

IAS 2026 – What Matters Most

A NATAP UPDATE

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OPINIONS EXPRESSED ARE MY OWN AND
DO NOT REPRESENT THOSE OF UNC



UNC

INSTITUTE FOR GLOBAL HEALTH
& INFECTIOUS DISEASES

IAS 2026: What Matters Most

PREVENTION

- PURPOSE 1 and 2 OLE
- LEN PrEP in US
- LA-CAB in women in OPERA
- LA-CAB PrEP US
- LA-CAB pregnancy safety
- PURPOSE 1 and 2 site selection
- CLARITY – ISRs CAB v LEN
- What PrEP do people want?
- DOXYPEP and STIs in US South, Australia
- DOXPEP Modelling

TREATMENT

Naive

- VOGUE: DTG/3TC v BFTAF
- Opti-DOR – TDF/3TC/DOR

Experienced/Switch

- ISL/LEN
- ISL + ULO
- DOR/ISL – Baseline ART resistance
- ARTISTRY-1 BIC/LEN treatment, satisfaction, metabolics
- LEN+bNAbs
- BFTAF v DTG/TC – DYAD 144w
- CAB/RPV adolescents LATA
- Adherence challenges - HERO

WELL-BEING

- New lipid guidelines, new lipid lowering meds and what this means for PWH
- Obesity definition
- PASO DOBLE – More on weight
- Fractures in RESPOND Cohort
- HBV in US HIV clinic
- Steatosis score
- Anal cancer risk factors – ANCHOR



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.
We owe them our gratitude.





PREVENTION

LEN PrEP: PURPOSE 1 Extension

Zero HIV Acquisitions With Twice-Yearly Subcutaneous Lenacapavir for PrEP During 52 Weeks of Open-Label Extension in PURPOSE 1

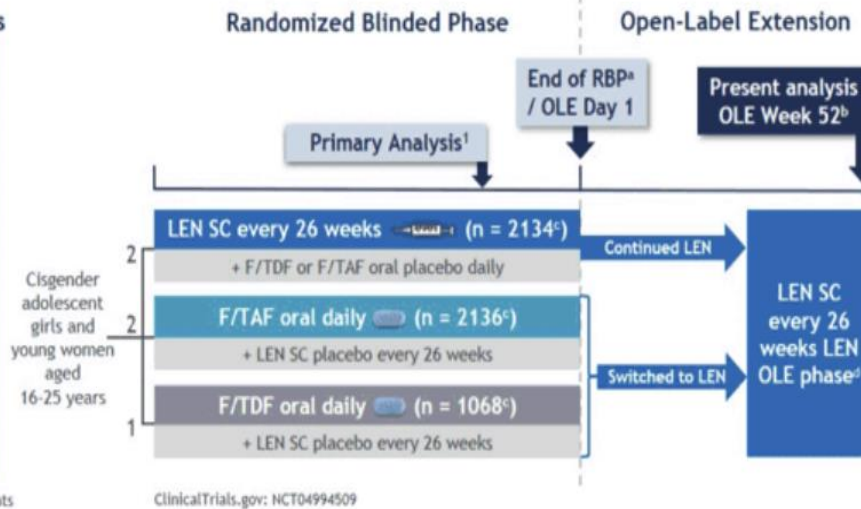
Noah Kiwanuka¹, Moelo Malahleha², Gonasagrie Nair³, Ishana Harkoo⁴, Flavia Matovu Kiweewa⁵, Sarah B Puryear⁶, Christoph C Carter⁶, Yuliang Chen⁶, Adam Akhtar⁶, Cheryl E Louw⁷, Leila E Mansoor⁴

