

“In Case You Missed It”: New Developments in HIV Prevention and Treatment



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Financial Relationships With Ineligible Companies (Formerly Described as Commercial Interests by the ACCME) Within the Last 2 Years

Dr Armstrong reported no relevant financial relationships with ineligible companies. (Updated November 16, 2025)

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Learning Objectives

After attending this presentation, learners will be able to:

- Compare and contrast options for preexposure prophylaxis (PrEP) and monitor patients on PrEP appropriately
- Describe the risks and benefits of starting patients with viremia on long-acting antiretroviral therapy
- Identify the consequences of funding losses to HIV programs in the US and globally

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Outline

- HIV Prevention
- HIV Treatment
- Policy



Slide 4

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What's new in HIV Prevention



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The HIV Biomedical Prevention Landscape



TDF/FTC
TAF/FTC



Cabotegravir



Lenacapavir

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Guidelines changes



TDF/FTC
TAF/FTC

Table 4. Recommendations for Currently Approved Biomedical HIV Prevention by Type of Exposure*

Type of exposure	Daily TDF/FTC	On-demand (2-1-1) TAF/FTC	Daily TAF/FTC	Every other month intramuscular long-acting cabotegravir†
Insertive anal/vaginal sex	✓	✓	✓	✓
Receptive anal sex	✓	✓	✓	✓
Receptive vaginal sex	✓	✓	✓	✓
Receptive intramuscular sex	✓	✓	✓	✓
Injection drug use‡	✓	✓	✓	✓
Recommended for pregnant and breastfeeding women	✓	✓	✓	✓
Initiate with a double dose	✓	✓	✓	✓
Recommended for individuals with reduced creatinine clearance (30-60 mL/min) or who have oligonephria or anephria	✓	✓	✓	✓

JAMA | Special Communication

Antiretroviral Drugs for Treatment and Prevention of HIV in Adults:
2024 Recommendations of the International Antiviral Society-USA Panel

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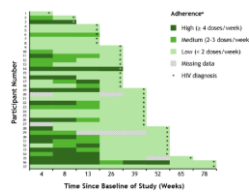
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Preexposure Prophylaxis for HIV: Updated Recommendations From the 2024 International Antiviral Society-USA Panel

"TAF/FTC is now recommended for the prevention of HIV acquisition from vaginal exposures for those in whom TDF/FTC is contraindicated or undesirable"

PURPOSE 1: 39 incident infections in the F/TAF arm. TFV-DP measures in dried blood spots in 37/39 of the incident cases. 35/37 with suboptimal or nonadherence. Of the two with high adherence, one had significant resistance (K65R + M184I)

Figure. Longitudinal Adherence of PURPOSE 1 Participants Diagnosed With Incident HIV in the F/TAF Group

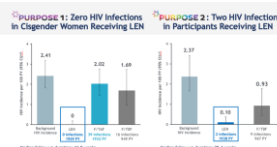


Kivweya et al., Adherence to F/TAF in cisgender women prevents HIV with low risk of resistance or diagnostic delay. CROI 2025, Abstract 194

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LEN for PrEP: The gift that keeps on giving...



PURPOSE 1

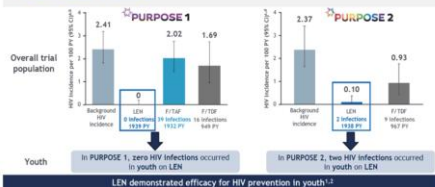
- 193 pregnant women on LEN (vs 208 on F/TAF and 95 on TDF)
- No transmissions on LEN (vs 4 and 1 respectively)
- Pregnancy outcomes were balanced and within norms for the population (live births, losses and congenital abnormalities)

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Lenacapavir for PrEP in youth, ages 16-25

