

Baseline Characteristics and Substance Use Among People Who Inject Drugs With Evidence of Active Use in HPTN 103/PURPOSE 4: A Phase 2 Study of Twice-Yearly Subcutaneous Lenacapavir for Pre-Exposure Prophylaxis

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Conclusions

- By leveraging intentional outreach and research-site engagement, we demonstrate the feasibility of enrolling a heterogeneous population of people who inject drugs (PWID) with substantial injection-related HIV vulnerability and social instability into the HPTN 103/PURPOSE 4 trial of twice-yearly subcutaneous (SC) lenacapavir (LEN) for pre-exposure prophylaxis (PrEP)
- These data highlight the importance of inclusive, community-informed trial design that reflects the characteristics and vulnerabilities of PWID encountered in real-world settings

Plain Language Summary

- Human immunodeficiency virus (HIV) prevention medicine, called pre-exposure prophylaxis (PrEP), lowers the chances of someone getting HIV
- People who inject drugs have a high chance of getting HIV but have often been underrepresented in HIV prevention studies
- Lenacapavir (LEN) is approved to help prevent HIV. It is given as an injection under the skin twice a year (every 6 months). Other PrEP medicines are available as tablets that people take by mouth every day
- The HPTN 103/PURPOSE 4 study is taking place in the United States. The study includes people who had recently injected drugs and shared injection equipment with others, which can increase the chance of getting HIV
- In this ongoing study, people received either LEN every 6 months or a daily oral tablet containing tenofovir disoproxil fumarate and emtricitabine
- In this analysis, researchers described how the HPTN 103/PURPOSE 4 study includes a diverse population of people who inject drugs in the United States

Introduction

- Globally, an estimated 15.2% of the 14.8 million PWID are living with HIV, underscoring the disproportionate burden of HIV in this population and the substantial unmet need for PrEP to prevent HIV acquisition¹
- Primary results from the Phase 3 PURPOSE 1 (NCT04994509) and PURPOSE 2 (NCT04925752) trials demonstrated robust efficacy and tolerability of twice-yearly SC LEN for PrEP compared with emtricitabine/tenofovir disoproxil fumarate (F/TDF), leading to global regulatory approvals of LEN for PrEP^{2,3}
- PWID, particularly those with active injection drug use, experience a disproportionate rate of HIV acquisition but have often been underrepresented in PrEP clinical trials
- HPTN 103/PURPOSE 4 (NCT06101342) is a Phase 2 clinical trial designed to address this inequity by evaluating LEN pharmacokinetics and safety for PrEP in PWID with evidence of active injection drug use in the United States

Objective

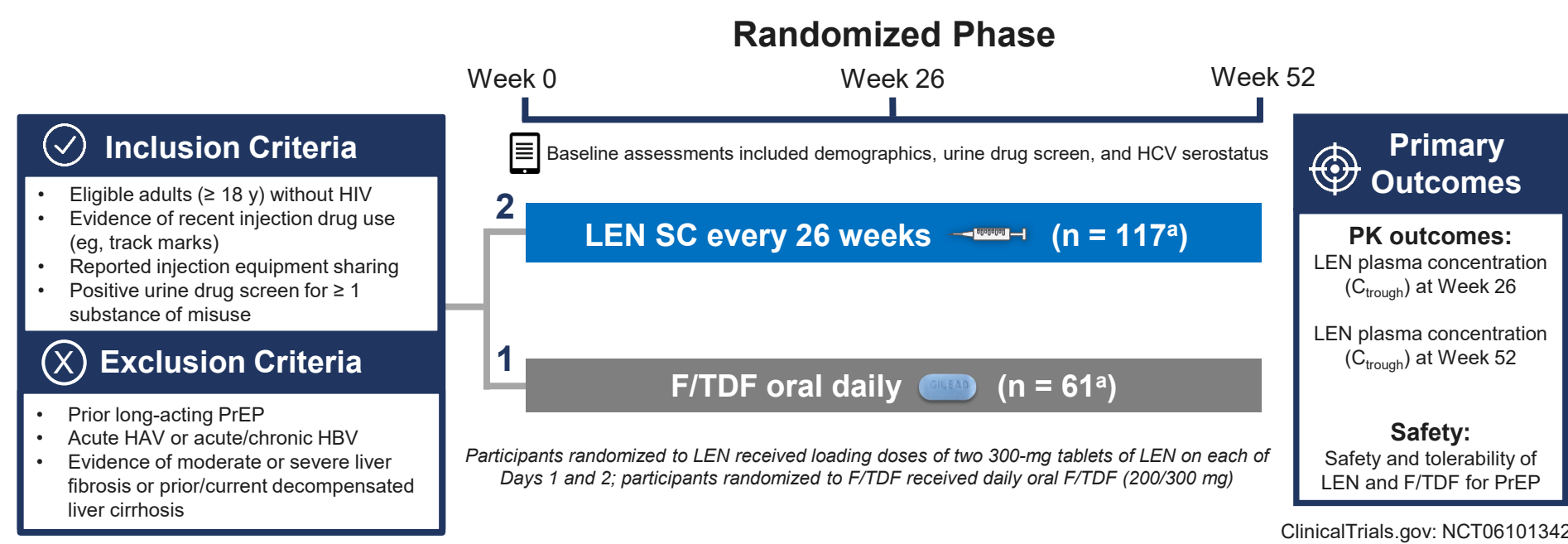
- To describe the trial design and baseline demographic, substance use, and hepatitis C virus (HCV) characteristics of participants in the HPTN 103/PURPOSE 4 study after close of enrollment

