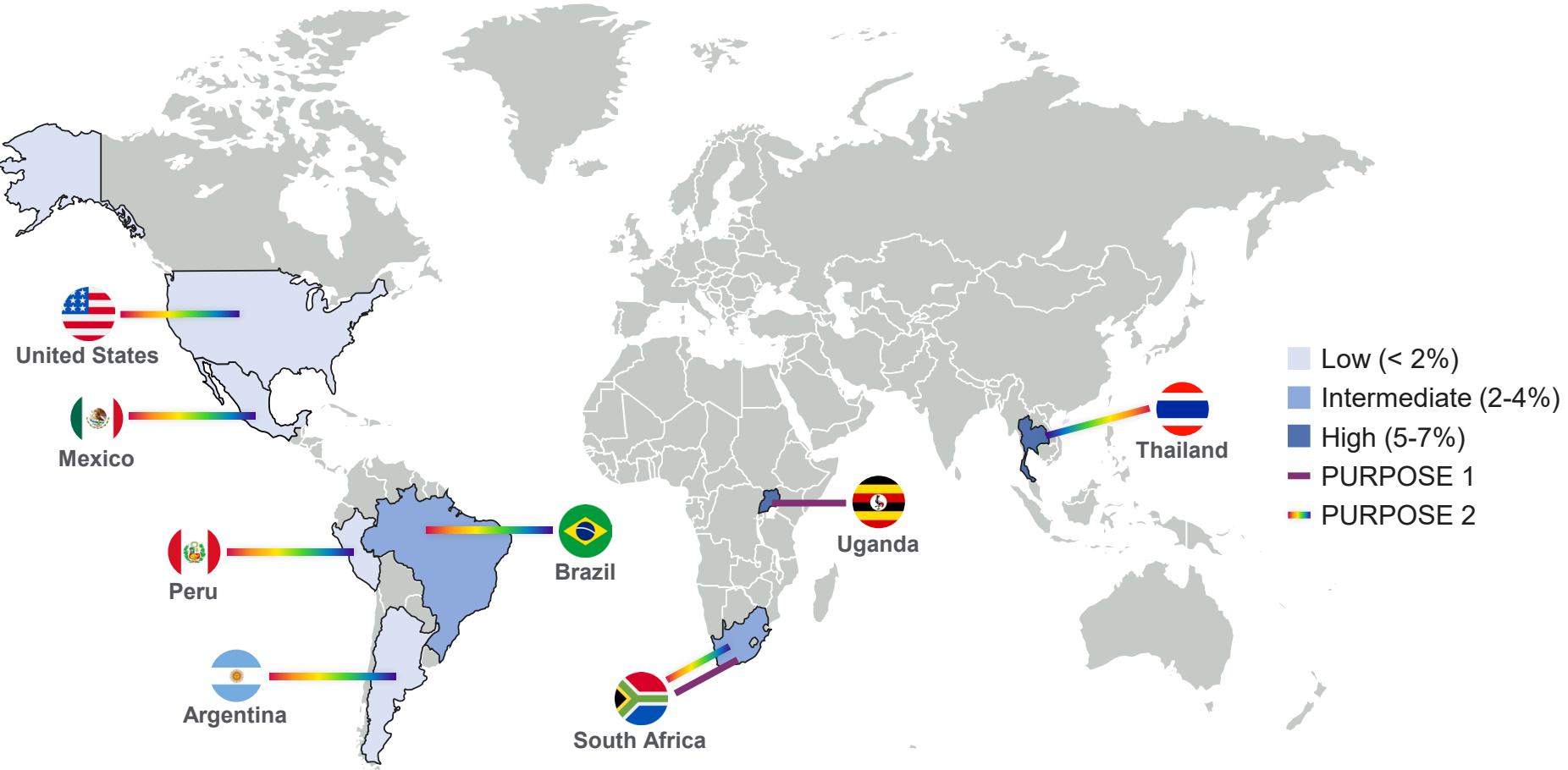
Plain Language Summary

- Human immunodeficiency virus (HIV) prevention medicine, called pre-exposure prophylaxis (PrEP), lowers the chances of someone getting HIV
- People who have a higher chance of getting HIV may also have a higher chance of getting other infections, including the hepatitis B virus (HBV). This is because HBV and HIV can spread in similar ways
- There is a widely used vaccine available to protect against HBV. However, not everyone gets the HBV vaccine and the protection from the vaccine can decrease over time
- Lenacapavir (LEN) is approved to help prevent HIV. It is given as an injection under the skin twice a year (every 6 months) and was shown to work well in protecting people from getting HIV in two clinical studies, called PURPOSE 1 and PURPOSE 2. People in PURPOSE 1 and PURPOSE 2 were offered HBV vaccines if they were not already immune
- Other PrEP medicines are available as tablets that people take by mouth every day
- This study looked at how many people included in PURPOSE 1 and PURPOSE 2 were already protected against HBV, how many received the HBV vaccination during the study, and how many people got HBV during the studies
- These results show that the number of people from PURPOSE 1 and PURPOSE 2 who got HBV vaccines was high, while the number who got HBV infection during the studies was very low