Only Two HIV Infections in Youth on LEN From PURPOSE 1 and 2



Gill K et al, IAS 2025 Abstract OAC0503

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Monitoring on PrEP



TDF/FTC
TAF/FTC



Cabotegravir



Lenacapavir

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CDC Clinical Guidance for PrEP

last update 2/10/2025

- Repeat HIV antigen/antibody and HIV-1 RNA tests at least every three months
- For those on injectable medications, test for HIV with Ag/Ab and HIV-1 RNA assays at month 1 and at least every 2 months starting in month 3

<https://www.cdc.gov/hiv/nexus/hcp/prep/index.html>, Accessed 11/12/2025

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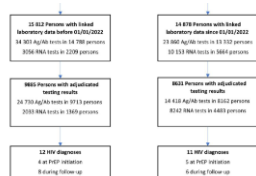
Limited Utility of HIV RNA Testing to Monitor Oral Preexposure Prophylaxis Use: A Real-World Cohort Study—United States, 2019–2023

Weiming Zhu,¹ Kevin P. Delaney,² Ya-lin A. Huang,² Ruqa R. Patel,² Athena P. Kourtis,² and Karen W. Hoover²

May 5, 2025

HIV Research Branch, Division of HIV Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

- Oral PrEP user cohort from the HealthVerity database 12/2018–8/2023 with linked laboratory data



*2021 CDC Guideline Update

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	Pre CDC guidelines change	Post CDC guidelines change
HIV RNA testing rate	14%	38%
Positivity rate of t/u Ag/Ab testing	0.03% (0.01–0.06)	0.04% (0.01–0.07)
Positivity rate of t/u RNA testing	1.39% (0.88–1.91)	0.22% (0.12–0.32)
False positive rate HIV RNA t/u	0.00% (0.00–0.27)	0.06% (0.02–0.14)
PPV HIV RNA t/u	100% (73.5–100)	66.7% (34.9–90.1)
Number needed to test		8226–9900 pts to detect 1 additional diagnosis earlier with HIV RNA testing than with Ag/Ab testing alone. None actually seen

HIV RNA testing did NOT provide additional value to Ag/Ab testing during routine follow-up of oral PrEP users.

*and should NOT be used for injectable PrEP users either who have even lower rates of seroconversions

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JAMA | Special Communication

Antiretroviral Drugs for Treatment and Prevention of HIV in Adults: 2024 Recommendations of the International Antiviral Society–USA Panel

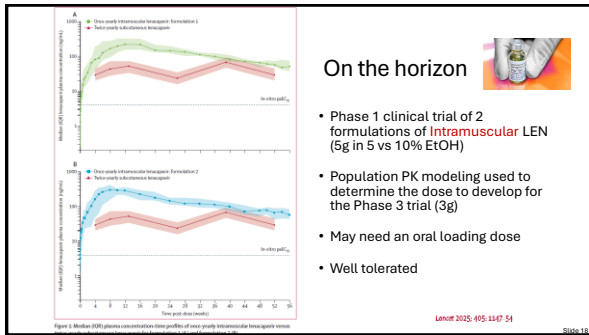
“Follow-up testing for cabotegravir PrEP breakthrough infections should not routinely include HIV RNA testing but should include a point-of-care rapid HIV antibody test and a laboratory-based antigen antibody test. RNA testing as part of routine monitoring for PrEP failure is not recommended because such testing has a low positive predictive value and false-positive results have significant negative sequelae.”

Preexposure Prophylaxis for HIV: Updated Recommendations From the 2024 International Antiviral Society–USA Panel

“RNA testing for routine monitoring for PrEP failure is not recommended [for lenacapavir].”