Methods

Study Design

- HPTN 103/PURPOSE 4 is an ongoing Phase 2, open-label, randomized trial evaluating the pharmacokinetics, safety, and acceptability of SC LEN versus daily oral F/TDF for PrEP in PWID (**Figure 1**)
- Study design and implementation stemmed from collaboration between academia, government, and industry partners and were informed by prior experience and stakeholder input to support inclusion of PWID
- Sites were selected in areas with intersectional substance use, HIV, and sociostructural disparities. Sites were also selected based on their experience and ability to serve PWID
- Sites incorporated case managers and referrals/access to harm reduction and HCV services

Figure 1. HPTN 103/PURPOSE 4 Study Design



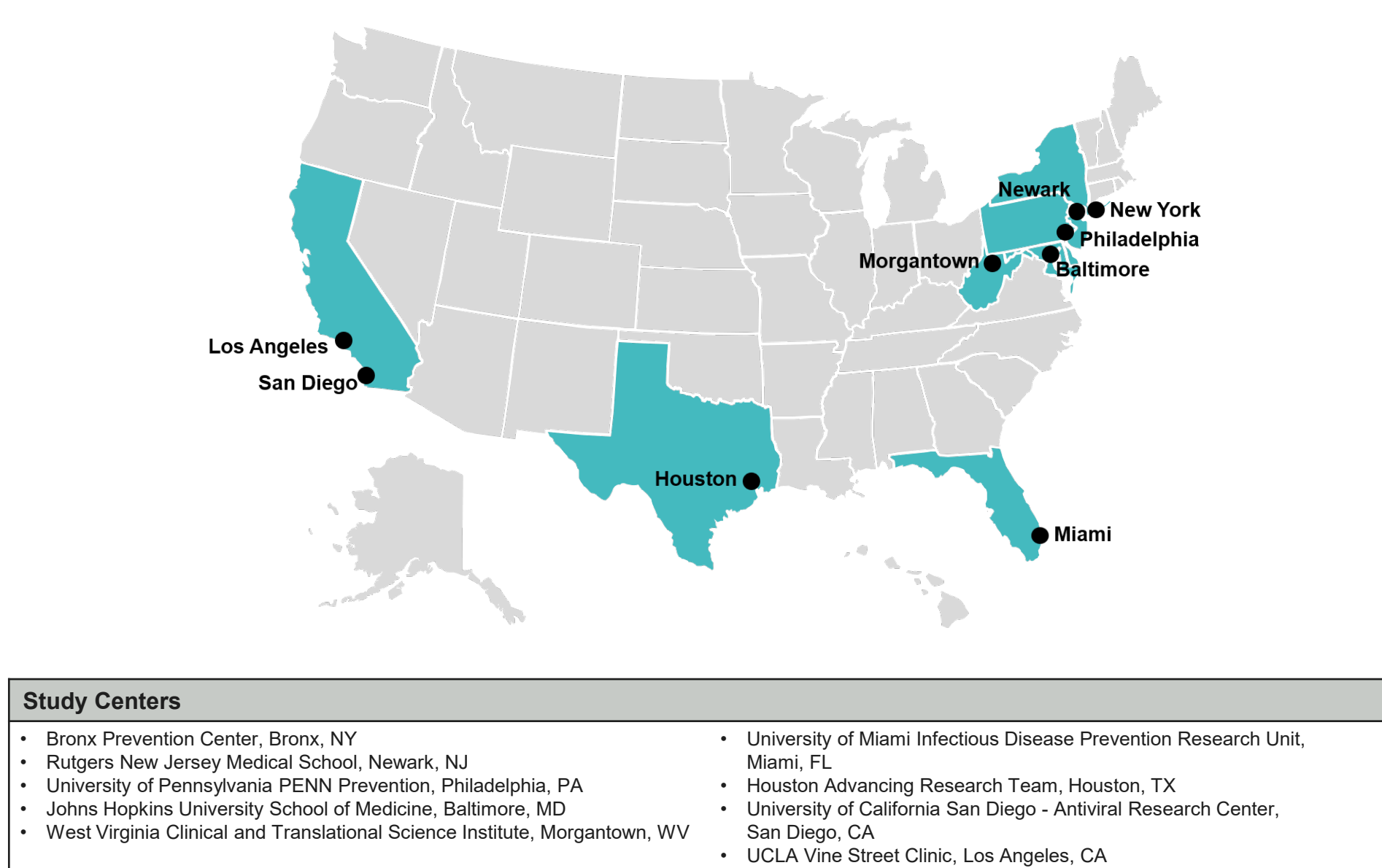
*Number of participants who received study drug.
C_{trough}, trough concentration; F/TDF, emtricitabine/tenofovir disoproxil fumarate; HAV, hepatitis A virus; HBV, hepatitis B virus; HCV, hepatitis C virus; LEN, lenacapavir; PK, pharmacokinetics; PrEP, pre-exposure prophylaxis; SC, subcutaneous; y, years.