- These findings, from around the time of PURPOSE 1 and PURPOSE 2 study start, show that screening, testing, and vaccinating against HBV can help protect people against HBV. This is especially important for people who have a higher chance of getting HIV

Introduction

- Twice-yearly subcutaneous LEN for PrEP demonstrated superior efficacy versus daily oral tenofovir-based PrEP in the Phase 3 PURPOSE 1 (NCT04994509) and PURPOSE 2 (NCT04925752) studies,^{1,2} leading to global regulatory approvals of LEN for PrEP.^{3,4}
- Due to shared modes of transmission, people with an increased likelihood of HIV acquisition are also at an increased risk of HBV acquisition⁵
- In 2019, around the time of PURPOSE 1 and PURPOSE 2 study initiation, the estimated global prevalence of chronic HBV infection was 4.1%,⁶ with varying degrees of HBV prevalence in PURPOSE 1 and PURPOSE 2 trial locations (**Figure 1**)
- Unlike LEN, both emtricitabine/tenofovir alafenamide (F/TAF) and emtricitabine/tenofovir disoproxil fumarate (F/TDF) have antiviral activity against HBV.^{7,8} Thus, we evaluated HBV acquisition in participants receiving LEN or tenofovir-based HIV PrEP from PURPOSE 1 and PURPOSE 2

Figure 1. Prevalence of HBV Infection in PURPOSE 1 and PURPOSE 2 Trial Locations



All-age HBV infection calculated using HBsAg seroprevalence data from 2019.⁶ HBV, hepatitis B virus; HBsAg, HBV surface antigen.