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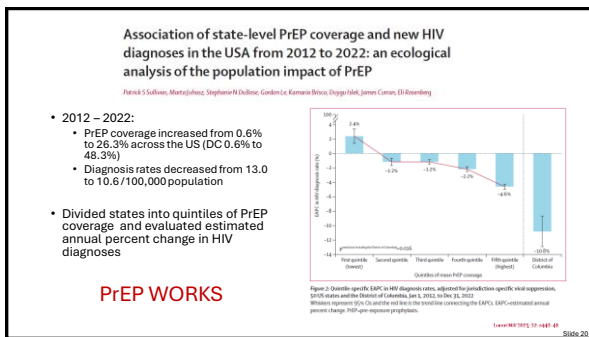
New Agents for PrEP

MK8527

- NRTTI (like islatravir)
- Once monthly oral agent
- Phase IIa study of 3 different doses MK-8527 in adults at low risk of HIV exposure
- Well-tolerated with good safety profile
- Phase 3 trials (EXPrESSIVE-10, -11) of 11 mg MK-8527 vs F/TDF underway

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What's new in HIV Treatment

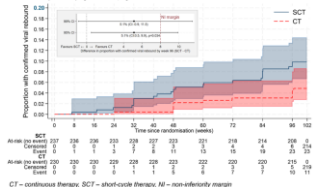
IAS-USA
International AIDS Society-USA

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BREATH-PLUS: Short cycle therapy is inferior to continuous therapy in adolescents living with HIV

Figure: BREATH-PLUS primary outcome - proportion with confirmed viral rebound (viral load ≥ 200 copies/mL) by week 96, by trial arm



Kekitiinwa A, et al, IAS 2025 Abstract OAS0104LB
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The Promise of Long-Acting ART

ACTG A5359 LATITUDE: Long-acting Cabotegravir + Rilpivirine vs. Oral ART in People Living with HIV with Adherence Challenges

Patients randomized to LA CAB/RPV vs continued oral therapy once VL < 200. Stopped early by the DSMB. 17% of patients randomized to LA CAB/RPV arm actually had VL > 200 at the time of medication start, one-third with VL > 10,000 copies/cc

Secondary Outcomes	LA CAB/RPV	Oral ART	Difference (%)
Virologic failure (n, %)	6 (7 %)	28 (25%)	-18.2 (-31.1 to -5.4)
Treatment-related failure (n, %)	9 (9.6 %)	29 (26%)	-16.6 (-29.9 to -3.3)
• Viral failure	6	28	
• Treatment discontinuation 2/2 AEs	3	1	

Rana et al, Abstract 212, CROI 2024

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Long-Acting Cabotegravir/Rilpivirine, Lenacapavir, and Ibalizumab Use Among Persons With HIV-1 Viremia at a Ryan White-Funded Clinic in the Urban US South

Jonathan A. Colasanti,^{1,2,3} Amelia Blumhagen,^{2,3} Leticia V. Miles-Carmona,^{1,2} Eudora Ochung,¹ Priyanka Pareek,¹ Vickie Robinson,¹ Erica Anderson,¹ Mary Gorman,¹ Hilary Sperry,¹ Bradley L. Smith,^{1,2} Joel Sussman,^{1,2} Eric Paul Lane,¹ Caitlin A. Moore,^{1,2,3} Meredith Lane,^{1,2} Wendy S. Anastos,^{1,2,3} and Laura F. Cullen,^{1,2,3}

- 361 pts initiated on LA-ART in this urban safety net population with significant barriers to care,
- 88 (22%) with viremia
 - 51% food insecurity, 35% housing instability, 25% unmet transportation needs
 - 51% with CD4<200, median VL 4.0, 16% with VL > 5 log, 46% with prior OIs
 - 9 perinatal infection
- 69% CAB/RPV, 27% with CAB +/- RPV + LEN, 4% CAB +/-RPV + LEN + IBA