Results

Participant Disposition and Demographics

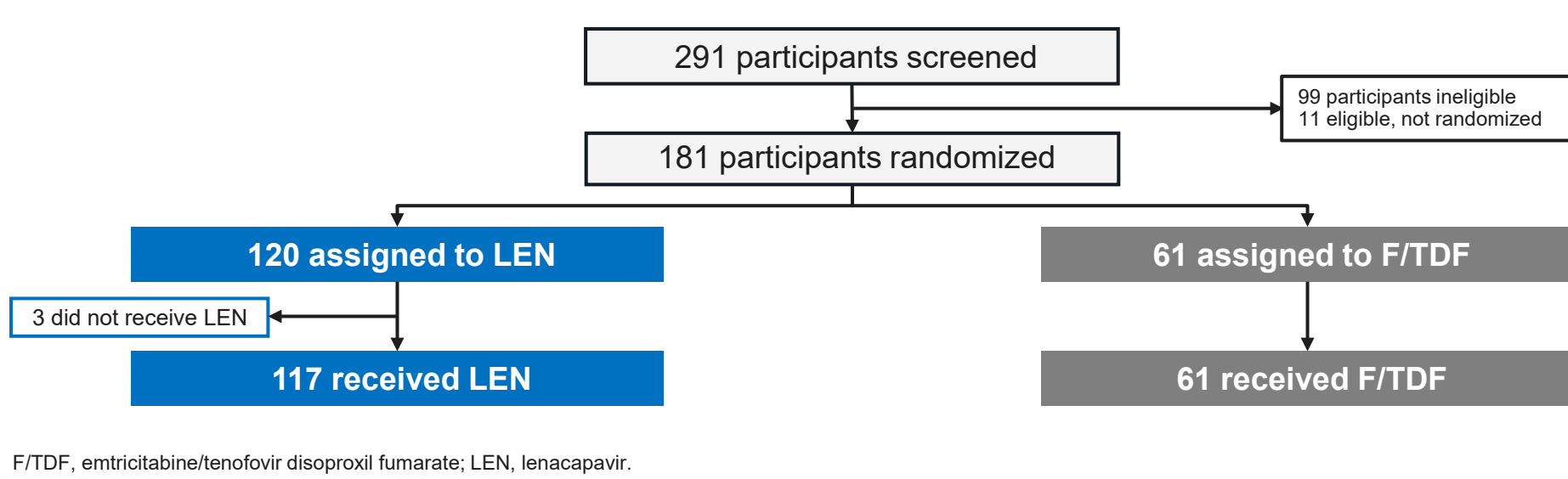
- In all, 291 participants were screened from nine sites in the US (**Figure 2**) of whom 181 (62%) were randomized; 178 participants received study drug (**Figure 3**)
- Key baseline demographics are shown in **Figure 4** (gender identity and race), **Figure 5** (socioeconomic vulnerability), and **Figure 6** (HCV infection), and summarized in **Table 1**
- At baseline, urine drug screen was positive for fentanyl in 70% of participants, opioids (excluding fentanyl) in 26%, and stimulants in 86%. Polysubstance use was identified in 65% of participants (**Figure 7**)