PURPOSE 1 Longer-Term Follow-up Through OLE Week 52

PURPOSE 1 Enrolled Participants

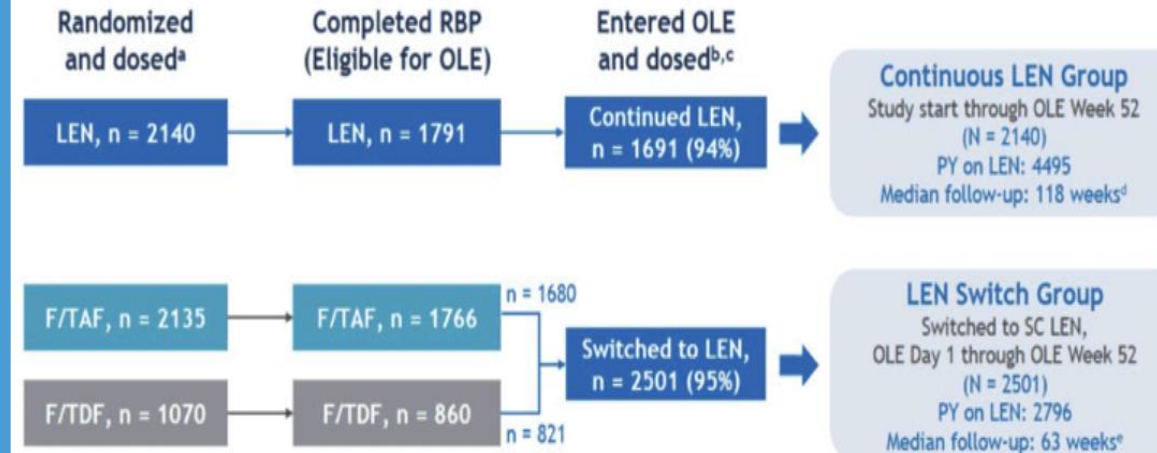


arker shading corresponds to a higher proportion of participants



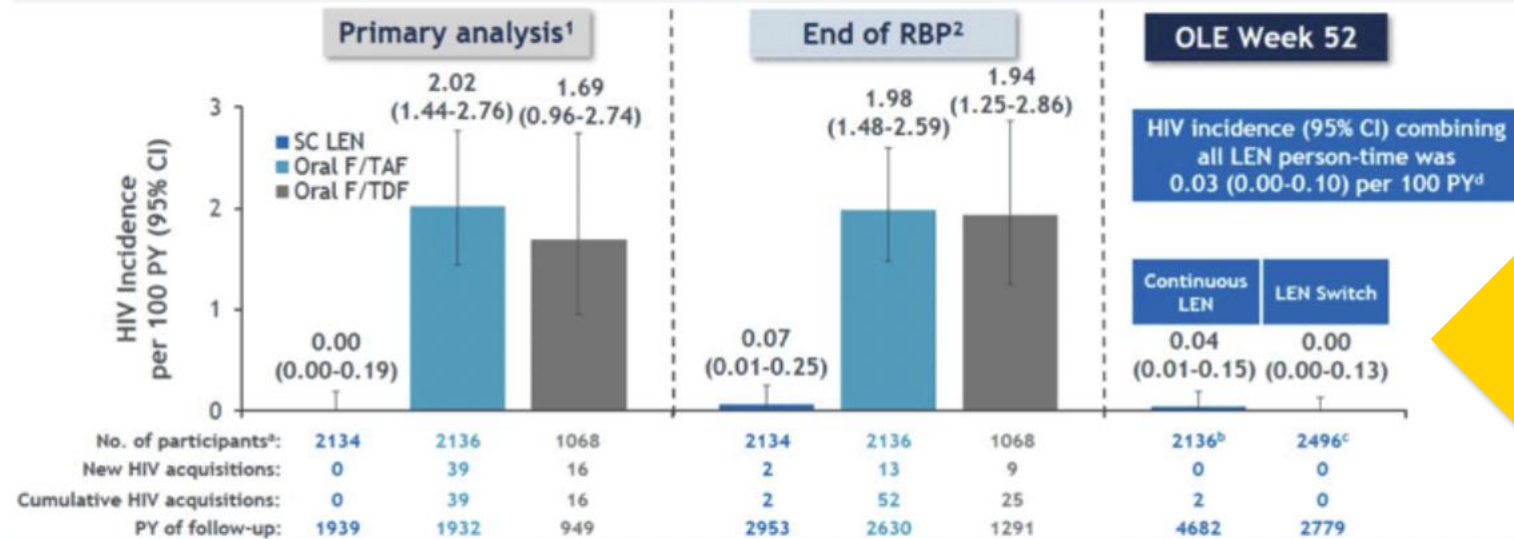
The present analysis includes over 7000 person-years on LEN