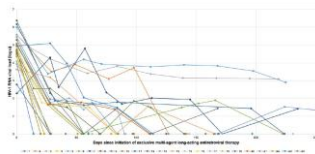
Colasanti, CROI 2025

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Results

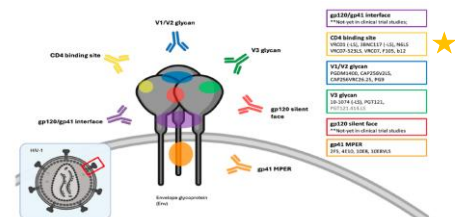
- 2 lost to follow-up
- 98% on time injections for CAB/RPV, 100% on time for LEN and IBA
- 92% with VS
 - 2 with LLV (50-200 copies/cc)
 - 2 with VL >200 and no resistance
 - 2 with VF with resistance
 - Both with dual class resistance (NNRTI + INSTI)



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Broadly Neutralizing Antibodies (bnAbs)



From: 2024, DE 101, <https://doi.org/10.1002/de.1001>

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Broadly neutralizing Abs: EMBRACE

Figure 1. EMBRACE QAM study design.

- Key inclusion/exclusion criteria**
- Aged 18-70 years
 - >2 HIV-1 RNA measurements <50 c/mL in the 12 months before screening
 - No prior ART switch due to VIF
 - CD4+ cell count >350 cells/mm³
 - On stable ART for ≥6 months
 - No active HBV co-infection^a
 - Phenotypic sensitivity to N6LS (IC₅₀ <2.0 µg/mL and MP1 >95%)^a

^arecombinant human hyaluronidase PH20

Griesel, EACS2025 PS09.1

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- The N6LS product, whether administered IV or via SC injection with IM CAB was safe, well tolerated, and acceptable in this Phase IIb study

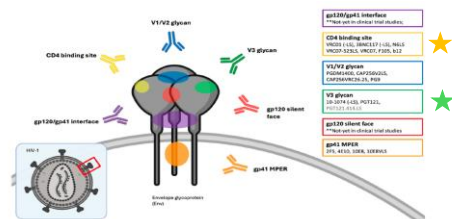
Table 2. N6LS-Related ISR Summary at Month 6^a

Outcome, n (%)	N6LS 60 mg/kg IV (N=50)	N6LS 3000 mg + rHuPH20 SC (N=49)
Participants reporting any ISR, n (%)	4 (8)	23 (51)
Number of ISR events, n ^b	4	70
Maximum grade based on all ISR events, n (%)		
1	4 (100)	39 (56)
2	0	20 (29)
3	0	11 (16)
4-5	0	0
ISR duration, median (range), days	2 (1-3)	4 (1-14)
Number of ISR events of interest		
Infusion site module	0	1 ^c
Infusion site erythema	1 ^c	26 ^d
ISRs leading to discontinuation	0	0

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Broadly Neutralizing Antibodies (bnAbs)



From: 2024, DE HIL, <https://doi.org/10.1016/j.jheale.2024.100000>

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LEN + teropavimab (TAB) + zinlirvimab (ZAB)

Key inclusion/exclusion criteria

- Age 18-65
- VL<50 x 12 months +
- Stable oral ART for 12 months
- CD4>=200 cells/mm3
- No HBV infection
- Pheno susc to TAB, ZAB

LEN 927 mg sc q6m + 2550 mg IV TAB q6m + 2550 mg IV ZAB q6m

n=53

stable baseline oral therapy

n=27

↑

Wk 36

↑

Wk 52

- Well-tolerated, 36 pts in the LEN/TAB/ZAB arm with ISRs to LEN, mostly Grade I
- No infusion related reactions
- 3 virologic failure in LEN/TAB/ZAB arm, none in oral therapy arm

Ogbuagu, EACS 2025, Abs PS09.2

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Assessment of Participants With Virologic Rebound

- Matching characteristics of all 3 participants: male, HIV-1 subtype B, weight >100 kg, lower bNAb exposure, experienced confirmed late virologic rebound late during dosing interval

Parameter	Participant 1	Participant 2	Participant 3
Baseline BMI, kg/m ²	30.8	38.3	36.3
Baseline weight, kg	109	143	118
Time of rebound	Wk 24	Wk 50	Wk 50
LEN C _{trough}	4th percentile	13th percentile	66th percentile
TAB C _{trough}	25th percentile	18th percentile	12th percentile
ZAB C _{trough}	37th percentile	18th percentile	6th percentile
Baseline TAB susceptibility IC ₅₀ , µg/mL	1.53	0.08	0.36
Baseline ZAB susceptibility IC ₅₀ , µg/mL	0.72	0.09	0.17

Ogbuagu, EACS 2025, Abstr PS09.2

Slide adapted from Clinical Care Options

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What could get in our way?