Figure 2. HPTN 103/PURPOSE 4 Study Sites



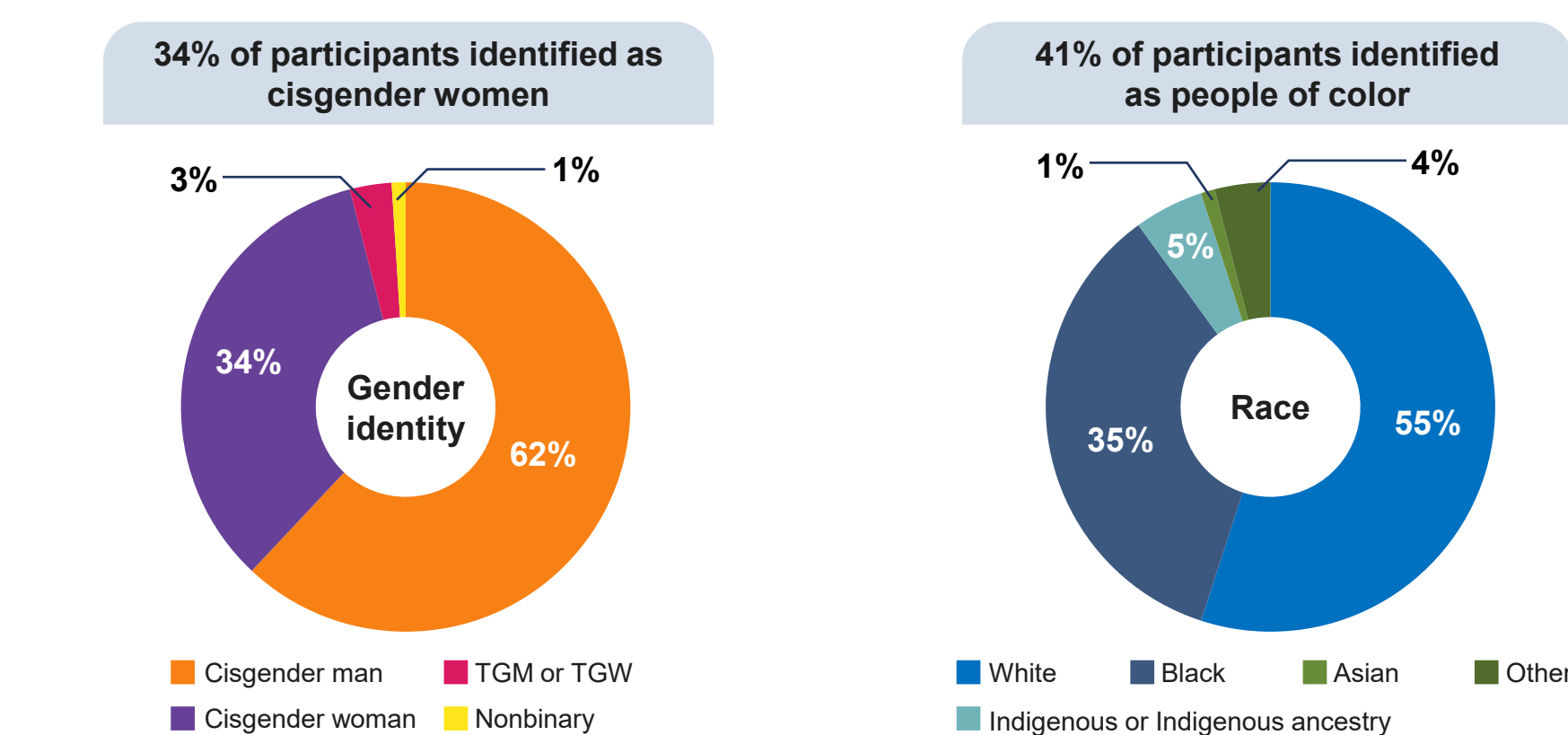
Results (cont.)