The Majority of Participants Chose Open-Label LEN



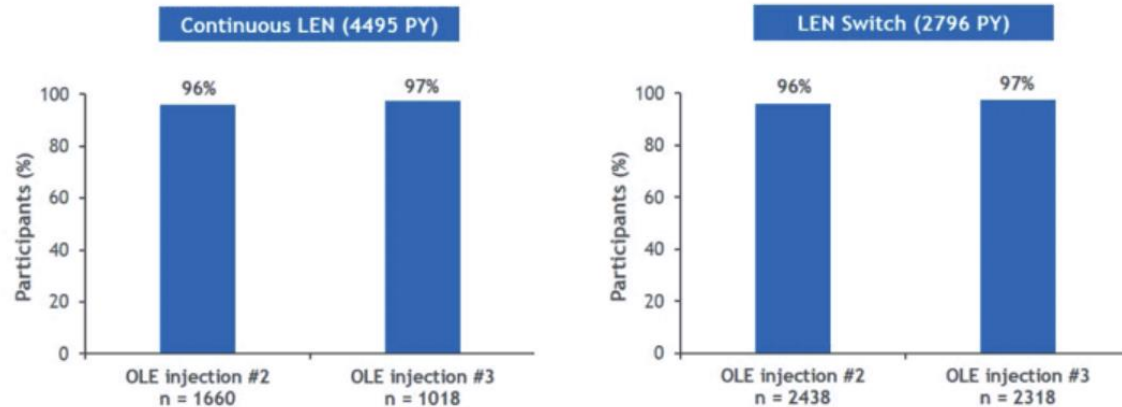
95% of participants who completed the RBP opted to continue or switch to LEN in the OLE

LEN Efficacy Remained High Through Longer-Term Follow-up



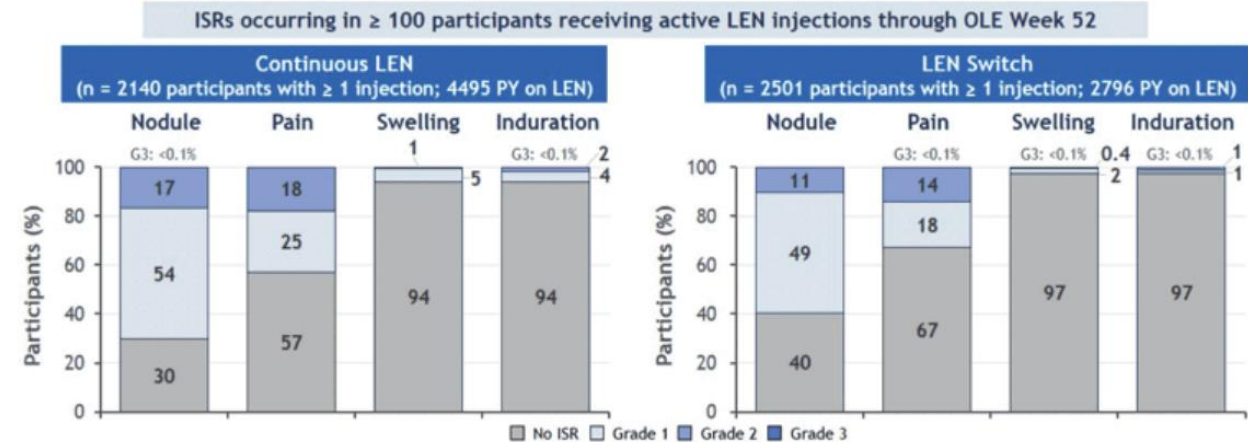
No new HIV acquisitions in women on open-label LEN, including among those who switched from oral PrEP to LEN

Adherence to Open-Label LEN Injections Was High Among LEN Switch Group



Adherence to open-label LEN injections was similarly high in participants who opted to continue or switch to LEN

ISR Incidence and Severity Were Similar in Continuous LEN and LEN Switch Groups



The majority of participants did not report ISRs other than expected injection site nodules

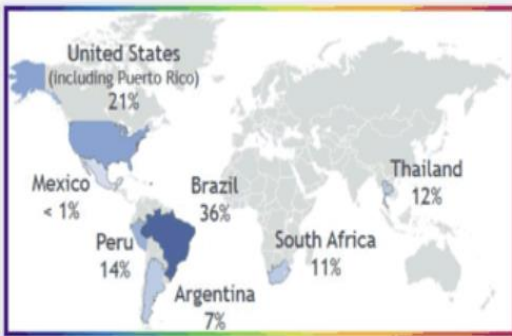
LEN PrEP: PURPOSE 2 Extension

High Efficacy of Twice-Yearly Subcutaneous Lenacapavir for PrEP Through 52 Weeks of Open-Label Extension in PURPOSE 2

