

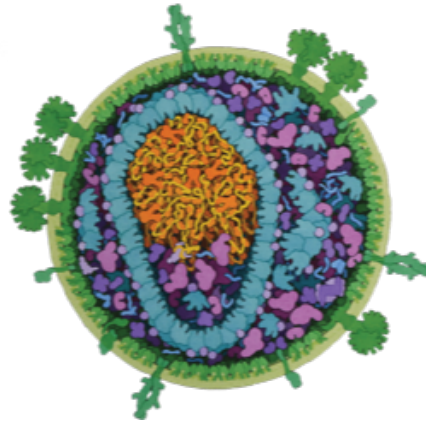
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INSTITUTE FOR GLOBAL HEALTH
& INFECTIOUS DISEASES

CROI 2026 – What Matters Most



CROI

Conference on Retroviruses
and Opportunistic Infections

A NATAP UPDATE

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CROI 2026: What Matters Most

PREVENTION

- Low level viremia and transmission modeling
- PURPOSE 1 & 2 Follow-Up Data (Breakthroughs, Safety, Resistance)
- LEN and CAB ISR - CLARITY Study
- LEN Drug Interactions in PrEP users
- ANRS PREVNIR Follow-Up
- PrEP user characteristics in US
- Real use of LA CAB in US
- EBONI LA CAB Black Women in US
- LA PrEP awareness among US MSM
- Overview of new agents (coming and possibly coming)

TREATMENT

Naive

- DOR-ISL vs BFTAF
- DTG/3TC->CAB/RPV VOLITION

Experienced/Switch

- DOR-ISL vs BFTAF - 96 week data
- DOR-ISL vs SOC - 96 week data
- ISL-LEN Weekly vs BFTAF - 96 week data
- BIC-LEN vs BFTAF
- BIC-LEN 96 week data
- N6LS + CAB EMBRACE
- LEN + TAB + ZAB
- Overview of new agents (coming and possibly coming)

WELL-BEING

- GLP-1 agonists and weight, liver fat, CVD risk, smoking, and more
- Inflammatory markers and CVD in REPRIEVE
- HTN in REPRIEVE
- New ACC/AHA lipid guidelines

OTHER MATTERS

- Science under siege
- Model of HIV diagnoses if Ryan White cut in US
- What you can do



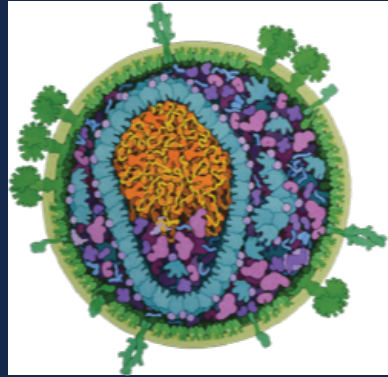
Thank You!

Acknowledgement

The vast majority of practice-changing and life-enhancing data to be presented were generated or supported by the US Federal government through the NIH, CDC, USAID, and other agencies staffed by people dedicated to our health and well-being.

Many are now unemployed.



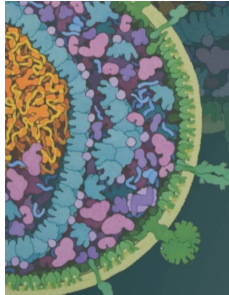


CROI

Conference on Retroviruses
and Opportunistic Infections

PREVENTION

HIV Prevention: Low-Level Viremia and Transmission



Themed Discussion-07
Tuesday, February 24, 2026

903 - Quantifying Uncertainty in HIV Transmission Risk From Persons With Low-Level Viremia

Michael Martin
The Johns Hopkins Bloomberg School of Public Health,
Baltimore, MD, USA

Financial Relationships:
Mr Martin reported no relevant financial relationships with ineligible companies.

CROI 2026

In 2023 the World Health Organization released a policy stating that “*People living with HIV who have a **suppressed but detectable [low-level viremia, 200 – 1000 copies/mL]** viral load and are taking medication as prescribed have **almost zero or negligible risk of transmitting HIV** to their sexual partner(s).*” Our goal was to **quantify transmission risk** (and uncertainty) associated with **low level viremia** and its **implications** in settings with infrequent VL monitoring.

EXISTING EVIDENCE

Among 323 transmission events, only **2 transmission events** were associated with a VL **<1,000 copies/mL** (Broyles et al., The Lancet, 2023).

However, among studies with index partners on treatment:



- **HPTN052:** **1/8** linked infections had index VL **<1,000 copies/mL** (Cohen et al., NEJM, 2016)
- **Partners PREP:** **1/3** linked infections had index VL **<1,000 copies/mL** (Mujugira et al., JAIDS, 2016)

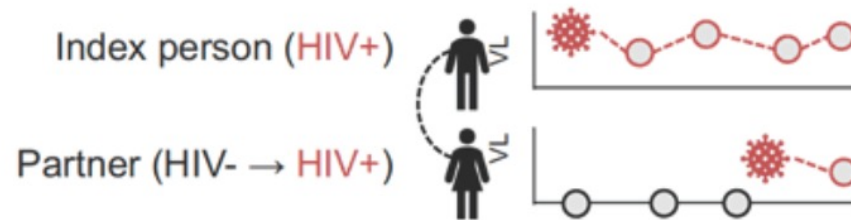
LLV is less stable than viral load (VL) that is undetectable, and no recent studies have rigorously quantified the resultant transmission risk. LLV does not always persist in individuals on treatment.

HIV Prevention: Low-Level Viremia and Transmission

METHODS: DATA

We utilized epidemiological and virological data from >15,000 participants with HIV in the population-based **Rakai Community Cohort Study (1995-2022)**.

TRANSMISSION COHORT: We utilized longitudinal HIV testing and viral load monitoring from monogamous cohabitating serodiscordant (HIV+/HIV-) couples. We estimated the relationship between index **viral load** and **rate of transmission** using a mechanistic model of viral transmission.



VIRAL LOAD COHORT: Paired viral load measurements from 91 people living with HIV on treatment were used to quantify stability of **low-level viremia** and simulate viral-load trajectories over 12-months of follow-up.

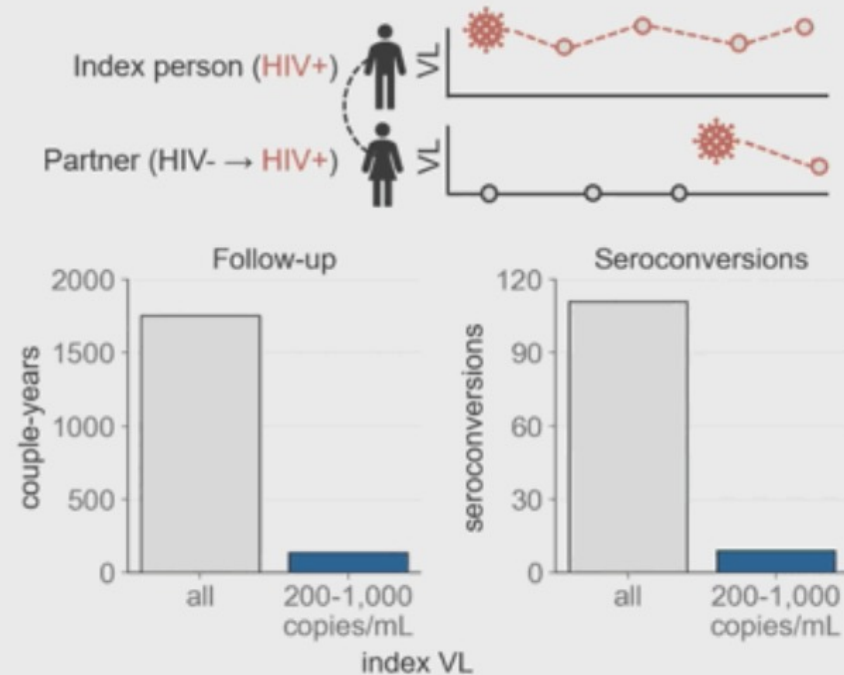
Data



**Rakai Health
Sciences Program**
Improved Health Through High Impact Research

Rakai Community Cohort Study

- Population-based open-cohort
- 1995 – 2022, ART uptake ~2010
- >15,000 participants living with HIV

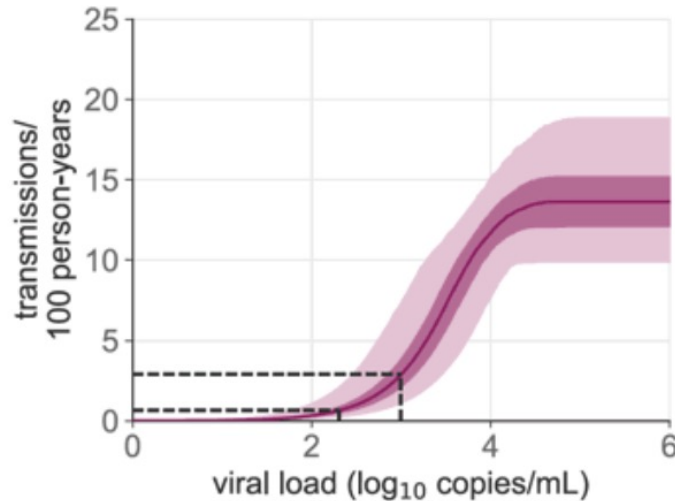


Nine of 111 (8%) seroconversions in monogamous cohabitating serodiscordant couples occurred with **low-level viremia** in index person

HIV Prevention: Low-Level Viremia and Transmission

RESULTS

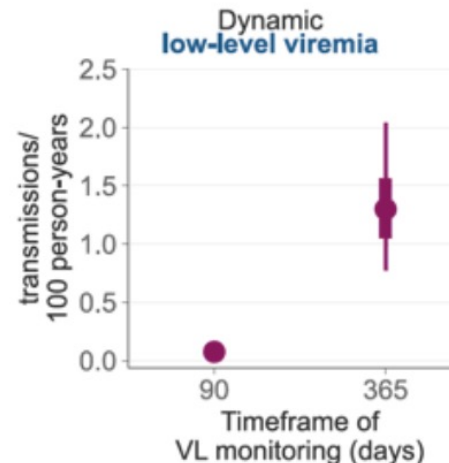
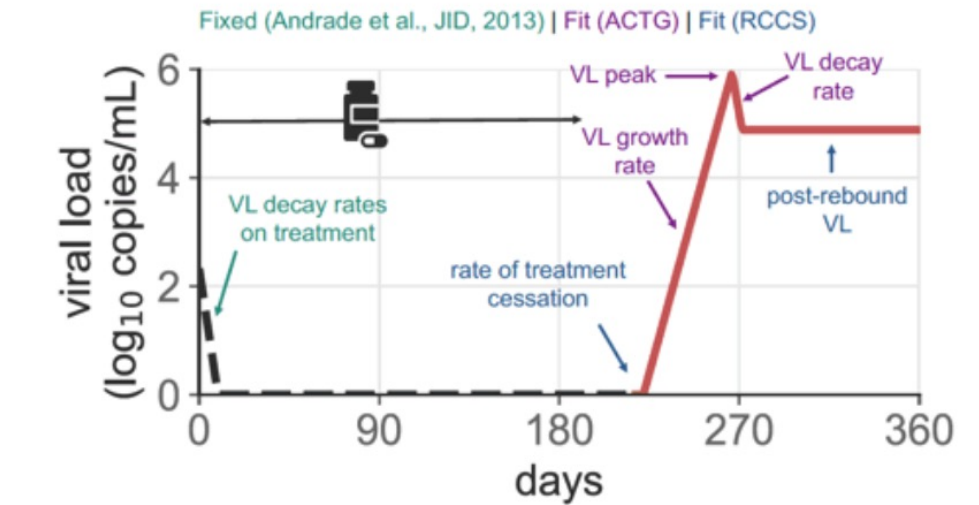
We fit this model to 93 seroconversions among 940 couple-years of follow-up from 415 monogamous serodiscordant couples. We focused on pre-treatment index partners as their viral loads are more stable and informative of the relationship between viral load and transmission rate.



We estimate **2.9 (95% CI 1.1-7.5) transmissions** per 100 person-years at a viral load of **1,000 copies/mL**

We estimate **0.6 (95% CI 0.2-2.1) transmissions** per 100 person-years at a viral load of **200 copies/mL**

We simulated **viral load dynamics** during 12 months of follow-up after initial **LLV**

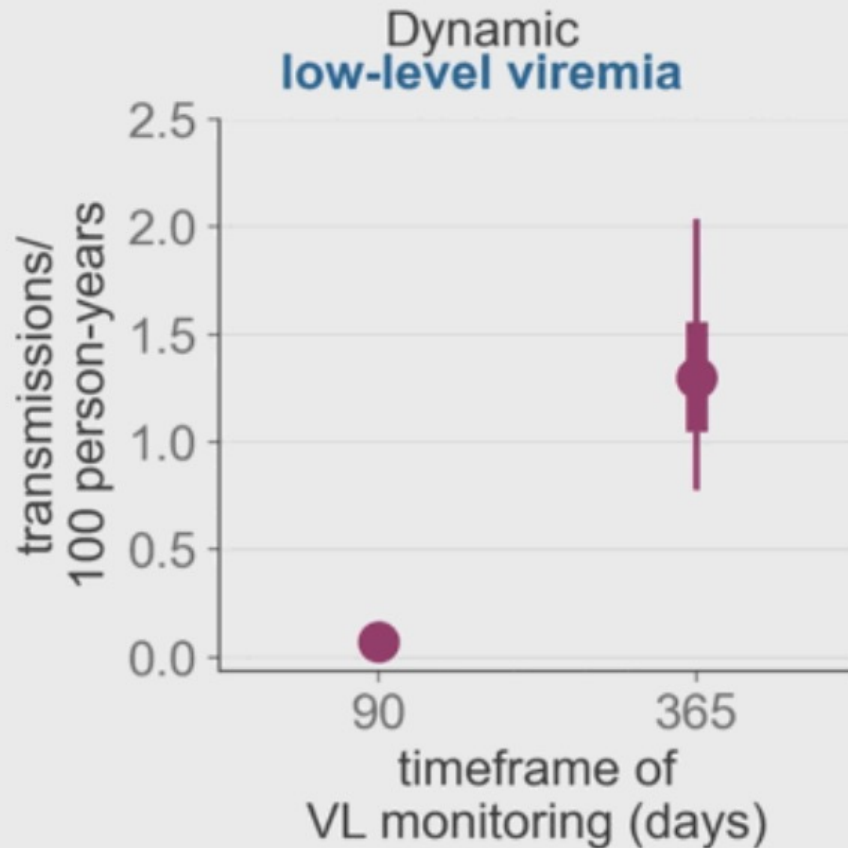


We estimate **1.3 (95% CI 0.8-2.0) transmissions** per 100 person-years from the average individual with **low-level viremia** accounting for **viral rebound**.

This risk could be reduced by 94% [93%-96%] with **90-day monitoring** vs. annually

HIV Prevention: Low-Level Viremia and Transmission

Results (continued)



Key takeaways

- **2.9 (95% CI 1.1-7.5) transmissions** per 100 person-years at a viral load of **1,000 copies/mL**
- **1.3 (95% CI 0.8-2.0) transmissions** per 100 person-years on average from individuals with **low-level viremia** accounting for **viral rebound**
- Only **6% (95% CI 4-7%)** of **transmissions** from people with **low-level viremia** on ART are predicted to occur in the first **90-days** post-monitoring, suggesting a role for **more frequent testing**

Transmission risk from individuals on treatment with low-level viremia may be sufficiently high to warrant reconsideration of recent policy guidance.



NIH NIAID R01AI155080 R01AI143333

HIV PrEP – Long-Acting LEN

The New York Times

Regulators Approve a Twice-Yearly Shot to Prevent H.I.V. Infection

The drug could change the course of the AIDS epidemic. But the Trump administration has gutted the programs that might have paid for it in low-income countries.

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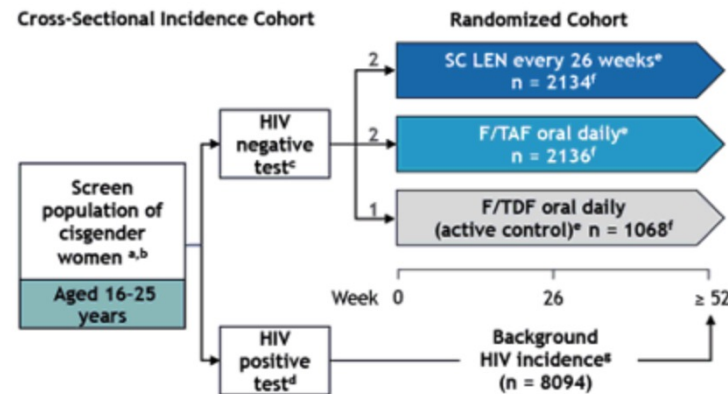
Lenacapavir is already sold as a treatment for H.I.V. infections that are resistant to other medications. Nardus Engelbrecht/Associated Press



By Apoorva Mandavilli

PURPOSE 1 and 2 Study Designs

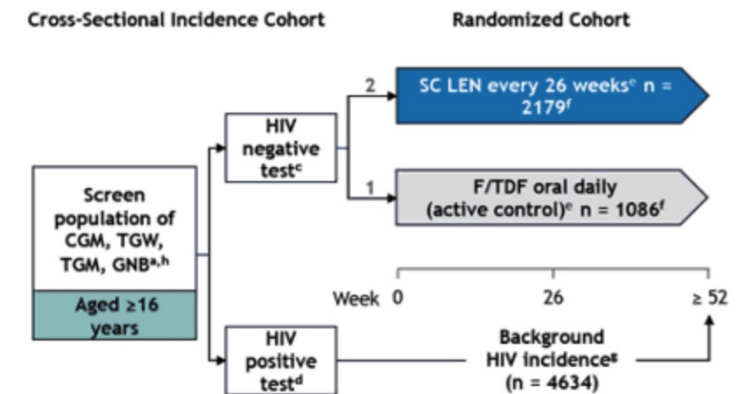
PURPOSE 1



ClinicalTrials.gov: NCT04994509

^aNot receiving PrEP and without HIV testing in past 3 months; ^bThe first participant was screened in August 2021, the 50th percentile participant was randomized in May 2023, and the last participant was randomized in September 2023; ^cParticipants also met eligibility criteria (including weight ≥ 35 kg, eGFR ≥ 60 mL/min, not pregnant); ^dReactivity assay data were used to estimate background HIV incidence (persons testing HIV positive were referred to HIV care); ^ePlus the alternative SC/oral placebo; ^fn numbers represent the full analysis set for efficacy analyses; ^gBackground HIV incidence is the incidence expected without PrEP that would have been expected in a placebo group (the counterfactual HIV incidence); ^hThe first participant was screened in June 2021, the 50th percentile participant was randomized in August 2023, and the last participant was randomized in December 2023. CGM, cisgender men; eGFR, estimated glomerular filtration rate; F/TAF^g, emtricitabine/tenofovir alafenamide; F/TDF^g, emtricitabine/tenofovir disoproxil fumarate; GNB^{a,h}, gender-nonbinary; LEN^a, lenacapavir; PrEP, pre-exposure prophylaxis; SC, subcutaneous; TGM, transgender men; TGW, transgender women.

PURPOSE 2



ClinicalTrials.gov: NCT04925752

Long-Acting LEN: Efficacy

The New York Times

Regulators Approve a Twice-Yearly Shot to Prevent H.I.V. Infection

The drug could change the course of the AIDS epidemic. But the Trump administration has gutted the programs that might have paid for it in low-income countries.

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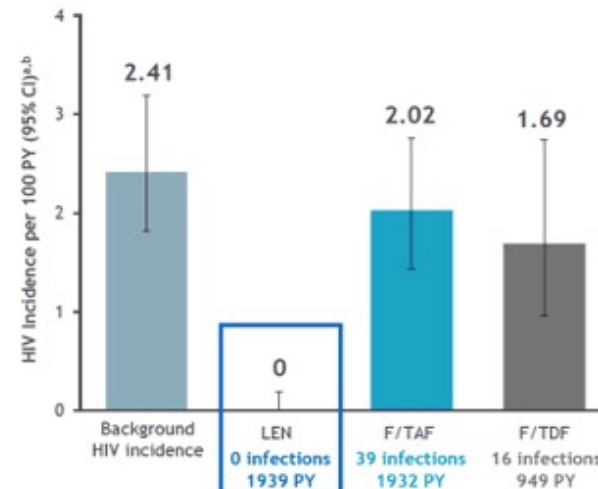


Lenacapavir is already sold as a treatment for H.I.V. infections that are resistant to other medications. Nardus Engelbrecht/Associated Press



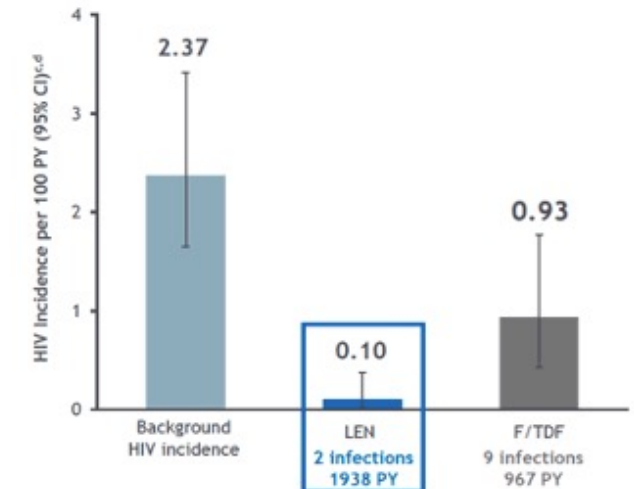
By Apoorva Mandavilli

PURPOSE 1: Zero HIV Infections in Cisgender Women Receiving LEN



Median follow-up duration: 44.0 weeks

PURPOSE 2: Two HIV Infections in Participants Receiving LEN



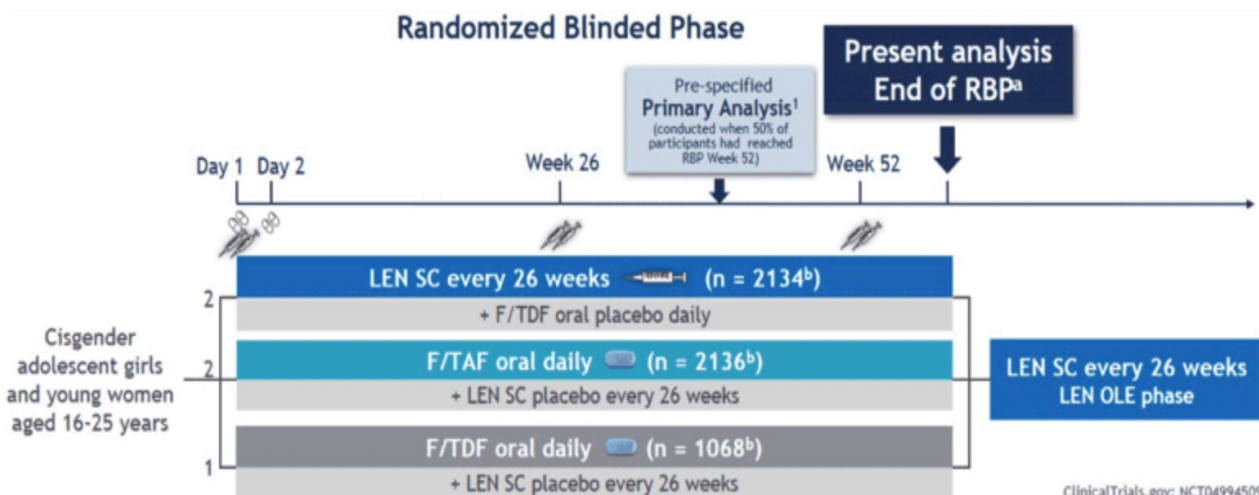
Median follow-up duration: 39.4 weeks

^aOverall n: background HIV incidence group, 8094; LEN, 2134; F/TAF, 2136; F/TDF, 1068. ^b95% CI: background HIV incidence group, 1.62-3.19; LEN, 0-0.19; F/TAF, 1.44-2.78; F/TDF, 0.96-2.74. ^cOverall n: background HIV incidence group, 4634; LEN, 2179; F/TDF, 1086. ^d95% CI: background HIV incidence group, 1.64-3.417; LEN, 0.012-0.373; F/TDF, 0.425-1.768. PY, person-years.

Long-Acting LEN Extended Follow-Up: Efficacy

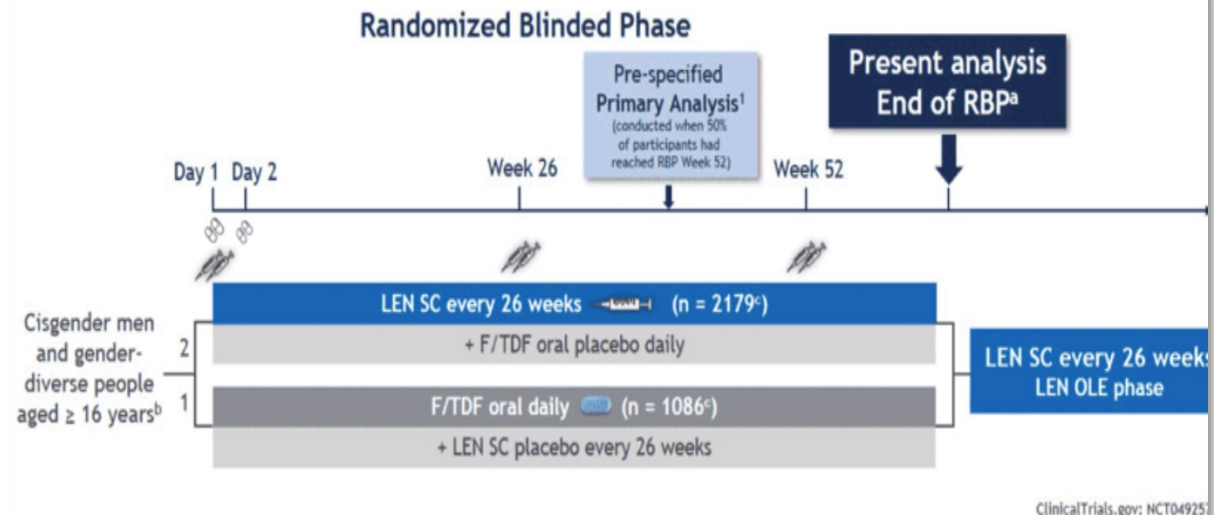
Twice-Yearly Subcutaneous Lenacapavir for PrEP: Updated HIV-1 Incidence and Safety Data in PURPOSE 1 at the End of the Randomized Blinded Phase

Nkosiphile Ndlovu,¹ Moelo Malahleha,² Yashna Singh,³ Flavia Matovu Kiweewa,⁴ Sarah B Puryear,⁵ Alexander Kintu,⁵ Christoph C Carter,⁵ Priyanka Arora,⁵ Yang Zhao,⁵ Cheryl Louw⁶



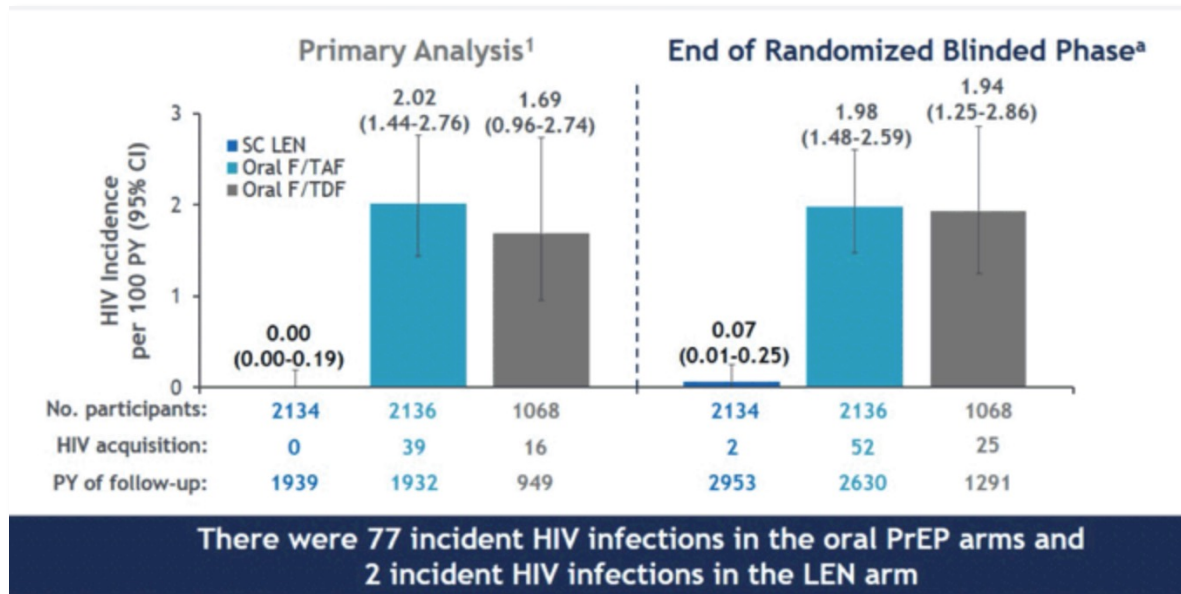
Lenacapavir for PrEP: HIV-1 Incidence and Safety from PURPOSE 2 at the End of Randomized Blinded Phase

Valeria D Cantos,¹ Kathryn Mngadi,² Khuanchai Supparatpinyo,³ Nkosiphile Ndlovu,⁴ Juan Carlos Hinojosa,⁵ Marcelo Losso,⁶ Namrata Shah,⁷ Susanne Doblecki-Lewis,⁸ J Carlo Hojilla,⁹ Lillian B Brown,⁹ Priyanka Arora,⁹ Pamela Wong,⁹ Christoph C Carter,⁹ Beatriz Grinsztejn,¹⁰ Susan Buchbinder¹¹

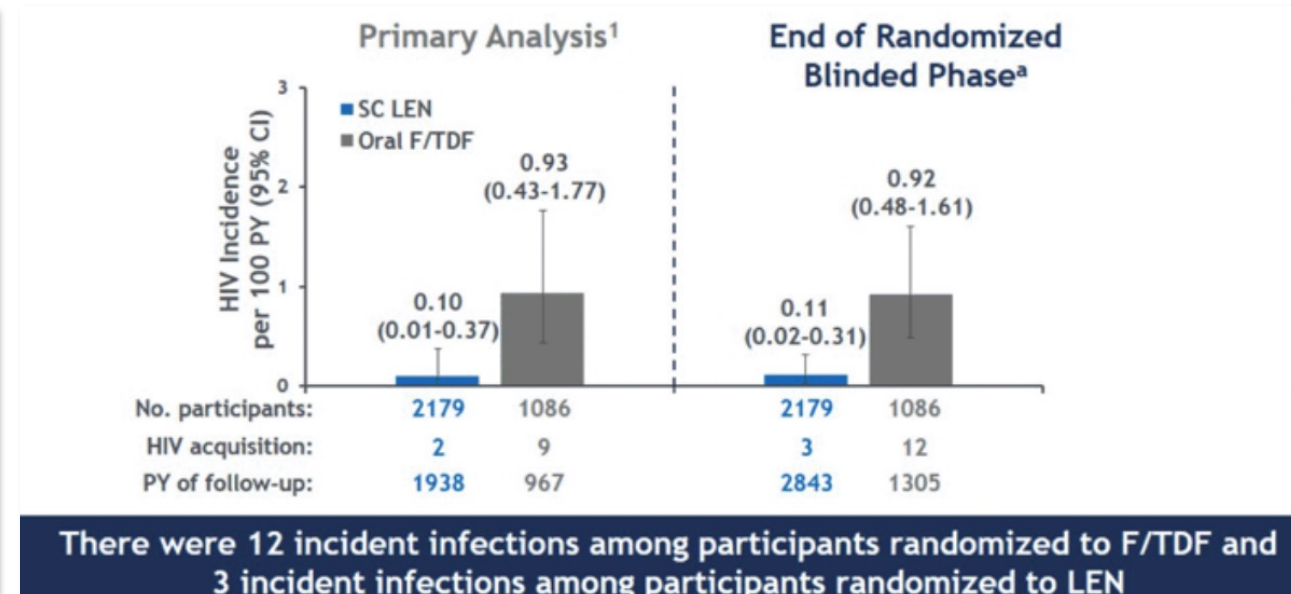


Long-Acting LEN Extended Follow-Up: Efficacy

PURPOSE 1

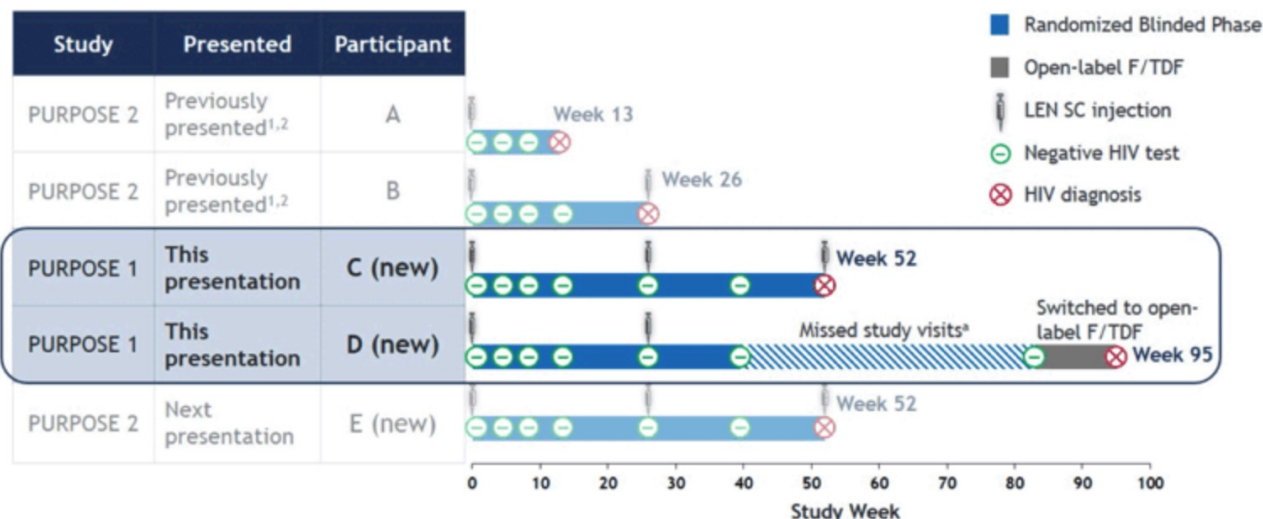


PURPOSE 2



Long-Acting LEN Extended Follow-Up: Efficacy

HIV Acquisition in LEN-Randomized Participants During PURPOSE 1 and PURPOSE 2

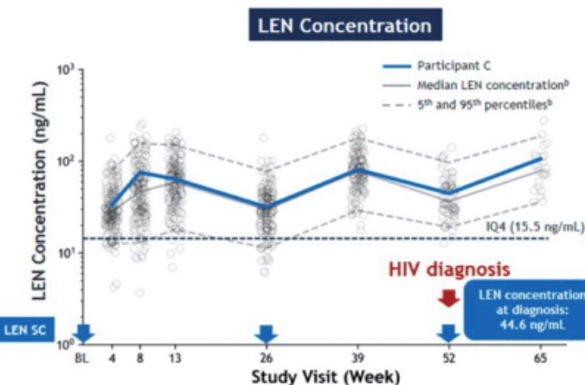


*Missed LEN injections.
F/TDF, emtricitabine/tenofovir disoproxil fumarate; LEN, lenacapavir; SC, subcutaneous.
1. Ogbuagu O, et al. Oral O49 presented at: HIV Glasgow; November 10-13, 2024; Glasgow, UK. 2. Kelley CF, et al. N Engl J Med. 2025;392:1261-76.

LEN Plasma Concentrations in Participant C

- Young woman tested positive for chlamydia at Week 52
- HIV diagnosed clinically on-study at Week 65 by typical serologic testing; retrospective RNA test found to be positive at Week 52/OLE Day 1

HIV Diagnostics	LEN (Randomized Blinded Phase)							LEN (OLE)
Study visit week	BL	4	8	13	26	39	52/OLE D1	65/OLE W13
Study day	0	30	57	92	183	274	365	456
Rapid Ag/Ab	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
Central Ag/Ab	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(+)
HIV-1/2 Ab diff								Ind.
Qualitative RNA								(+)
Quantitative RNA, c/mL	(-)					(-)	47 ^a	78



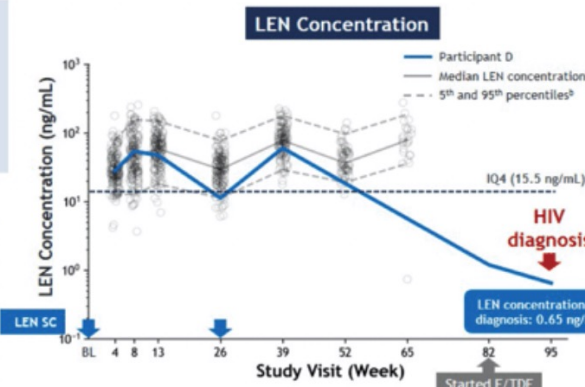
Participant C received all LEN injections on time and was diagnosed with standard HIV serologic testing; LEN concentrations were within the range of the prespecified subset of participants analyzed for PK^b

^aRetrospective. ^bIn the prespecified subset of participants analyzed for LEN PK at W4 (n = 165), W8 (n = 158), W13 (n = 163), W26 (n = 156), W39 (n = 129), W52 (n = 73), W65 (n = 23), indicated as circles in the graph. IQ4 was defined as the protein-adjusted 95% effective concentration in MT-4 cells, and IQ4 as 4x the protein-adjusted 95% effective concentration, in vitro.
1. Margot N, et al. Poster O-324 presented at: HIV Glasgow; 5-8 October 2020; Glasgow, UK.