Figure 3. HPTN 103/PURPOSE 4 Disposition



F/TDF, emtricitabine/tenofovir disoproxil fumarate; LEN, lenacapavir.

Figure 4. Distribution of Participants in HPTN 103/PURPOSE 4 by Gender Identity and Race



See Table 1 footnotes for information on race definitions and percentage calculations.
TGM, transgender man; TGW, transgender woman.

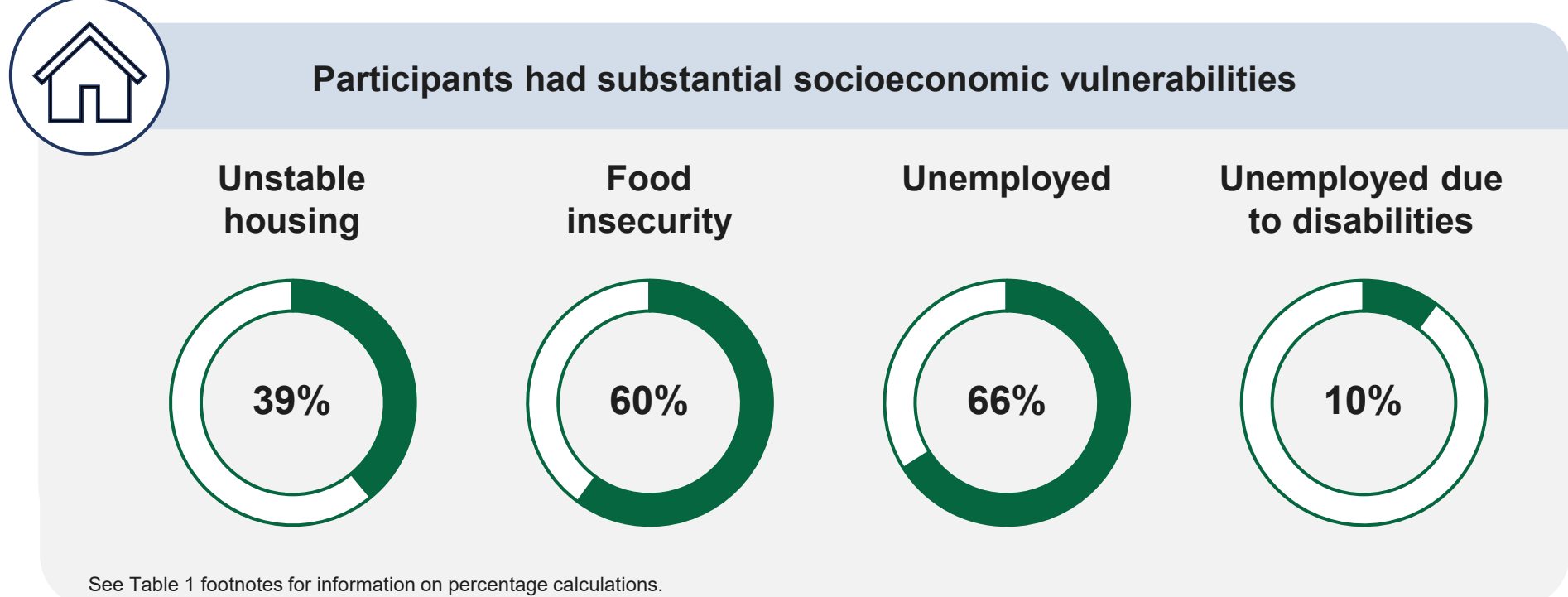
Table 1. Baseline Demographic, Clinical, and Socioeconomic Characteristics of Participants Enrolled in HPTN 103/PURPOSE 4