Objective

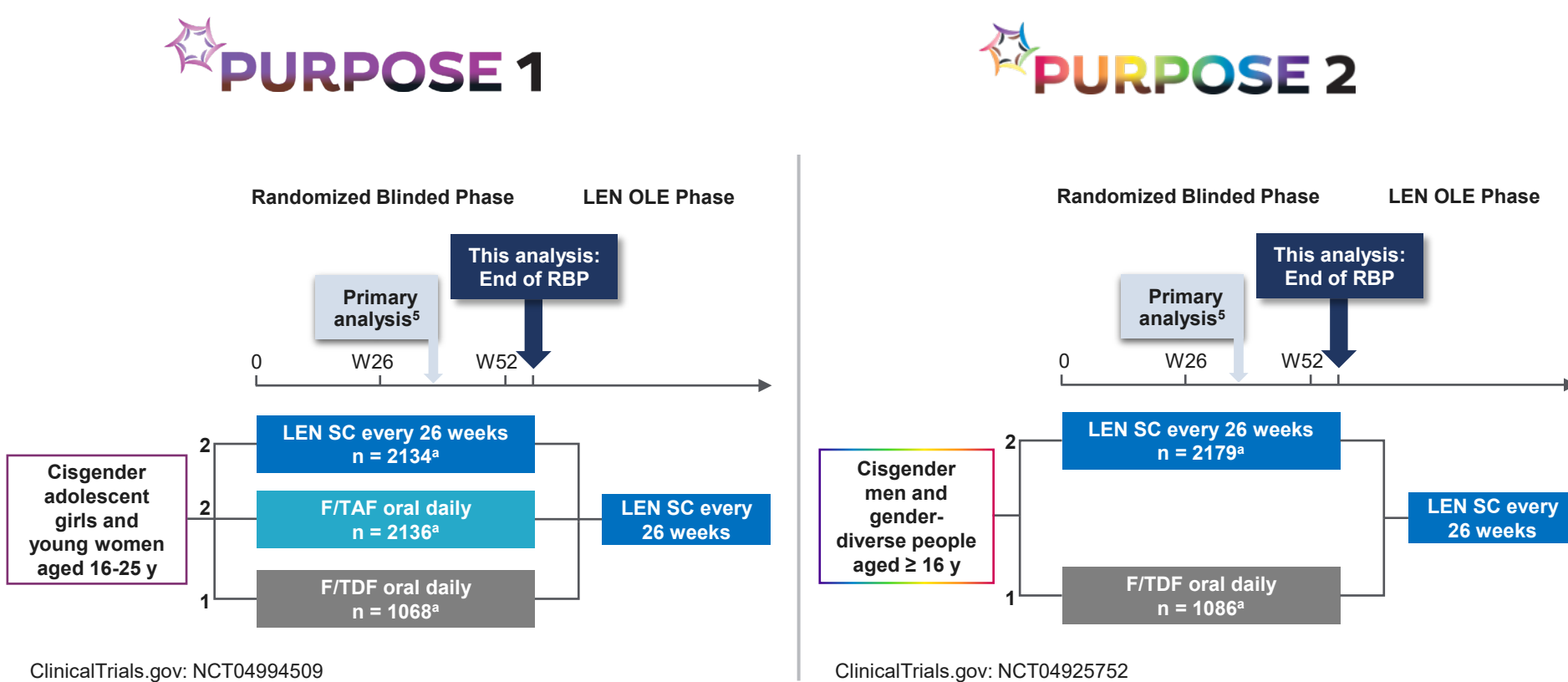
- To evaluate HBV baseline immunity, immunization, and incident infection in the context of LEN for HIV PrEP in PURPOSE 1 and PURPOSE 2

Methods

Study Design

- In PURPOSE 1 (cisgender girls and women aged 16-25 years in South Africa and Uganda) and PURPOSE 2 (cisgender men and gender-diverse individuals aged ≥ 16 years in the United States, Brazil, Thailand, South Africa, Peru, Argentina, and Mexico), participants were randomized in a blinded fashion to LEN or tenofovir-based PrEP along with tablet or injection placebo (**Figure 2**)
- HBV serology, including HBV surface antigen (HBsAg), HBV surface antibody (HBsAb), and HBV core antibody (HBcAb), was assessed at screening and every 26 weeks after randomization
- Participants who were either HBV nonimmune or immune from either vaccination or prior HBV exposure were included in the study
- Participants with positive HBsAg at screening were excluded
 - Positive HBcAb with negative HBV DNA were eligible
- Participants identified as HBV nonimmune (HBsAb negative) at screening were offered free HBV vaccinations at the study sites
- We assessed incident HBV infection during the studies' randomized blinded phases based on investigator adverse event (AE) reporting

Figure 2. PURPOSE 1 and PURPOSE 2 Study Designs



^{1,2}Included in the full analysis set for primary efficacy analyses (additional participants are included in the safety analysis).^{1,2} F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; LEN, lenacapavir; OLE, open-label extension; RBP, randomized blinded phase; SC, subcutaneous; W, week; y, years.

Acknowledgments: We extend our thanks to the PURPOSE 1 and PURPOSE 2 participants, their families, and all participating investigators. We also acknowledge Stephanie Cox and Stephen Yant (both Gilead Sciences) who assisted with the lenacapavir HBV activity analysis. This study was funded by Gilead Sciences, Inc. Medical writing support was provided by Simon Wigfield, PhD (Aspire Scientific Ltd, UK), and was funded by Gilead Sciences, Inc.

Methods (cont.)