LEN Plasma Concentrations in Participant D

- Young woman had last LEN injection at Week 26, then missed Week 52 injection
- Transitioned to open-label F/TDF at Week 82; HIV-negative at that time
- HIV diagnosed at Week 95, 487 days after last LEN injection

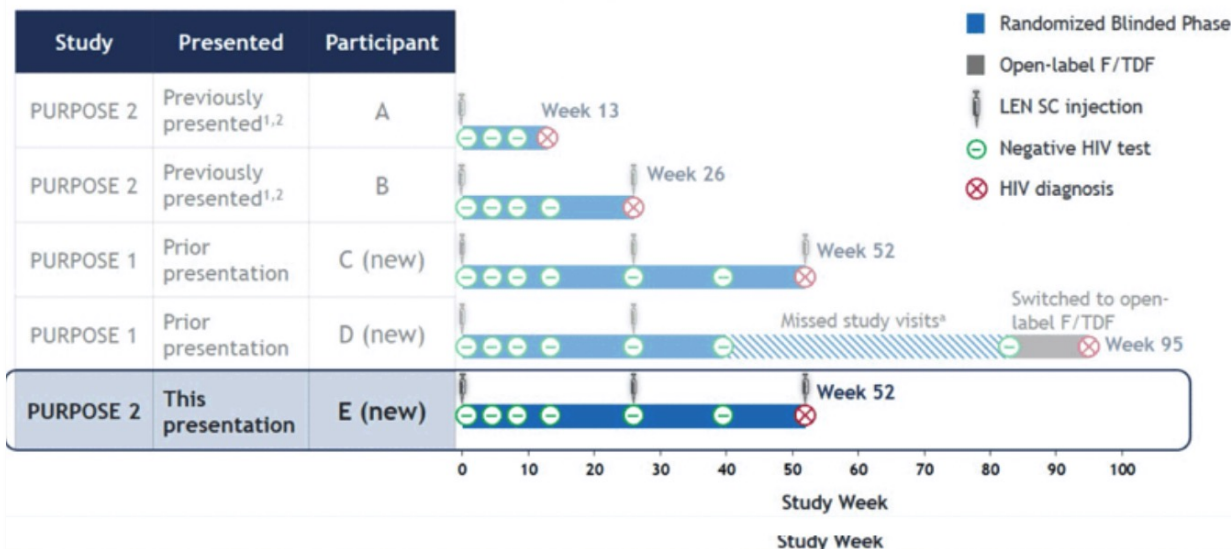
HIV Diagnostics	LEN (Randomized Blinded Phase)							Open-label F/TDF	
Study visit week	BL	4	8	13	26	39	52	82	95
Study day	0	30	57	92	183	271		579 ^a	670
Rapid Ag/Ab	(-)	(-)	(-)	(-)	(-)	(-)	Missed	(-)	(+)
Central Ag/Ab	(-)	(-)	(-)				Missed	(-)	(+)
HIV-1/2 Ab diff									(HIV-1+)
Qualitative RNA									
Quantitative RNA, c/mL	(-)							(-)	134,000



Participant D was diagnosed with HIV-1 after LEN discontinuation, while receiving open-label F/TDF, approximately 16 months after the last LEN injection

Long-Acting LEN Extended Follow-Up: Efficacy

HIV Acquisition in LEN-Randomized Participants During PURPOSE 1 and PURPOSE 2



^aMissed LEN injections.

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

1. Ogbuagu O, et al. Oral O49 presented at: HIV Glasgow; November 10-13, 2024; Glasgow, UK. 2. Kelley CF, et al. *N Engl J Med*. 2025;392:1261-76.

^aMissed LEN injections.

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

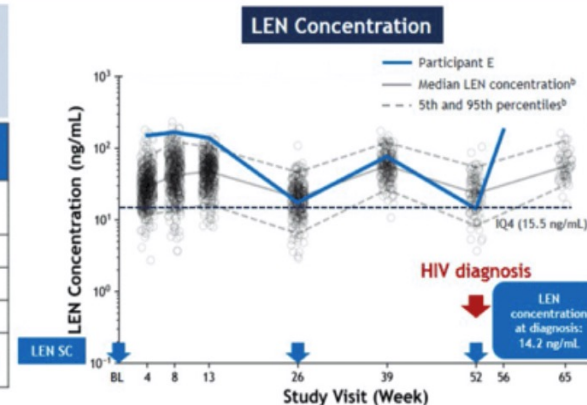
1. Ogbuagu O, et al. Oral O49 presented at: HIV Glasgow; November 10-13, 2024; Glasgow, UK. 2. Kelley CF, et al. *N Engl J Med*. 2025;392:1261-76.

LEN Plasma Concentrations in Participant E with Seroconversion

- Young gender-diverse person with history of rectal chlamydia at screening and Week 26 (Day 176), and rectal gonorrhea at Week 26 (Day 176)
- Diagnosed with HIV at Week 52 (Day 352)

HIV Diagnostics	LEN (Randomized Blinded Phase)						
Study visit week	BL	W4	W8	W13	W26	W39	W52/OLE D1
Rapid Ag/Ab	(-)	(-)	(-)	(-)	(-)	(-)	(-)
Central Ag/Ab	(-)	(-)	(-)	(-)	(-)	(-)	(+)
HIV-1/2 Ab diff							Ab (-)
Quantitative RNA, c/mL	ND					ND ^a	2,020,000

HIV diagnosis

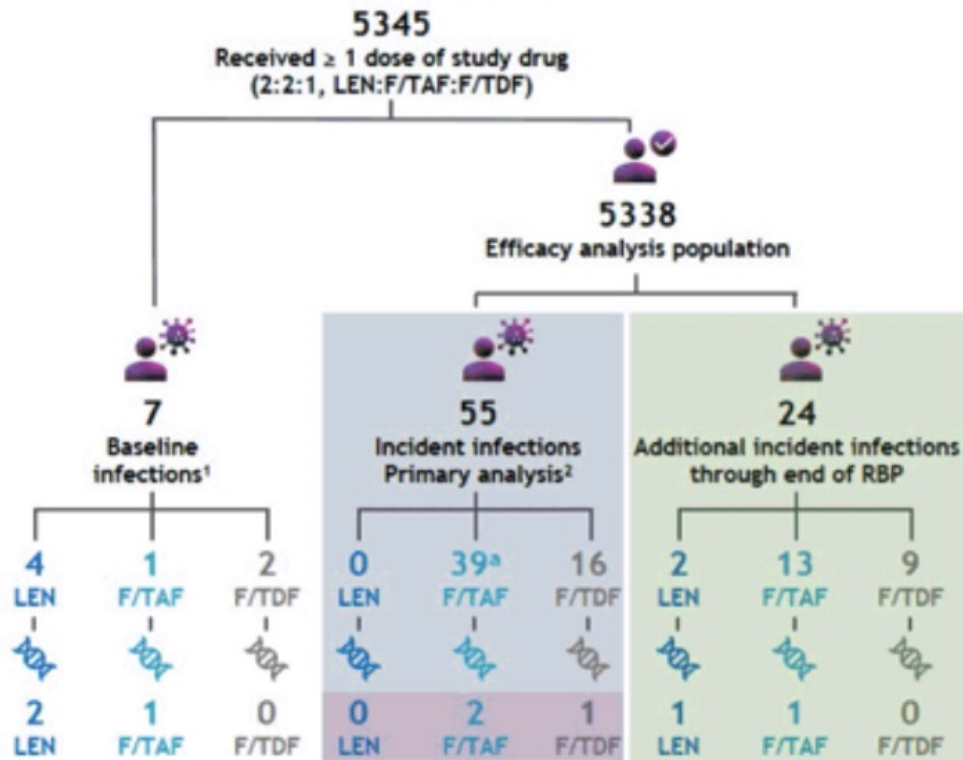


Participant E was diagnosed with standard HIV testing at Week 52. This participant received all injections on time and LEN concentrations were generally within the range of the prespecified subset of participants analyzed for PK^b

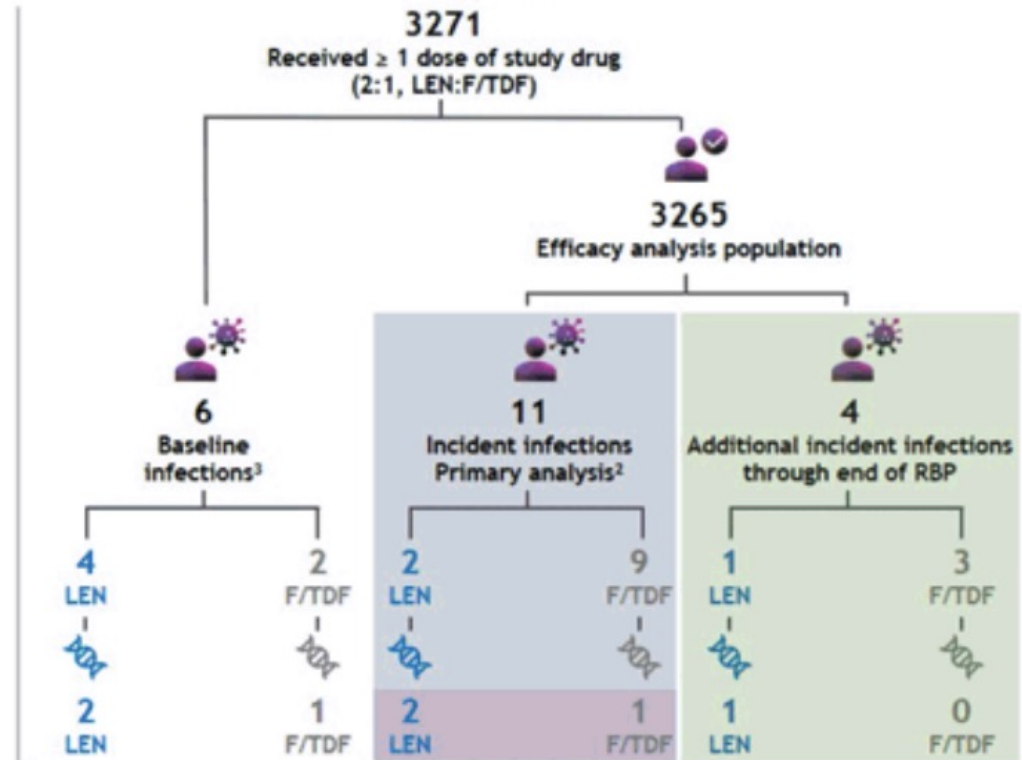
Long-Acting LEN Extended Follow-Up: Resistance

Participants Who Acquired HIV

PURPOSE 1



PURPOSE 2



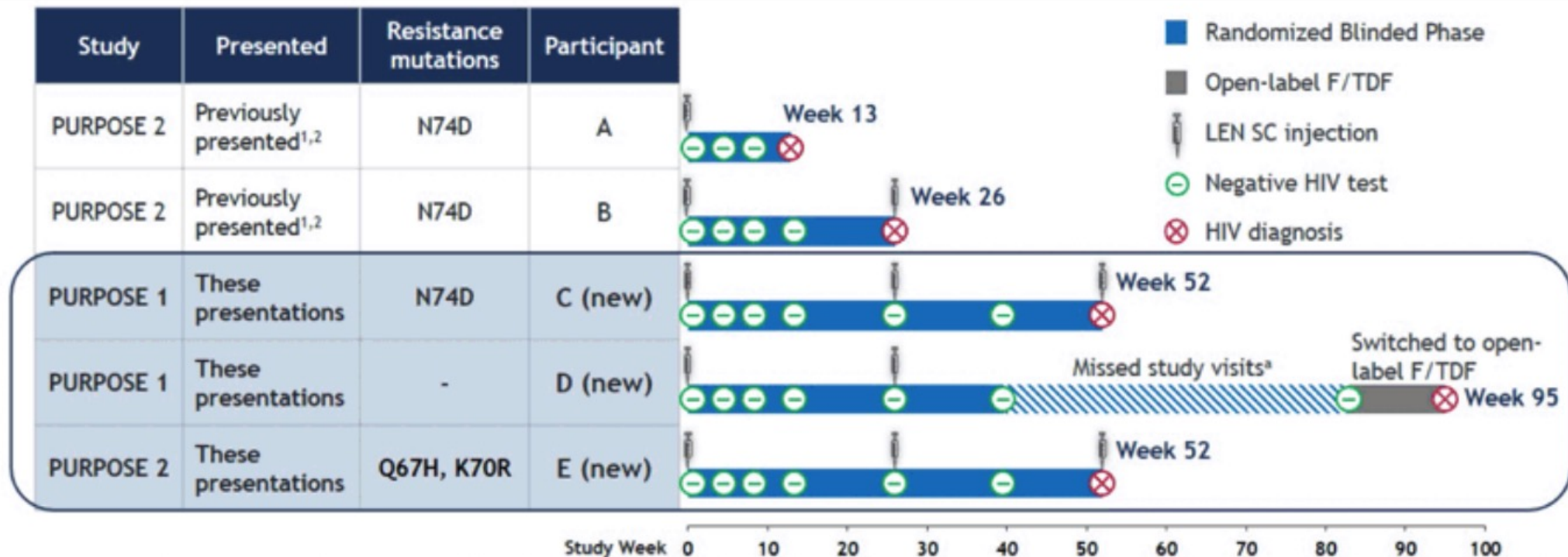
^aTwo participants in the F/TAF arm of PURPOSE 1 were not included in the resistance analysis population due to viral load of < 200 copies/mL or withdrawn consent.

F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; LEN, lenacapavir; RBP, randomized blinded phase.

¹ Bekker LG, et al. *N Engl J Med*. 2024;391:1179-92. ² Cox S, et al. *J Infect Dis*. 2026;233:e203-11. ³ Kelley CF, et al. *N Engl J Med*. 2025;392:1261-76.

Long-Acting LEN Extended Follow-Up: Resistance

HIV Incidence and Resistance in LEN-Randomized Participants During PURPOSE 1 and PURPOSE 2



Of the 5 HIV infections acquired on LEN in the PURPOSE studies, 3 had the N74D resistance mutation

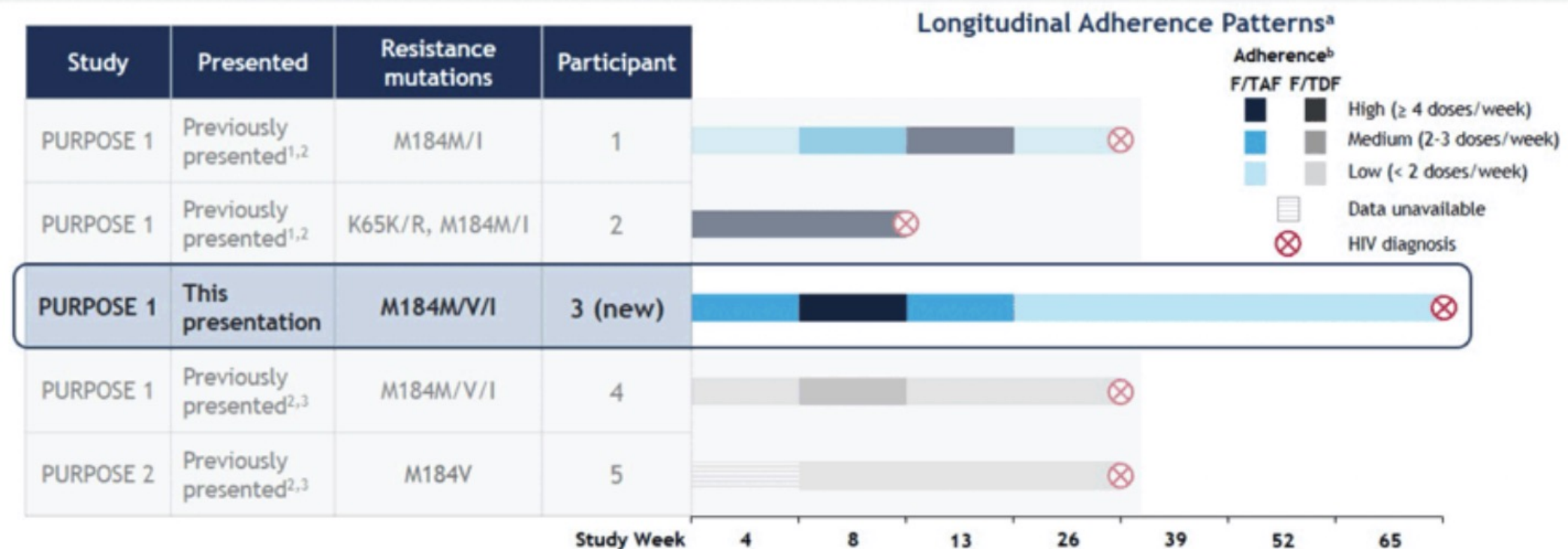
^aMissed LEN injections.

- Indicates no resistance mutation was detected. F/TDF, emtricitabine/tenofovir disoproxil fumarate; LEN, lenacapavir; SC, subcutaneous.

1. Ogbuagu O, et al. Oral O49 presented at: HIV Glasgow; November 10-13, 2024; Glasgow, UK. 2. Kelley CF, et al. *N Engl J Med*. 2025;392:1261-76.

Long-Acting LEN Extended Follow-Up: Resistance

HIV Resistance in F/TAF- and F/TDF-Randomized Participants in PURPOSE 1 and PURPOSE 2



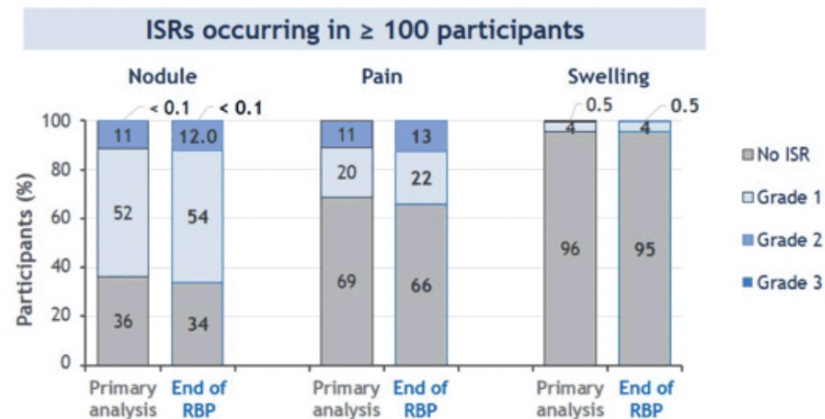
Of the 89 HIV infections acquired on F/TAF or F/TDF in the PURPOSE studies, only 5 participants had resistance with the majority from suboptimal study drug adherence

^aEach box represents DBS-based adherence for the corresponding time period. ^bBy TFV-DP DBS levels. For F/TAF, adherence was categorized as the following: low, < 450 fmol/punch (dosing < 2 days/week); medium, ≥ 450 to < 950 fmol/punch (dosing 2-3 days/week); high, ≥ 950 fmol/punch (dosing ≥ 4 days/week). For F/TDF, adherence was categorized as the following: low, < 350 fmol/punch (dosing < 2 days/week); medium, ≥ 350 to < 700 fmol/punch (dosing 2-3 days/week); high, ≥ 700 fmol/punch (dosing ≥ 4 days/week). DBS, dried blood spot; F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; TFV-DP, tenofovir diphosphate.

Long-Acting LEN Extended Follow-Up: ISR

PURPOSE 1

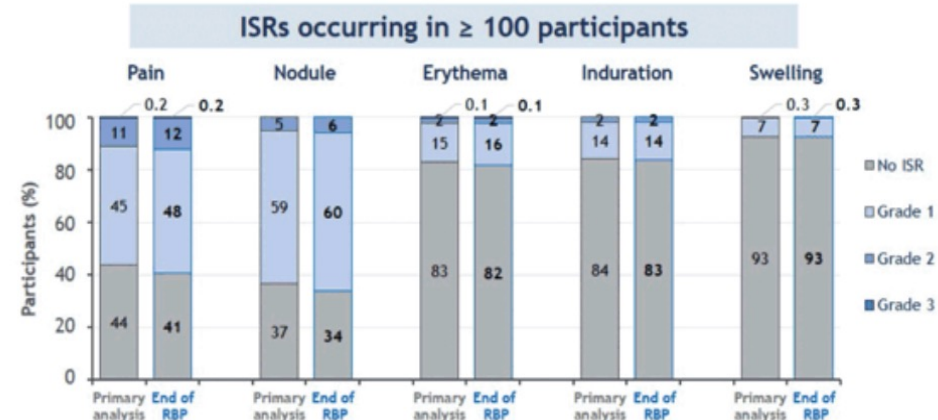
ISR Incidence and Severity in the LEN Group Remained Consistent with the Primary Analysis¹



The majority of participants did not report ISRs other than expected injection site nodules; there were no new discontinuations due to ISRs

PURPOSE 2

ISR Incidence Was Consistent with the Primary Analysis¹ and Most Were Low-Grade

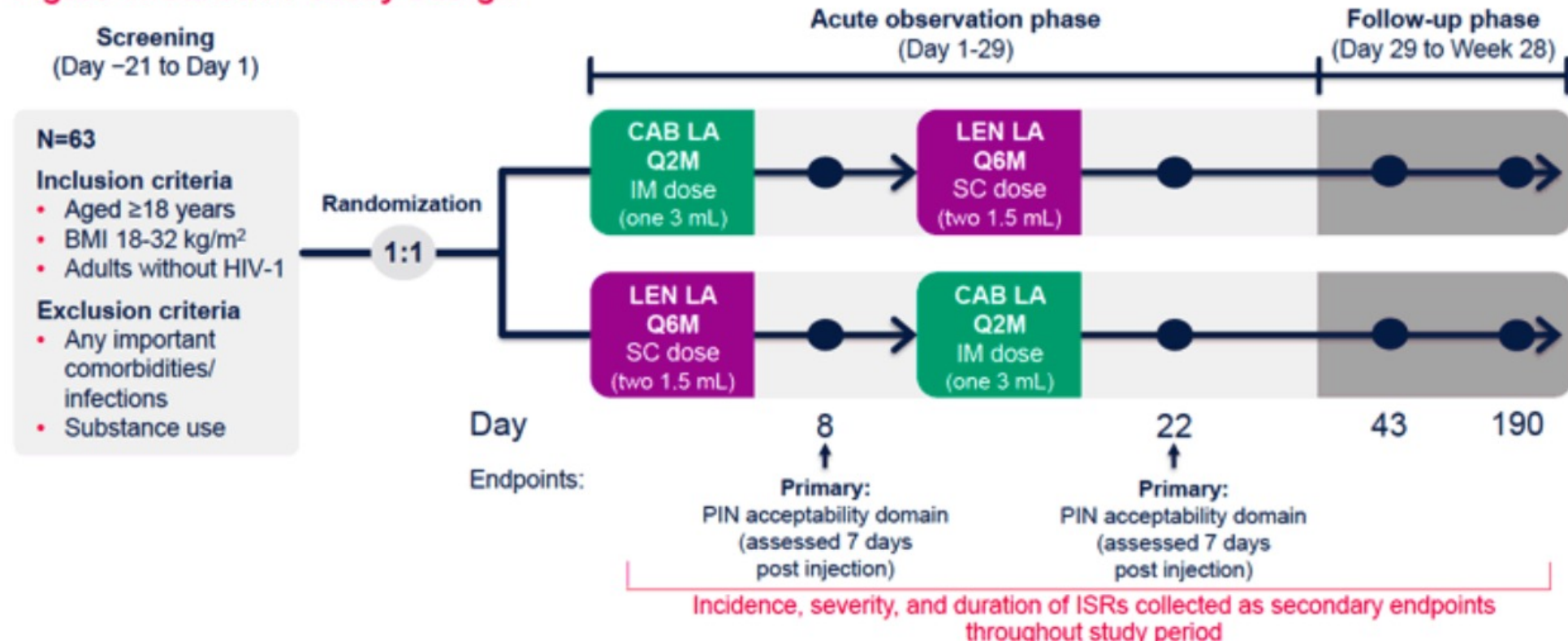


After the primary analysis, there were no new discontinuations due to ISRs through the end of the RBP

LEN^{SQ} vs CAB^{IM} ISR: CLARITY Trial

- CLARITY is an open-label, randomized crossover study comparing a single dose each of CAB LA and LEN LA in 63 people without HIV-1 (Figure 1)
- A single dose of CAB LA consists of 1 intramuscular gluteal injection, and a single dose of LEN LA consists of 2 subcutaneous abdominal injections

Figure 1. CLARITY Study Design



LEN^{SQ} vs CAB^{IM} ISR: CLARITY Trial

Results

Participant Baseline Demographics

- A diverse group of 63 participants (33% female, 38% Hispanic or Latine, and 29% Black or African American) were enrolled

Frequency of ISR Events Among Participants

- Participants experienced fewer ISR events after CAB LA compared with LEN LA injections (Table 1)
 - The median (range) number of ISRs per participant was 2 (0-8) after CAB LA and 10 (3-20) after LEN LA

Table 1. Participant-Level Summary of ISR Frequency Through Day 190^a

Variable, n (%)	CAB LA (n=61) ^b	LEN LA (n=62) ^b
Participants who experienced any ISR event	55 (90)	62 (100)
Number of ISR events ^c		
0	6 (10)	0
1	18 (30)	0
2	14 (23)	0
3 to 5	18 (30)	7 (11)
≥6	5 (8)	55 (89)

^aIn participants who received ≥1 injection. ^bOne participant received CAB LA on Day 1 but did not receive LEN LA on Day 15. ^cParticipants could experience more than 1 type of ISR event in response to injection.

LEN^{SQ} vs CAB^{IM} ISR: CLARITY Trial

Table 2. Summary of Overall ISRs Through Day 190^a

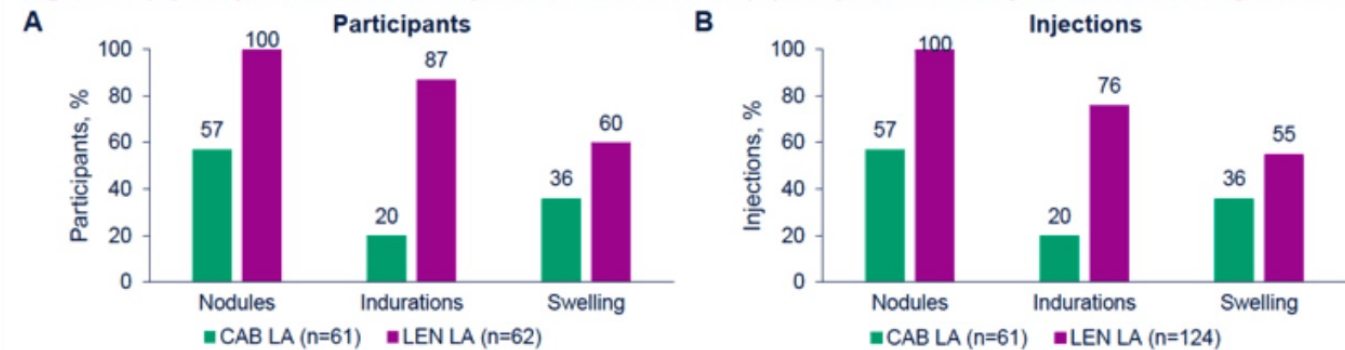
Variable, n ^b	CAB LA (n=61) ^c	LEN LA (n=62) ^c
Total injections ^d	61	124
ISR events	150	642
Visible ISR events, n (% of all events) ^e	43 (29)	331 (52)
Maximum grade, n (% of all injections)		
Grade 1	37 (61)	59 (48)
Grade 2	13 (21)	59 (48)
Grade 3	5 (8)	6 (5)
Outcome, n (% of all events) ^f		
Recovered/Resolved	146 (97)	504 (79)
Not recovered/not resolved	4 (3)	138 (22)

^aIn participants who received ≥1 injection. ^bUnless otherwise noted. ^cOne participant received CAB LA on Day 1 but did not receive LEN LA on Day 15. ^dA single dose of CAB LA requires 1 injection; a single dose of LEN LA requires 2 injections. ^eDefined as having any erythema, hyperpigmentation, and/or visible nodules, indurations, or swelling. ^fPercentages may total >100% due to rounding.

Summary of Nodule, Induration, and Swelling Events

- Fewer participants experienced nodules (CAB LA, 57%; LEN LA, 100%), indurations (CAB LA, 20%; LEN LA, 87%), and swelling (CAB LA, 36%; LEN LA, 60%) after CAB LA vs LEN LA injections (Figure 2)
- The proportions of nodules (14% vs 63%), indurations (83% vs 89%), and swelling events (77% vs 87%) that were visible were lower after CAB LA than LEN LA injections (Table 3)

Figure 2. (A) Proportions of Participants With ISRs and (B) Proportions of Injections Resulting in ISRs^a



^aA single dose of CAB LA consists of 1 injection; a single dose of LEN LA consists of 2 injections.

- The duration of nodules was shorter after CAB LA vs LEN LA injection, with 2 (6%) nodules with CAB LA persisting >180 days vs 101 (82%) nodules with LEN LA (Table 3)

LEN^{SQ} vs CAB^{IM} ISR: CLARITY Trial

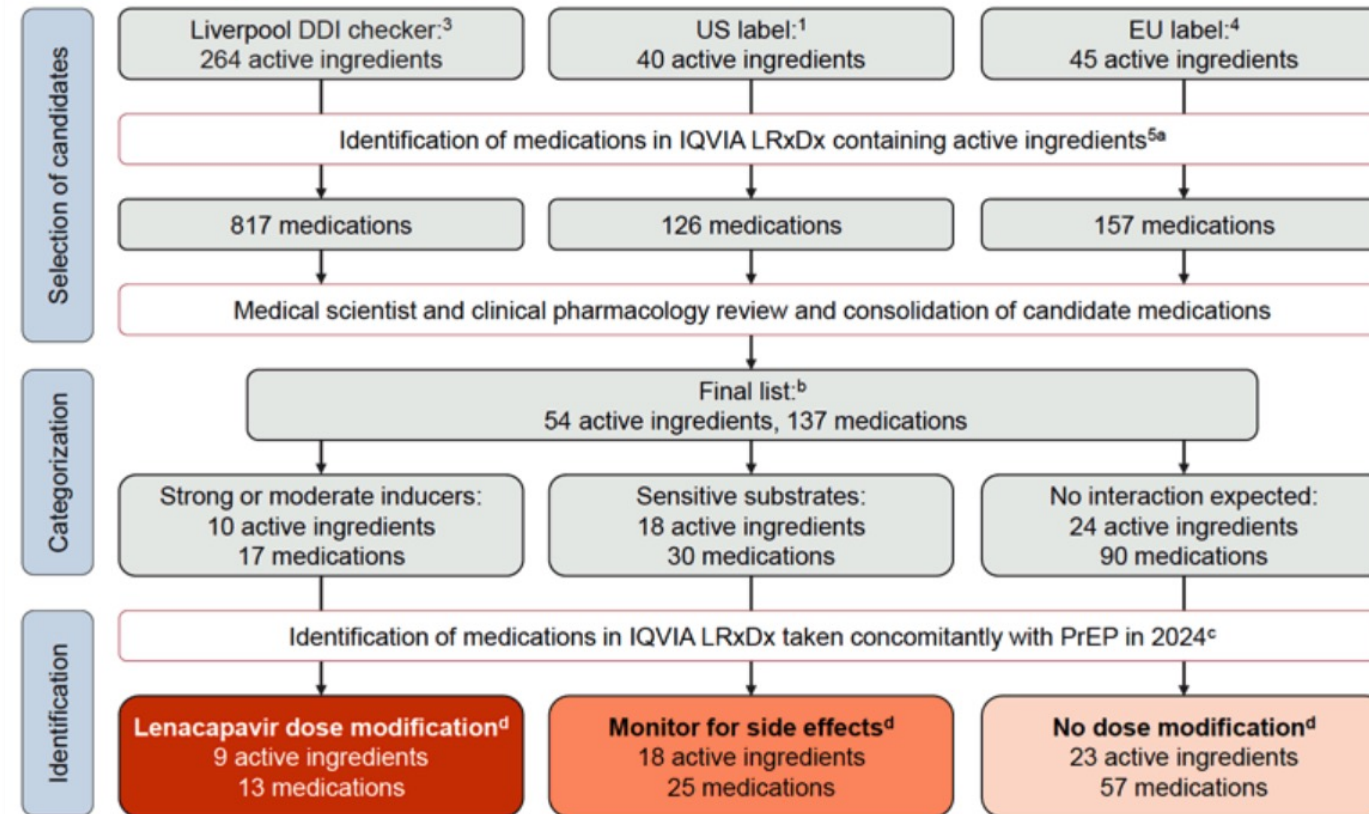
Table 3. Summary of Nodules, Indurations, and Swelling^a

Characteristic	CAB LA (n=61) ^b	LEN LA (n=62) ^b
Nodules, n	35	124
Nodules unresolved by Day 190, n (%)	4 (11)	120 (97)
Duration of nodules, median (range), days ^c	64.0 (7-182)	196.5 (2-224)
Nodules visible at any time, n (%)	5 (14)	78 (63)
Indurations, n	12	94
Indurations unresolved by Day 190, n (%)	0 (0)	0 (0)
Duration of indurations, median (range), days ^c	12.0 (2-42)	14.0 (2-59)
Indurations visible at any time, n (%)	10 (83)	84 (89)
Swelling, n	22	68
Swelling unresolved by Day 190, n (%)	0 (0)	0 (0)
Duration of swelling, median (range), days ^c	5.0 (2-36)	7.0 (2-202)
Swelling visible at any time, n (%)	17 (77)	59 (87)

^aIn participants who received ≥1 injection. ^bOne participant received CAB LA on Day 1 but did not receive LEN LA on Day 15. ^cIncludes both resolved and unresolved ISRs (up to data cut-off date of Dec 29, 2025).