Characteristic, n (%)	LEN (n = 117)	F/TDF (n = 61)	TOTAL (N = 178)
Median age, years (range)	42 (21-67)	44 (25-65)	43 (21-67)
Sex assigned at birth			
Female	41 (35)	22 (36)	63 (35)
Male	76 (65)	39 (64)	115 (65)
Gender identity			
Cisgender man	74 (63)	37 (61)	111 (62)
Cisgender woman	39 (33)	22 (36)	61 (34)
Transgender man or woman	4 (3)	1 (2)	5 (3)
Nonbinary	0	1 (2)	1 (1)
Sexual orientation ^a			
Heterosexual	93/115 (81)	50/61 (82)	143/176 (81)
Gay, lesbian, or bisexual	20/115 (17)	10/61 (16)	30/176 (17)
Other	2/115 (2)	1/61 (2)	3/176 (2)
Ethnicity ^{a,b}			
Hispanic/Latine	23/116 (20)	8/59 (14)	31/175 (18)
Not Hispanic/Latine	93/116 (80)	51/59 (86)	144/175 (82)
Race ^{a,b}			
Black ^c	45 (38)	17/60 (28)	62/177 (35)
White	61 (52)	37/60 (62)	98/177 (55)
Indigenous or Indigenous ancestry ^d	6 (5)	2/60 (3)	8/177 (5)
Asian	1 (1)	1/60 (2)	2/177 (1)
Other ^e	4 (3)	3/60 (5)	7/177 (4)
High school education or less	70 (60)	44 (72)	114 (64)
Marital status			
Never married	83 (71)	40 (66)	123 (69)
Married	12 (10)	5 (8)	17 (10)
Separated/divorced/widowed	22 (19)	16 (26)	38 (21)
HCV infection			
Prior HCV infection	29 (25)	18 (30)	47 (26)
Active HCV infection	27 (23)	9 (15)	36 (20)
Socioeconomic characteristics ^a			
Unstable housing	45/115 (39)	24/60 (40)	69/175 (39)
Food insecurity	71/116 (61)	34/60 (57)	105/176 (60)
Unemployed	77/115 (67)	40/61 (66)	117/176 (66)
Unemployed due to disabilities	11/115 (10)	6/61 (10)	17/176 (10)

^aParticipants who reported 'not permitted', 'preferred not to answer', or where data were missing were excluded from the percentage calculations. ^bRace and ethnic group were reported by the participants. ^cThe 'Black' category included all participants who identified as being Black or as being of Black ancestry and included the terms 'Black', 'Black/White', and 'Black/Asian'. ^dThe 'Indigenous or Indigenous ancestry' category included the terms 'White/American Indian or Alaska Native', 'American Indian or Alaska Native', 'Asian/American Indian or Alaska Native', 'Asian/Native Hawaiian or Other Pacific Islander', and 'White/Native Hawaiian or Other Pacific Islander'. ^eThe 'Other' category includes 'multiracial - other' and 'not multiracial - other'. F/TDF, emtricitabine/tenofovir disoproxil fumarate; HCV, hepatitis C virus; LEN, lenacapavir.