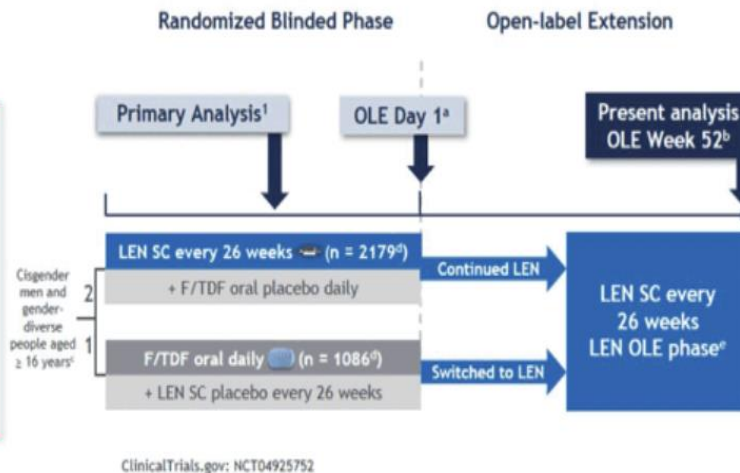
Marcelo H Losso¹, Breno Santos², Javier R Lama³, Kenneth H Mayer⁴, Anchalee Avihingsanon⁵, Nkosi Ndlovu⁶, Namrata Shah⁷, Olivia van Gerwen⁸, Stephanie Cox⁹, Lillian B Brown⁹, Christoph C Carter⁹, Pamela Wong⁹, Priyanka Arora⁹, Jose Pilotto¹⁰, Beatriz Grinsztejn¹¹