HIV PrEP – Long-Acting LEN DDIs

Figure 1. Identification of Concomitant Medications Metabolized Through CYP3A and/or P-gp and Categorization by Potential Lenacapavir DDIs



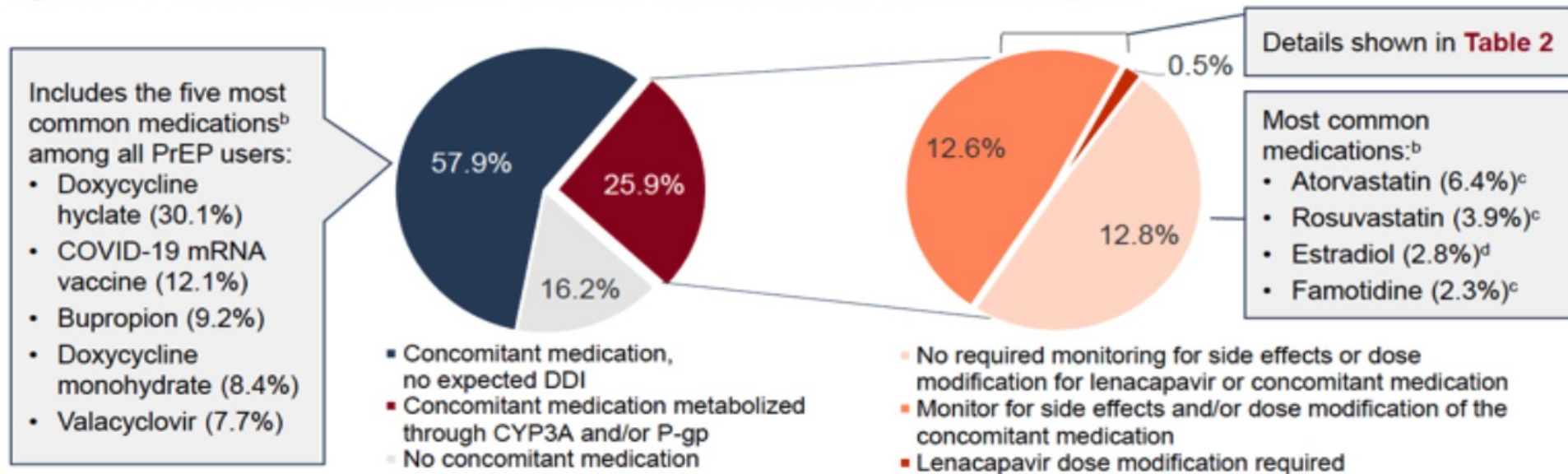
	All PrEP users	PrEP users with any concomitant medication	PrEP users with a concomitant medication metabolized through CYP3A and/or P-gp
Total, n (%)	457,402 (100)	383,221 (83.8)	118,531 (25.9)

HIV PrEP – Long-Acting LEN DDIs

Concomitant Medication Use

- Most (83.8%) PrEP users were taking at least one concomitant medication in 2024 (**Table 1**)
- In total, 25.9% PrEP users had concomitant use of at least one medication metabolized through CYP3A and/or P-gp (**Table 1**)
- If lenacapavir were used in place of the current PrEP option, 0.5% of all PrEP users in 2024 would have required lenacapavir dose modification and 12.6% would have required monitoring for side effects or consideration of dose modification of the concomitant medication (**Figure 2**)
 - No monitoring for side effects or dose modification of either medication would have been required for the remaining 12.8% of PrEP users with potential DDIs

Figure 2. Concomitant Medication Use and Potential DDIs^a With Lenacapavir



^aDefined here as medications metabolized through CYP3A and/or P-gp. ^bIncludes all medication users; not mutually exclusive. ^cNo clinically significant interaction per the US product label. ¹

^dNo clinically significant interaction found in prior study.⁶

HIV PrEP – Long-Acting LEN DDIs

Medication With Lenacapavir DDIs

- The most common concomitant medications requiring lenacapavir dose modifications were oxcarbazepine (0.3% of all PrEP users), carbamazepine (0.1%) and rifampin (<0.1%) (**Table 2**)
- The most common medications requiring monitoring with potential dosage change were erectile dysfunction medications (10.7%), e.g., tadalafil (7.5%), sildenafil (4.1%), and vardenafil (0.1%) (individuals may have received more than one ED medication; **Table 2**)

Table 2. Concomitant Medications Requiring Dose Modification or Monitoring^a

DDI category	Drug class	Indication	N	Proportion of all PrEP users (%)	Mean duration (days)	Prescription fills (n)
Lenacapavir dose modification (all)			2433	0.53	125	4
Oxcarbazepine	Anticonvulsant	Seizure disorders, nerve pain, ^b bipolar disorder ^b	1502	0.33	132	4
Carbamazepine			465	0.10	144	4
Phenytoin			117	0.03	142	4
Phenobarbital			101	0.02	102	4
Rifampin	Antibacterial	Bacterial infections (including tuberculosis)	193	0.04	58	2
Rifabutin			43	0.01	18	1
Rifapentine			28	0.01	62	2
Enzalutamide	Antiandrogen	Prostate cancer	8	<0.01	145	6
Apalutamide			6	<0.01	118	5

HIV PrEP – Long-Acting LEN DDIs

Monitoring for side effects or dose modification of concomitant medication (all)				57,736	12.62	113	4
	Tadalafil for ED (>2.5 mg/day)	Vasodilator (PDE5 inhibitor)	Erectile dysfunction, pulmonary arterial hypertension ^d	34,082	7.45	134	4
	Taladafil for PAH ^c			405	0.09	87	3
	Sildenafil for ED (>25 mg/day)			18,603	4.07	79	3
	Sildenafil for PAH			4331	0.95	79	3
	Vardenafil (>5 mg/day)			328	0.07	52	3
	Simvastatin (>10 mg/day)	Statin	High cholesterol and triglycerides	2407	0.53	200	4
	Lovastatin (>20 mg/day)			155	0.03	204	4
	Dexamethasone	Corticosteroid	Inflammation, immune overactivity	2038	0.45	9	1
	Hydrocortisone/cortisone			323	0.07	127	3
	Rivaroxaban	Anticoagulant	Prevent/treat blood clots	1362	0.30	167	4
	Warfarin			513	0.11	216	5
	Dabigatran			55	0.01	167	4
	Edoxaban			2	<0.01	195	4
	Triazolam	Sedative	Insomnia	555	0.12	18	2
	Midazolam		Anesthesia, seizure management	82	0.02	27	2
	Digoxin	Antiarrhythmic	Heart failure, atrial fibrillation	111	0.02	158	3
	Dihydroergotamine ^e	Ergot derivative	Migraine and cluster headaches	28	0.01	79	3
	Ergotamine ^e			5	<0.01	62	3
No interaction expected and no dose adjustments needed (all) ^f				58,362	12.8%	141	3

HIV PrEP – 2:1:1

Final Results of the ANRS Prevenir Study with Daily or On Demand Oral PrEP with TDF/FTC in Paris, France

JM. Molina, J. Ghosn, DH. Vu, G. Liegeon, L. Beniguel, G. Pialoux, C. Katlama, M. Ohayon, N. Derche, B. Spire, S. Halfen, M. Costa, C. Delaunay, L. Assoumou, D. Costagliola and the Prevenir Study Group



Study Design

Open-Label Prospective Cohort Study in the Paris Region

n ≥ 3,000

May 3rd 2017

May 2nd 2025

- HIV-negative high risk adults
- Inconsistent Condom use
- eGFR ≥ 50 mL/mn
- HbS Ag negative if On Demand

TDF/FTC
Daily

TDF/FTC
On Demand

Show 15% reduction
in new HIV diagnoses
among MSM and TGW
in the Paris Region

- Participants opted for either daily or on demand PrEP and could switch between regimen
- FU every 3 months with 4G HIV test and creatinine, then every 6 months starting May 2021
- STI screening at physicians' discretion
- Condoms, gels, risk reduction and adherence counseling, Q on sexual behavior

HIV PrEP – 2:1:1



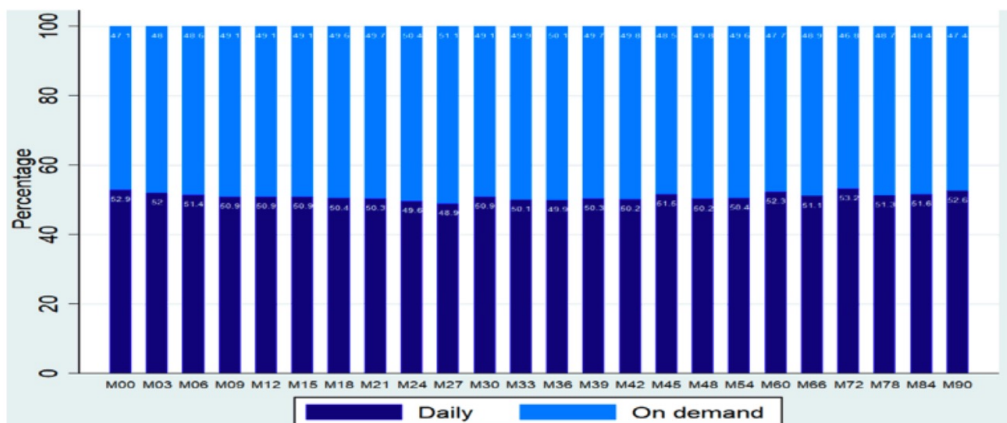
Baseline Characteristics

Characteristics (Median, IQR) or (n, %)	N = 3209
Age (years)	36 (29-43)
Caucasian	2720 (84.8)
MSM	3168 (98.7)
Heterosexual men or women	27 (0.8)
Transgender	14 (0.4)
Country of Birth - France	2646 (82.5)
Africa	146 (4.6)
Other	415 (12.9)
Bachelor's degree	2256 (70.3)
History of PrEP use	1872 (58.3)
Use of Chemsex*	461 (14.4)
On Demand dosing regimen	1512 (47.1)
Nb condomless sex acts in prior 4 weeks	2 (0 - 5)
Nb sexual partners in prior 3 months	10 (5 - 20)

* at last sexual intercourse : cocaine, GHB, MDMA, mephedrone



Dosing Regimen over Time



Post-hoc classification of PrEP users in 3 categories

Daily PrEP users (38.4%)
daily PrEP > 75% of FU
Median Daily use: 100% (89.5-100)

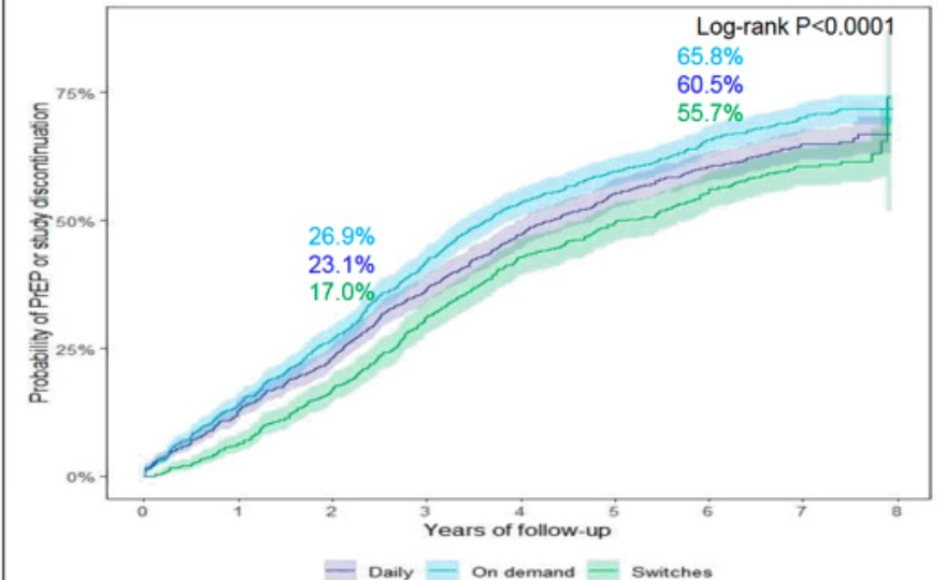
On demand PrEP users (38.3%)
on demand >75% of FU
Median On demand: 100% (90.9-100)

Switch users (23.3%)
Median Daily use: 50% (37-62)

Study Discontinuation Incidence/100 PY

Daily PrEP users: 15.0
On demand PrEP users: 17.4
Switch users: 12.8

Study Discontinuation



Liegeon G. et al OFID 2024

HIV PrEP – 2:1:1



HIV Incidence

Global HIV Incidence: 0.99/1000 PY (95% CI: 0.5-1.7) (13 cases)*

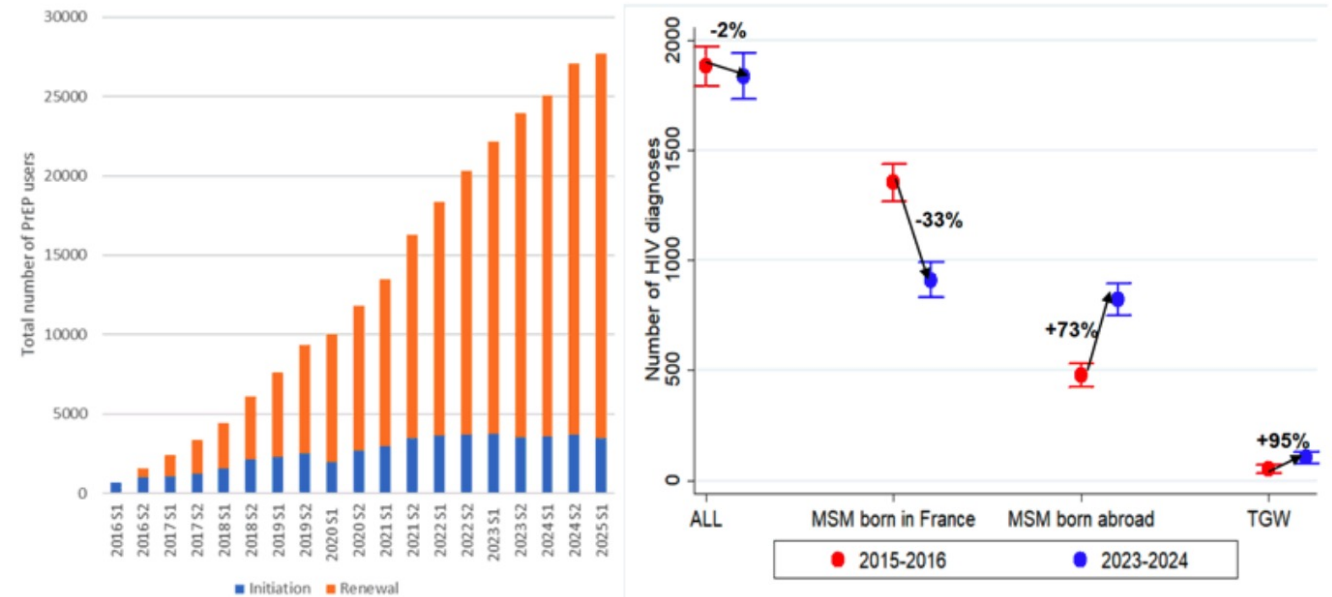
Mean Follow-up of 49.1 months and 13130 Person-Years

PrEP Dosing Regimen	Follow-Up Pts-years	Nb Cases	HIV Incidence /1000 PY (95% CI)	P-value
Daily PrEP Users	4974	3	0.6 (0.1 – 1.8)	0.4
On Demand PrEP users	4786	7	1.5 (0.6 - 3.0)	
Switch PrEP users	3370	3	0.9 (0.2 – 2.6)	

* 1 case on daily PrEP reported in the abstract not presented since informed consent for study extension not signed



Number of PrEP Users and of HIV Diagnoses among MSM and TGW in Paris



Real World PrEP: US PrEP users

Prescriptions for Oral vs Injectable HIV Preexposure Prophylaxis, 2012-2025

METHODS

- Retrospective cohort analysis of PrEP initiation using patient-level data harmonized in Epic Cosmos.
- Evaluated four PrEP medications:
 - emtricitabine/tenofovir disoproxil fumarate [FTC/TDF] (Approved 2012)
 - emtricitabine/tenofovir alafenamide [FTC/TAF] (Approved Oct. 2019)
 - Cabotegravir [CAB] (Approved Dec. 2021)
 - Lenacapavir [LEN] (Approved Jun. 2025)
- PrEP initiation defined as the first documented medication event (prescribed, dispensed, or hospital-administered) for an individual without an HIV diagnosis code.
- HIV Prevalence determined using diagnostic and lab codes.
- Described PrEP initiation by modality, sex, race, ethnicity, rurality, and Social Vulnerability Index (SVI) at the ZIP Code level.

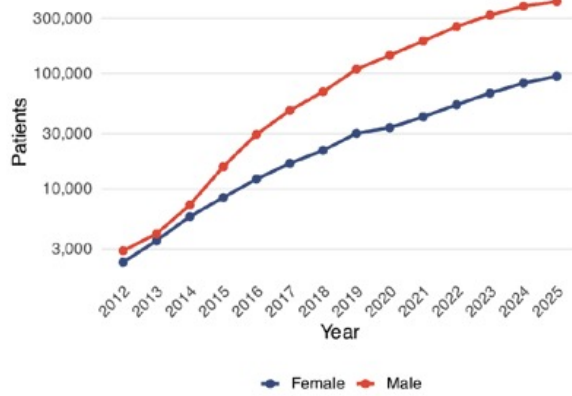
Table 1. Characteristics of individuals with documented PrEP initiations in Epic Cosmos (n=819,044), 2012-2025.

Characteristic	N = 819,044
Mean age in years at initiation (SD)	35.81 (12.56)
Sex	
Female	231,012 (28.21%)
Male	585,571 (71.49%)
Unknown	2,461 (0.30%)
Race/Ethnicity	
Asian Non-Hispanic	35,599 (4.35%)
Hispanic Any Race	113,456 (13.85%)
Non-Hispanic Black or African American	144,029 (17.59%)
Non-Hispanic White	358,972 (43.83%)
Other Non-Hispanic	16,206 (1.98%)
*Combined/Unknown	150,782 (18.41%)
Rurality	
Rural	45,631 (5.57%)
Urban	759,027 (92.67%)
Missing	14,386 (1.76%)
SVI (overall)	
<25%	100,749 (12.30%)
>=25% & <50%	165,343 (20.19%)
>=50% & <75%	200,050 (24.42%)
>=75%	336,997 (41.15%)
Missing	15,905 (1.94%)
Agent at initiation	
FTC/TDF	632,768 (77.26%)
FTC/TAF	173,632 (21.20%)
Cabotegravir	11,693 (1.43%)
Lenacapavir	951 (0.12%)

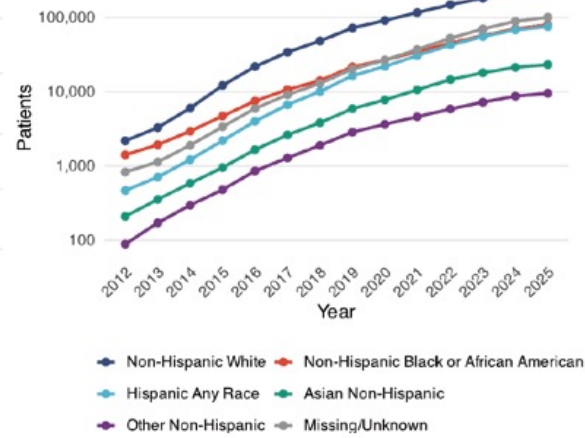
RESULTS

- Between 2012 and 2025, 819,044 individuals initiated PrEP, with majority initiating FTC/TDF (632,768; 77.26%), followed by FTC/TAF (173,632; 21.20%), CAB (11,693; 1.43%), and LEN (951; 0.12%).
- The average age at PrEP initiation was 35.8 years of age
- Geographically, 759,027 (92.67%) resided in urban areas and 45,631 (5.57%) in rural areas.
- By SVI, 336,997 (41.15%) individuals were in the highest quartile ($\geq 75\%$), and 100,749 (12.30%) were in the lowest quartile ($<25\%$).

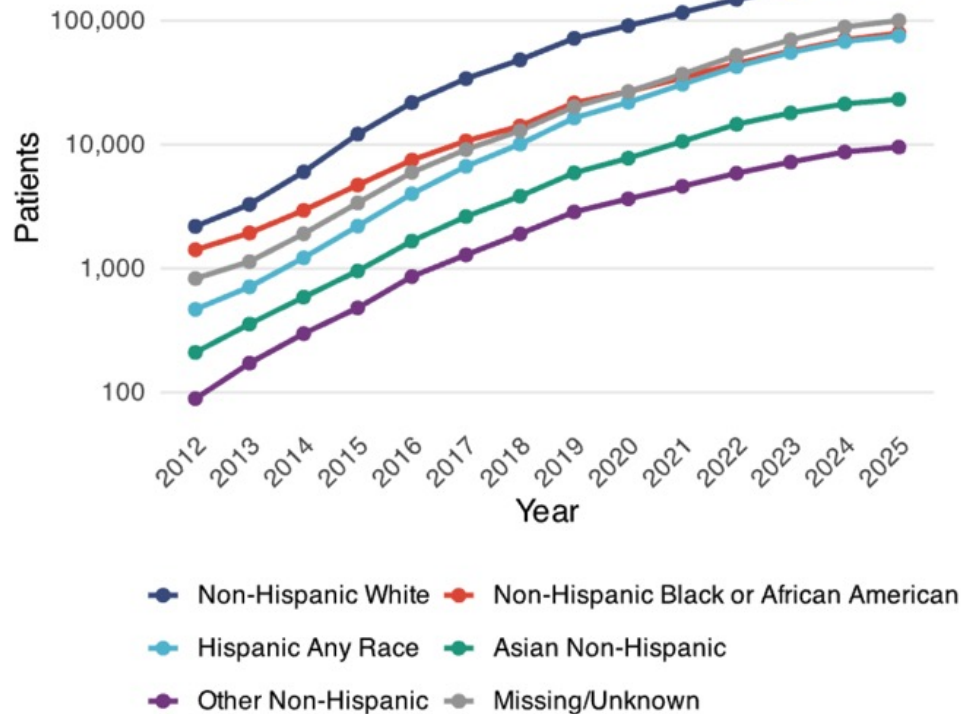
Cumulative Initiation by Sex



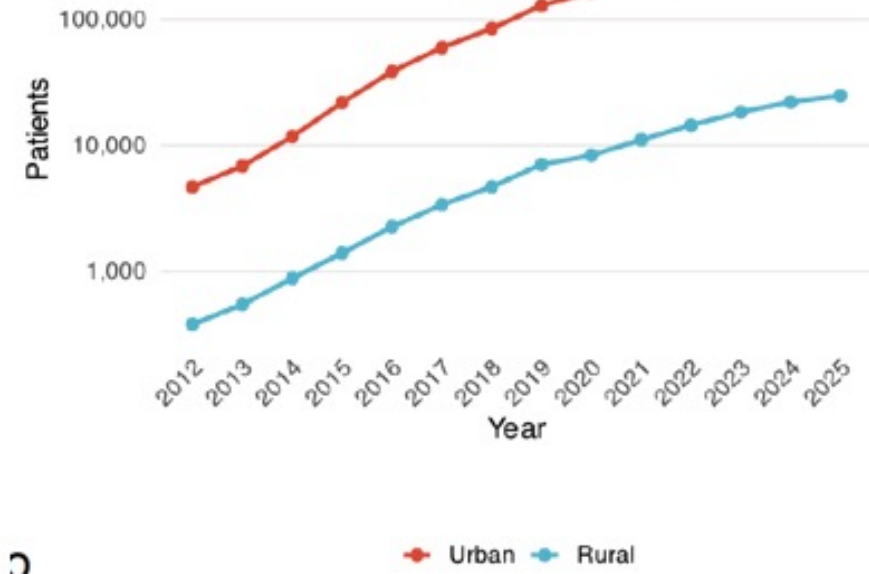
Cumulative Initiation by Race and Ethnicity



Cumulative Initiation by Race and Ethnicity



Cumulative Initiation by Rurality



Real World PrEP: US PrEP users

National LAI-PrEP Use and Retention in Care in the United States, 2022-2024

METHODS

- **Data Source:** PrEP pharmacy and medical claims data from a national claims database
- **Study period:** Jan 2022 – Dec 2024
- **Study population:** Persons with ≥ 1 claim for any PrEP drug during the study period
- **PrEP user classification**
 - Oral PrEP: ≥ 1 claim for oral PrEP
 - LAI-PrEP: ≥ 1 claim for injectable cabotegravir
- **Analysis 1:** Oral and LAI-PrEP users stratified by sex, race/ethnicity and insurance type
- **Analysis 2:** LAI-PrEP retention in care over a two-year period
 - Yearly retention: ≥ 1 claim for cabotegravir in each 4-month period
 - 2023-2024 cohort: ≥ 1 year of follow-up from initiation to end of data period
 - 2022-2024 cohort: ≥ 2 years of follow-up from initiation to end of data period

RESULTS

Distribution of PrEP users

- 4% of all PrEP users were LAI-PrEP users ($n=15,121/361,087$) in the most recent quarter
- Medicaid coverage was higher among LAI-PrEP users (26%) than oral PrEP users (14%)

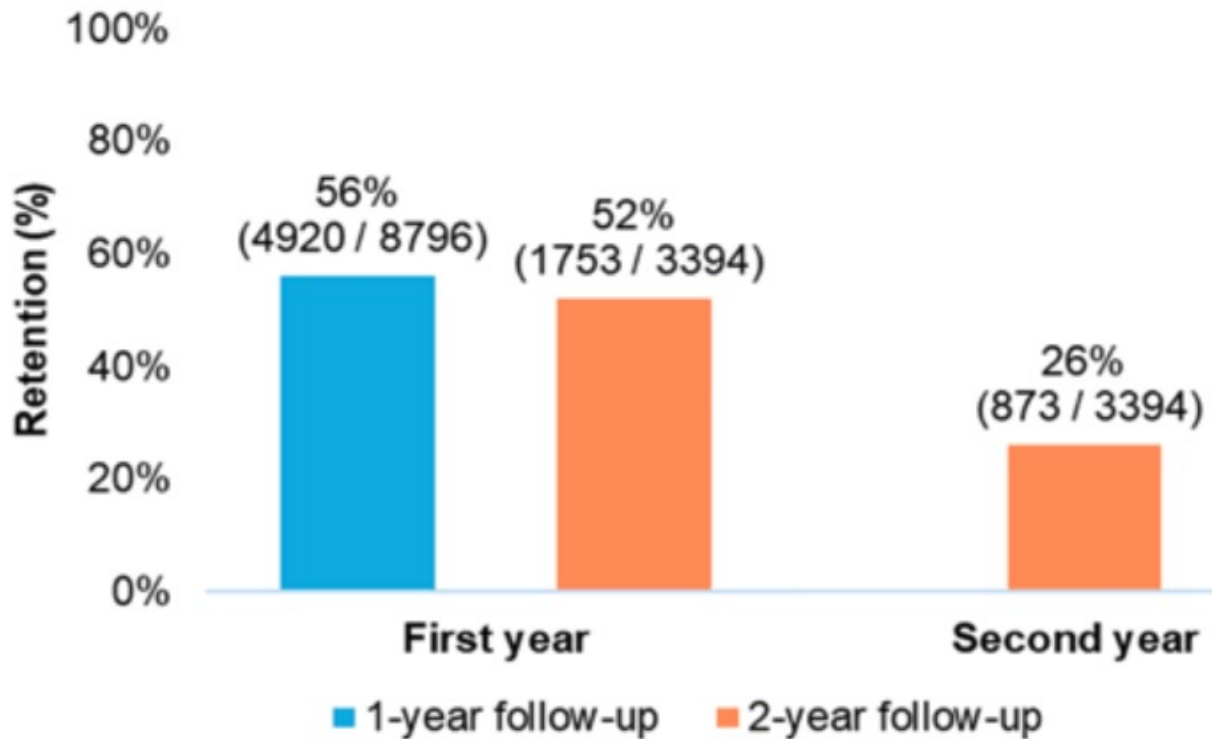
Table 1: PrEP users in the US from 2022 to 2024 by sex, race and ethnicity, and insurance type

Variable	All PrEP Users (n = 781,156) n (%)	Oral PrEP (n = 770,846) n (%)	LAI-PrEP (n = 24,306) n (%)
Sex			
Male	695,494 (89%)	687,551 (89%)	20,747 (85%)
Female	85,643 (11%)	83,277 (11%)	3,558 (15%)
Race and Ethnicity ¹			
Asian	25,427 (3%)	25,106 (3%)	690 (3%)
Black/African American	125,616 (16%)	123,857 (16%)	4,576 (19%)
Hispanic	131,776 (17%)	129,665 (17%)	4,543 (19%)
White/Caucasian	484,478 (62%)	478,302 (62%)	14,050 (58%)
Others	13,859 (2%)	13,916 (2%)	447 (2%)
Insurance Type			
Commercial	520,116 (67%)	513,752 (67%)	16,441 (68%)
Government	15 (<1%)	3 (<1%)	20 (<1%)
Medicare	21,594 (3%)	21,224 (3%)	851 (4%)
Medicaid	111,932 (14%)	108,591 (14%)	6,257 (26%)
Assistance Programs	118,658 (15%)	118,534 (15%)	509 (2%)
Cash	3,369 (<1%)	3,278 (<1%)	207 (1%)

¹ Hot-deck imputation was performed for missing data using observed sex, insurance plan and state information

Real World PrEP: CAB use in the US

LAI-PrEP Retention in Care



Long-acting injectable PrEP was hailed as a game changer in HIV prevention, but uptake remained **modest** (3.1% of all PrEP users; 2022-2024), and many **did not remain in care** (1-yr retention 56%, 2-yr retention 26%)

Real World PrEP: CAB use by Black Women in US

EBONI M12 Results: High Real-World Effectiveness and Acceptance of CAB LA for PrEP in Black Women

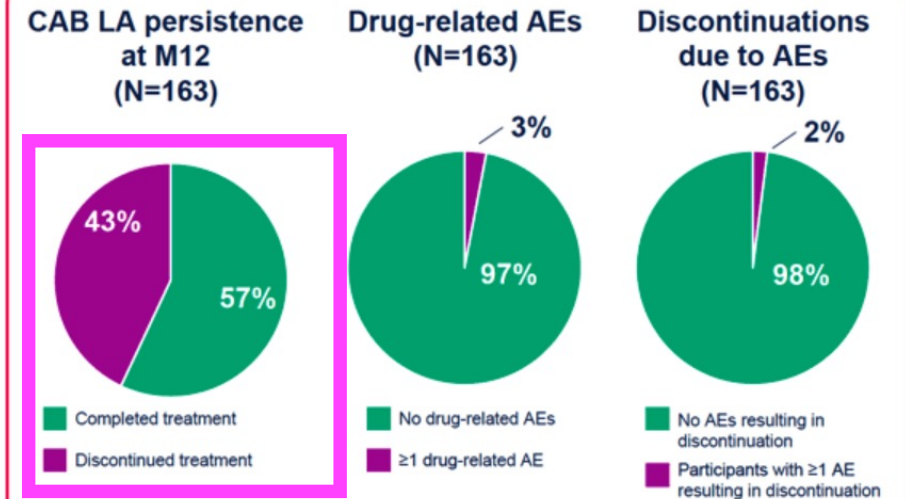
Methods

- EBONI was a 12-month, phase 4, hybrid effectiveness-implementation science trial assessing CAB LA integration at 20 practice sites in Black cisgender and transgender women
- Clinical assessments included HIV incidence, persistence, safety, and tolerability
- M12 implementation questionnaires assessed acceptability of CAB LA, as well as injection pain, local reactions, and overall experiences with CAB LA
 - Acceptability of CAB LA was evaluated using the validated Acceptability of Intervention Measure
- Table 1 depicts patient participant demographics at baseline and M12
 - At baseline, 163 women initiated CAB LA, with 99 completing M12 implementation questionnaires
 - At M12, the median age was 37 (IQR, 30-43) years and 21% of participants were transgender women



No cases of HIV acquisition occurred among Black women in EBONI

Figure 1. CAB LA Persistence and Adverse Events Through M12



AE, adverse event.

- Almost half (44%, 67/151) of participants had not taken oral PrEP in the 6 months before initiating CAB LA
- The majority (61%; n=100/163) of participants were of childbearing potential, of whom 6% (n=6/100) experienced a pregnancy
- Persistence on CAB LA was 74% at M6 (120/163) and 57% at M12 (n=93/163), with 69% to 89% receiving injections within the ± 7 -day window through M12 (Figure 1)
- Drug-related adverse events (3%; n=5/163) were rare, with 2% (n=3) of participants discontinuing due to adverse events

Real World PrEP: Awareness Among US MSM

Trends in Long-Acting PrEP Awareness, Willingness, and Uptake Among Men Who Have Sex With Men

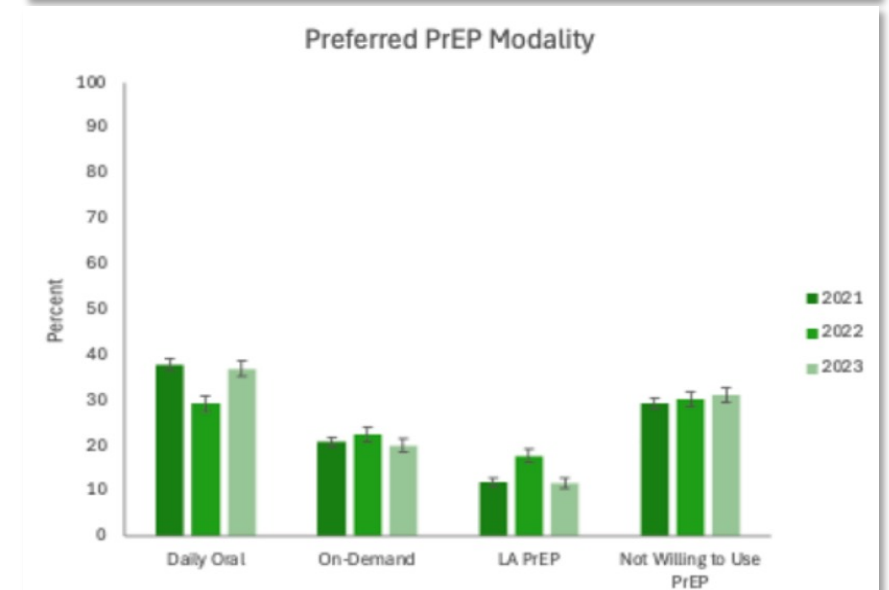
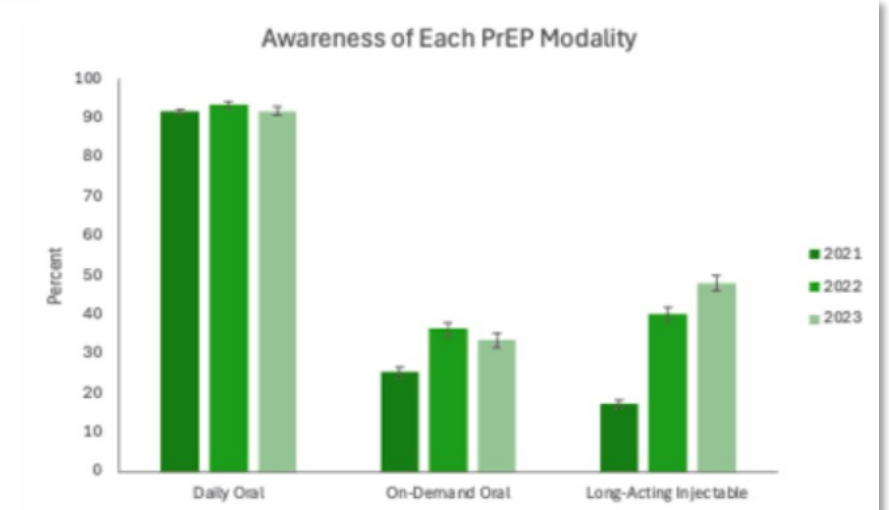
METHODS

- We analyzed data from the 2021, 2022, and 2023 cycles of the American Men's Internet Survey (AMIS)
- AMIS is a serial, annual, cross-sectional survey of MSM in the United States
- Recruitment is conducted online and participants complete an uncompensated, 45-minute survey

RESULTS

- 15,993 MSM participated across the three cycles (n = 7,638 in 2021; 4,443 in 2022; 3,912 in 2023)
- Almost all participants were aware of daily oral PrEP; awareness of on-demand oral and CAB LA PrEP increased over the study period
- Oral options for PrEP were most preferred
- Among those who had used PrEP in the past 12 months, 1.4% and 3.5% reported CAB LA PrEP use in the 2022 and 2023 cycles, respectively
- Black MSM were more likely than White MSM to report CAB LA PrEP use (OR = 2.3, 95%CI: 1.1, 4.4) and rural MSM were much less likely than urban MSM to use CAB LA PrEP (OR = 0.4, 95%CI: 0.1, 1.2)

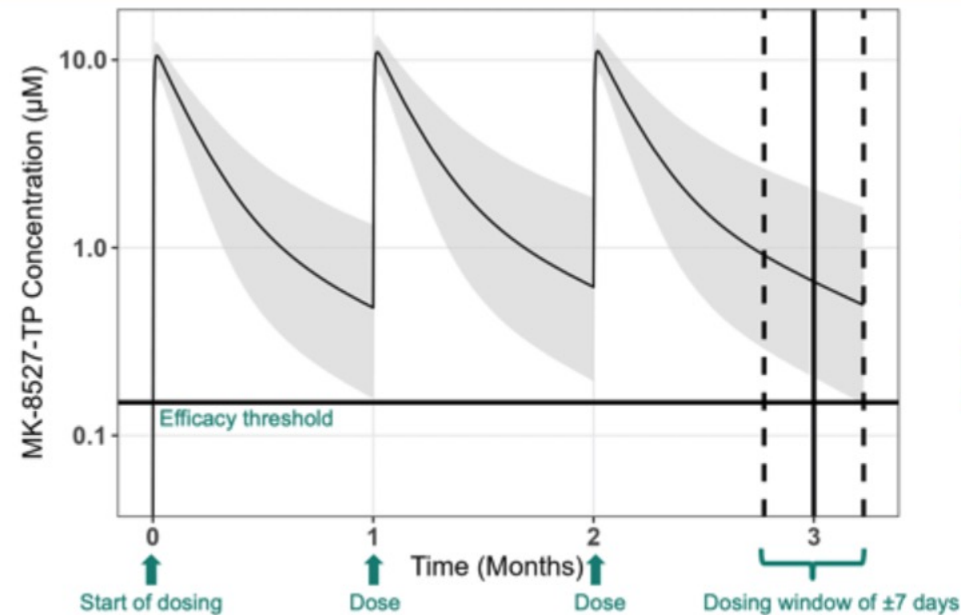
Jones J, et al.



PrEP Pipeline

- Monthly oral MK-8527^{NRTTI}
- Every 12-month LEN IM
- Broadly neutralizing antibodies (bNAbs)
- Tenofovir rectal douche
- Implants?

MK-8527 11 mg qm are predicted to maintain MK-8527-TP concentrations above the PK preventive efficacy threshold



- ✓ Fast onset of action (within an hour)
- ✓ Coverage for the whole month after the first dose
- ✓ Provides a ± 7 -day dosing window

Month = 31 days. Bands represent fifth and 95th PI.