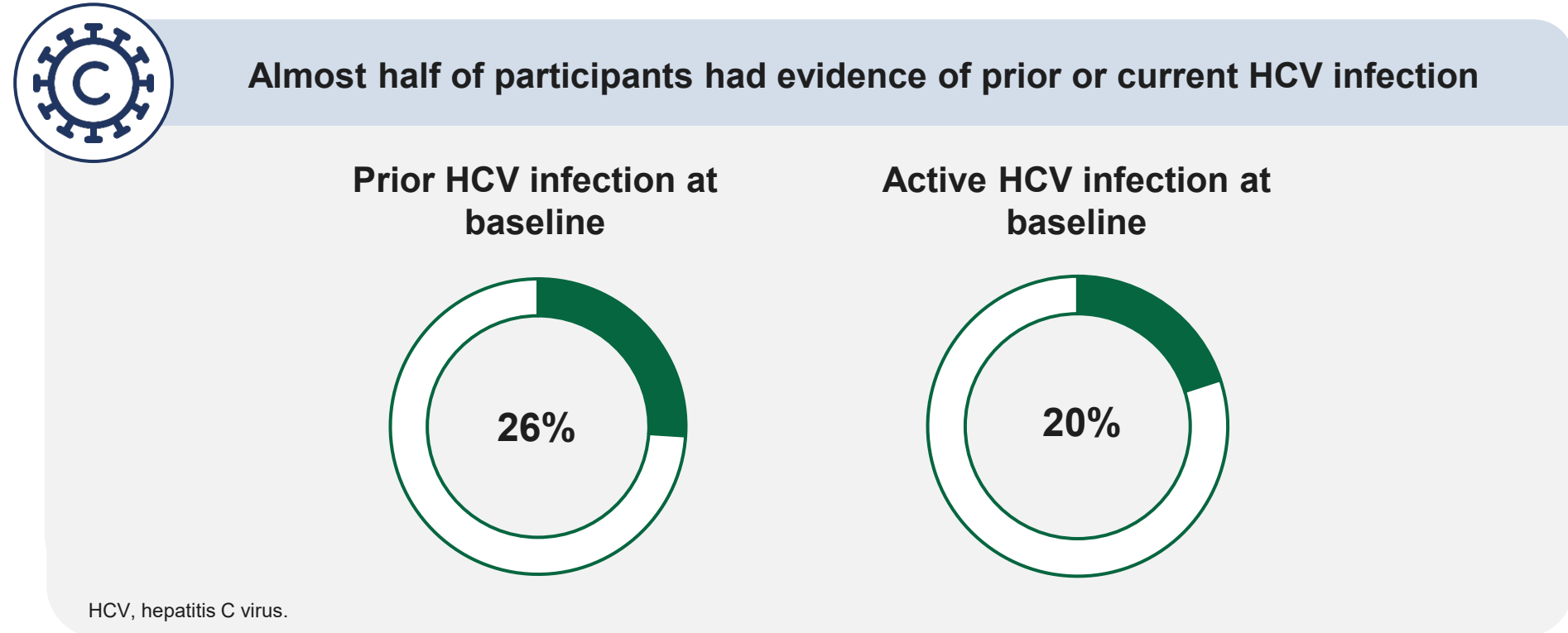
Disclosures: SSo has received research grants from Abbott Laboratories and Gilead Sciences, Inc.; and honoraria from Gilead Sciences, Inc. and MSD. SD-L has received research grants from Gilead Sciences, Inc. and Merck Inc. JC has received consulting fees from Gilead Sciences, Inc. and Viiv Healthcare. JB has received support from and reports research grants to her institute from Gilead Sciences, Inc. EM has received research grants from Gilead Sciences, Inc. SH is on the HIV Advisory Committee. SM has received research grants from Abbott Laboratories.