LEN HBV antiviral assay

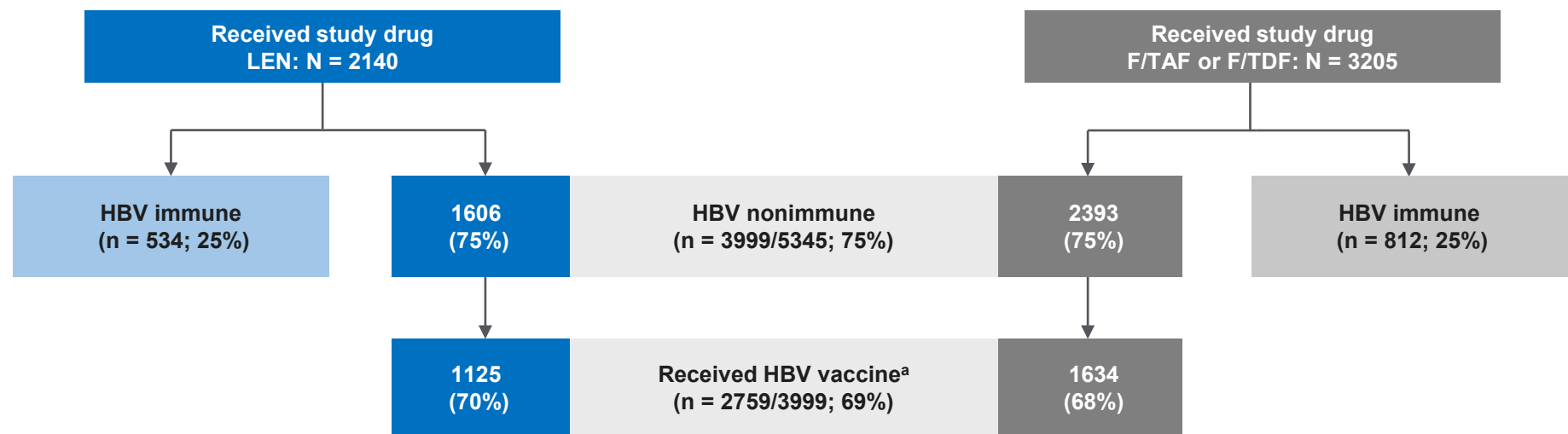
- Briefly, immortalized human hepatocytes expressing HBV receptor (HepG2-NTCP) were infected with HBV AD38 and plated in 384-well plates prespotted with 3-fold serial dilutions of LEN, lamivudine (positive control; a nucleoside reverse transcriptase HBV inhibitor), or dimethyl sulfoxide control. After 5 days of incubation, cells were lysed and supernatant HBV DNA content was quantified using the QuantiGene 2.0 DNA assay kit (Thermo Fisher Scientific)

Results

HBV Vaccination in PURPOSE 1 and PURPOSE 2

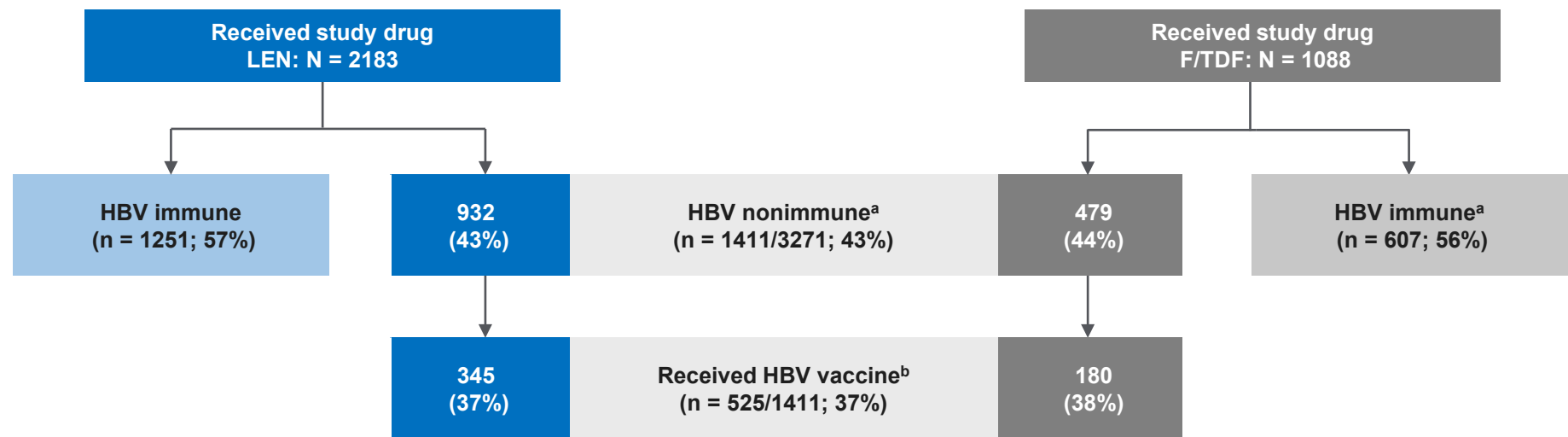
- In PURPOSE 1, 5345 participants received study drug (2140 LEN, 2135 F/TAF, 1070 F/TDF); 3999 (75%) were HBV nonimmune at screening, of whom 2759 (69%) received HBV vaccination (**Figure 3**)
- In PURPOSE 2, 3271 participants received study drug (2183 LEN, 1088 F/TDF); 1411 (43%) were HBV nonimmune at screening, of whom 525 (37%) received HBV vaccination (**Figure 4**)