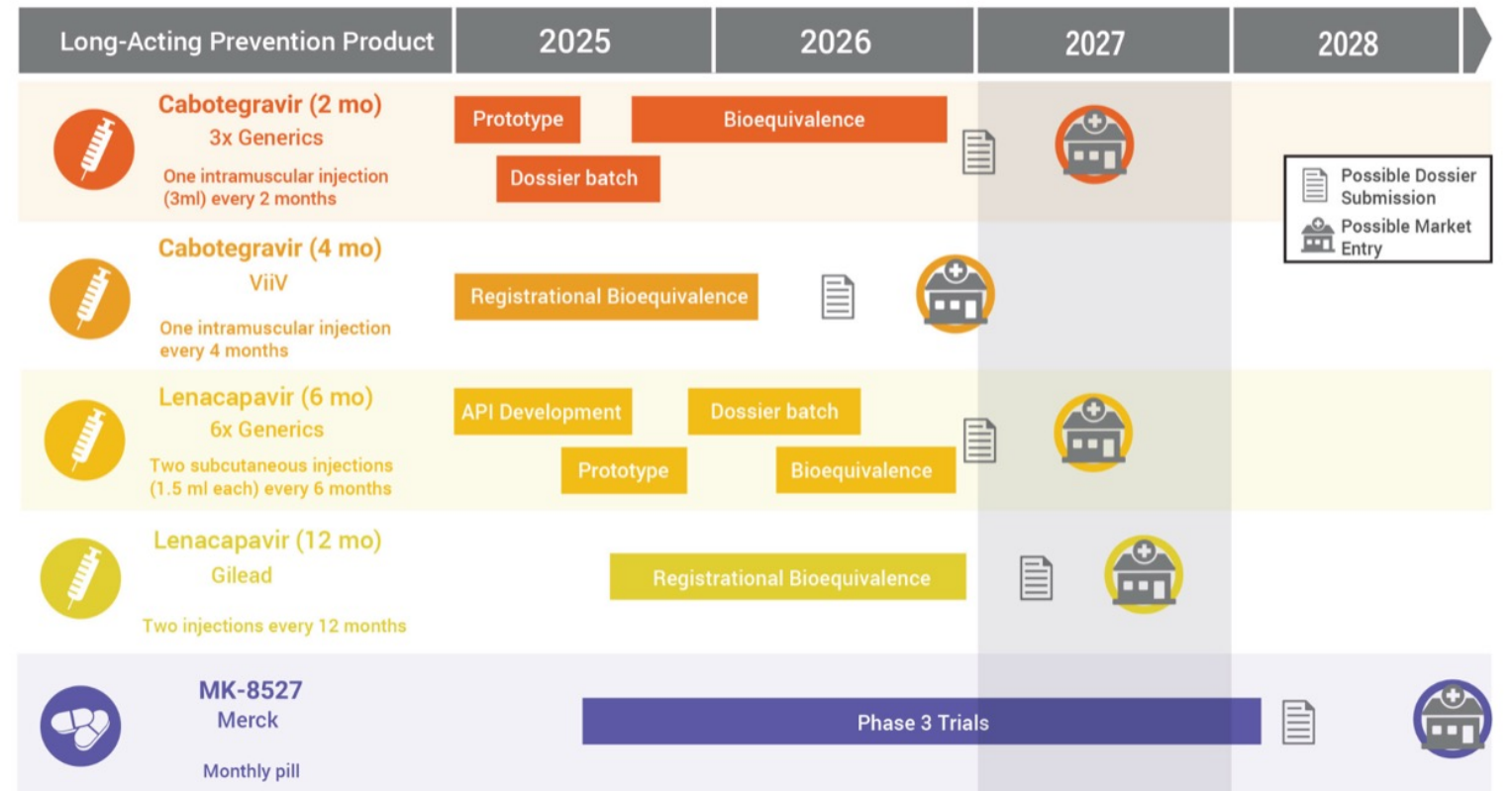
PI, prediction interval; PK, pharmacokinetics; qm, once-monthly; TP, triphosphate.

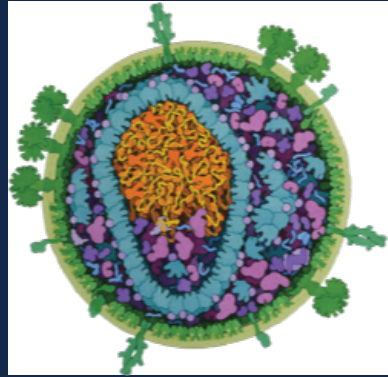
Kapoor Y, et al.

PrEP Pipeline

- Monthly oral MK-8527^{NRTTI}
- Every 12-month LEN IM
- Broadly neutralizing antibodies (bNAbs)
- Tenofovir rectal douche
- Implants?

An “Innovation Pile-Up” In Next-Generation LA-PrEP is Possible





CROI

Conference on Retroviruses
and Opportunistic Infections

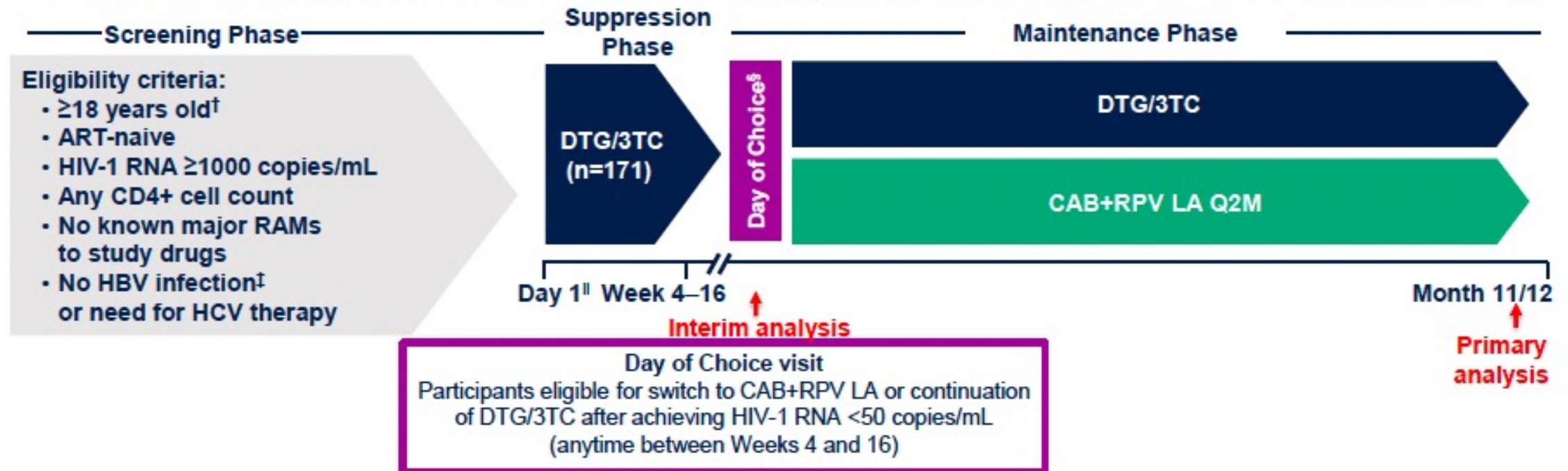
TREATMENT

[Naïve] VOLITION: LA-ART Shared Decision Making in PWH Suppressed on DTG/3TC

Methods

Figure 1. VOLITION Study Design*

Phase 3b, multicenter, non-randomized, parallel-group, open-label, implementation-effectiveness study



[Naïve] VOLITION: LA-ART Shared Decision Making in PWH Suppressed on DTG/3TC

Results

Table 1. A Diverse Population of Participants Chose to Switch to CAB+RPV LA at DoC

Parameter	CAB+RPV LA (n=129)
Median years (range)	31 (18–67)
<35 years, n (%)	79 (61)
35–<50 years, n (%)	37 (29)
≥50 years, n (%)	13 (10)
Women (self-reported gender), n (%)	34 (26)
Race, n (%)	
Black or African American	42 (33)
White	77 (60)
Other races*	5 (4)
Not reported or unknown	5 (4)
Hispanic/Latinx ethnicity, n (%)	66 (51)
Region, n† (%)	
North America	63 (49)
Europe	30 (23)
South America	36 (28)
Median (IQR) weight (kg)	77.7 (65.3, 86.0)
Median (IQR) BMI (kg/m ²)	25.5 (22.4, 29.4)
BMI (kg/m ²) category, n (%)	
Overweight (25 to <30)	47 (36)
Obesity (≥30)	27 (21)
Median (IQR) CD4+ cell (cells/mm ³)	555 (427, 668)
CD4+ cell (cells/mm ³) category, n (%)‡	
<100	1 (<1)
100 to <200	7 (6)
200 to <350	20 (16)
≥350	98 (78)

- Overall, 171 participants enrolled in the study and initiated DTG/3TC, 151 (88%) of whom were eligible and were offered the choice to switch to CAB+RPV LA at DoC§.
- Of those offered the choice, 129 (85%) participants chose to switch to CAB+RPV LA.
- A diverse population of participants was represented, comprising 51% Hispanic/Latinx, 33% Black or African American, and 26% women (Table 1).

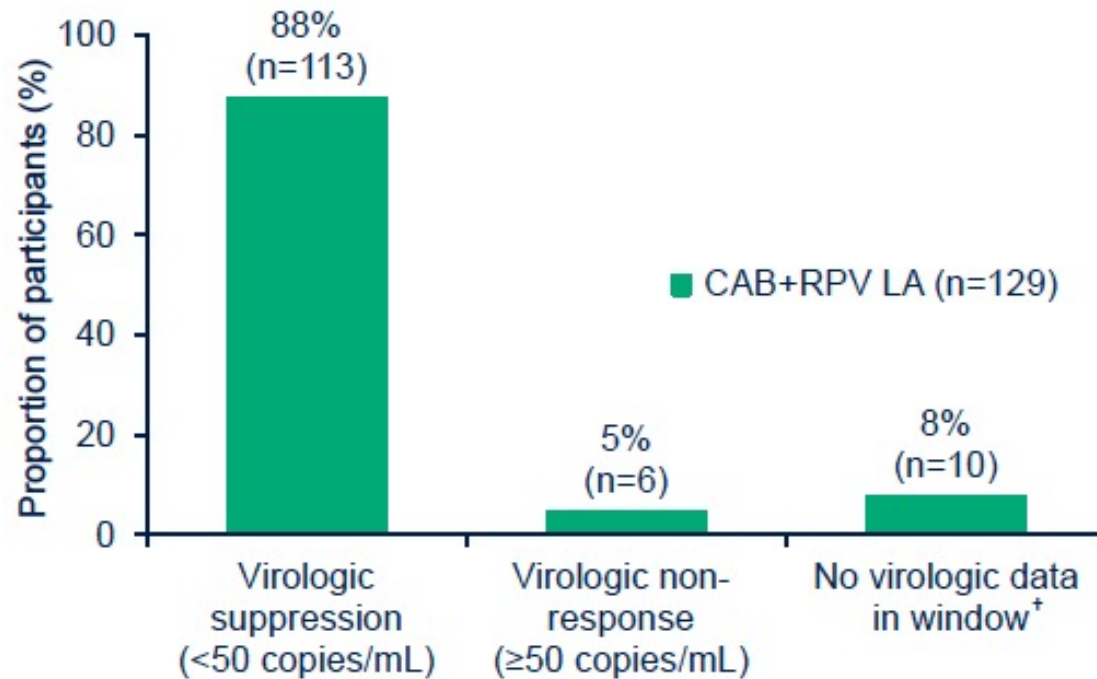
*Other race participants: Multiple, n=3; Asian, n=2. †North America includes United States (including Puerto Rico; n=54) and Canada (n=9); Europe includes France (n=8), Germany (n=4), Italy (n=9), and Spain (n=11); South America includes Argentina (n=20) and Chile (n=16). ‡n=126. §Four participants withdrew during the suppression phase; reasons for ineligibility for switch were: did not achieve virologic suppression (defined as HIV-1 RNA <50 copies/mL; n=15); and baseline resistance to NNRTI [E138A] (n=1).

3TC, lamivudine; BMI, body mass index; CAB, cabotegravir; DoC, Day of Choice; DTG, dolutegravir; IQR, interquartile range; LA, long-acting; NNRTI, non-nucleoside reverse transcriptase inhibitor; RPV, rilpivirine.

[Naïve] VOLITION: LA-ART Shared Decision Making in PWH Suppressed on DTG/3TC

Figure 2. High Rate of Virologic Suppression at Month 11

A. Modified* Snapshot



- One (<1%) participant met CVF criteria with emergent INSTI and NNRTI resistance (Table 2).

Participant*	
Sex at birth, age range (years)	Male, 20–29
BMI (kg/m ²)†	≥30
HIV-1 subtype	B
Viral load at Day 1 (copies/mL; cobas 6800)	55,700
RAMs at DoC (proviral DNA)	None
Time to virologic failure (months)	9
Viral load at SVF/CVF (copies/mL; cobas 6800)	405/1410
Viral load at SVF/CVF (copies/mL; RealTime)	285/1213
RAMs at failure	NNRTI: M230L INSTI: E138K, Q148K
ART following CAB+RPV LA discontinuation	DRV/COBI/FTC/TAF‡

[Naïve] DOR/ISL vs BFTAF

177 - DOR/ISL (100/0.25 mg) vs BIC/FTC/TAF for Initial HIV-1 Therapy: Week 48 Results of a Phase III Study

Jürgen K. Rockstroh
Bonn University Hospital, Bonn, Germany

Double-Blind DOR/ISL (100/0.25 mg) vs BIC/FTC/TAF

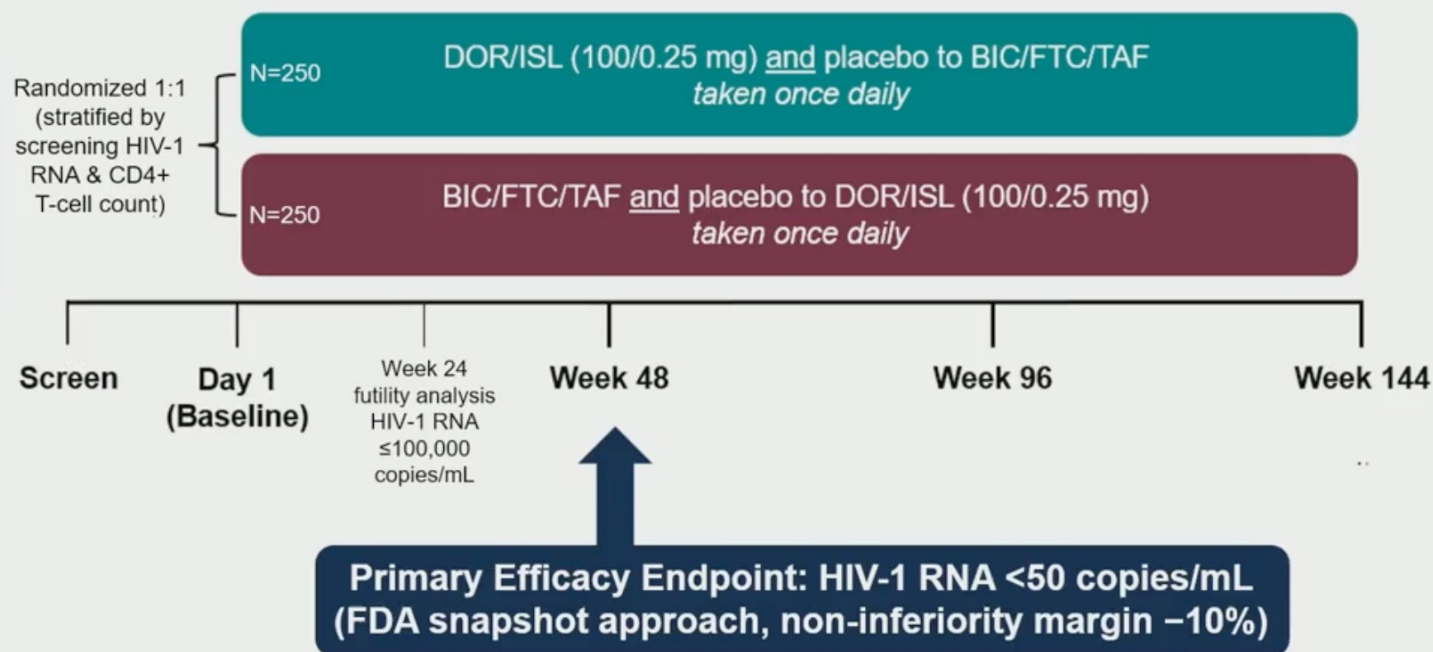
Population

- Adults with plasma HIV-1 RNA ≥ 500 copies/mL at screening
- Treatment-naïve
- No documented or known resistance to study intervention^a
- No active hepatitis B

^aBased on the following list of RAMs:

DOR specific RAMs: V106A/M, V108I, Y188L, H221Y, P225H, F227C/L/V, M230I/L, L234I, P236L, Y318F

NRTI RAMs: K65R/E/N, T69insert, K70E, Q151M, M184I/V, or ≥ 3 TAMs (M41L, D67N, K70R, L210W, T215F/Y, K219E/Q)



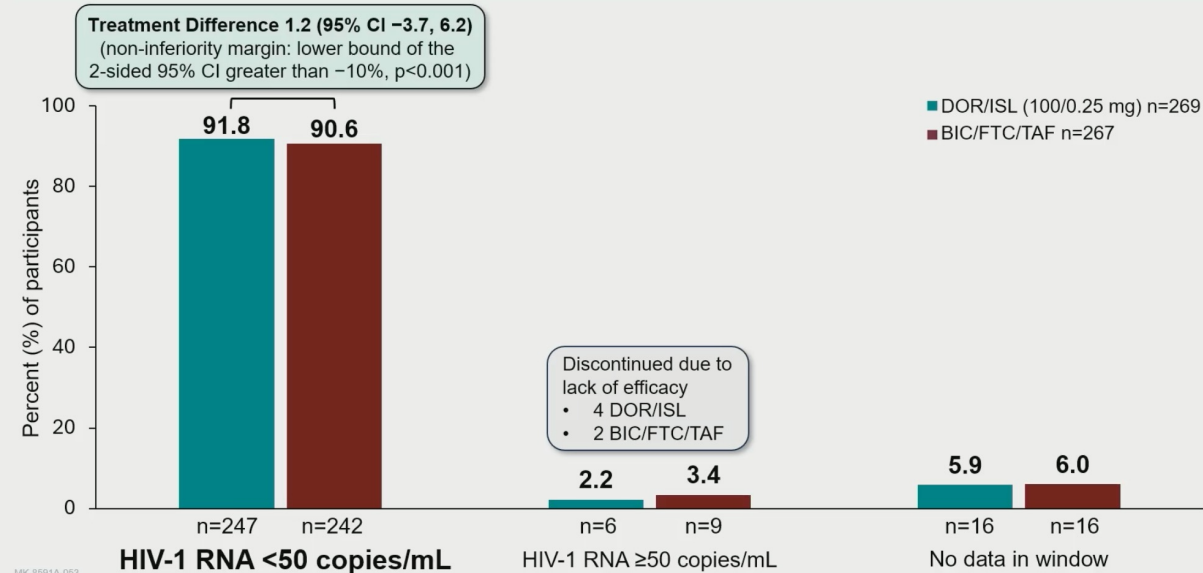
[Naïve] DOR/ISL vs BFTAF

Demographics Balanced Across Treatment Groups

Baseline Demographics	DOR/ISL (100/0.25 mg) n=269	BIC/FTC/TAF n=267	Total Population N=536
Age (years), median (IQR)	33 (26-41)	32 (26-39)	32 (26-40)
Female sex at birth, n (%)	65 (24.2)	69 (25.8)	134 (25.0)
Race, n (%): White	110 (40.9)	115 (43.1)	225 (42.0)
Black or African American	89 (33.1)	82 (30.7)	171 (31.9)
Asian	29 (10.8)	29 (10.9)	58 (10.8)
Hispanic or Latino/a ethnicity, n (%)	104 (38.7)	110 (41.2)	214 (39.9)
CD4+ T-cell count (cells/mm ³), median (IQR)	384 (238-531)	359 (254-531)	370 (247-531)
CD4+ T-cell count <200 cells/mm ³ , n (%)	54 (20.1)	38 (14.2)	92 (17.2)
HIV-1 RNA (copies/mL), median (IQR)	53,800 (15,000-190,000)	56,700 (17,600-179,000)	55,000 (16,550-184,000)
HIV-1 RNA >100,000 (copies/mL), n (%)	96 (35.7)	101 (37.8)	197 (36.8)
HIV-1 RNA >500,000 (copies/mL), n (%)	27 (10.0)	28 (10.5)	55 (10.3)
HIV-1 subtype: B	138 (51.3)	145 (54.3)	283 (52.8)
C	59 (21.9)	43 (16.1)	102 (19.0)
Non-B/non-C	72 (26.8)	79 (29.6)	151 (28.2)
Anti-HBs negative and anti-HBc negative	131 (48.7)	146 (54.7)	277 (51.7)

[Naïve] DOR/ISL vs BFTAF

DOR/ISL Non-Inferior to BIC/FTC/TAF at Week 48 US FDA Snapshot



TE Resistance to DOR/ISL Observed in 2 of 269 Participants

CD4+ T Cell Count at Baseline (cells/mm ³)	HIV-1 RNA at Screening/ Baseline (copies/mL)	Mutations Observed at Baseline ^a	Phenotypic Fold-Shift (assessment) ^b	HIV-1 RNA at Discontinuation (copies/mL)	Mutations Observed at Discontinuation ^a	Phenotypic Fold-Shift (assessment) ^b
31	2,260,000/ 801,000	RT: V90I, Y181Y/C, G190S	DOR 1.83 (S) ISL 0.42 (S)	951,000 (week 16) ^c	RT: V90I, M184I , Y188L , G190S	DOR >max (R) ISL 2.42 (S)
171	1,580,000/ 1,690,000	RT: T69T/N, V179E, T215T/A	Assay failure	228,000 (week 24) ^d	RT: L74I , V106A , V179E, M184V , F227L	DOR >max (R) ISL 6.69 (S)

^aGenotypic resistance was evaluated using the GenoSure PRIme® next-generation sequencing assay.

^bPhenotypic fold-shift was determined using the PhenoSense® assay. Assessment of susceptibility for DOR was determined using clinical cutoffs defined by Monogram Biosciences in the PhenoSense® and PhenoSense® Integrase assays. A clinical cutoff of 20 fold-shift was used for ISL susceptibility as the model-predicted steady state islatravir-triphosphate concentration 24h after the 0.25 mg daily dose is approximately 20-fold above the target for efficacy (defined as an inhibitory quotient of 5).

^cDOR and ISL plasma concentrations relatively low suggesting possible incomplete adherence between Week 4 and 8.

^dDOR and ISL plasma concentrations quantifiable at all visits suggesting adherence at time of study visit.

RT, reverse transcriptase; TE, treatment-emergent.

- Similar CD4 cell count gains in both arms. No evidence of cellular toxicity of DOR/ISL
- Similar AE rates. In DOR/ISL one case of DRESS and one case of liver injury
- 3 HBV infections in the DOR/ISL arm

[Naïve] DOR/ISL vs BFTAF

Increase in Weight Was Similar with DOR/ISL and BIC/FTC/TAF

Mean change in weight at Week 48^a

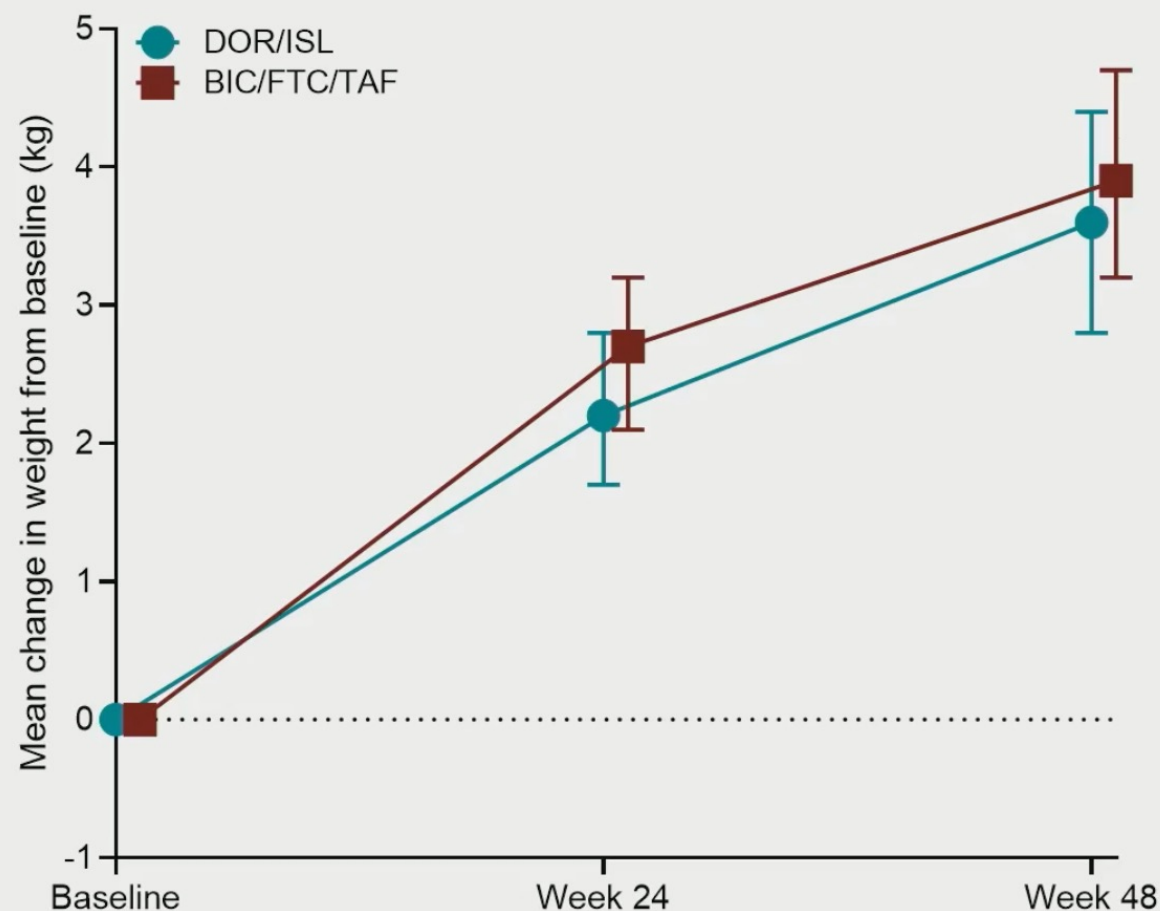
DOR/ISL

- 3.6 kg (95% CI 2.8, 4.4)

BIC/FTC/TAF

- 3.9 kg (95% CI 3.2, 4.7)

Difference: -0.3 (95% CI -1.5, 0.9; p=0.57)



^aPrespecified secondary endpoint: superiority of DOR/ISL to BIC/FTC/TAF for a lower mean increase from baseline weight would be concluded if the upper bound of the two-sided multiplicity-adjusted 95% CI for the between-group treatment difference was less than 0 kg.

[Switch] SUPLA - CAB/RPV vs SOC in Viremic PWH

Week-24 Outcomes of Long-Acting Injectable ART in People With HIV and Suboptimal Viral Suppression

530

Nan-Yu Chen^{1,2}, M.D., Ph.D., Cheng-Pin Chen³, M.D., Yi-Chun Lin³, M.D., Shu-Hsing Cheng³, M.D., Shien-Shian Huang⁴, M.D., Jun-Yuan Zheng⁴, Ching-Tai Huang^{1,2,5}, M.D., Ph.D., Ting-Shu Wu^{1,2}, M.D., Ph.D., Ting-Yi Su^{1,5}, M.D., Shian-Sen Shie¹, M.D., Jung-Jr Ye⁴, M.D., Chun-Fu Yeh¹, M.D., Peng-Hao Chang¹, M.D., Chong Kei Lao¹, M.D., Shu-Yuan Lee³, Yu-Hsiang Hsiao¹, M.S., Zhuo-Hao Liu^{2,6}, M.D., Ph.D., and Chien-Yu Cheng^{3,7}, M.D., Ph.D., for the SUPLA Study Team

1. Division of Infectious Diseases, Department of Internal Medicine, Linkou Chang Gung Memorial Hospital, Taoyuan, Taiwan, 2. School of Medicine, Chang Gung University, Taoyuan, Taiwan, 3. Department of Infectious Diseases, Taoyuan General Hospital, Ministry of Health and Welfare, Taoyuan, Taiwan, 4. Division of Infectious Diseases, Keelung Chang Gung Memorial Hospital, Keelung, Taiwan, 5. Division of Infectious Diseases, Taipei Chang Gung Memorial Hospital, Taipei, Taiwan, 6. Department of Neurosurgery, Chang Gung Memorial Hospital Linkou Branch, Taiwan, 7. Institute of Public Health, School of Medicine, National Yang-Ming Chiao Tung University, Taipei, Taiwan

Key Entry Criteria:

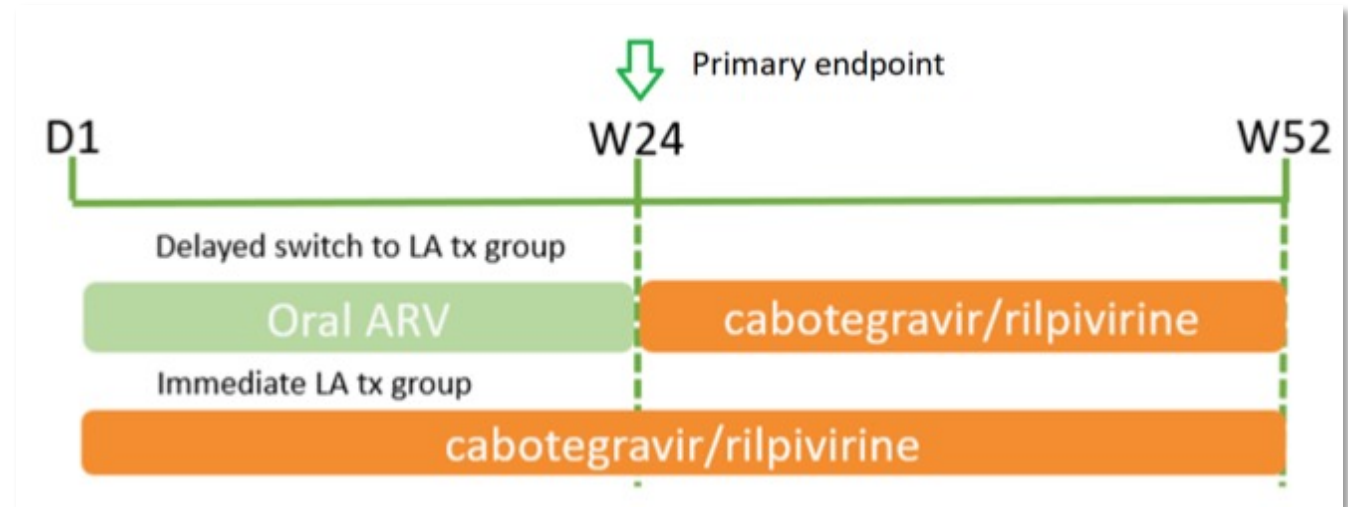
- ART-experienced PWH aged ≥ 18 years weighing ≥ 35 kg
- HIV diagnosis for more than 12 months
- HIV-1 RNA ≥ 200 copies/mL at enrollment
- No drug resistance mutations (DRMs) to CAB or RPV

Key Exclusion Criteria:

- DRMs to CAB or RPV identified through medical records or screening genotyping
- Individuals who cannot receive hepatitis B treatment during the period of transitioning to LA CAB+RPV, if they are hepatitis B carriers

Participants were randomized 1:1 to either:

- **Immediate LA treatment group:** Participants were prescribed immediate 8-weekly LA CAB+RPV for 52 weeks. No oral lead-in period before LA CAB+RPV
- **Delayed switch to LA treatment group:** Participants continued on oral ART until Week 24 when they were switched to LA CAB+RPV for another 28 weeks



[Switch] SUPLA - CAB/RPV vs SOC in Viremic PWH

	Immediate LA (n= 25)	Delayed LA (n= 20)	Total (n= 45)
Age			
years, median (IQR)	45 (29–49)	39 (33–47)	40 (33–49)
Sex at birth (% , n)			
Male	92% (23)	90% (18)	91% (41)
Female	8% (2)	10% (2)	9% (4)
CD4 (cells/ μ L)			
median (IQR)	382 (203–453)	268 (134–355)	319 (160–435)
CD4 (cells/ μ L, % , n)			
< 200	24% (6)	30% (6)	27% (12)
$\geq$ 200	76% (19)	70% (14)	73% (33)
Viral load (copies/mL)			
median	28,800	42,950	35,000
IQR	1,950–188,500	25,700–372,000	3,630–225,000
Viral load (copies/mL, % , n)			
< 10 ⁵	64% (16)	55% (11)	60% (27)
10 ⁵ –10 ⁶	32% (8)	35% (7)	33% (15)
$\geq$ 10 ⁶	4% (1)	10% (2)	7% (3)

Subtype (% , n)			
B	56% (14)	65% (13)	60% (27)
CRF01_AE	12% (3)		7% (3)
CRF07_BC	8% (2)	25% (5)	16% (7)
No data	24% (6)	10% (2)	18% (8)
BMI (kg/m ²)			
median (IQR)	23.3 (21.0–24.6)	23.8 (20.7–26.8)	23.3 (20.7–26.1)
Substance use (% , n)			
	56% (14)	65% (13)	60% (27)
Years since HIV diagnosis			
years, median (IQR)	12 (5–18)	9.5 (6.5–17)	10 (5.5–17.5)
Source of recruitment (% , n)			
Call back	44% (11)	70% (14)	56% (25)
Self-arranged appointment	32% (8)	10% (2)	22% (10)
Scheduled appointment	24% (6)	20% (4)	22% (10)
Pattern of last oral ART			
Irregular (% , n)	44% (11)	25% (5)	36% (16)
Interrupted (% , n)	56% (14)	75% (15)	64% (29)
Duration of ART interruption			
months, median (IQR)	12 (5–24)	7 (4–22)	10 (4–23.5)
Top 3 ART regimens before study entry (% , n)			
TAF/FTC/BIC	56% (14)	60% (12)	58% (26)
ABC/3TC/DTG	28% (7)	15% (3)	22% (10)
3TC/DTG	8% (2)	15% (3)	11% (5)

[Switch] SUPLA - CAB/RPV vs SOC in Viremic PWH

	Immediate LA	Delayed Switch	p value	Relative Risk (95% CI)
Primary endpoint				
HIV-1 RNA <200 copies/mL (% , n)				
Modified Intention to Treat	88.0% (22/25)	55.0% (11/20)	0.0264	0.2667 (0.0830, 0.8565)
Per Protocol	91.7% (22/24)	64.7% (11/17)	0.0551	0.2361 (0.0540, 1.0318)
Secondary endpoints				
HIV-1 RNA <50 copies/mL (% , n)				
Modified Intention to Treat	76.0% (19/25)	40.0% (8/20)	0.0220	0.4000 (0.1826, 0.8761)
Per Protocol	79.2% (19/24)	47.1% (8/17)	0.0421	0.3935 (0.1601, 0.9674)
Week 24 HIV-1 RNA, copies/mL (median, IQR)	21.6 (0–46)	62 (22–21,760)	0.0071	--
Change of CD4 cell count, cells/ μ L	70 (-9–157.5)	137 (24–170)	0.4473	--
Lost to follow-up (% , n)	4% (1/25)	15% (3/20)	0.3087	--
Discontinuation of ART for any treatment-related reason (% , n)	8% (2/25)	0 (0/20)	0.4949	--
Change of body weight, kg (median, IQR)	1.4 (0.1–3.7)	3.95 (2.2–5.95)	0.0085	--

Modified intention to treat: missing cases were classified as virally not suppressed; Per protocol: missing cases were excluded from the analysis; Relative Risk (RR): RR values represent the risk of the outcome (e.g., failing to achieve viral suppression) comparing the Immediate LA group to the Delayed Switch group

Table 2. Week 24 efficacy outcome in SUPLA Study

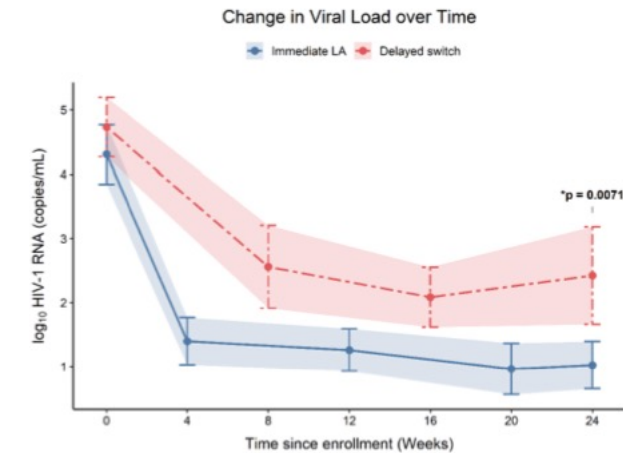


Figure 3. Longitudinal HIV-1 RNA viral load over 24 weeks. Shaded areas indicate 95% confidence intervals

[Switch] DOR/ISL vs BFTAF Blinded 96 Week Data

Figure 1. Double-blind DOR/ISL vs continuing BIC/FTC/TAF

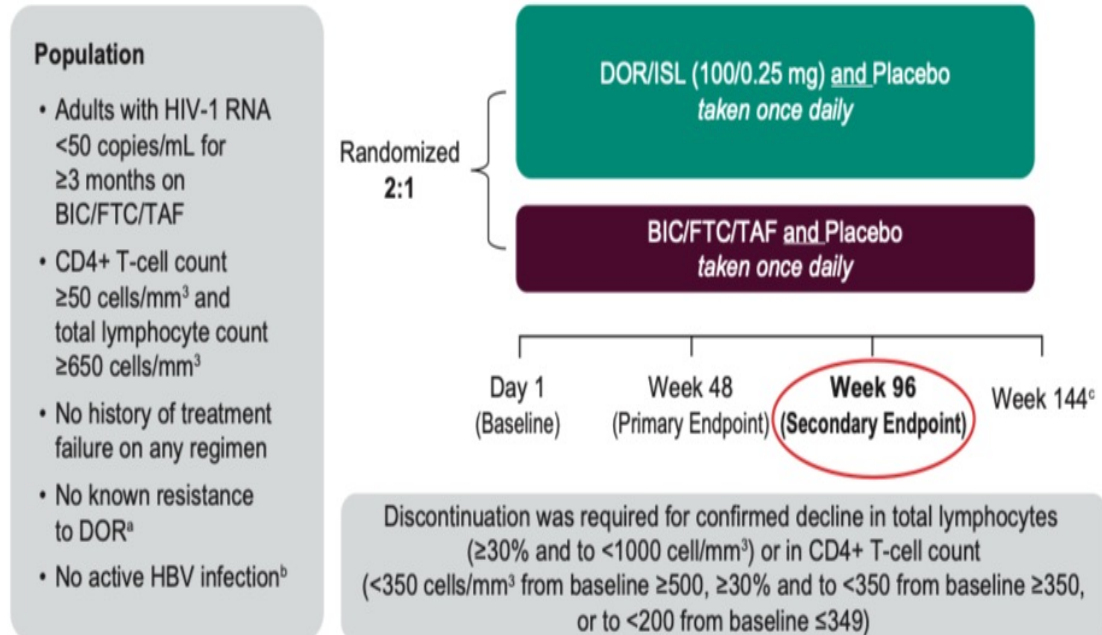
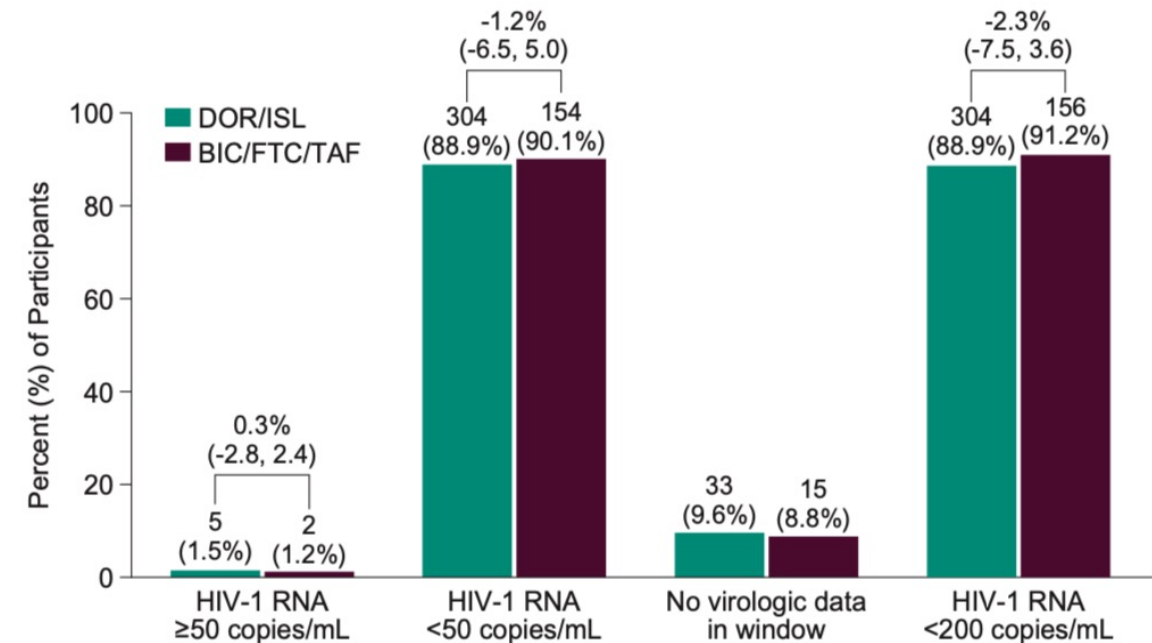


Figure 2. Efficacy at Week 96 (FDA snapshot approach) was similar between DOR/ISL and BIC/FTC/TAF



Conclusions

- Switching to DOR/ISL (100/0.25 mg) from BIC/FTC/TAF maintained a high rate (89%) of virologic suppression and had similar efficacy to continuing BIC/FTC/TAF at Week 96
- DOR/ISL was generally well tolerated over 96 weeks; the AE profiles of DOR/ISL and BIC/FTC/TAF were comparable
- A switch to DOR/ISL had no adverse effects on total lymphocyte and CD4+ T-cell counts through Week 96

These findings are consistent with the study's primary Week 48 results.