Figure 5. Socioeconomic Vulnerability in HPTN 103/PURPOSE 4



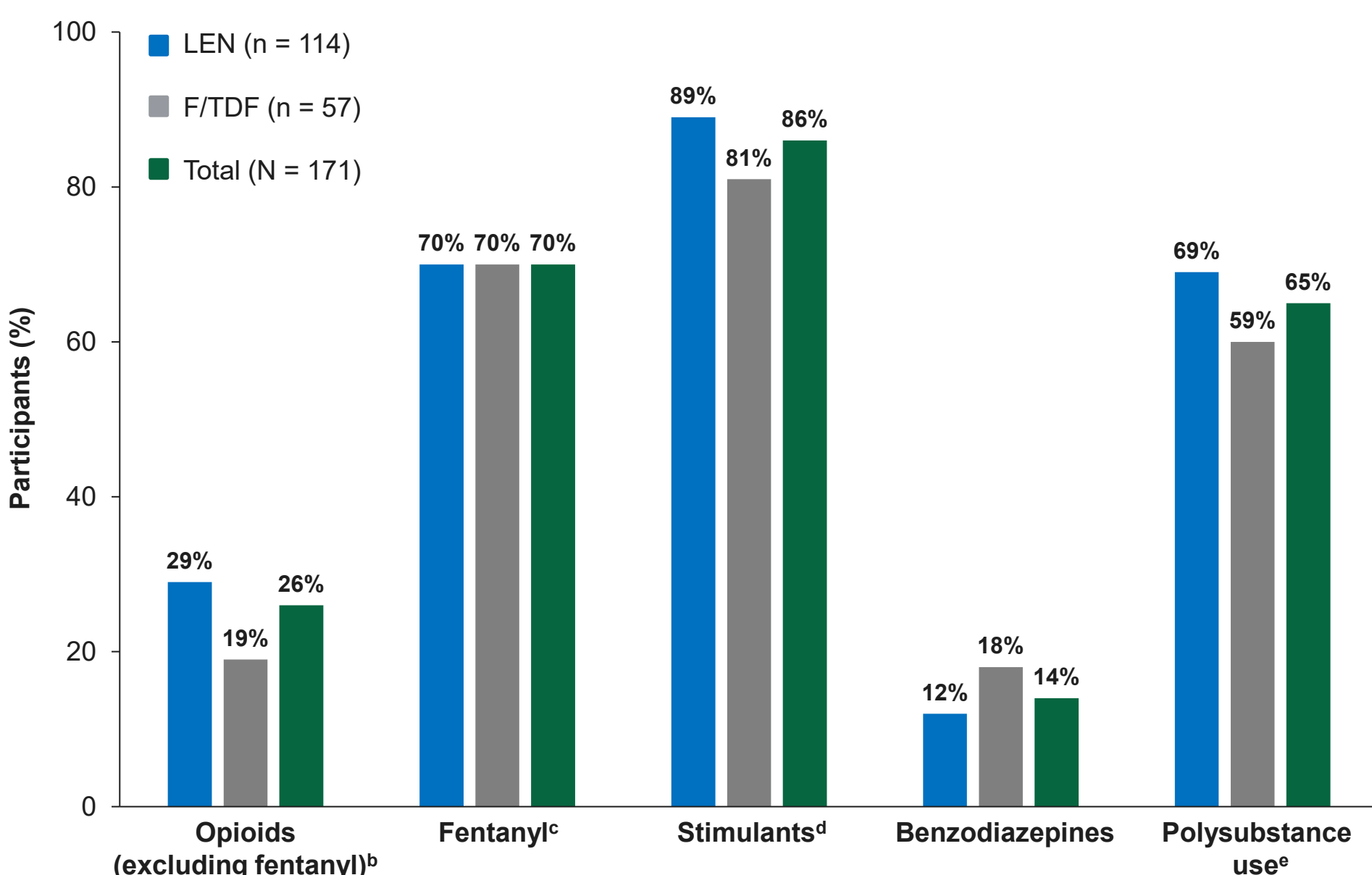
See Table 1 footnotes for information on percentage calculations.

Figure 6. HCV Infection in HPTN 103/PURPOSE 4



HCV, hepatitis C virus.

Figure 7. Baseline Substance Use Characteristics at Baseline^a



^aCombined point-of-care and central urine screening. ^bOpioids included codeine, hydromorphone, morphine, oxycodone, and heroin metabolites (6-monoacetylmorphine).

^cTotal participants was 163 (109 LEN; 54 F/TDF). ^dStimulants included amphetamine, cocaine, methamphetamine, and 3,4-methylenedioxymethamphetamine (MDMA).

^ePolysubstance use is defined as tested positive for ≥ 2 categories of drugs of misuse (opioid [excluding fentanyl], fentanyl, stimulants, or benzodiazepines), excluding the combination of opioids and fentanyl. Total participants was 168 (112 LEN; 56 F/TDF).

F/TDF, emtricitabine/tenofovir disoproxil fumarate; LEN, lenacapavir.

Disclosures (cont.): SSh has received research grants from Alkermes Inc., Gilead Sciences, Inc., and Indivior Inc.; consulting fees from Lilly Inc. and Clear Scientific Inc.; and is a site Principal Investigator for Altimmune Inc. DRB, AM, DF, AA, BJD, LK, CL, LS-T, VV, and GL do not have any disclosures to report. SBP, CCC, and RD are employees and shareholders of Gilead Sciences, Inc.

References: 1. Degenhardt L, et al. *Lancet Global Health*. 2023;11:e659-72. 2. Bekker LG, et al. *N Engl J Med*. 2024;391:1179-92. 3. Kelley CF, et al. *N Engl J Med*. 2025;392:1261-76.

Acknowledgments: We extend our thanks to the HPTN 103/PURPOSE 4 participants, their families, and all participating investigators. 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.