PURPOSE 2 Longer-Term Follow-up Through OLE Week 52

PURPOSE 2 Enrolled Participants

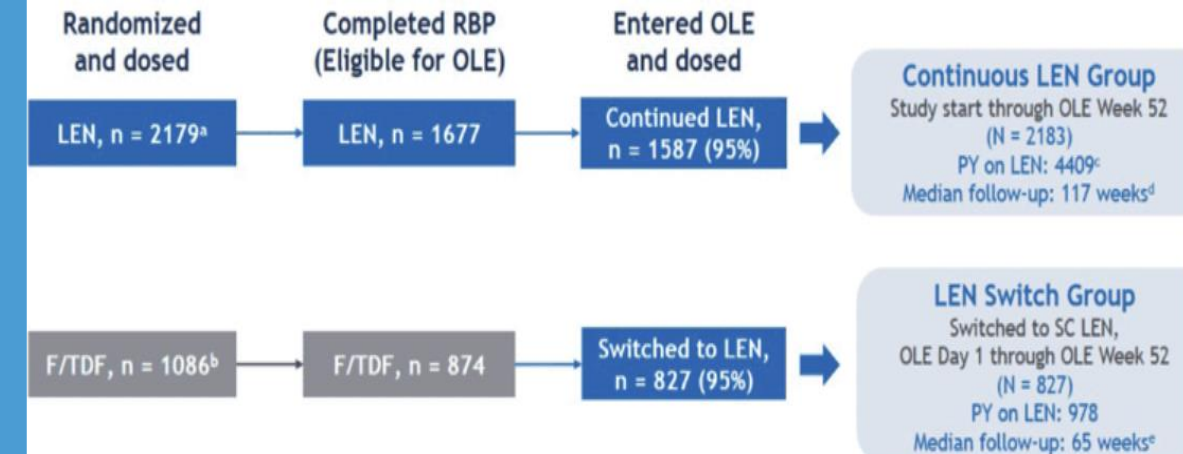


Darker shading corresponds to a higher proportion of participants



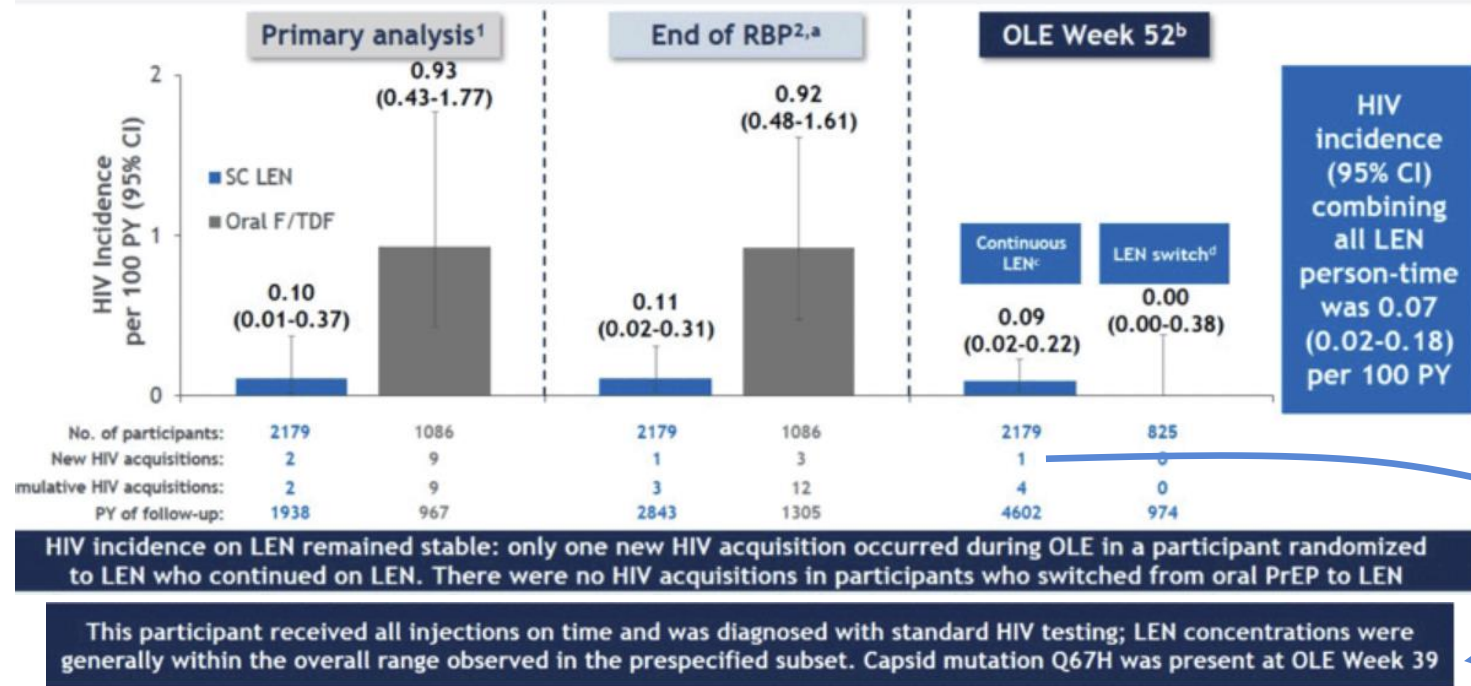
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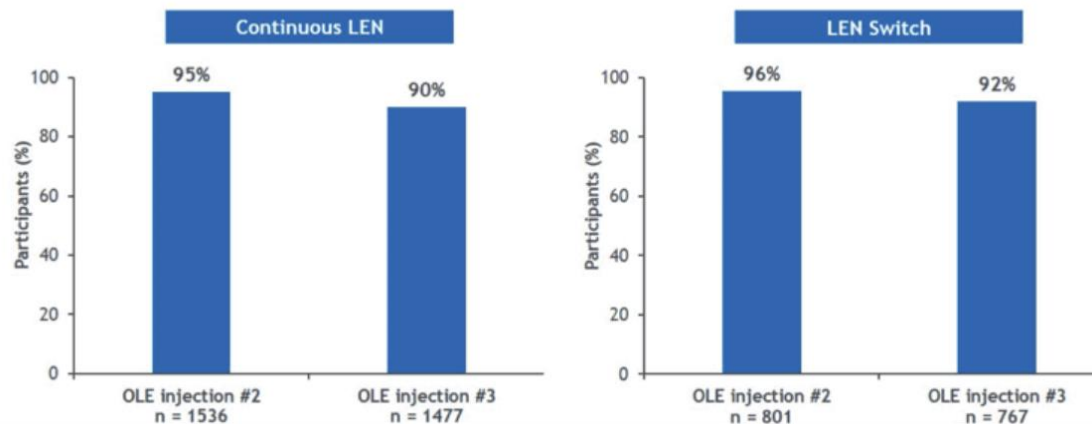