[Switch] DOR/ISL vs BFTAF Blinded 96 Week Data

Figure 1. Double-blind DOR/ISL vs continuing BIC/FTC/TAF

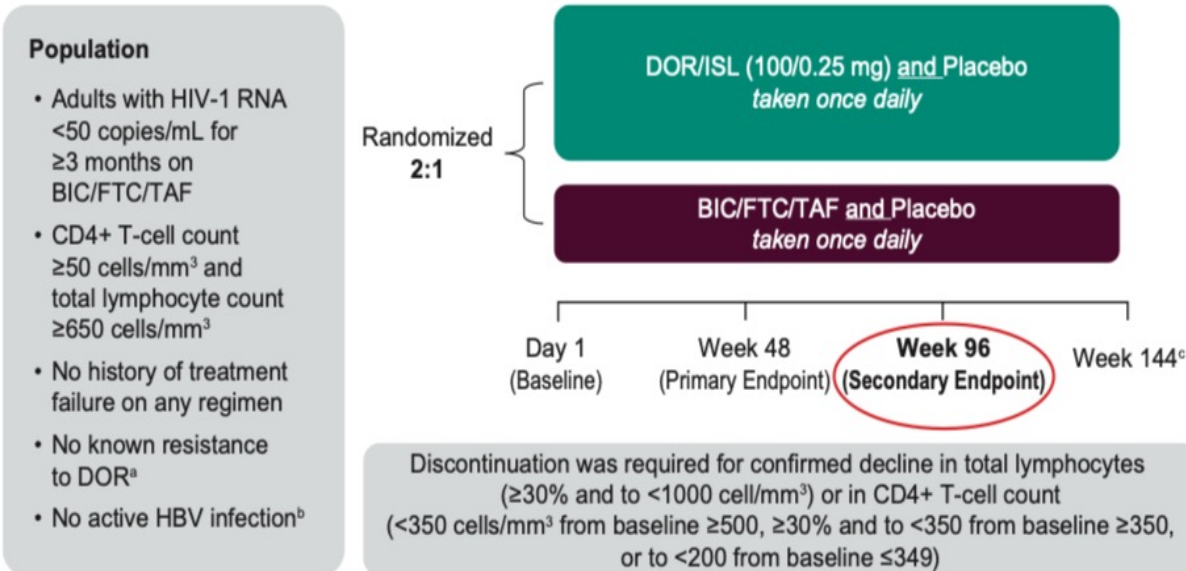


Table 4. Mean changes from baseline to Week 96 in weight, lipids, insulin resistance, and renal function were comparable between groups

Measure	DOR/ISL		BIC/FTC/TAF		Treatment Difference (95% CI) ^b
	n	Mean change ^a	n	Mean change ^a	
Weight, kg	304	0.34 (-0.38, 1.06)	156	0.43 (-0.37, 1.24)	-0.03 (-1.18, 1.11)
Fasting LDL-C, mg/dL	289	-1.76 (-4.99, 1.47)	146	0.36 (-4.05, 4.77)	-2.02 (-7.06, 3.01)
Fasting non-HDL-C, mg/dL	289	-4.65 (-8.24, -1.06)	146	-2.57 (-7.29, 2.15)	-2.23 (-7.69, 3.22)
Insulin resistance (HOMA-IR)	241	-0.13 (-0.69, 0.43)	124	0.47 (0.11, 0.84)	-0.29 (-0.98, 0.40)
eGFR from creatinine, mL/min/1.73m ²	304	7.08 (5.77, 8.39)	155	-0.28 (-2.18, 1.63)	7.28 (5.02, 9.53)
eGFR from cystatin C, mL/min/1.73m ²	298	-2.41 (-3.52, -1.30)	154	0.93 (-0.61, 2.47)	-3.54 (-5.35, -1.72)

^aWith 95% CIs based on the t-distribution. ^bWith 95% CIs calculated from ANOVA models.

eGFR, estimated glomerular filtration rate. HOMA-IR, homeostatic model assessment for insulin resistance. n, number of participants with corresponding baseline and post-baseline data at Week 96.

Conclusions

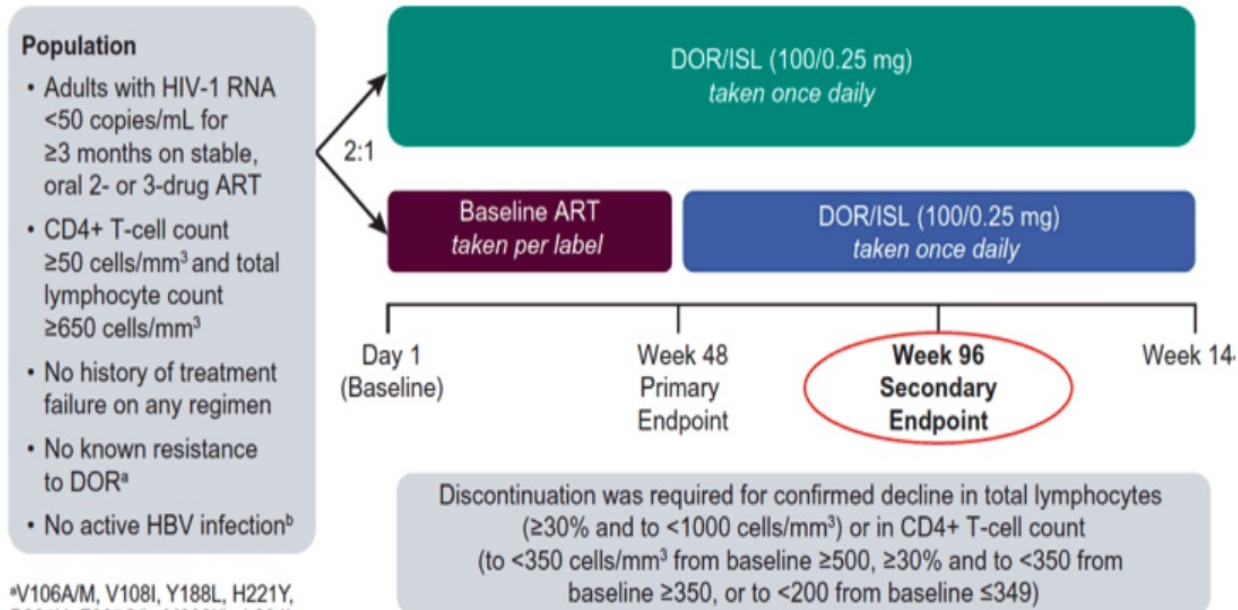
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These findings are consistent with the study's primary Week 48 results.

[Switch] DOR/ISL vs Standard ART Open Label

96 Week Data

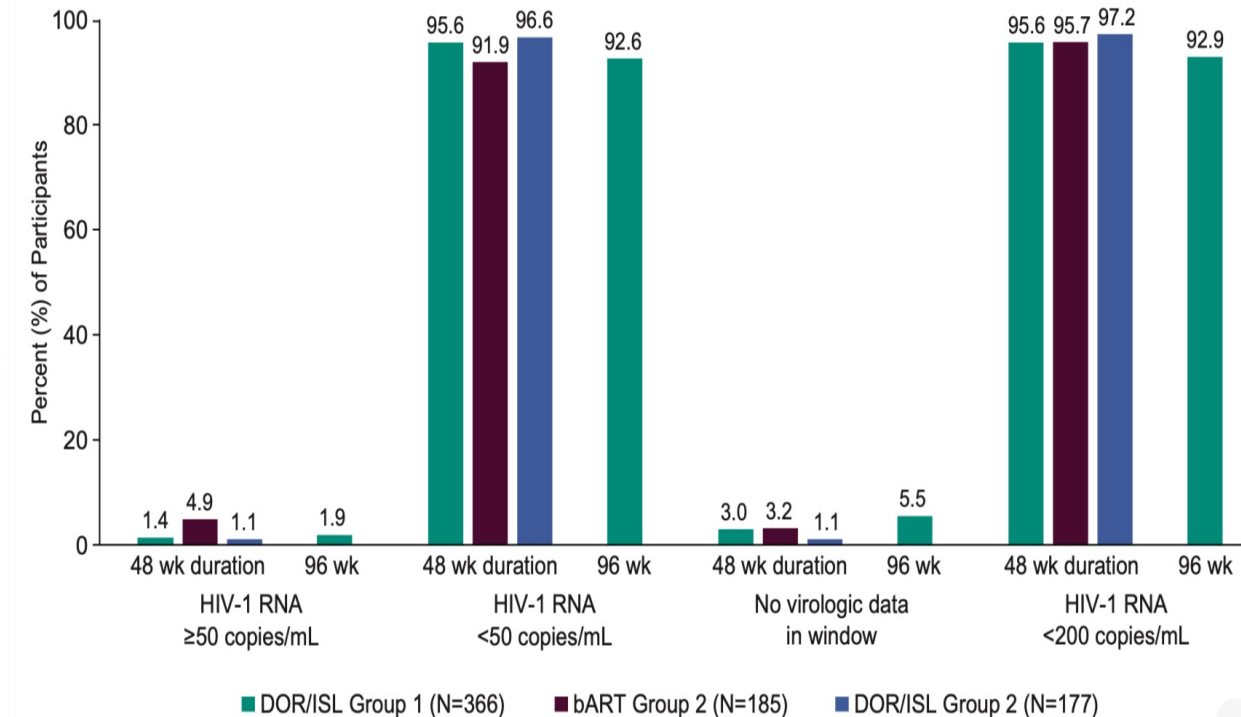
Figure 1. MK-8591A-051: a Phase 3, randomized, open-label switch study



^aV106A/M, V108I, Y188L, H221Y, P225H, F227C/L, M230I/L, L234I, P236L or aY318F.

^bNegative surface antigen and DNA tests.

Figure 2. Virologic outcomes at Week 48 and Week 96 (FDA snapshot approach)



Conclusions

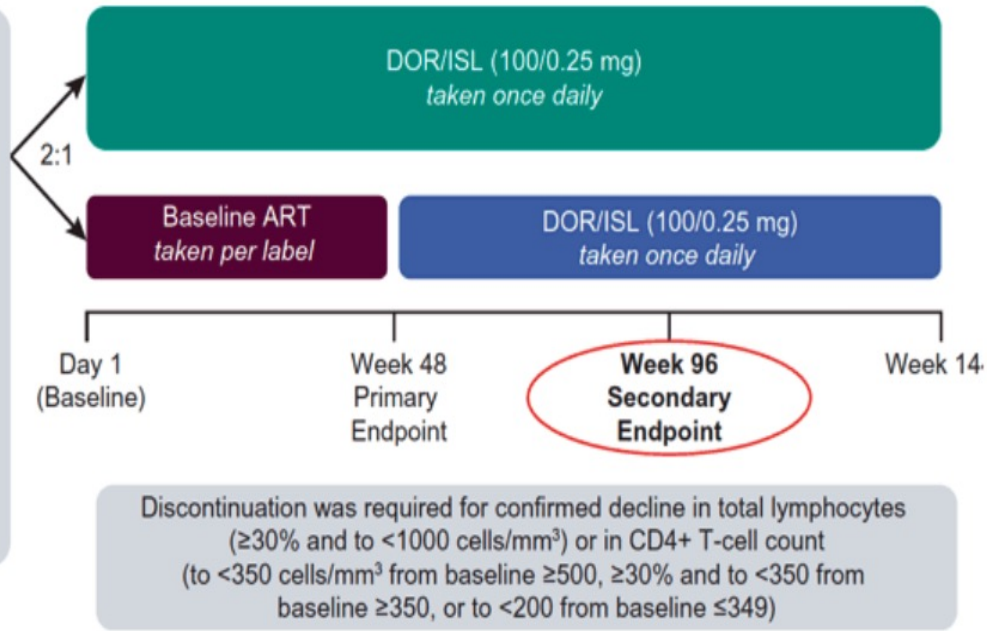
- Switching to DOR/ISL (100/0.25 mg) maintained high rates of virologic suppression (HIV-1 RNA <50 copies/mL) through 96 weeks of treatment
 - 48 weeks of DOR/ISL: 95.6% in Group 1 (Week 0-48) and 96.6% in Group 2 (Week 48-96)
 - 96 weeks of DOR/ISL: 92.6% in Group 1 (Week 0-96)
- No treatment-emergent resistance to DOR or ISL was observed through Week 96
- Switching to DOR/ISL had no adverse effects on total lymphocyte or CD4+ T-cell counts through Week 96
- DOR/ISL maintained a favorable safety and tolerability profile over 96 weeks

[Switch] DOR/ISL vs Standard ART Open Label 96 Week Data

Figure 1. MK-8591A-051: a Phase 3, randomized, open-label switch study

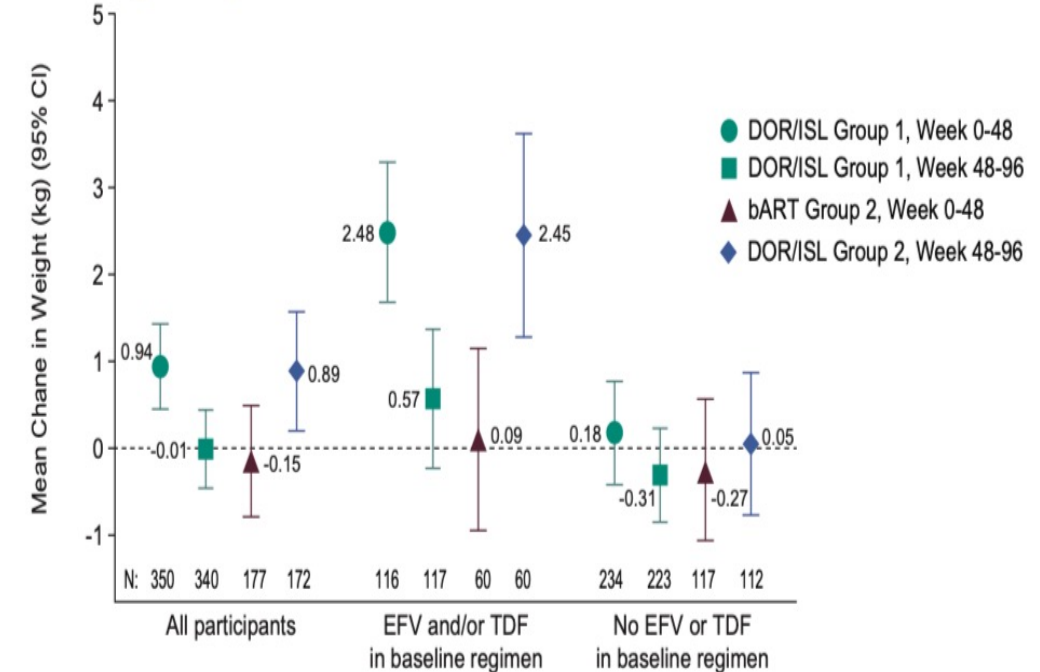
Population

- Adults with HIV-1 RNA <50 copies/mL for ≥3 months on stable, oral 2- or 3-drug ART
- CD4+ T-cell count ≥50 cells/mm³ and total lymphocyte count ≥650 cells/mm³
- No history of treatment failure on any regimen
- No known resistance to DOR^a
- No active HBV infection^b



^aV106A/M, V108I, Y188L, H221Y, P225H, F227C/L, M230I/L, L234I, P236L or aY318F.

Figure 4. Mean change in weight at Week 48 and Week 96



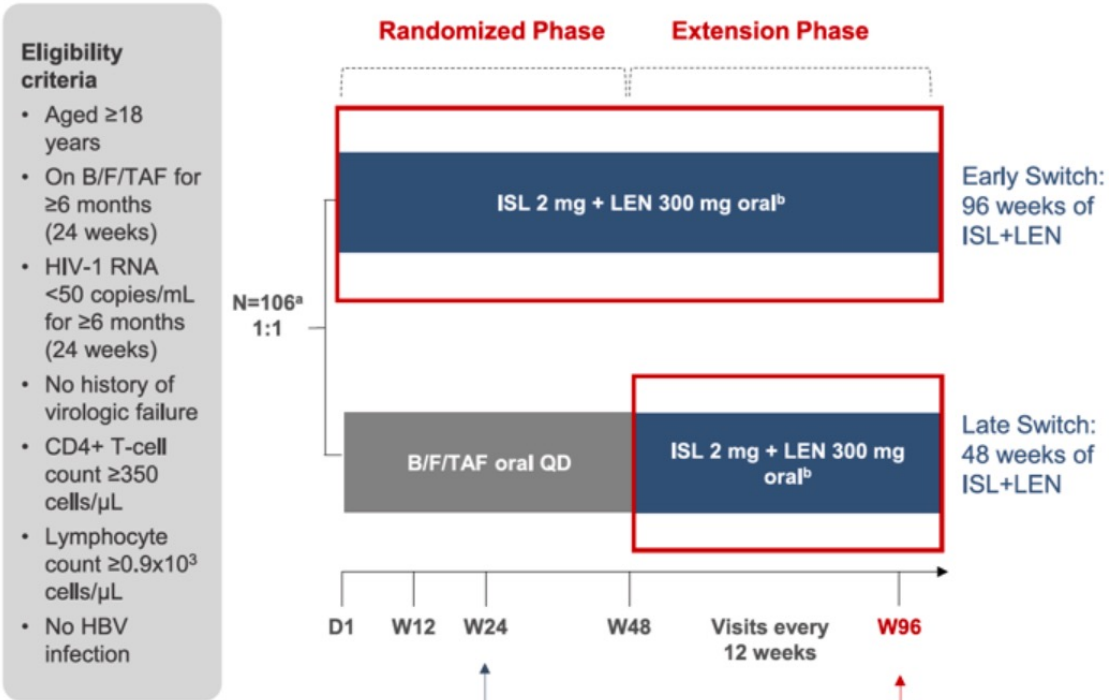
Conclusions

- Switching to DOR/ISL (100/0.25 mg) maintained high rates of virologic suppression (HIV-1 RNA <50 copies/mL) through 96 weeks of treatment
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- DOR/ISL maintained a favorable safety and tolerability profile over 96 weeks

[Switch] Weekly ISL^{Oral}/LEN^{Oral} vs BFTAF

96 Week data

Figure 1. Study Design



Primary endpoint:¹¹

- Proportion with HIV-1 RNA ≥50 copies/mL at Week 24 per FDA Snapshot Algorithm

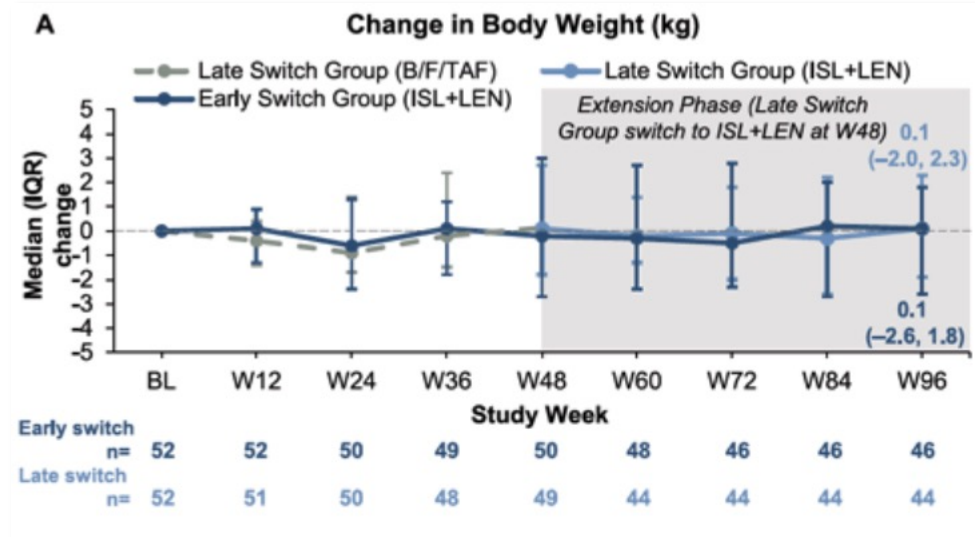
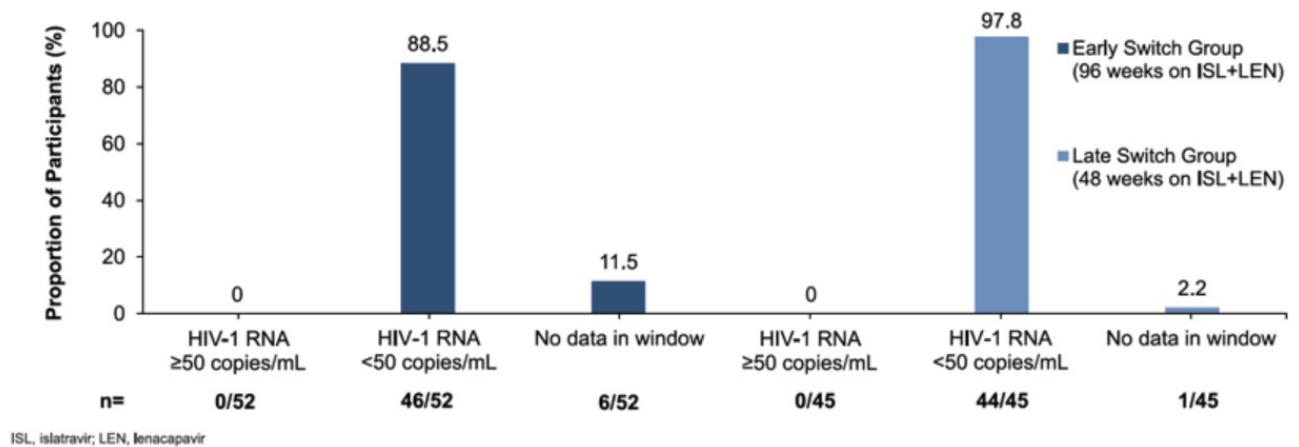
Results included in this presentation:

- Proportion with HIV-1 RNA ≥50 copies/mL
- Proportion with HIV-1 RNA <50 copies/mL
- Change from baseline in CD4+ T-cell and lymphocyte count
- AEs

Other assessments:

- Change in BMI, body weight, and adherence by pill count

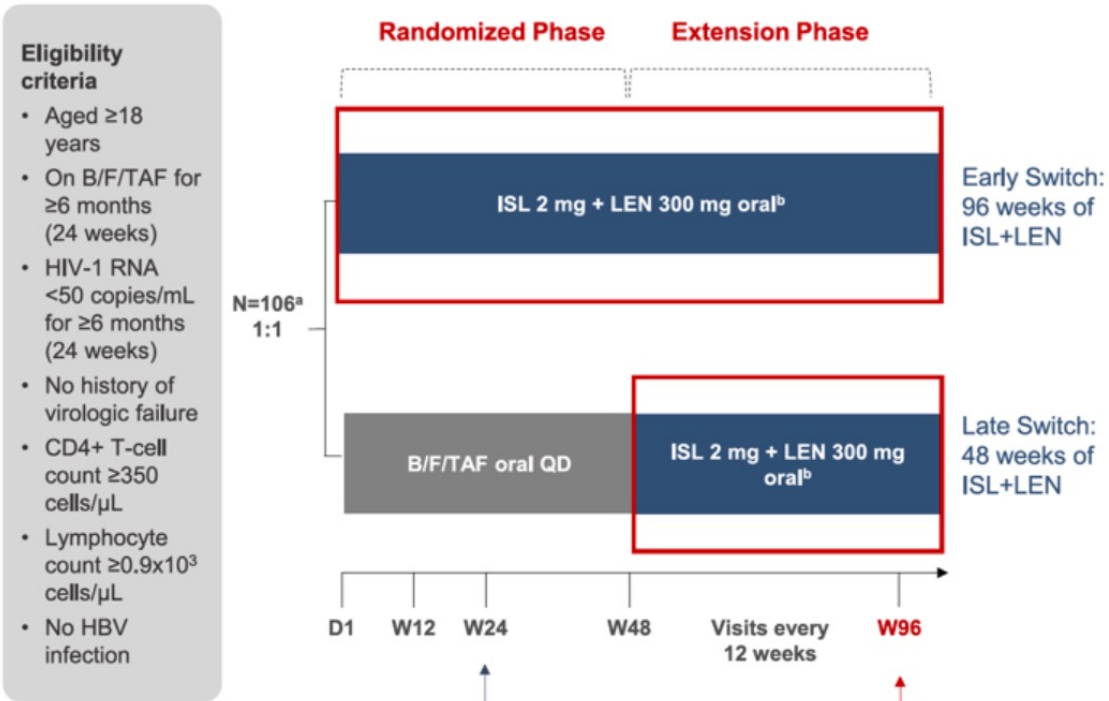
Figure 2. Study Week 96 Virologic Outcomes for Early Switch Group and Late Switch Group



[Switch] Weekly ISL^{Oral}/LEN^{Oral} vs BFTAF

96 Week data

Figure 1. Study Design



Primary endpoint:¹¹

- Proportion with HIV-1 RNA ≥50 copies/mL at Week 24 per FDA Snapshot Algorithm

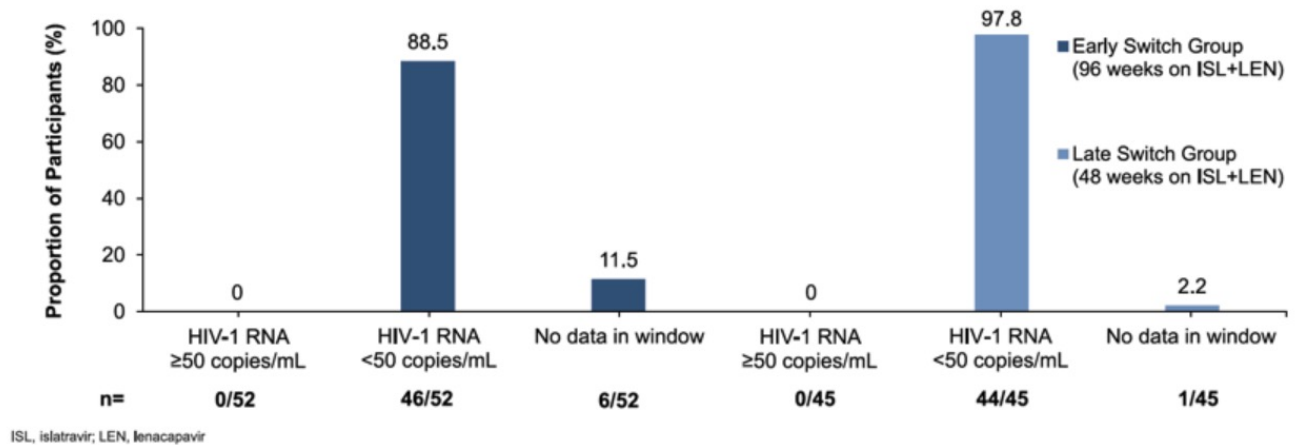
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- Proportion with HIV-1 RNA <50 copies/mL
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Other assessments:

- Change in BMI, body weight, and adherence by pill count

Figure 2. Study Week 96 Virologic Outcomes for Early Switch Group and Late Switch Group

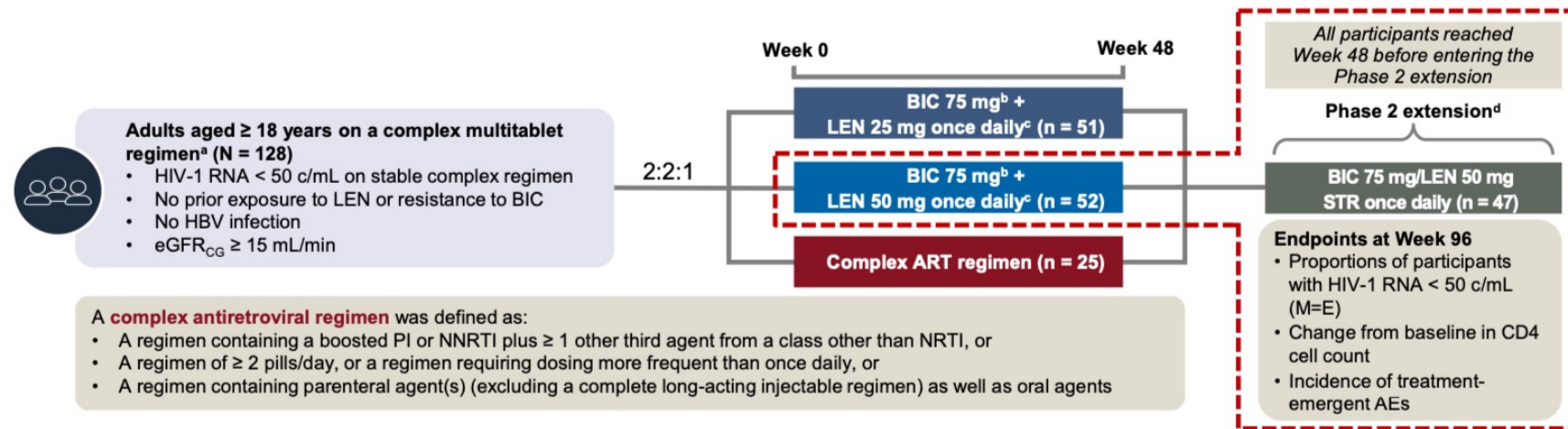


Conclusions

- All participants receiving once-weekly oral islatravir (ISL) + lenacapavir (LEN) maintained virologic suppression at study Week 96
 - No participant in either group had HIV-1 RNA ≥50 copies/mL at study discontinuation
 - No emergent resistance to ISL or LEN was detected
- Once-weekly oral ISL+LEN was well tolerated; no Grade ≥3 adverse events (AEs), serious AEs, or AEs leading to study drug discontinuation were related to ISL+LEN
- CD4+ T-cell counts and lymphocyte counts remained stable in both groups
- These results support ISL+LEN as a potential first, once-weekly complete oral HIV-1 treatment regimen
- Two ongoing Phase 3 studies (ISLEND-1, NCT06630286; ISLEND-2, NCT06630299) are investigating an ISL/LEN fixed-dose combination in virologically suppressed people with HIV-1 (PWH)

[Switch] ARTISTRY-1: BIC/LEN^{Oral} 96 Week Data

Study Design of the Phase 2 Portion of the Phase 2/3 ARTISTRY-1 Trial



^aDue to viral resistance, intolerance, or contraindication to existing STRs. ^bBIC 75 mg single agent provides exposure consistent with BIC 50 mg as part of B/F/TAF. ^cAll participants taking BIC + LEN took an oral loading dose of LEN 600 mg on Days 1 and 2 of treatment. ^dParticipants who switched from a complex ART regimen in the extension phase took the oral loading doses of LEN. AE, adverse event; ART, antiretroviral therapy; BIC, bictegravir; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; c, copies; CD4, cluster of differentiation 4; eGFR_{CG}, estimated glomerular filtration rate by Cockcroft-Gault equation; HBV, hepatitis B virus; LEN, lenacapavir; PI, protease inhibitor; M = E, missing = excluded; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; STR, single-tablet regimen.