Figure 3. HBV Immunity Status at Screening in PURPOSE 1



^aParticipants received > 1 HBV vaccine. F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; HBV, hepatitis B virus; LEN, lenacapavir.

Figure 4. HBV Immunity Status at Screening in PURPOSE 2



^aTwo participants in the F/TDF group had missing HBV immunity status at screening. ^bParticipants received > 1 HBV vaccine. F/TDF, emtricitabine/tenofovir disoproxil fumarate; HBV, hepatitis B virus; LEN, lenacapavir.

HBV Immunity in PURPOSE 1 and PURPOSE 2

- Rates of HBV immunity increased from screening to Week 52 in both studies (**Table 1**)

Table 1. HBV Serology in PURPOSE 1 and PURPOSE 2

	Screening (N = 5345)	Week 52 (N = 4567)
PURPOSE 1		
HBV immune (HBsAb+), n (%) ^a	1346 (25)	3512 (77)
HBcAb positive	132 (10)	181 (5)
HBcAb negative	1214 (90)	3331 (95)
HBV nonimmune (HBsAb-), n (%) ^b	3999 (75)	1055 (23)
HBcAb positive ^c	40 (1)	21 (2)
HBcAb negative	3959 (99)	1034 (98)
HBsAg positive	0	0
Missing serology	0	0
PURPOSE 2		
HBV immune (HBsAb+), n (%) ^a	1858 (57)	1952 (74)
HBcAb positive	238 (13)	243 (12)
HBcAb negative	1620 (87)	1708 (88)
HBV nonimmune (HBsAb-), n (%) ^b	1411 (43)	692 (26)
HBcAb positive ^c	24 (2)	16 (2)
HBcAb negative	1387 (98)	676 (98)
HBsAg positive	1 (< 1)	0
Missing serology	2 (< 1)	0

^aDenominator for HBcAb-positive and HBcAb-negative participants is HBV immune (HBsAb+). ^bDenominator for HBcAb-positive, HBcAb-negative, and HBsAg positive participants is HBV nonimmune (HBsAb-). ^cParticipants were HBV RNA negative. ^dOne participant was HBsAb positive with missing HBcAb data at Week 52. HBV, hepatitis B virus; HBcAb, HBV core antibody; HBsAb, HBV surface antibody; HBsAg, HBV surface antigen.