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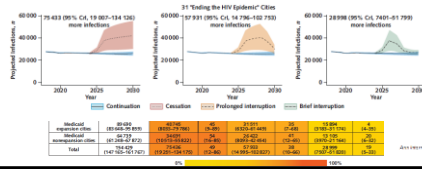
The IAS–USA Annual Virtual Course Update: Emerging Challenges in HIV Medicine, December 4, 2025

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The Potential Impact of Ending the Ryan White HIV/AIDS Program on HIV Incidence: A Simulation Study in 31 U.S. Cities

Ryan Foster, PhD; Melissa Schure, PhD; Joyce Jones, MD; Catherine Lesko, PhD; D. Scott Batey, PhD, MSW; Isabelle Butler, MD, MPH; Dafina Ward, JD; Karen Magrover, PhD, MEd; Keri N. Akhtar, PhD, MPH; Marnita K. Jain, MD, MPH; Kasia A. Gebro, MD, MPH; David W. Dowdy, MD, PhD; Manank Shah, MD, PhD; Parvati Kessie, PhD; and Anthony T. Fojo, MD, MHS

Modeled impact on HIV incidence and excess infections under three conditions between now and 2030



doi:10.7554/mbe.25.18137

834-835

The impact of cuts in the US President's Emergency Plan for AIDS Relief funding for HIV pre-exposure prophylaxis in sub-Saharan Africa: a modelling study

Jack Stone, Kennedy Kipkech Mutai, Adeline Arterio, Ramcín Sílhol, Mario-Claude Bolly, Jinai Rutevosian, Chris Beyer, Peter Vickerman

Least MSF 2022: 11/27/22

- Cessation of PEPFAR-funded PrEP for one year will prevent 719,000 + people from accessing PrEP across 28 sub-Saharan African countries
- This could lead to 6671 new infections during 1 year and 10,313 additional (secondary) infections over the next 5 years

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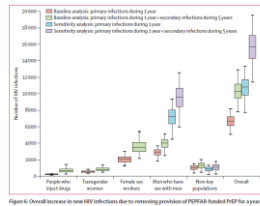


Figure 6: Overall increase in new HIV infections due to removing provision of PEPFAR funded PrEP for a year

Stone, IAS2025, OAS0103LB

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Conclusions

- There are several options for PrEP (oral and long-acting) that can be used across multiple populations and monitoring only requires routine testing which prevents over-medicalization and barriers to care
- Longer acting oral agents are promising as are longer acting preparations of LEN
- Long acting injectable therapy offers new hope for patients for whom oral therapy is difficult.
- Pairing injectable ARVs with bnAbs has promise
- Science has allowed us to have options to end the epidemic but all this is at risk with recent policy changes that affect access in the US and worldwide.

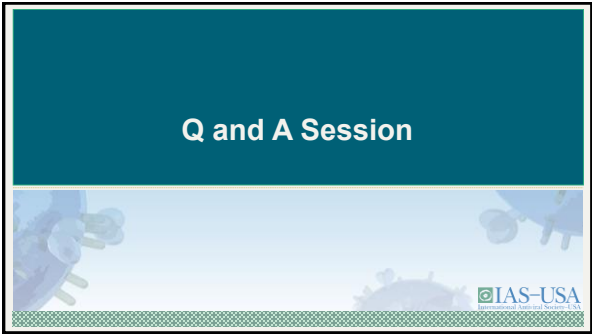
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