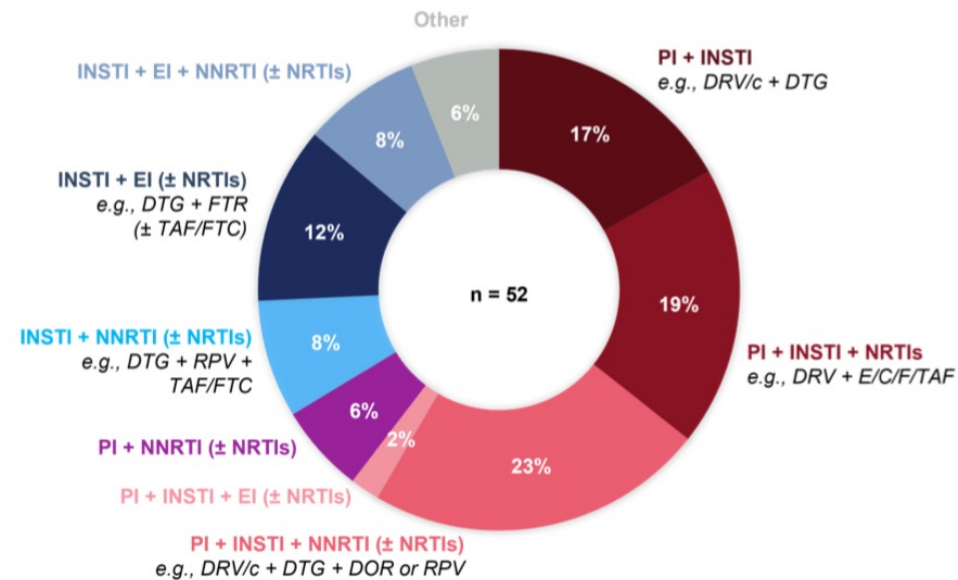
- ARTISTRY-1 (NCT05502341) is an ongoing, randomized, open-label, multicenter, active-controlled Phase 2/3 trial
- Participants who reached Week 48 and completed the end of randomized treatment visit were invited to enter the extension period and took a once-daily STR of BIC 75 mg/LEN 50 mg
- This analysis includes data from all participants originally randomized to take BIC 75 mg + LEN 50 mg, who either discontinued the study during the randomized period or continued into the extension

[Switch] ARTISTRY-1: BIC/LEN^{Oral}

96 Week Data

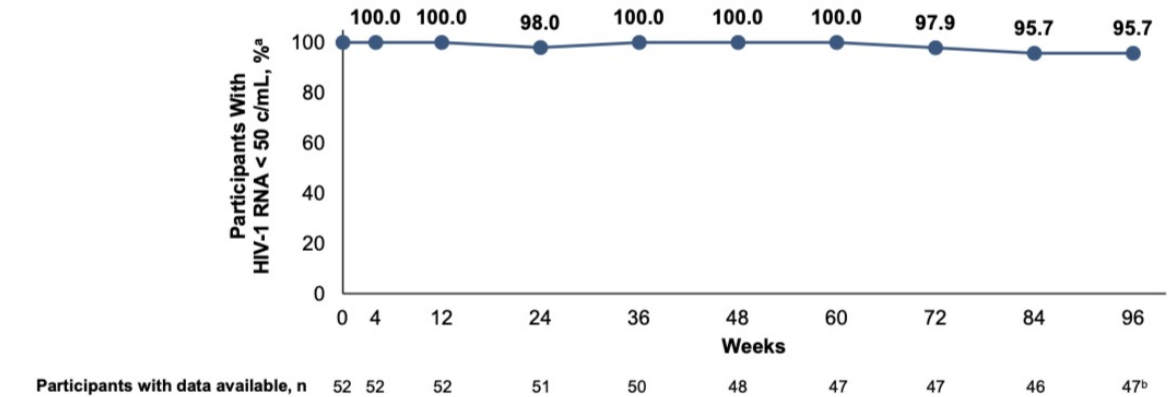
- Overall, 52 PWH were originally randomized to take BIC 75 mg + LEN 50 mg once daily
 - Of these, 5 discontinued during the randomized period, and 47 entered the extension period and took BIC 75 mg/LEN 50 mg STR once daily

Complexity of ART Regimens in Participants Randomized to BIC 75 mg + LEN 50 mg in Phase 2



71% of participants were on a PI, and of those, 62% were taking a PI + INSTI

Virologic Outcomes Through Week 96 (M = E)

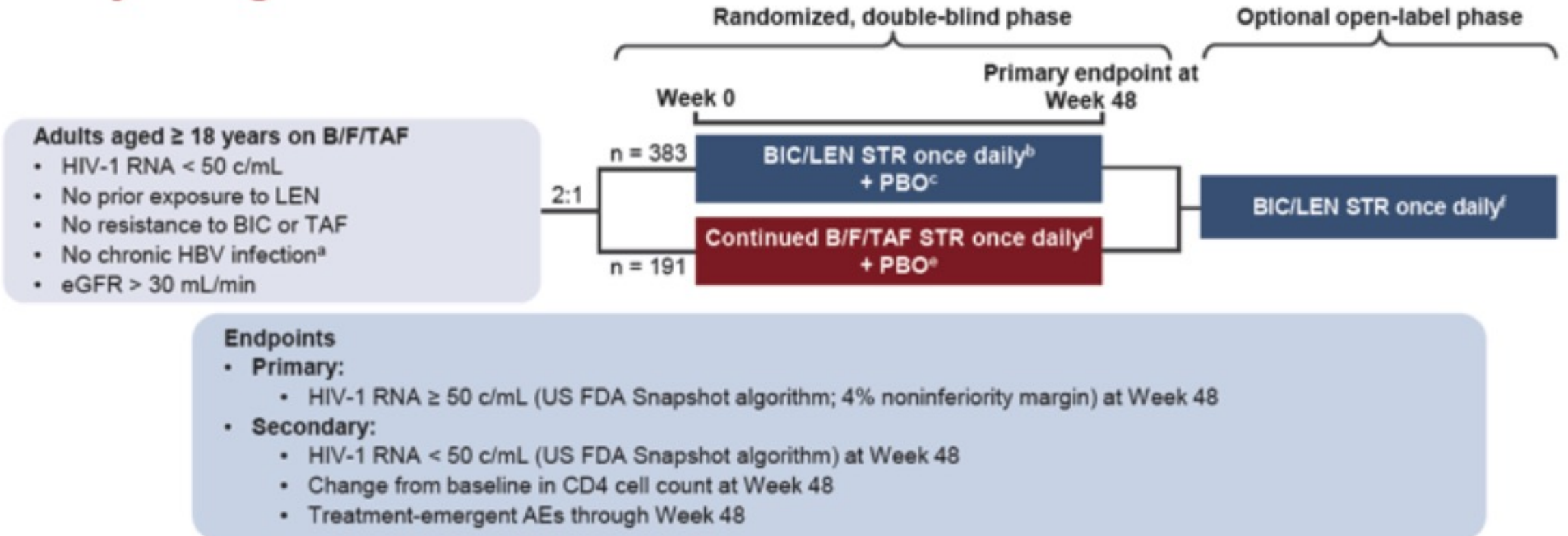


Conclusions

- In Phase 2 of the Phase 2/3 ARTISTRY-1 trial, bicitgravir (BIC) and lenacapavir (LEN) maintained high levels of virologic suppression after a longer-term follow-up of 96 weeks in people with HIV (PWH) who switched from complex regimen (CR)
- BIC + LEN and BIC/LEN single-tablet regimen (STR) were generally well tolerated
- These findings support continued evaluation of the combination of BIC and LEN to optimize treatment in PWH with virologic suppression on a CR
- A BIC/LEN STR is being assessed in Phase 3 of ARTISTRY-1 and in ARTISTRY-2

[Switch] ARTISTRY-2: BIC/LEN^{Oral} vs BFTAF

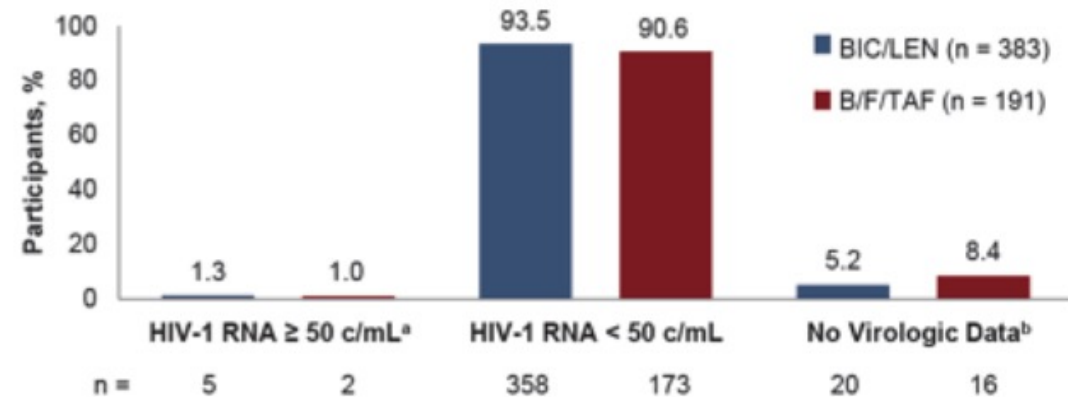
Study Design of ARTISTRY-2



[Switch] ARTISTRY-2: BIC/LEN^{Oral} vs BFTAF

Virologic Outcomes at Week 48 (US FDA Snapshot Analysis)

Virologic Outcome at Week 48



^aDiscontinued study drug due to other reasons and last available HIV-1 RNA was ≥ 50 c/mL: BIC/LEN n = 3, B/F/TAF n = 2. ^bDiscontinued study drug due to adverse event or death: BIC/LEN n = 6, B/F/TAF n = 4; discontinued study drug due to other reasons and last available HIV-1 RNA was < 50 c/mL: BIC/LEN n = 14, B/F/TAF n = 12. ^cDifference in percentages of participants between treatment groups (BIC/LEN minus B/F/TAF) and two-sided CIs were constructed based on Mantel-Haenszel stratum weights and Koch variance estimator and adjusted by geographic region (US vs non-US). BIC, bictegravir; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; c, copies; FDA, Food and Drug Administration; LEN, lenacapavir.

Post-Baseline Resistance Analyses

- Two participants on BIC/LEN and two participants on B/F/TAF underwent resistance analysis
- Of these, one participant on BIC/LEN and both participants on B/F/TAF had no treatment-emergent resistance through Week 48
- One participant on BIC/LEN had an isolated R263K integrase substitution at Week 36
 - This participant had a history of prior exposure to raltegravir and dolutegravir
 - The R263K isolate remained phenotypically susceptible to BIC
 - No capsid mutations were detected

- In the BIC/LEN group, four of five participants with HIV-1 RNA ≥ 50 copies (c)/mL at Week 48 had low-level viremia (HIV-1 RNA < 1000 c/mL)
- One participant in the BIC/LEN group had HIV-1 RNA 10,700 c/mL at Week 48 and resuppressed following change to a protease inhibitor-containing regimen

[Switch] EMBRACE - N6LS (LVB)^{IV} or SC q4M/CAB^{IM} q1M vs SOC

Maintenance of HIV Suppression at 12 Months With Lotivibart (VH3810109, N6LS) Q4M + CAB LA QM: The EMBRACE Study

Charlotte-Paige Rolle, MD, MPH¹; Anne Luetkemeyer, MD²; Christopher Bettacchi, MD³; William Towner, MD⁴; Peter Leone, MD⁵; Margaret Gartland, MSc⁶; Paul Wannamaker, BA⁶; Rulan Griesel, PhD⁶; Michael Warwick-Sanders, BM, BSc⁷; Riccardo D'Agostino, PhD⁷; David Dorey, MMath⁸; Kathryn Brown, PhD⁹; Christina Donatti, PsyD⁶; Sherene Min, MD, MPH⁵; Jan Losos, PhD⁵

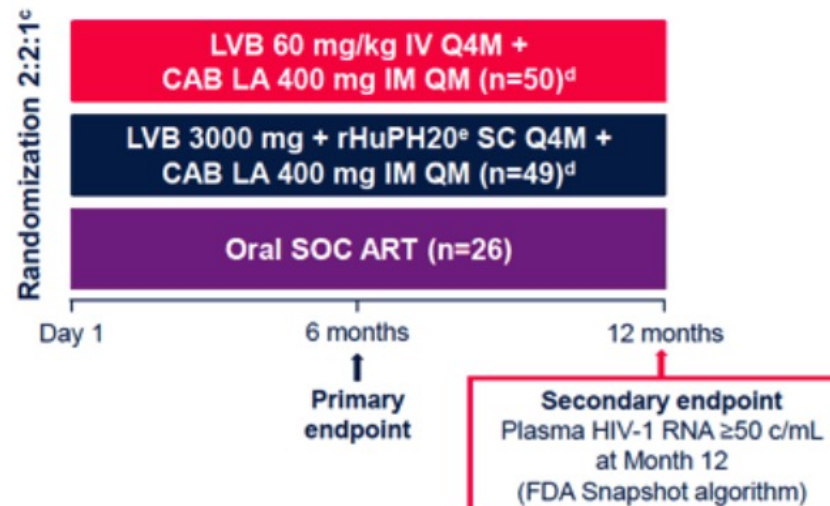
- Lotivibart (LVB; VH3810109, N6LS) is a broadly neutralizing CD4-binding site antibody in development for ULA HIV-1 treatment
- Part 1 of the EMBRACE study evaluated efficacy, safety, and tolerability of LVB Q4M + monthly intramuscular CAB LA to maintain HIV-1 suppression
 - At Month 6, LVB IV and SC maintained virologic suppression in 96% and 88% of participants with baseline LVB sensitivity, respectively; IV showed more favorable safety and tolerability
- Here, we present 12-month efficacy, safety, tolerability, and participant-reported outcome results from a planned interim analysis of EMBRACE part 1

Study Design

Randomized, open-label, multicenter, phase 2b study conducted at 45 sites in the United States and Puerto Rico

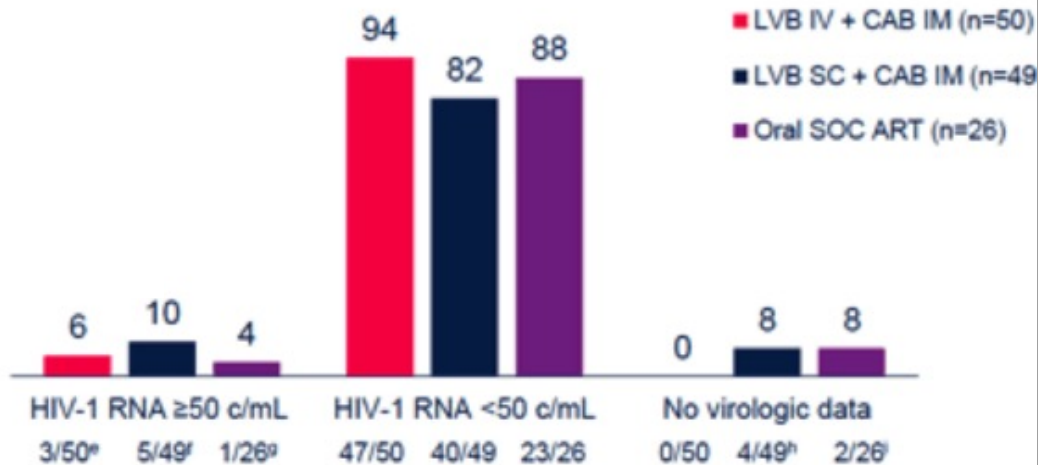
Key inclusion/exclusion criteria

- Aged 18-70 years
- On stable ART for ≥6 months
- ≥2 HIV-1 RNA measurements <50 c/mL in the 12 months before screening
- Phenotypic sensitivity to LVB (IC₉₀ ≤2.0 µg/mL and MPI >98%)^a
- No prior ART switch due to VF
- CD4+ cell count ≥350 cells/mm³
- No active HBV co-infection^b



[Switch] EMBRACE - N6LS (LVB)^{IV} or SC q4M/CAB^{IM} q1M vs SOC

Efficacy at Month 12 (FDA Snapshot, full analysis set)



No Participants in the LVB IV Group Met CVF Between Months 6 and 12

Parameter	LVB IV + CAB IM (n=50)		LVB SC + CAB IM (n=49)		Participant 3	Oral SOC ART (n=26)
	Participant 1	Participant 2	Participant 1	Participant 2		Participant 1 ^a
Baseline LVB IC ₉₀ , µg/mL	1.26	0.60	0.80	0.94	1.26	—
Baseline INSTI RAMs	None	None	None	None	None	None
Time of rebound	Month 3	Month 6	Month 3	Month 1 ^e	Month 12	Month 9
HIV-1 RNA at CVF, c/mL	1810	3200	363,000	1290	114,000	214
LVB IC ₉₀ at CVF, µg/mL ^b	>50	3.34	1.08 ^c	0.66 ^f	11.98	—
CAB RAMs at CVF ^b	None	None	Q148R ^d	None	T97A, N155H	L74I ^g
CAB fold-change at CVF ^b	0.52	1.34	2.17	1.33	2.60	0.58

- LVB SC group: 2 participants met CVF by Month 6; there was 1 additional CVF by Month 12
- No participants in the LVB IV group and 2 participants in the LVB SC group had CAB RAMs at CVF
- 3/5 participants in LVB groups had baseline LVB IC₉₀ ≤1 µg/mL; phenotypic sensitivity alone does not explain CVF
- 3/5 participants developed reduced sensitivity to LVB at CVF (IV, n=2; SC, n=1)

Conclusions

At 12 months, LVB with CAB LA maintained virologic suppression, demonstrating durable efficacy in an adult population with baseline LVB sensitivity

- LVB IV demonstrated a more favorable safety and tolerability profile than LVB SC
 - No new safety signals or additional AEs were identified between Month 6 and Month 12
- These findings support the continued evaluation of LVB IV Q6M with CAB LA IM Q2M in part 2 of EMBRACE, which is fully enrolled
- LVB is part of ViiV Healthcare's broader efforts to develop innovative ultra-long-acting therapies that address the diverse needs of people affected by HIV and transform HIV care

[Switch] LEN-TAB-ZAB^{q6m} 52 Week Resistance Data

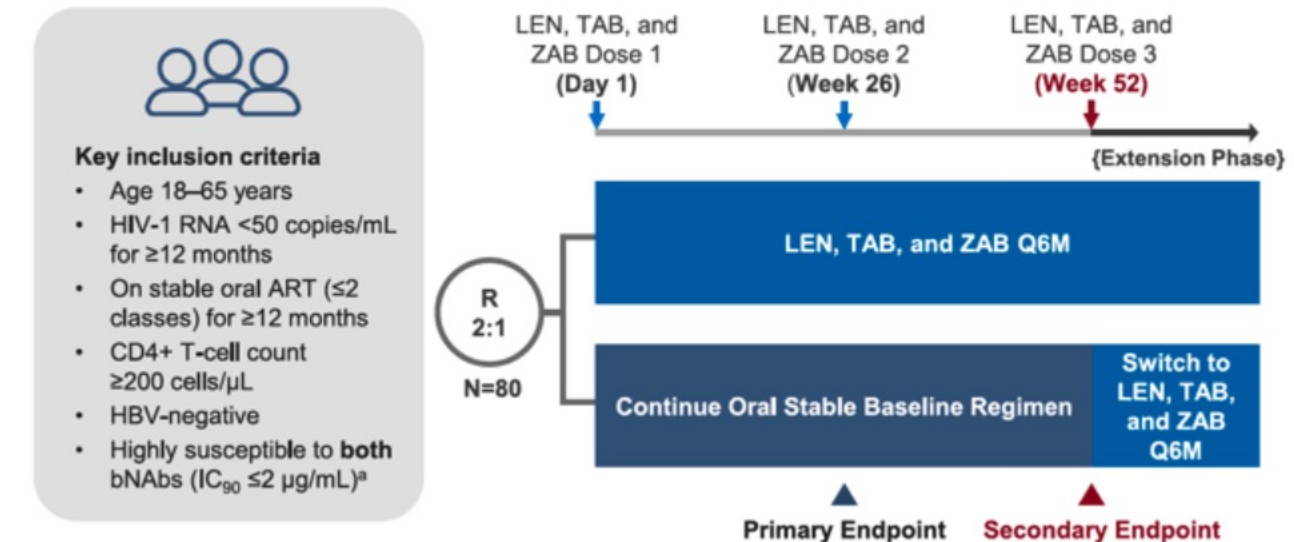
Laurie A. VanderVeen^{1*}, Lisa Selzer¹, Yu Hu¹, Jiani Li¹, Ross Martin¹, Nan Zhang¹, Kwad Mponponsuo¹, Joseph Eron², Sean E. Collins¹, Christian Callebaut¹

¹Gilead Sciences, Inc., Foster City, CA, USA; ²University of North Carolina, Chapel Hill, NC, USA

*Presenting author

- LEN, the first-in-class HIV-1 capsid inhibitor, is approved for the treatment of multidrug-resistant HIV-1 and for HIV-1 prevention, and can be administered subcutaneously twice yearly⁵⁻⁷
- TAB (3BNC117-LS, GS-5423) and ZAB (10-1074-LS, GS-2872) are bNAbs that target the HIV envelope (ENV) and can also be dosed twice yearly⁸
 - TAB targets the CD4-binding site while ZAB targets the V3 glycan on the HIV-1 ENV⁸
- In a Phase 2, ongoing, open-label study (NCT05729568; **Figure 1**), LEN, TAB, and ZAB are being investigated in combination as a twice-yearly treatment for HIV-1
 - Twice-yearly LEN, TAB, and ZAB maintained virological suppression (HIV-1 RNA <50 copies/mL) in 96% and 89% of participants with HIV-1 highly susceptible to both bNAbs at Weeks 26 and 52, respectively (**Figure 2**)^{1,2}

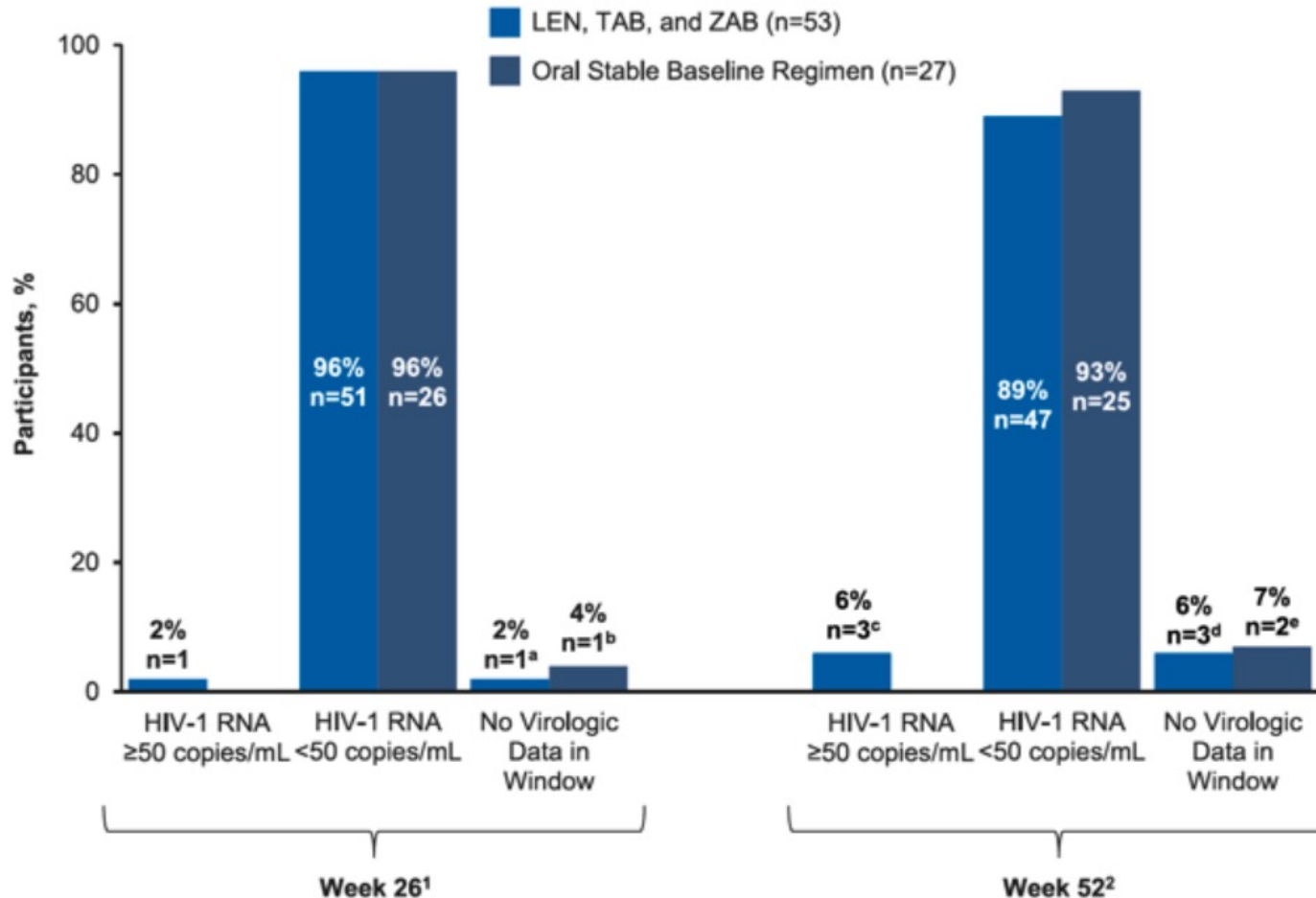
Figure 1. Phase 2 Study Design



^aBy PhenoSense® HIV mAb Assay (Monogram Biosciences).
ART, antiretroviral therapy; bNAb, broadly neutralizing antibody; HBV, hepatitis B virus; IC₉₀, 90% inhibitory concentration; LEN, lenacapavir; mAb, monoclonal antibody; Q6M, every 6 months; R, randomized; TAB, teropavimab; ZAB, zinlirvimab.

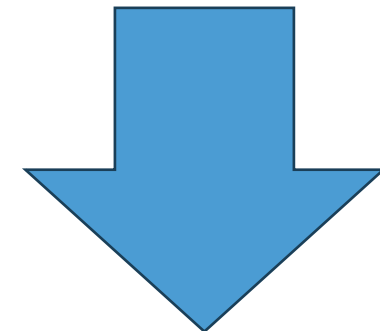
[Switch] LEN-TAB-ZAB^{q6m} 52 Week Resistance Data

Figure 2. Virologic Outcomes by US FDA Snapshot Algorithm at Weeks 26 and 52



On-Treatment (Post-Baseline thru Week 52) Analysis

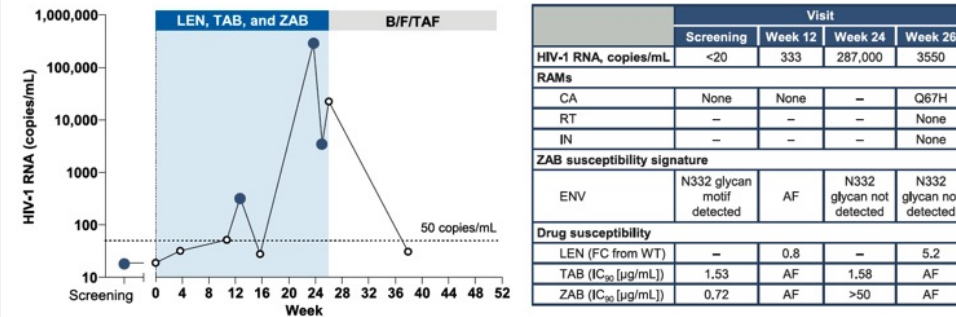
3 participants (5.7%) in the LEN, TAB, ZAB arm and 0 in the SBR arm met resistance analysis criteria



Relative Exposures to LEN, TAB, and ZAB Through Week 52

- Exposures of LEN (Figure 8A), TAB (Figure 8B), and ZAB (Figure 8C) in the three participants with virologic rebound were relatively lower than the study population median; however, they still fell within the range observed in participants who remained virologically suppressed

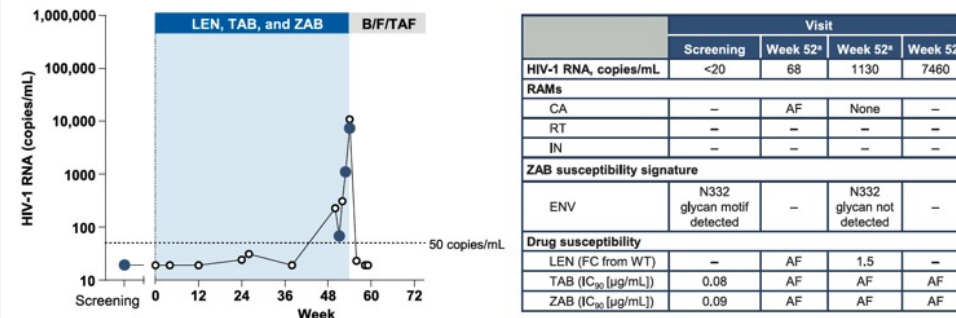
Figure 4. Virologic Analysis of Participant 1



“—” = not tested. Blue circles indicate resistance testing visits. AF, assay failure; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; CA, capsid; ENV, envelope; FC, fold change; IC₉₀, 90% inhibitory concentration; IN, integrase; LEN, lenacapavir; RAM, resistance-associated mutation; RT, reverse transcriptase; TAB, teropavimab; WT, wild-type; ZAB, zinlirvimab.

- Participant 1 developed LEN resistance (Q67H) and resistance to ZAB (IC₉₀ >50 μg/mL) at Week 24
- This participant had rapid HIV-1 RNA suppression after switching to oral bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF)

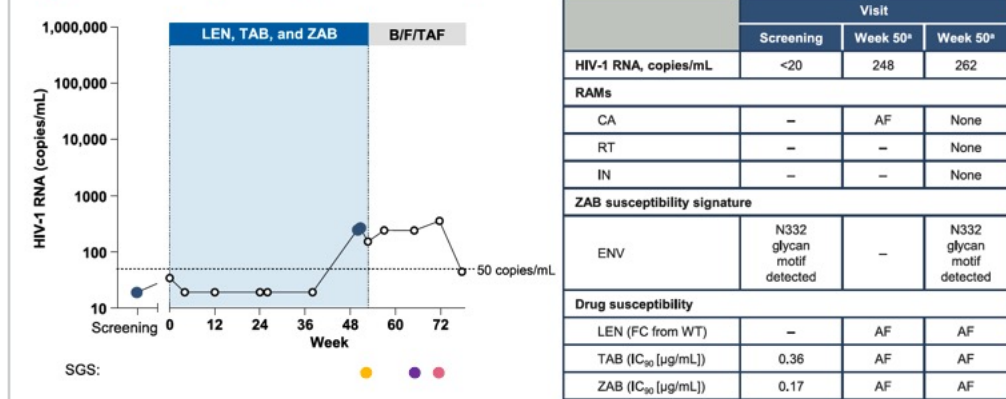
Figure 5. Virologic Analysis of Participant 2



“—” = not tested. *These were re-tests for virologic rebound confirmation as per protocol. Blue circles indicate resistance testing visits. AF, assay failure; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; CA, capsid; ENV, envelope; FC, fold change; IC₉₀, 90% inhibitory concentration; IN, integrase; LEN, lenacapavir; RAM, resistance-associated mutation; RT, reverse transcriptase; TAB, teropavimab; WT, wild-type; ZAB, zinlirvimab.

- Participant 2 had predicted loss of ZAB susceptibility at Week 52 without LEN resistance
- This participant had rapid HIV-1 RNA suppression after switching to oral B/F/TAF

Figure 6. Virologic Analysis of Participant 3



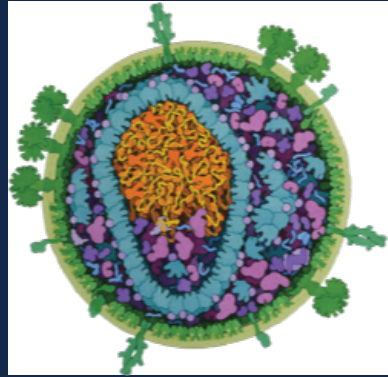
“—” = not tested. *These were re-tests for virologic rebound confirmation as per protocol. Blue circles indicate resistance testing visits. AF, assay failure; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; CA, capsid; ENV, envelope; FC, fold change; IC₉₀, 90% inhibitory concentration; IN, integrase; LEN, lenacapavir; RAM, resistance-associated mutation; RT, reverse transcriptase; SGS, single-genome sequencing; TAB, teropavimab; WT, wild-type; ZAB, zinlirvimab.

- Participant 3 had persistent low-level viremia after restarting oral B/F/TAF with no resistance detected
- This participant resuppressed 180 days following initiation of oral B/F/TAF

Exposures of LEN, TAB, and ZAB in the 3 participants with viral rebound were relatively lower than the study population median but fell within the range observed in participants who remained suppressed

ART Pipeline

- Ultra-Long CAB^{INSTI}
 - Phase I PK data and modelling support Q4M IM
- GS-3242^{INSTI}
 - Next gen INSTI with potential for q4M injectable dosing in pre-clinical study
- VH184^{INSTI}
 - Next gen INSTI with phase I PK data exploring q6M SC dosing
- VH-499^{Capsid Inhibitor}
 - Phase I PK data support Q6M dosing of IM and maybe SC



CROI

Conference on Retroviruses
and Opportunistic Infections

Well-Being

GLP-1 Agonists at CROI

- Weight Loss and lower A₁C Crane H, et al
- Weight, BMI, BP, CVD Risk Lee D, et al
- Liver Fibrosis Ma J, et al
- Subclinical CVD Risk Eckard A, et al
- Smoking Crane H, et al



GLP-1 Agonists at CROI

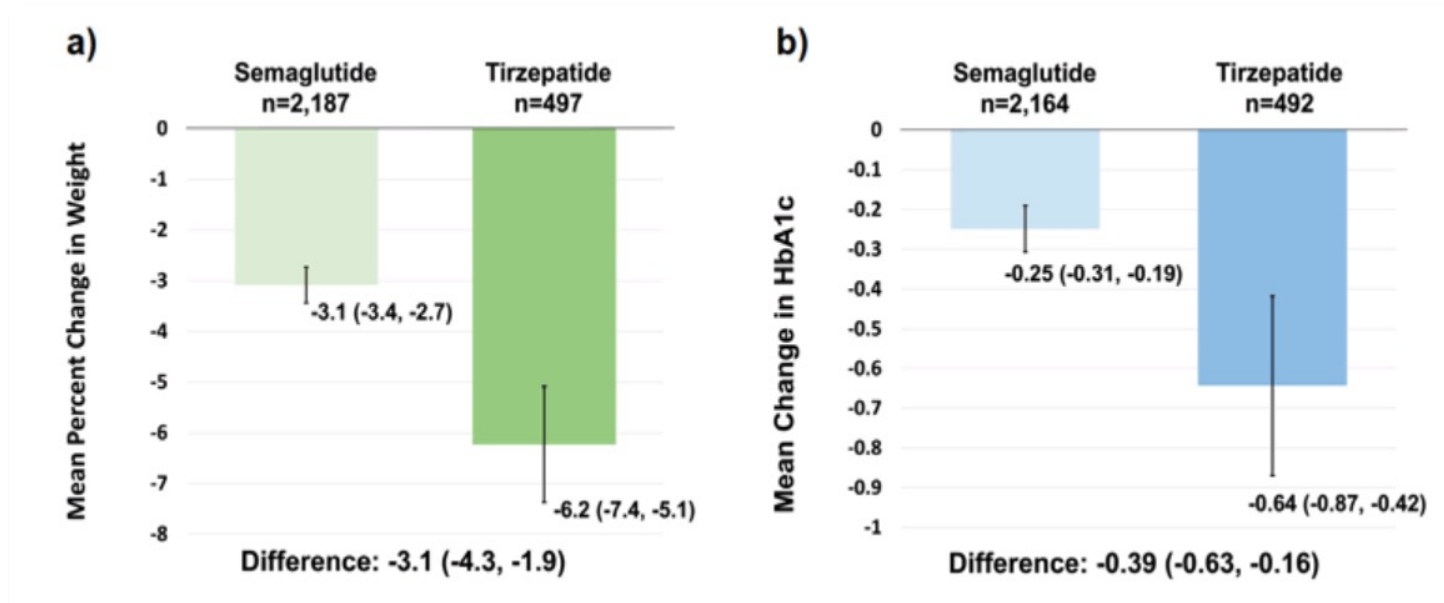
- Weight Loss and lower A₁C Crane H, et al



Setting & Participants
Centers for AIDS Research Network of Integrated Clinical Systems (CNICS) Cohort

CNICS is a 10-site cohort of adult PWH engaged in care at academic clinics across the US

New-users of semaglutide or tirzepatide were included in this study



GLP-1 Agonists at CROI

- Weight, BMI, BP, CVD Risk^{Lee D, et al}

- 61 PWH were prescribed tirzepatide (22 had concurrent diabetes [PWH/D], 39 did not have diabetes [PWH/nD])
- 26.2% (16/61) of PWH discontinued tirzepatide prior to 1 year: GI side effects (3), non-GI side effects (3), supply issues (2), insurance issues (7), lack of efficacy (1)

Tirzepatide use in PWH led to statistically significant reductions in body weight, BMI, systolic blood pressure, A1C, and 10-year ASCVD risk scores. However, 26.2% (16/61) of PWH discontinued tirzepatide prior to 1 year due to insurance/supply-related challenges.

CONCLUSIONS

1. PWH who initiated tirzepatide (whether for obesity or for DM) lost mean weight of ~14.5 kg (31.9 lbs) or 13.8% of their baseline total body weight at 12 months
2. This degree of weight loss is slightly less than that seen in people without HIV – 17% weight loss at 12 months [5]
3. As expected, PWH/nD lost more weight than PWH/D
4. Statistically significant reductions were seen in BMI, A1C, SBP with significant increase in HDL; all improvements likely contributed to lowering 10-Year ASCVD risk scores
5. Unfortunately, ~26.2% of PWH discontinued tirzepatide prior to the end of 12 months due to a combination of side effects, insurance and supply-related challenges

GLP-1 Agonists at CROI

- Liver Fibrosis^{Ma J, et al}

METHODS

- Setting:** 10 geographically diverse sites of the CFAR Network of Integrated Clinical Systems (CNICS) cohort⁴
- Inclusion:** all adult PWH initiating semaglutide for diabetes and/or weight loss with data for FIB-4 calculations (4/2018 – 11/2024)

Table 3. Change in FIB-4 after semaglutide initiation^a in PWH with moderate-to-advanced fibrosis using adjusted^a linear mixed models with *a priori* stratifications.