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LEN Efficacy Remained High Through OLE Week 52

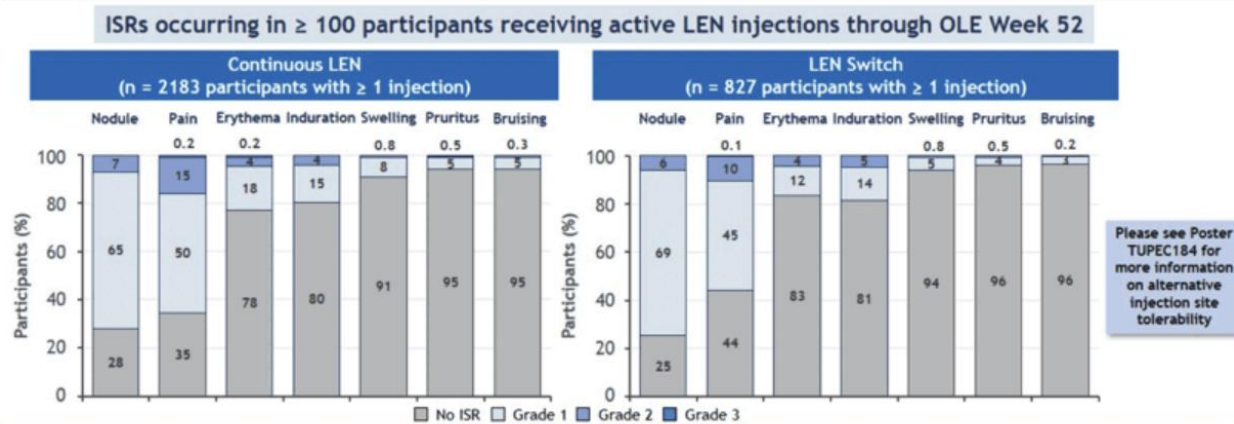


On-Time Injection Adherence to Open-Label LEN Injections Was High



Adherence to open-label LEN injections in both groups was high

ISR Incidence and Severity Were Similar in Continuous LEN and LEN Switch Groups



Please see Poster TUPEC184 for more information on alternative injection site tolerability

Early days of LEN PrEP in the US

Aaron Siegler asiegle@emory.edu



PrEP in Motion

The first six months of national injectable lenacapavir PrEP prescribing and equity, United States, June-December 2025

Main question

Using US national claims data, describe the use and equity of lenacapavir injectable PrEP (LEN), cabotegravir injectable PrEP (CAB), and oral PrEP.

Findings

From June 2025 – December 2025, among PrEP users 1% used LEN, 5% used CAB, and 95% used oral PrEP. For all regimens, PrEP equity was lower for Black persons, Hispanic persons, and younger persons.

Number of users by medication type, 01 June 2025 – 31 Dec 2025, and years on market





AIDS 2026

National claims analyses provide unique insights

Long acting cabotegravir persistence in care over 2 years

Persistence in care among 24,194 CAB users (2022-2024) lower than previously estimated, with persistence similar or lower than oral PrEP

Abstract | JAMA Network Open | Vol. 5, No. 6

Original Investigation | Infectious Diseases

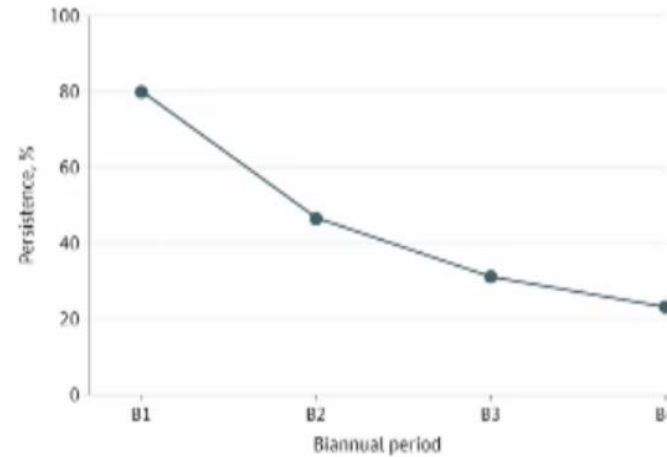
Long-Acting Injectable Cabotegravir Use and Persistence Over 2 Years