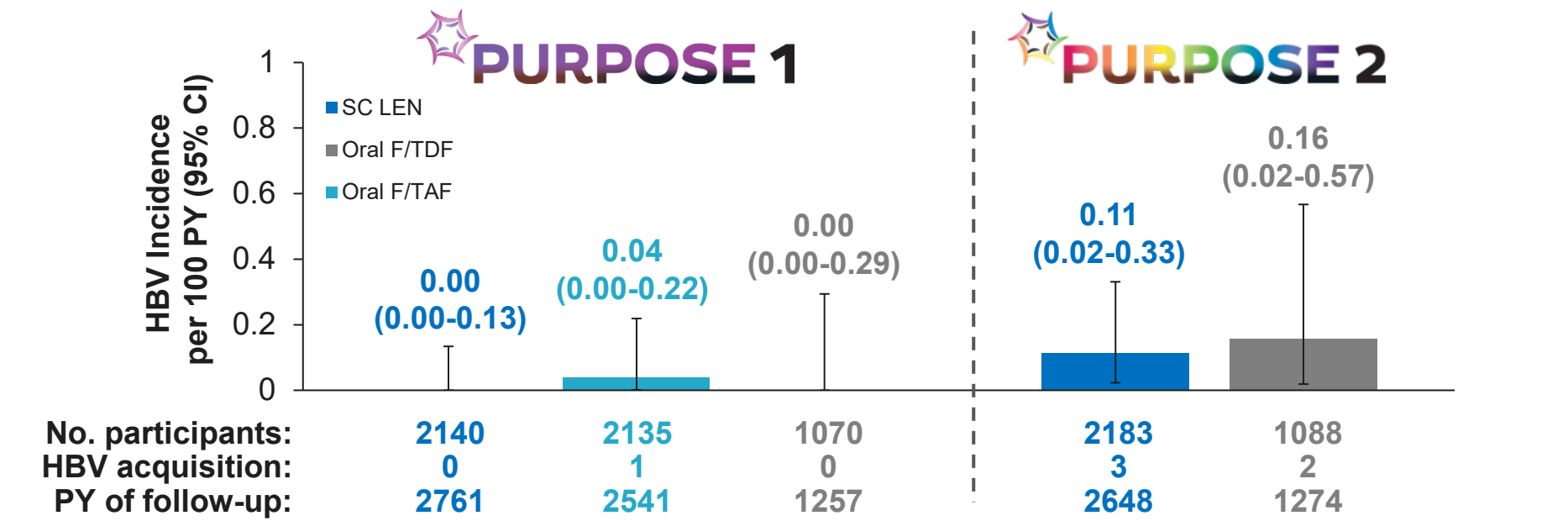
Disclosures: ALA has received consulting fees from Gilead Sciences, Inc. and Viiv Healthcare; and has received research grants from Gilead Sciences, Inc. JVRM has received consulting fees from Gilead Sciences, Inc., MSD, GSK, and J&J. AA has received research grants from Gilead Sciences, Inc., Viiv Healthcare, and MSD; and travel support to attend conferences. CCC, SBP, and RE are employees and shareholders of Gilead Sciences, Inc. JRL, MM, and NK do not have any disclosures to report.

Results (cont.)

HBV Incidence in PURPOSE 1 and PURPOSE 2

- There was only one incident HBV infection in PURPOSE 1, which occurred in a participant randomized to F/TAF (incidence rate [IR]: 0.04 per 100 person-years [PY]; 95% confidence interval [CI]: 0.00-0.22) (**Figure 5**)
- There were five incident HBV infections in PURPOSE 2, three in the LEN group (IR: 0.11 per 100 PY; 95% CI: 0.02-0.33) and two in the F/TDF group (IR: 0.16 per 100 PY; 95% CI: 0.02-0.57) (**Figure 5**)
- Case details of these six incident HBV infections are shown in **Table 2**

Figure 5. HBV Incidence During the RBP of PURPOSE 1 and PURPOSE 2



CI, confidence interval; F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; HBV, hepatitis B virus; LEN, lenacapavir; PY, person-years; RBP, randomized blinded phase; SC, subcutaneous.