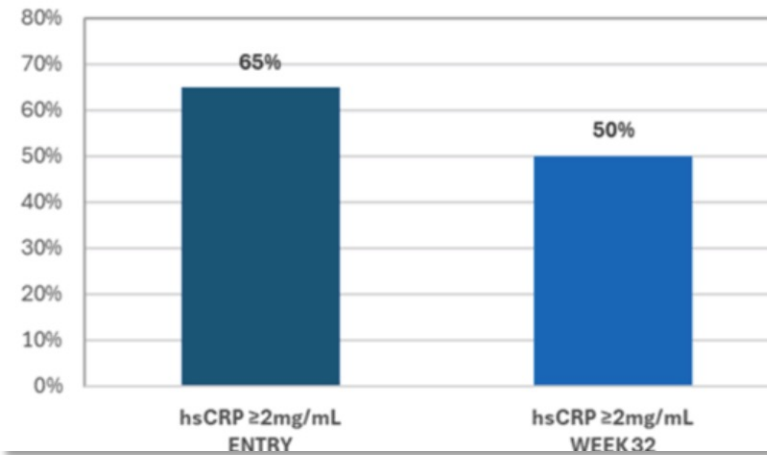
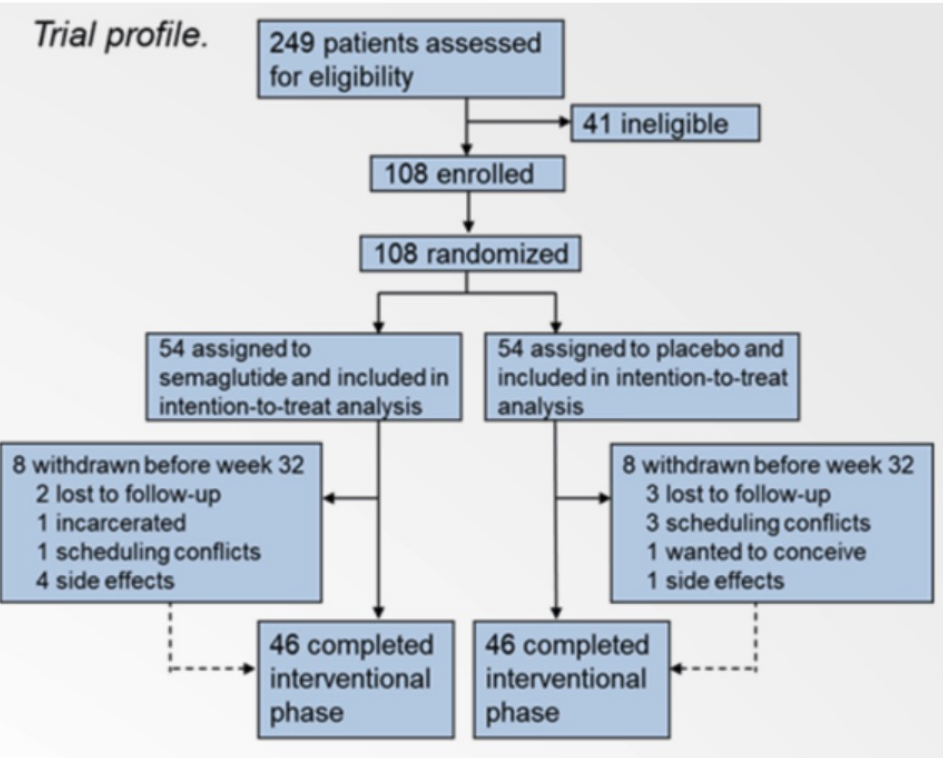
Baseline Stratum in PWH with Moderate-to-Advanced Fibrosis		N	# Obs	ΔFIB-4	95% CI	P
Hepatitis B	No HBV	434	4,945	-0.13	-0.20, -0.06	<0.001
	HBV	48	765	0.03	-0.18, 0.23	0.8
Hepatitis C	No HCV	374	4,146	-0.13	-0.20, -0.05	<0.01
	HCV	108	1,564	-0.07	-0.22, 0.07	0.3
Recent Alcohol Use ^b	No Alcohol Use	149	2,043	-0.08	-0.18, 0.02	0.11
	Any Alcohol Use	168	1,682	-0.06	-0.18, 0.05	0.3
	Hazardous Use	59	525	-0.14	-0.37, 0.09	0.2
Semaglutide Dose ^c	Low dose	284	3,124	-0.16	-0.25, -0.07	<0.001
	High dose	46	695	-0.21	-0.43, 0.01	0.06
	Unknown dose	152	1,891	-0.01	-0.13, 0.11	0.9

Semaglutide was associated with reductions in FIB-4 score in moderate-to-advanced liver fibrosis with the greatest declines in advanced fibrosis.

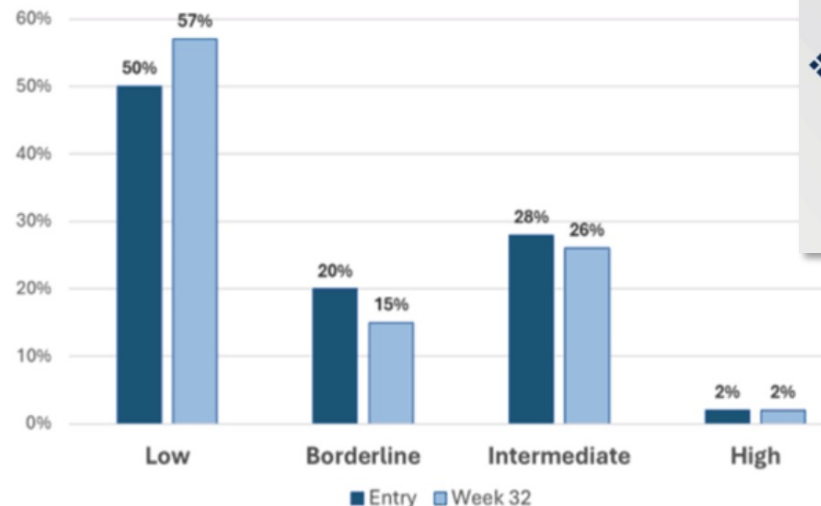
GLP-1 Agonists at CROI

- Subclinical CVD Risk^{Eckard A, et al}

Trial profile.



% of Participants in the Semaglutide Group by 10-Year ASCVD Risk Category at Entry and Week 32



SUMMARY OF RESULTS

- ❖ In the current analysis, we did not demonstrate any statistically significant effects of semaglutide on measures of subclinical vascular function and calcified atherosclerotic plaque.
- ❖ However, significant effects were seen in 10-year ASCVD risk estimate and hsCRP, both established measures of CVD risk, and a trend toward improved oxygen consumption, a measure of cardiometabolic health.

GLP-1 Agonists at CROI

- Smoking^{Crane H, et al}

METHODS

- *Setting:* Centers for AIDS Research Network of Integrated Clinical Systems (CNICS) Cohort
- CNICS is a 10-site cohort of adult PWH engaged in care at academic clinics across the United States
- *Observation Period:* 04/2018-03/2025
- *Participants:* PWH who self-reported ongoing cigarette use at the time of semaglutide initiation for weight or diabetes management

Outcome: Change in smoking intensity (cigarettes per day) from pre-initiation to post-initiation of semaglutide

RESULTS

204 PWH reported smoking at semaglutide initiation



76% male
24% female

Mean smoking:
10.5 cigs/day
9.3 pack-years



Mean age:
51 years (± 10)



Mean time on SG:
375 days (± 327)

78% had BMI ≥ 30
55% had diabetes
69% hypertension



CONCLUSIONS

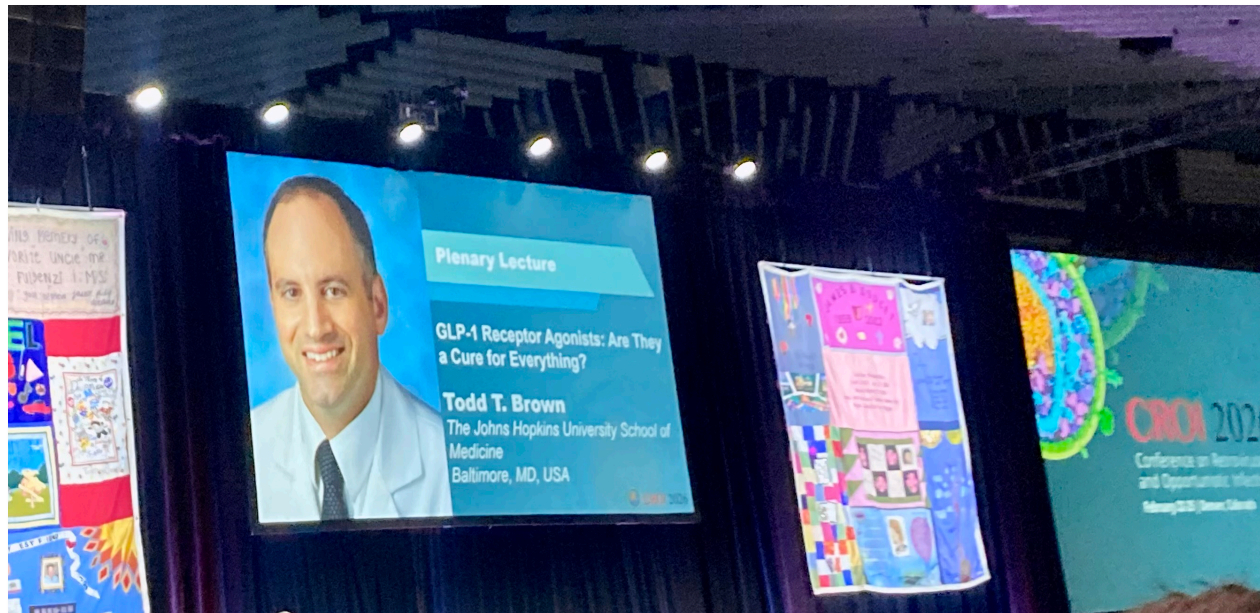
PWH reduced their smoking intensity by 2.7 cigarettes per day, or 26%, after initiating semaglutide for management of weight or diabetes

Findings should be verified over a longer period of time

We confirmed that smoking intensity was stable in this cohort during the control period prior to initiation

Semaglutide may result in additional benefit to overall health in PWH

GLP-1 Agonists at CROI



GLP-1 Receptor Agonists: Are They a Cure for Everything?

Is our exuberance rational or irrational?

Todd T. Brown, MD, PhD
Professor of Medicine and Epidemiology
Division of Endocrinology, Diabetes, & Metabolism
Johns Hopkins University
Baltimore, Maryland, USA

GLP-1 Agonists at CROI

GLP1RA for Obesity-related Conditions

Condition	Efficacy	FDA approval	Comments
CVD	↓ 20% MACE (SELECT)	Semaglutide	Secondary Prevention
Heart Failure	↑ 13% Clin Summary Score ↓ 40% HF Events		Preserved Ejection Fraction
MASH	↓ 29% Steatohepatitis Resolution ↓ 14% Fibrosis	Semaglutide	
Sleep Apnea	↓ 64% sleep apnea events (apnea-hypopnea index)	Tirzepatide	
Chronic Kidney Disease	↓ 20% albuminuria ↓ 22% in composite kidney endpoint (FLOW)		FDA approved for diabetic kidney disease (semaglutide)
Knee Osteoarthritis	↓ 21% WOMAC Pain Score		

MACE: Major Adverse Cardiovascular Event; MASH: Metabolic-Dysfunction Associated Steatohepatitis

Kosiborod, NEJM, 2023; Kosiborod, Lancet, 2024; Sanyal NEJM, 2025; Malhorta, NEJM, 2024; Apperloo, Nature Med, 2025

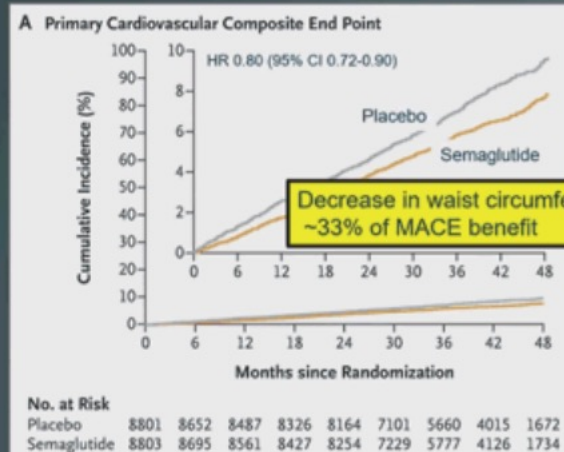
GLP-1 Agonists at CROI

GLP1RA for Obesity-related Conditions

Condi
CVD
Heart Fail
MASH
Sleep Apr
Chronic K
Disease
Knee
Osteoarth
MACE: M

Are CVD benefits of GLP-1 RAs mediated by weight loss? : SELECT Trial

Primary Cardiovascular Endpoint



MACE: CVD death,
non-fatal MI, non-fatal stroke
Deanfield, Lancet 2025

GLP-1 Agonists at CROI

GLP1RA for Obesity-related Conditions

Condi

CVD

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MASH

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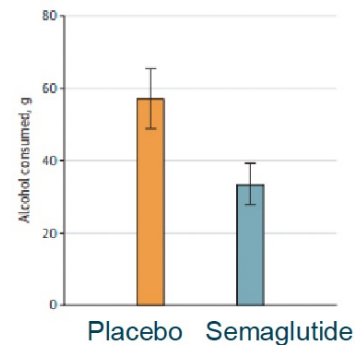
Kosiborod, NE

Deanfield,

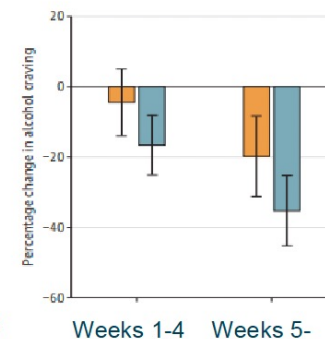
Are CVD benefits of GLP-1 RAs mediated by GLP1 RA in the Treatment of Substance Use Disorders

- GLP-1 receptors found in brain reward areas
- Robust pre-clinical data in animal models of:
 - Alcohol
 - Opioids
 - Nicotine
 - Psychostimulant addictions
- Randomized phase 2 clinical trial evidence emerging
- > 20 RCTs ongoing including three in PWH
 - Cocaine use disorder
 - Alcohol use disorder

Lab self-administration of alcohol (g)



Change from baseline in craving



Weekly Semaglutide in Adults with Alcohol Use Disorder

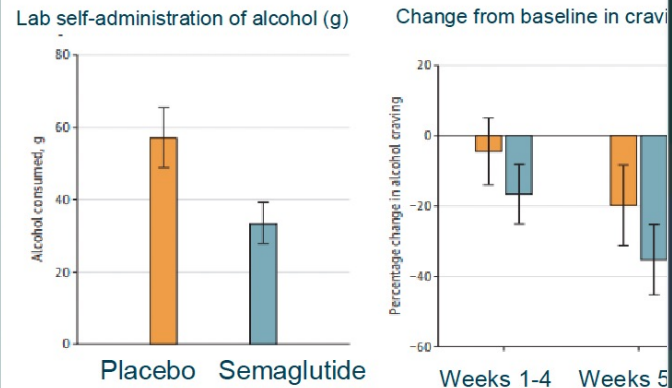
- 9 week randomized, controlled trial in 48 people with AUD
- Weekly Semaglutide: 0.25 mg x 4w; 0.5 mg x 4w
- Lab alcohol self-administration, craving
- Significant decrease in cigarettes/day

GLP-1 Agonists at CROI

GLP1RA for Obesity-related Conditions

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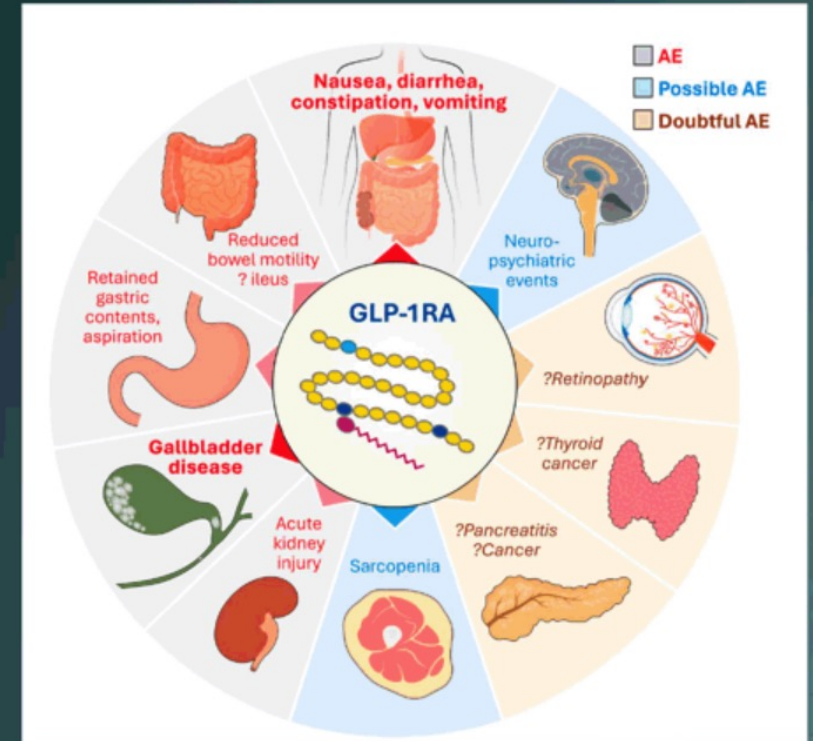
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Srinivasan, J Endo Soc, 2025

Hendershot, JAMA Psychiatry, 2025

CROI 2026

Adverse Effects of GLP1 RAs



GLP-1 Agonists at CROI

GLP1RA for Obesity-related Conditions

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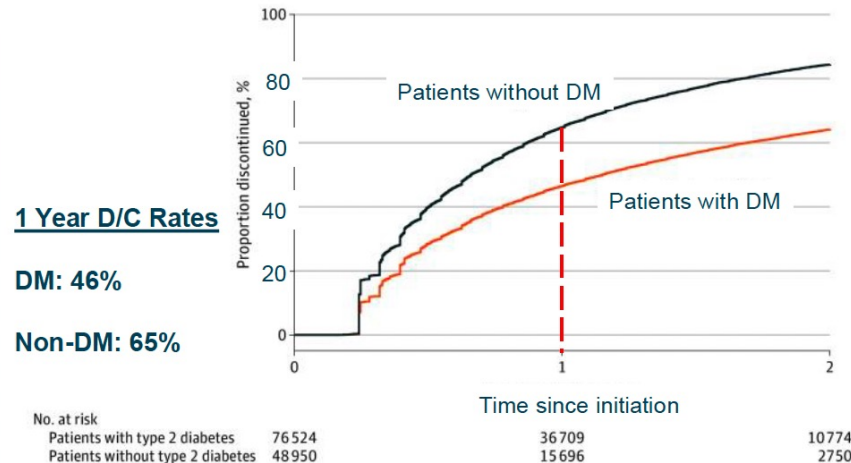
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Srinivasan, J Endo Soc, 2025

Adverse Effects of GLP1 RAs

GLP1 RA Discontinuation Rates

Time to discontinuation of GLP-1 RA



Factors Associated with D/C

- Age ≥ 65 years
- Black race
- Low Income
- Less weight loss
- GI adverse effects

Rodriguez, JAMA Network Open, 2025

n=125, 474 initiated on GLP-1 RA

CROI 2026

GLP-1 Agonists at CROI

GLP1RA for Obesity-related Conditions

Are CVD benefits of GLP-1 RAs mediated by GLP1 RA in the Treatment

- GLP-1 receptors found in brain reward
- Robust pre-clinical data in animal models
 - Alcohol
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- Randomized phase 2 clinical trial evidence emerging
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 - Cocaine use disorder
 - Alcohol use disorder

Srinivasan, J Endo Soc, 2025

Adverse Effects of GLP1 RAs

GLP1 RA Discontinuation Rates

Weight Regain after GLP1 RA Discontinuation

Comparison

Intervention

Pharmacological interventions currently or previously licensed for weight loss

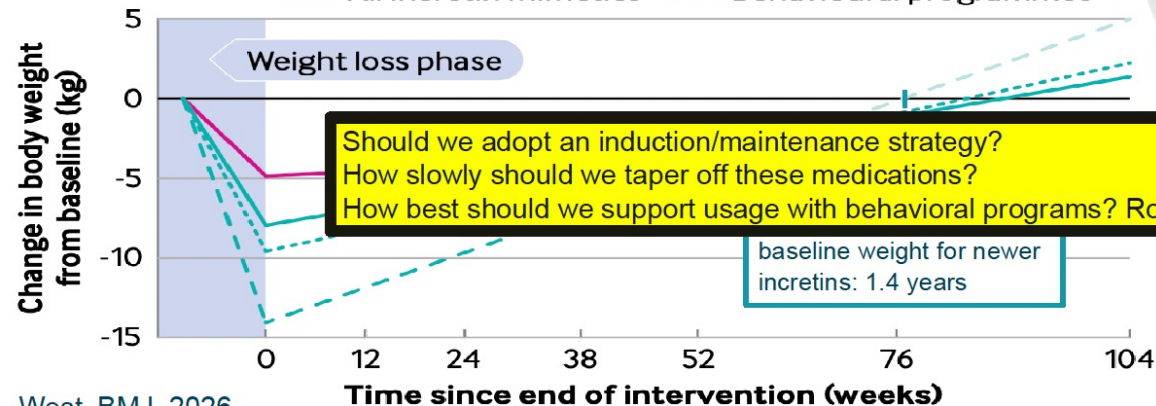
6322

Control

Non-pharmacological weight loss interventions or placebos

3019

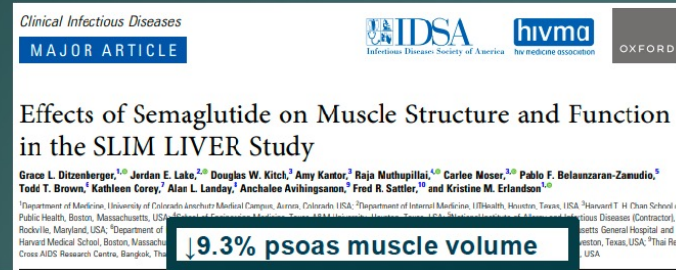
Outcomes



Adverse Effects of GLP1 RAs

GLP1 RA in Older Adults: Loss of Lean Mass

- ## Change in Lean Mass in GLP-1 RA Clinical Trials



Parameter	Baseline	Week 24	Change, Baseline to Week 24 (estimate, 95% CI)	P-value
5x Chair Rise (seconds)	12.5 (3.6)	11.9 (3.3)	-0.66 (-1.4, 0.07)	0.077

Muscle mass clinically relevant in certain populations?
Weight loss matter for muscle mass?
With protein intake and/or resistance training?

Presence of slow gait speed (<1 meters/second)	No: 16 (61%) Yes: 31 (63%)	No: 26 (64%) Yes: 22 (46%)	RR: 0.78 (0.66, 0.91)	0.029
--	-------------------------------	-------------------------------	-----------------------	-------



Time since end of intervention (weeks)

GLP-1 Agonists at CROI

GLP1RA for Obesity-related Conditions

- Condition
- CVD
- Heart Failure
- MASH
- Sleep Apnea
- Chronic Kidney Disease
- Knee Osteoarthritis
- MACE: Major Adverse Cardiovascular Events
- Kosiborod, NEJM

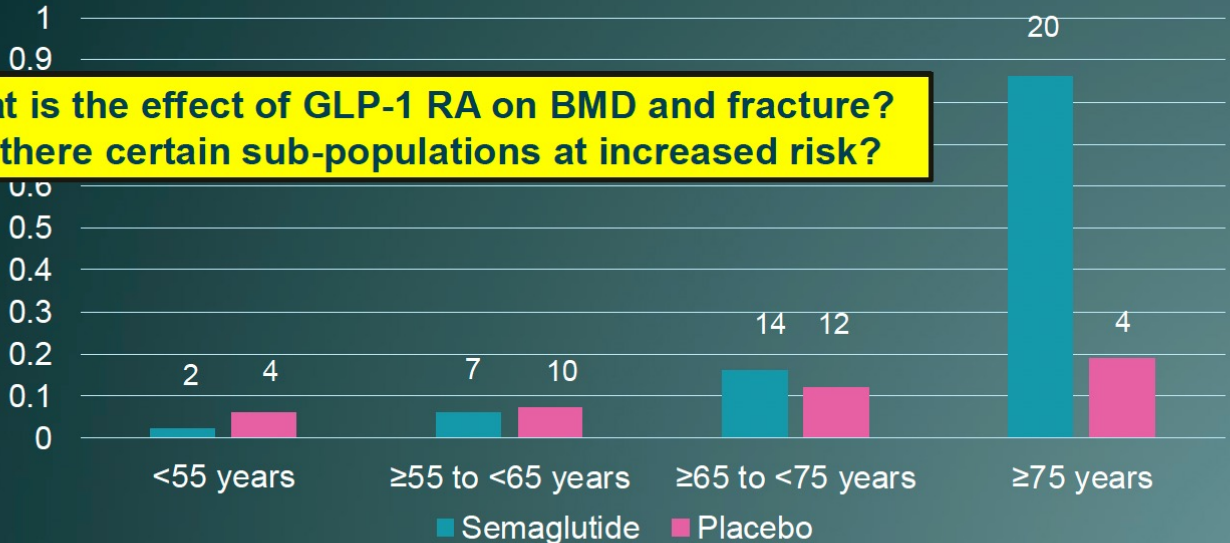
Are CVD benefits of GLP-1 RAs mediated by GLP1 RA

- GLP-1 receptor agonists
- Robust pre-clinical evidence
 - Alcohol
 - Opioids
 - Nicotine
 - Psychosocial
- Randomized clinical trials emerging
- > 20 RCTs
 - Cocaine
 - Alcohol

Adverse Effects of GLP1 RAs

GLP1 RA in Older Adults: Loss of Lean Mass

Rate of Hip/Pelvis Fractures per 100 Person-years in SELECT by Age



Kushner, Obesity, 2025, calculated from Table S5; numbers above columns represent absolute number of events

on

al weight
r placebos

CROI 2024

Week
P-value
0.077

ns?

0.029

AI coaching?

26

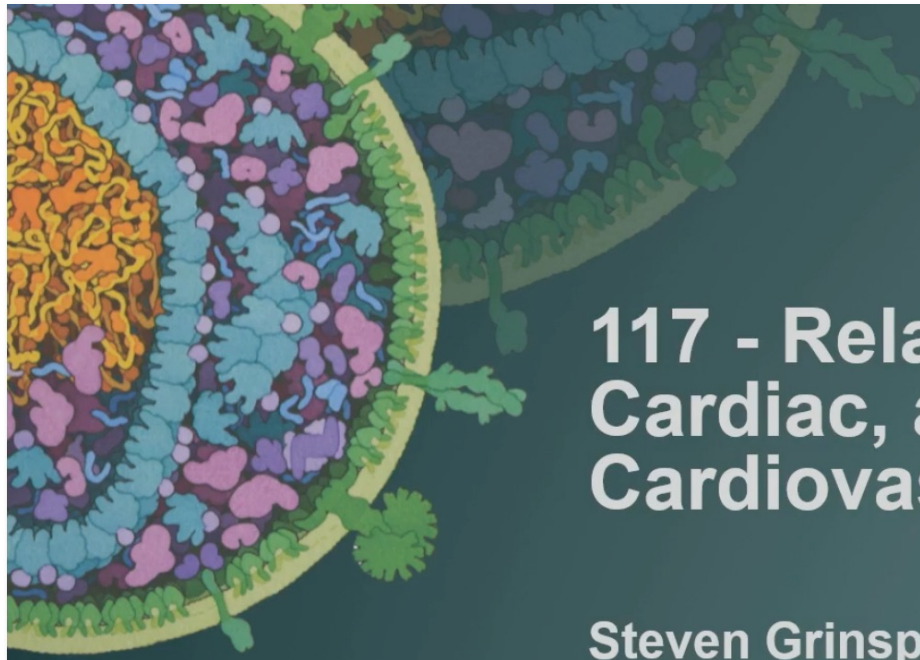
2026

Is our exuberance for GLP-1 RAs rational or irrational?

- This class of medications has transformed the treatment of multiple diseases
- We are only at the beginning of this transformation.
- Data should guide GLP-1 RA use, not enthusiasm
- Global access will be a major challenge that requires careful management.



Predictive Markers for CVD in REPRIEVE



Oral Abstract Session-03

Monday, February 23, 2026

117 - Relationship of Inflammatory, Cardiac, and Lipid Biomarkers to Cardiovascular Events in REPRIEVE

Steven Grinspoon

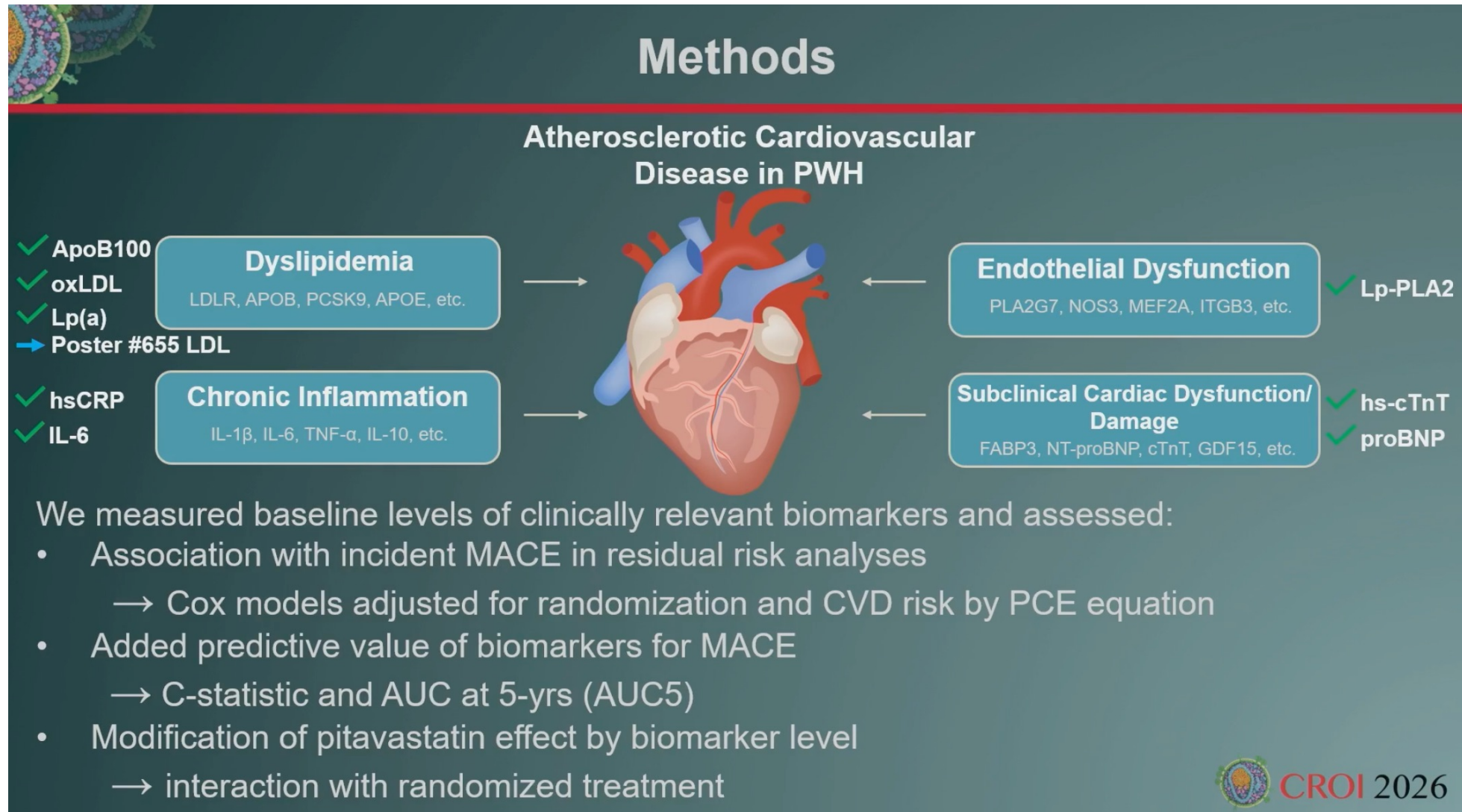
Massachusetts General Hospital, Boston, MA, USA

Financial Relationships:

Dr Grinspoon reported Self: Grants/grants pending with Gilead Sciences, Inc, Kowa Pharmaceuticals America, Inc, and ViiV Healthcare.

CROI 2026

Predictive Markers for CVD in REPRIEVE



Predictive Markers for CVD in REPRIEVE

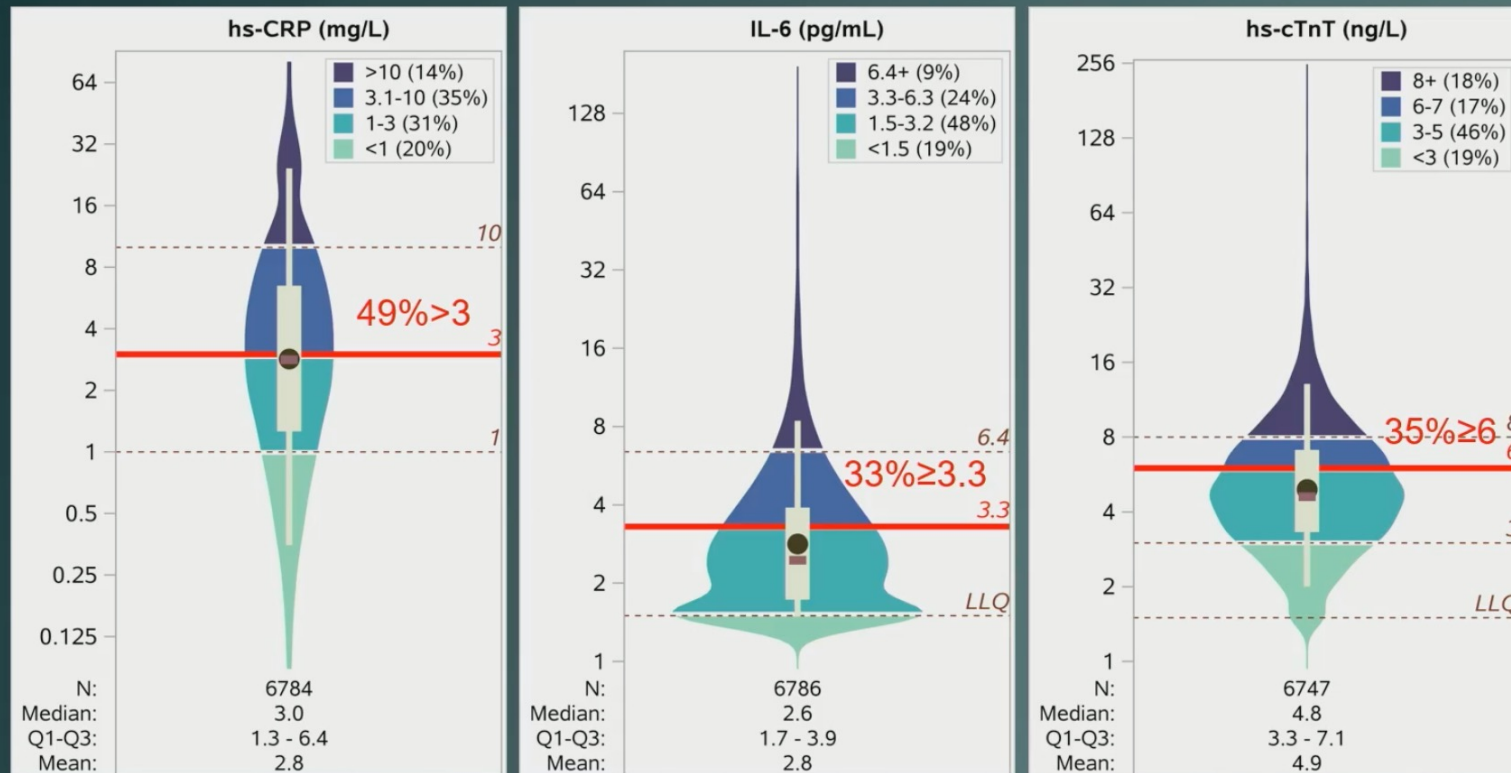
Participant Characteristics

		All (N=7005)	Without MACE (N=6819)	With MACE		
				Pooled Groups (N=186)	Pitavastatin (N=74)	Placebo (N=112)
Natal sex	Male	68%	68%	73%	72%	74%
Age (years)	Median (Q1, Q3)	50 (45, 55)	50 (45, 55)	53 (49, 56)	53 (49, 56)	53 (49, 57)
GBD Super Region	High Income	55%	55%	78%	78%	79%
	Latin Am. and Carib	16%	16%	10%	14%	7%
	S.East/East Asia	8%	8%	5%	4%	5%
	South Asia	4%	4%	4%	1%	6%
	Sub-Saharan Africa	16%	17%	3%	3%	3%
Race	Black or AA	44%	44%	46%	45%	46%
	White	35%	35%	38%	42%	36%
	Asian	13%	13%	9%	5%	12%
PCE risk score (%)	Median (Q1, Q3)	4.5 (2.1, 7.0)	4.4 (2.1, 7.0)	6.4 (4.4, 9.3)	6.3 (3.9, 9.3)	6.7 (4.8, 9.2)
CD4 count (cells/mm³)	Median (Q1, Q3)	455, 834	629 (455, 835)	616 (448, 799)	620 (429, 784)	612 (465, 826)
HIV-1 RNA (copies/mL)	<LLQ	87%	87%	83%	82%	84%
	LLQ -< 400	11%	10%	14%	15%	13%
	400+	2%	2%	3%	3%	3%



Predictive Markers for CVD in REPRIEVE

Increased Inflammation and Subclinical Cardiac Dysfunction in Asymptomatic Low-Moderate Risk ART-treated PWH



— Clinical threshold for elevated values

The estimated probability density function, and mean (circle), median (dash), Q1-Q3 (box) and P5-P95 (whiskers).

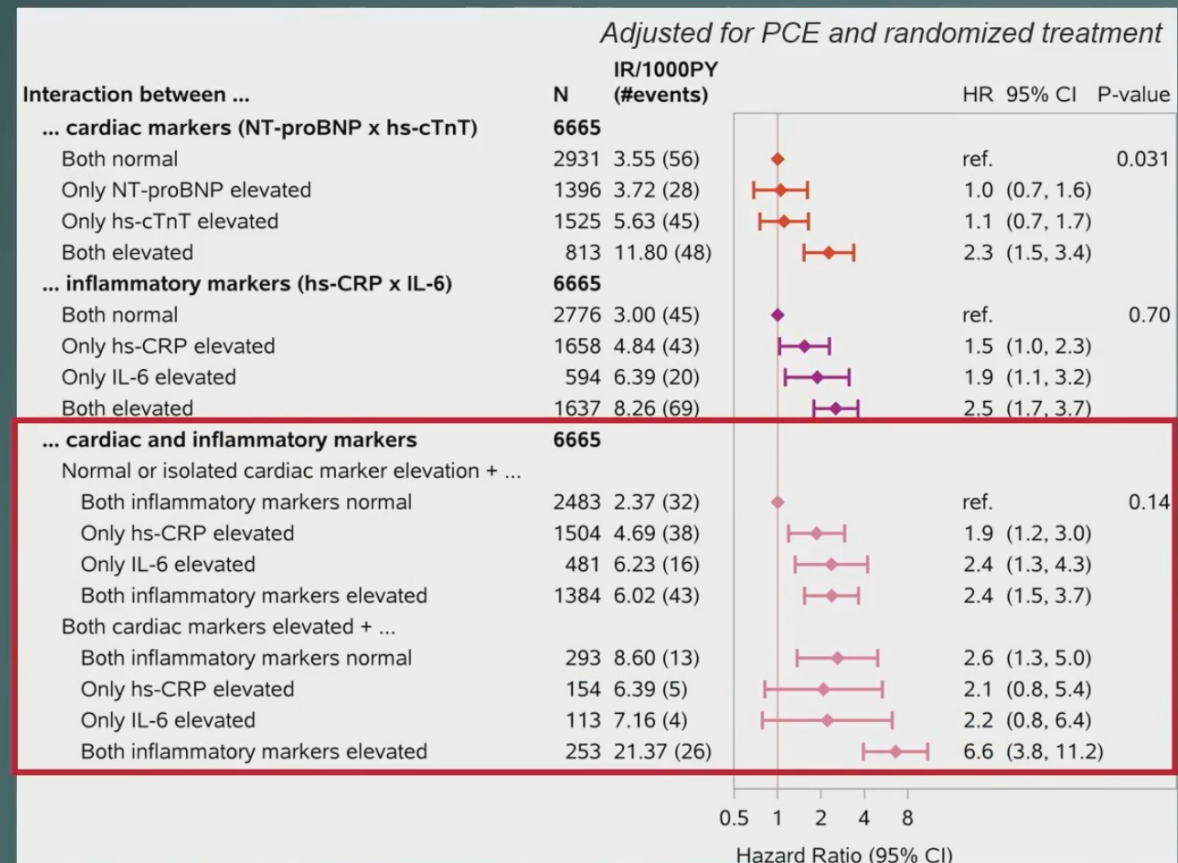


CROI 2026

Predictive Markers for CVD in REPRIEVE

Estimated Effects of Baseline Cardiac and Inflammatory Biomarker Interactions on MACE Hazard (Ad Hoc Analysis)

- Elevations in each inflammatory biomarker alone was associated with a higher hazard of MACE
 - Even higher hazard with elevations in both
- Markedly higher MACE hazard among those with elevations in all cardiac and inflammatory markers
 - Although small numbers





Conclusions and Future Directions

- Asymptomatic PWH with low-moderate traditional cardiovascular risk, well-treated on ART are characterized by inflammation and subclinical cardiac dysfunction
- Inflammatory pathways, particularly IL-6, representing innate immune activation, and subclinical myocardial dysfunction related strongly to MACE in residual risk analyses
- Clinically relevant biomarkers in these pathways used in combination may improve risk prediction for CVD in PWH
- Further research is needed to better understand:
 - Mechanisms by which specific inflammatory and cardiac pathways contribute to MACE
 - Utility of biomarkers from these pathways for HIV specific CVD risk prediction algorithms
 - Role of adjunctive therapies for residual immune activation in combination with statins

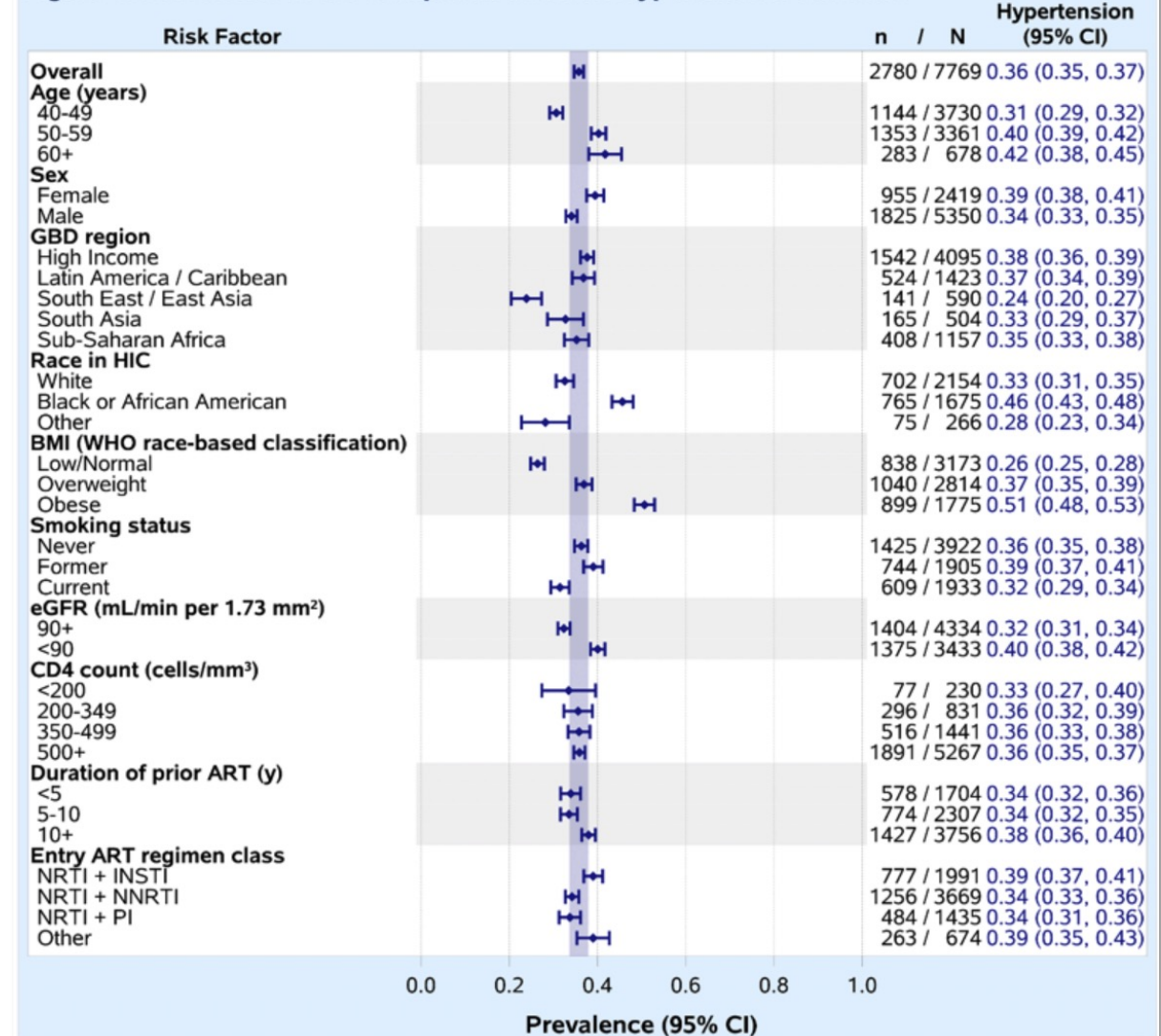


Hypertension in REPRIEVE

RESULTS

- 7,769 participants enrolled from 5 global burden of disease (GBD) regions: median age 50 years (IQR 45, 55) and 2,419 (31%) women; 88% virologically suppressed (<400 copies/mL)
- Prevalence of baseline hypertension: 36% (95%CI 35, 37);** varied by GBD region; more common in women (Figure 1)
 - 1,911 participants (69%) had pre-existing hypertension
 - 1,578 were on antihypertensive medications (including 29 started on antihypertensive medications at baseline)
 - 333 not on medications
 - 869 (31%) previously undiagnosed
- Hypertension more common with traditional risk factors:
 - Older age (50+ yrs), Black or African American race in high-income region, higher BMI, reduced renal function (GFR < 9 mL/min) (Figure 1)
- Among 1,882 participants with pre-existing hypertension, 39% (95%CI 37, 41) were uncontrolled**
 - Varied by region with control most common in high income countries (Figure 2)

Figure 1: Prevalence of the composite baseline hypertension outcome



AHA/ASA Journals

JOURNALS | BROWSE | RESOURCES | INFORMATION | ALERTS

Circulation

CURRENT ISSUE | ARC

REVIEW ARTICLE | Originally Published 13 March 2026 | 

2026

ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/A
PhA/ASPC/NLA/PCNA Guideline on the
Management of Dyslipidemia: A Report of
the American College of
Cardiology/American Heart Association
Joint Committee on Clinical Practice
Guidelines

Writing Committee Members, Roger S. Blumenthal, MD, FACC, FAHA, FASPC, FNLA, Chair, Pamela B. Morris, MD, FACC, FAHA, FASPC, FNLA, Vice Chair, Mario Gaudino, MD, FAHA, FACC, JC Liaison, Heather M. Johnson, MD, MS, FAHA, FACC, FASPC, JC Liaison, Timothy S. Anderson, MD, MAS, Vera A. Bittner, MD, MSPH, FACC, FAHA, MNLA, AACVPR, ... [SHOW ALL](#) ... , and John T. Wilkins, MD, MSc, FAHA | [AUTHOR INFO & AFFILIATIONS](#)

Circulation • New online • <https://doi.org/10.1161/CIR.0000000000001423>

Key updates:

- **Early prevention:** Screening and lifestyle interventions should begin in childhood, with earlier pharmacologic therapy—especially for those with familial hypercholesterolemia or LDL ≥ 160 mg/dL in young adults.
- **New risk tool:** The **PREVENT-ASCVD equations** replace the older pooled cohort equations to estimate **10- and 30-year cardiovascular risk** for adults aged 30–79, guiding treatment decisions.
- **Lower LDL-C targets:**
 - <100 mg/dL for borderline/intermediate risk
 - <70 mg/dL for high risk
 - <55 mg/dL for very high-risk patients or secondary prevention.
- **Testing and biomarkers:** A **once-in-a-lifetime Lp(a)** check and **apolipoprotein B** testing are now recommended to refine risk assessment. **Coronary artery calcium (CAC)** scoring is advised when treatment decisions are uncertain.
- **Therapy approach:** Statins remain first-line, but **ezetimibe**, **PCSK9 inhibitors**, **bempedoic acid**, **inclisiran**, and **evinacumab** are recognized as important add-ons when targets aren't met.
- **Lifestyle foundation:** Diet, exercise, healthy weight, tobacco avoidance, and adequate sleep remain the cornerstone of prevention and treatment.

Overall, the guideline's central theme is **"lower LDL earlier and for longer"** to reduce lifetime cardiovascular risk and prevent heart attack and stroke.

New ACC/AHA Lipid Guidelines

☰

AHA/ASA Journals

JOURNALS | BROWSE | RESOURCES | INFORMATION | ALERTS

Circulation

CURRENT ISSUE | ARCHIVE

REVIEW ARTICLE | Originally Published 13 March 2026 |

2026

ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/A
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Circulation • New online • <https://doi.org/10.1161/CIR.0000000000001423>

CVD

ASCVD

Heart Failure

Sex*

☒ Male ☐ Female

Age (years)*

30-79

SBP (mmHg)*

90-200

Total Cholesterol (mg/dL)*

130-320

HDL Cholesterol (mg/dL)*

20-100

eGFR (mL/min/1.73m²)*

15-140

BMI (kg/m²)*

18.5-39.9

Diabetes

Any history of diabetes.

☒ No ☐ Yes

Current Smoking

Any cigarette use within the last 30 days

☒ No ☐ Yes

Lipid-lowering medication

Current use of statin medication to lower cholesterol

☒ No ☐ Yes

Anti-hypertensive medication

Current use of any medication for hypertension

☒ No ☐ Yes

The following three predictors are optional for further personalization of risk assessment. When they are clinically indicated or available,

If available or indicated, select "Yes" and enter the value.

UACR (mg/g)

UACR is clinically indicated for individuals with chronic kidney disease, diabetes, or hypertension

☒ No ☐ Yes

HbA1C

HbA1c is clinically indicated for individuals with diabetes, prediabetes, overweight, or obesity, or those with history of gestational diabetes

☒ No ☐ Yes

Zip Code

valid 5-digit zip code is needed to estimate social deprivation index [SDI]

☒ No ☐ Yes

Calculate

Reset

- Use PREVENT-ASCVD Calculator

REVIEW ARTICLE | Originally Published 13 March 2026 | 

 Check for updates

2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/A PhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

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Circulation • New online • <https://doi.org/10.1161/CIR.0000000000001423>

- Start early
- Go low

Lipid Lowering to Reduce ASCVD Risk

Screen
EARLIER



- Screen at **age ≥2y** if family history of premature ASCVD, severe hypercholesterolemia, or FH
- Screen at **ages 9–11y** to identify FH and other lipid disorders

Check
REGULARLY



- Screen lipids again at age **19y**
- Recheck at least every **5y** and use PREVENT-ASCVD to identify risk

Aim for
LOWER LDL-C



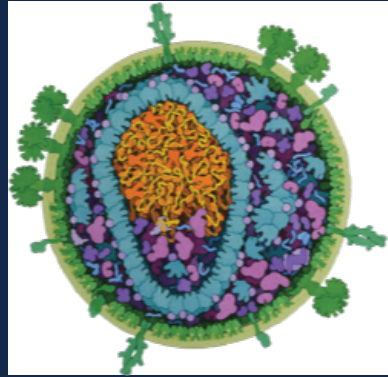
- LDL-C goal:
- **<100 mg/dL** for PREVENT-ASCVD <10%
 - **<70 mg/dL** for PREVENT-ASCVD ≥10%, FH, DM with risk factors, CAC ≥100 AU
 - **<55 mg/dL** for clinical ASCVD at very high risk*

Treat
LONGER



- Check lipids **4–12wk** after start or dose change of lipid-lowering therapy, then **every 6–12mo** thereafter
- Benefits increase with longer therapy; tailor duration to individual risk

Promote lifelong healthy lifestyle behaviors



CROI

Conference on Retroviruses
and Opportunistic Infections

OTHER MATTERS

Other matters that matter: Defunding Science

HEALTH

The Trump administration restructures federal health agencies, cuts 25% of staff

MARCH 28, 2025 · 4:14 AM ET

HEARD ON [MORNING EDITION](#)

By [Selena Simmons-Duffin](#), [Michel Martin](#)



[World](#) ▾ [Business](#) ▾ [Markets](#) ▾ [Sustainability](#) ▾ [Legal](#) ▾ [Commentary](#) ▾ [More](#) ▾

US to cut \$600 million in public health grants to Democrat-led states, Bloomberg reports

By Reuters

February 10, 2026 2:09 AM GMT+1 · Updated February 10, 2026



 World Report

www.thelancet.com Vol 407 February 21, 2026

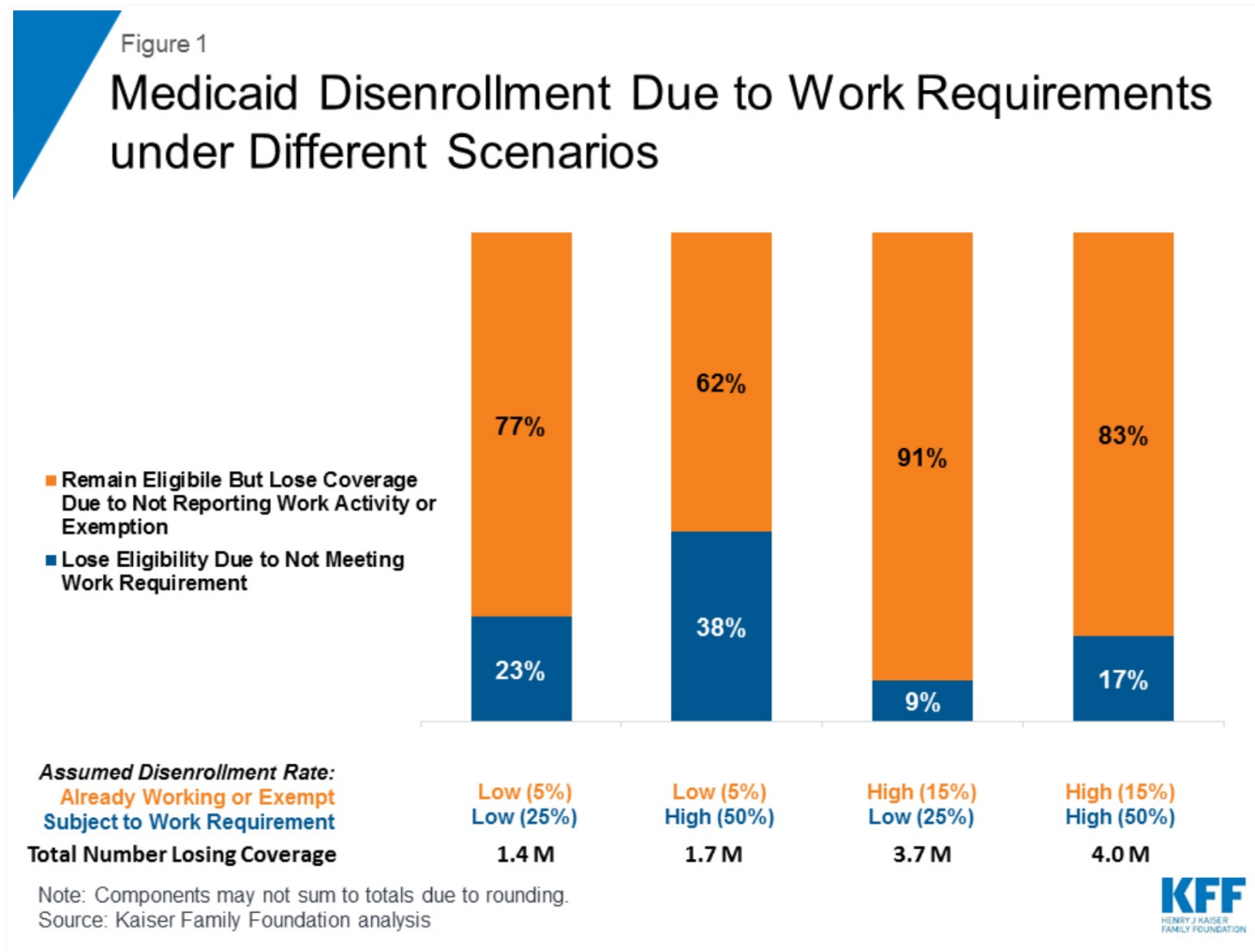


Congress compels the Trump Administration to spend science and health funding

Proposals for huge cuts to NIH and CDC budgets have been rejected, to the relief of scientists.
[Susan Jaffe reports from Washington, DC.](#)

Other matters that matter: Defunding Assistance

2. CBO estimates of national work requirements show lower federal spending and an increase in the number of uninsured, but no increase in employment.



Other matters that matter: What if Ryan White went away?

HIV Incidence Could Rise by 73% in 30 States if Ryan White Ends: A Simulation Study

Melissa Schnure¹, Ryan Forster², Joyce L. Jones¹, Catherine R. Lesko², D. Scott Batey³, Isolde Butler⁴, Dafina Ward⁵, Karen Musgrove⁶, Keri N. Althoff⁷, Mamta K. Jain⁷, Kelly A. Gebo¹, David W. Dowdy², Maunank Shah¹, Parastu Kasaie², Anthony T. Fojo¹

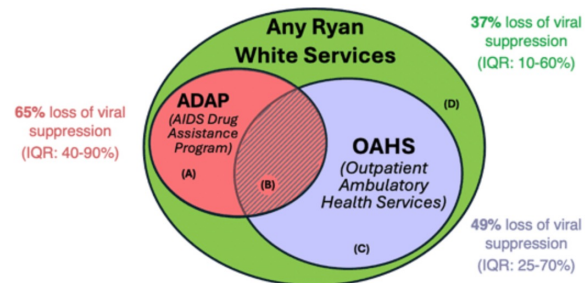
¹Johns Hopkins University School of Medicine; ²Johns Hopkins Bloomberg School of Public Health; ³Tulane School of Social Work; ⁴Crescent Care; ⁵Southern AIDS Coalition; ⁶Birmingham AIDS Outreach; ⁷UT Southwestern Medical Center

What happens to HIV incidence if the Ryan White program were discontinued?

(or temporarily interrupted)

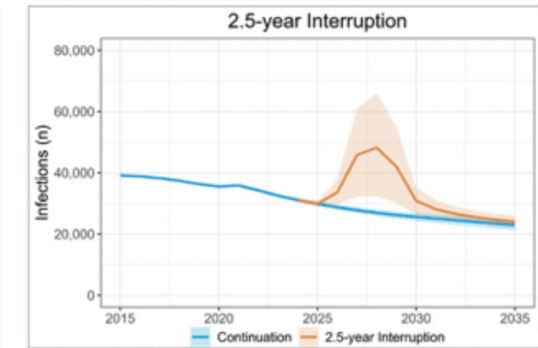
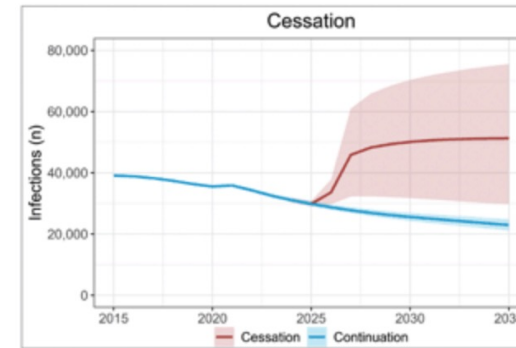
"If all Ryan White programs ended indefinitely, what percentage of virally suppressed individuals would stop taking ART consistently among these groups?"

Survey responses

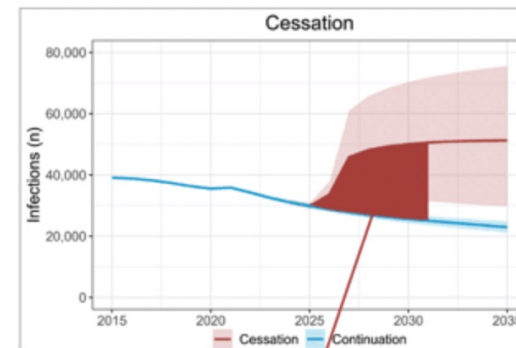


180 responses from 41 states

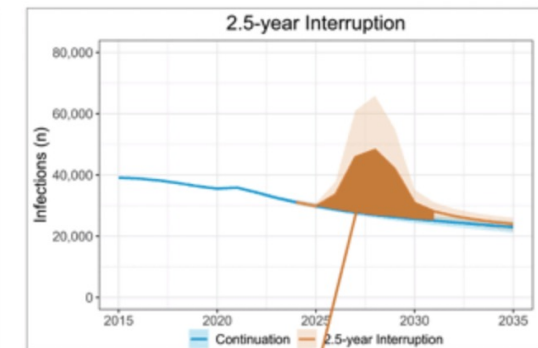
Projected results: 30 states, aggregated



Projected results: 30 states, aggregated



117,431 [30,863 – 213,440]
more infections
73% [19 – 132%]



68,264 [18,180 – 123,309]
more infections
43% [11 – 77%]

Other matters that matter: What if Ryan White went away?

HIV Incidence Could Rise by 73% in 30 States if Ryan White Ends: A Simulation Study

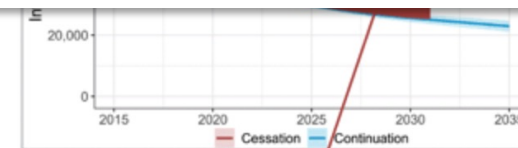
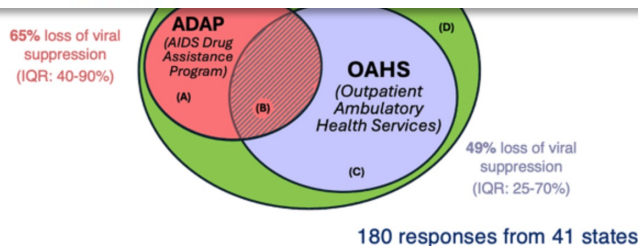
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Melissa Sch
Karen Musgr
Anthony T. F

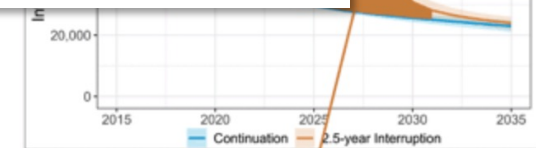
¹Johns Hopkin:
⁴Crescent Carr

Conclusions

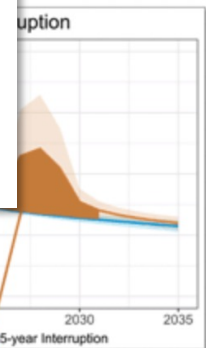
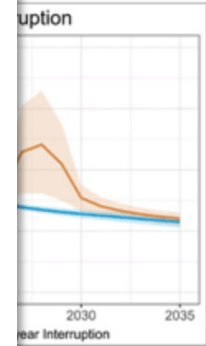
- HIV incidence could rise by 73% in 30 States if Ryan White ends, or by 43% if programs experience a 2.5-year interruption
- Impacts of cessation vary substantially at the state level, ranging from 42% in Indiana to 147% in Colorado
- **Ryan White services play a critical role in preventing transmission of HIV**



117,431 [30,863 – 213,440]
more infections
73% [19 – 132%]



68,264 [18,180 – 123,309]
more infections
43% [11 – 77%]



Other matters that matter: Devaluing science has consequences

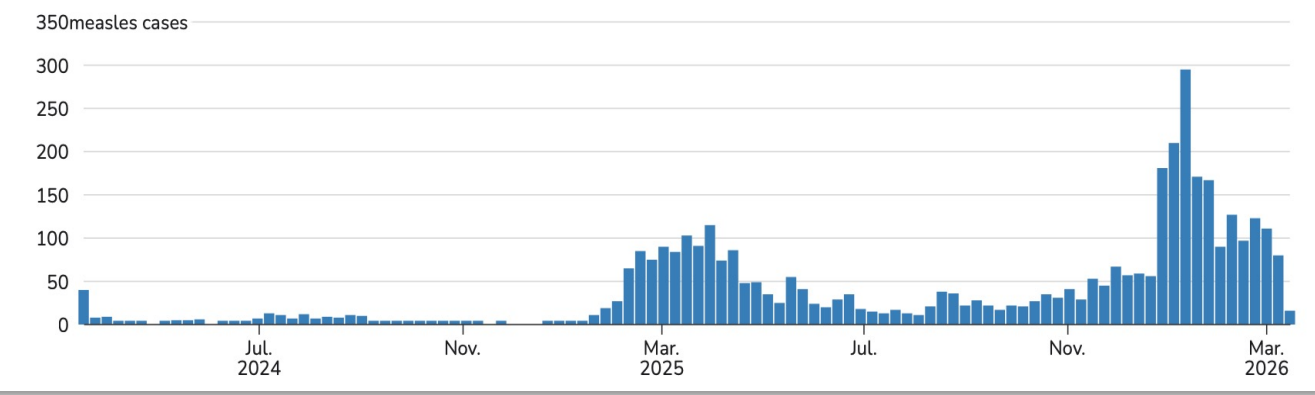


Measles (Rubeola)

EXPLORE THIS TOPIC

Weekly measles cases by rash onset date

2022–2026* (as of March 19, 2026)



U.S. Hospitalizations

	2026	2025
Total Hospitalized	5% (74 of 1,487 cases)	11% (242 of 2,285 cases)
Percent of Age Group Hospitalized		
Under 5 years	7% (23 of 314)	18% (106 of 584)
5-19 years	3% (23 of 781)	6% (57 of 1,015)
20+ years	7% (27 of 385)	12% (79 of 673)
Age unknown	14% (1 of 7)	0% (0 of 13)

Other matters that matter: Devaluing science has consequences

[Home](#) | [JAMA](#) | [New Online](#)

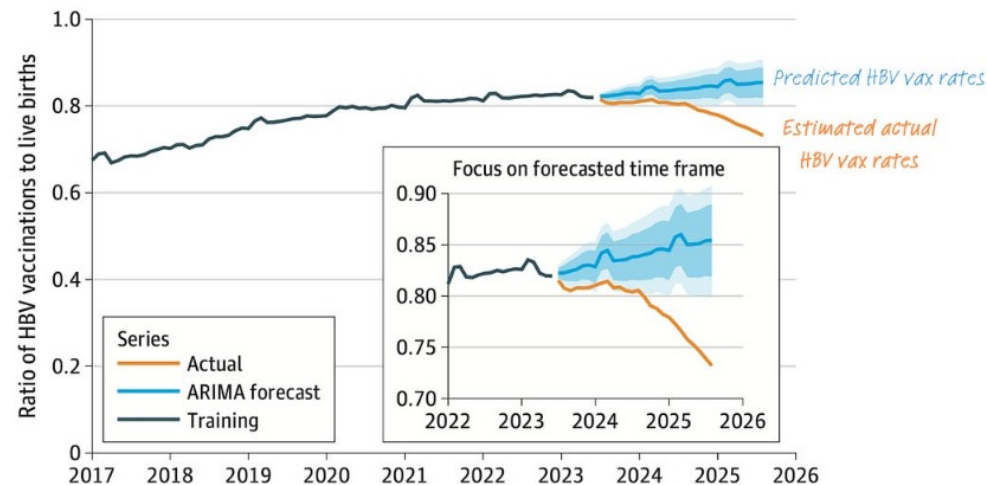
Research Letter

US Newborn Hepatitis B Virus Vaccination Rates

Joshua M. Rothman, MD, MS¹; Brian Kwan, MD, MS^{2,3}; Christopher A. Longhurst, MD, MS^{1,3}; [et al](#)

» [Author Affiliations](#) | [Article Information](#)

Predicted vs. actual Hep B birth doses per live births, U.S. estimates



Source: [Rothman et al., 2026](#)

March 5, 2026 | 3 min read

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Tylenol orders in pregnant people plummeted after Trump falsely linked the medicine to autism

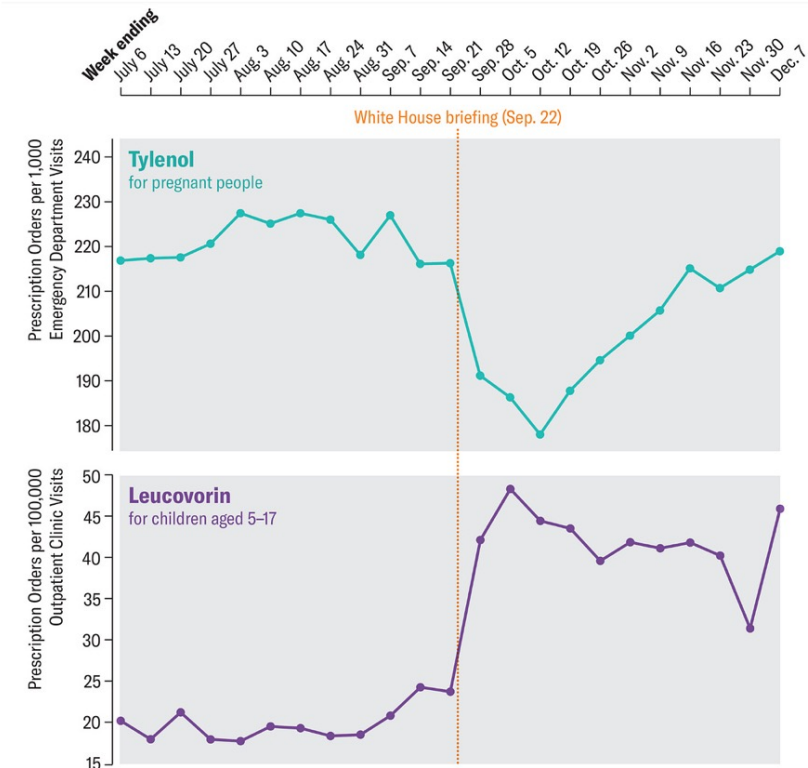


Figure Source: [Scientific American](#).

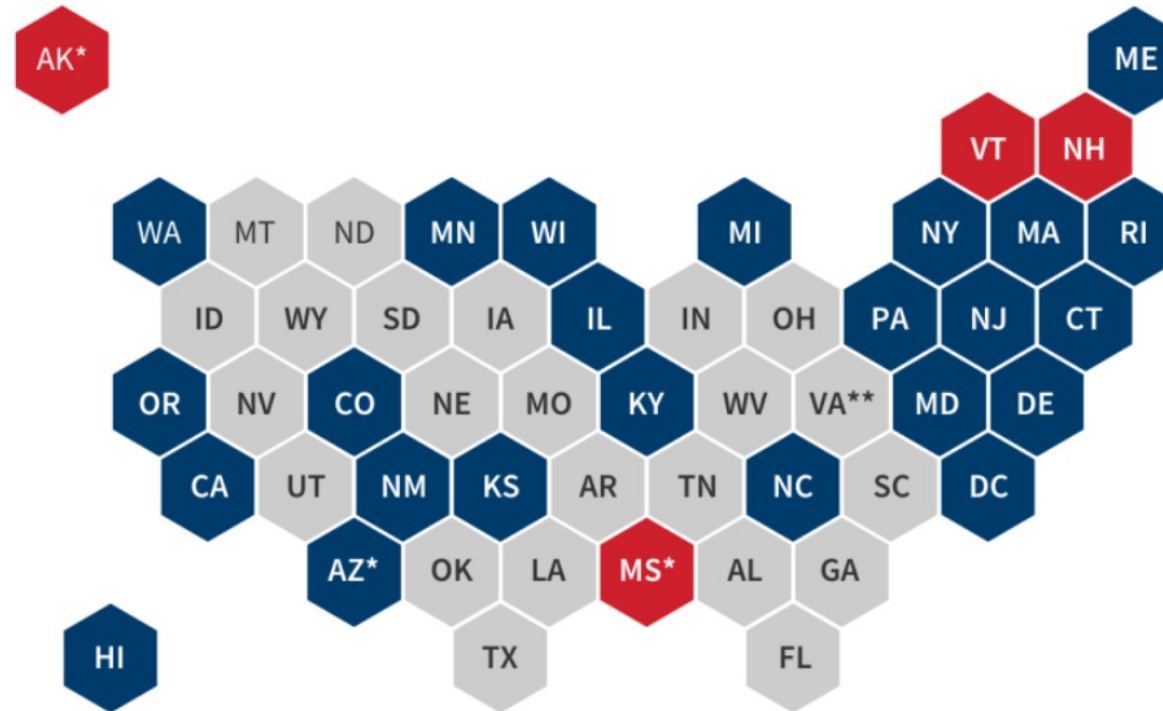
Other matters that matter: Distrusting politicized public health leadership

Most States Now Depart From Federal Guidelines for Childhood Vaccines, Including All States with Democratic Governors

States relying on non-federal sources for some or all routine childhood vaccine recommendations, by governor's party ID, as of Jan. 20, 2026.

- Republican Governor
- Democratic Governor

Note: *Has departed from federal recommendations for at least one childhood vaccine. **Virginia's governor is a Democrat as of Jan. 17, 2026; the state may choose to change its position regarding vaccine recommendations soon.
Source: KFF, State Recommendations for Routine Childhood Vaccines: Increasing Departure from Federal Guidelines



KFF

Other matters that matter:

- **Vote**
 - Local, State, National
 - Midterm, term, special elections
 - Make sure you are registered
 - Need an ID? Get an ID.
 - Mail-in ballots early (follow the instructions!)
- **Unite**
 - Speak up
 - Show up
- **Be a force for truth**
 - Resist nonsense
 - Control cynicism
 - Embrace logic