Table 2. Investigator-Reported HBV Case Details

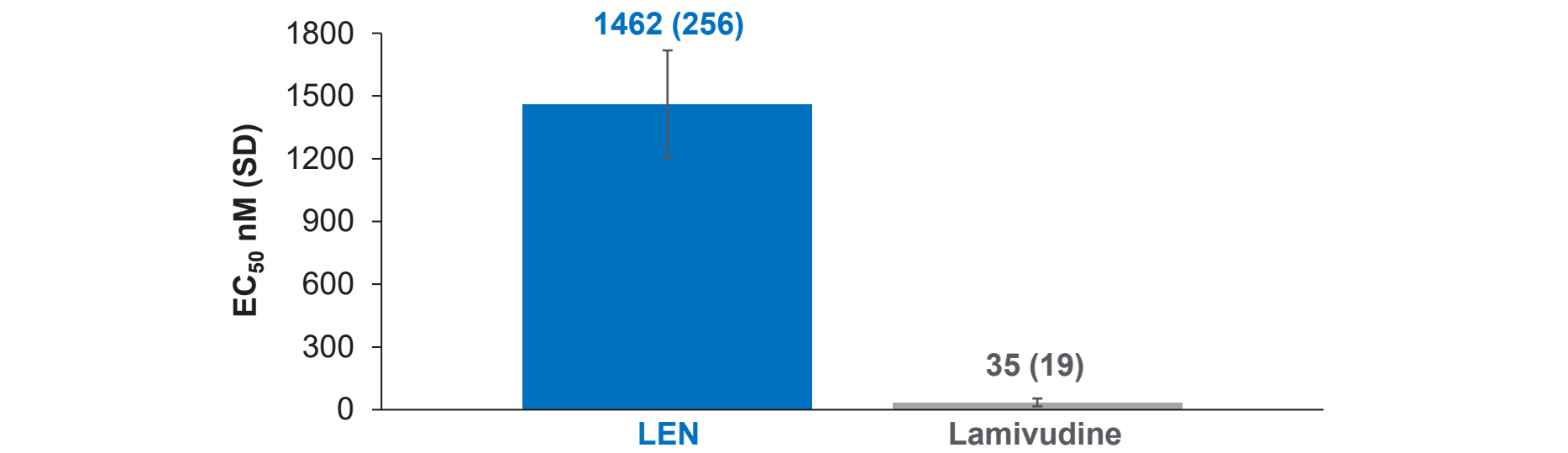
Participant	Study	Group	Coded AE Term	AE Start Day	Screening HBsAb	Screening HBsAg	Screening HBcAb	HBV Vaccination	Clinical Details
A	PURPOSE 1	F/TAF	Hepatitis B	377	Positive	Negative	Negative	Day 20, Day 92, and Day 277	• HBcAb seroconversion • No chronic infection ^a
B	PURPOSE 2	F/TDF	Hepatitis B	546	Positive	Negative	Negative	None	• HBcAb seroconversion • HBsAg negative • No chronic infection ^a
C	PURPOSE 2	LEN	Hepatitis B	184	Negative	Negative	Negative	None	• HBcAb and HBsAb seroconversion • HBsAg negative • No chronic infection
D	PURPOSE 2	LEN	Acute hepatitis B	176	Negative	Negative	Negative	Day 11, Day 39	• HBcAb and HBsAb seroconversion • HBsAg negative • No chronic infection
E	PURPOSE 2	LEN	Hepatitis B	63	Positive	Negative	Negative	None	• HBcAb seroconversion • HBsAg negative • No chronic infection ^a
F	PURPOSE 2	F/TDF	Hepatitis B	8	Positive	Negative	Negative	None	• HBcAb seroconversion • HBsAg negative • No chronic infection ^a

^aIn participants with baseline HBsAb positivity, subsequent incident HBcAb positivity may be the result of prior natural infection (with intermittently detectable HBcAb levels), assay false positivity, or on-study incident HBV infection. AE, adverse event; F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; HBV, hepatitis B virus; HBcAb, HBV core antibody; HBsAb, HBV surface antibody; HBsAg, HBV surface antigen; LEN, lenacapavir.

LEN HBV activity

- LEN displays a higher EC₅₀ value versus lamivudine, demonstrating LEN is approximately 40 times less potent at blocking HBV replication than lamivudine, a clinically utilized HBV replication inhibitor (**Figure 6**)
 - The observed activity of LEN against HBV is approximately 25,000 weaker than its activity against HIV-1

Figure 6. LEN Low Potency *in vitro* Against HBV



A high EC₅₀ means a higher concentration of drug is required to produce 50% of its maximal effect versus a drug with a low EC₅₀; therefore, LEN is less potent against HBV versus HIV. EC₅₀, half maximal effective concentration; HBV, hepatitis B virus; LEN, lenacapavir; SD, standard deviation.

References: 1. Bekker LG, et al. *N Engl J Med*. 2024;391:1179-92. 2. Kelley CF, et al. *N Engl J Med*. 2025;392:1261-76. 3. Yeztugo (lenacapavir) USP, Gilead Sciences, Inc., June 2025. 4. Yeztugo (lenacapavir) EU SmPC, Gilead Sciences Ireland UC, May 2026. 5. CDC. <https://www.cdc.gov/hepatitis/hcp/populations-settings/hiv.html> (accessed Oct. 6, 2026). 6. GBD 2019 Hepatitis B Collaborators. *Lancet Gastroenterol Hepatol*. 2022;7:796-829. 7. Fung S, et al. *J Hepatol*. 2017;66:11-18. 8. Li J, et al. *BMC Infect Dis*. 2021;21:567