Shi Hao Ermen Koh, MPH¹, Wenting Huang, PhD², Eric W. Hall, PhD³,
Jill Jones, PhD⁴, Xiao Zang, PhD⁵, Courtney R. Yarbrough, PhD⁶, Edwin S. Carlin-Gutierrez, MA⁷, Patrick S. Sullivan, DVM, PhD⁸,
Aaron J. Siegle, PhD⁹

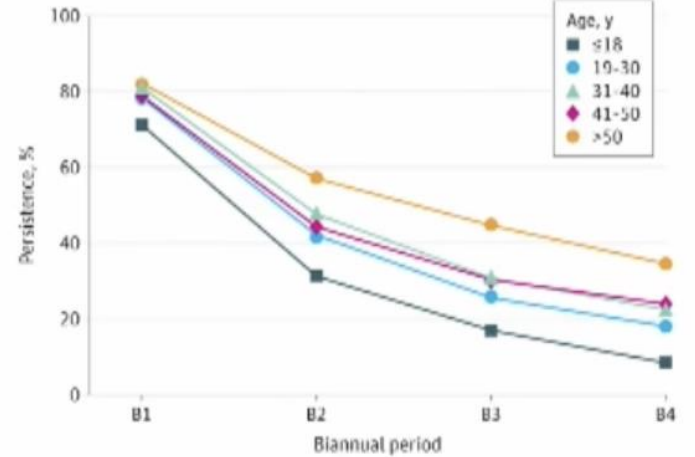
26-31 July • Rio de Janeiro, Brazil

aids2026.org

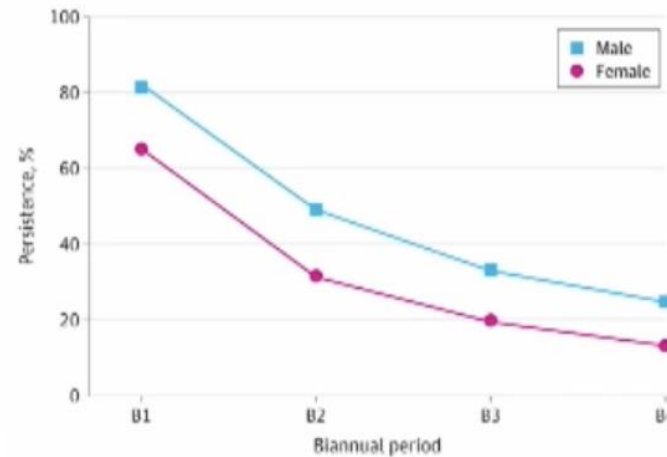
A Overall



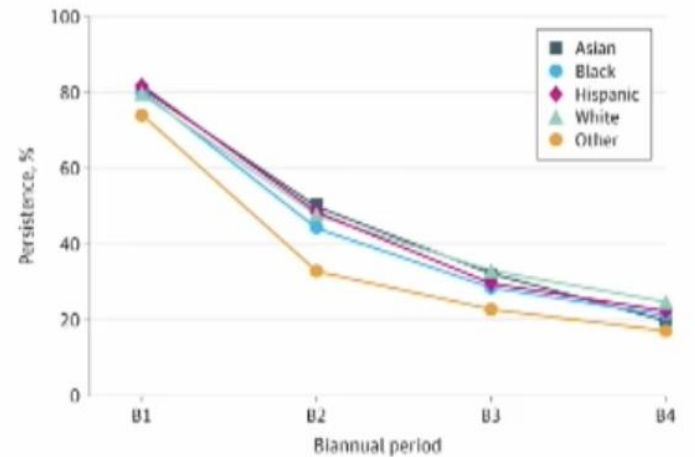
B Age



C Sex



D Race and ethnicity



	Lenacapavir		Cabotegravir		Oral PrEP	
	n	%	n	%	n	%
Gender						
Male	6,045	85%	27,381	86%	487,271	91%
Female	1,089	15%	4,487	14%	46,603	9%
Race/ethnicity						
Black	1,186	17%	5,934	19%	80,737	16%
Hispanic	1,213	17%	5,675	18%	84,743	16%
White	4,233	61%	18,076	58%	328,293	63%
Others	361	5%	1,398	5%	26,361	5%
Age (years)						
≤ 24	558	8%	2,554	8%	48,961	9%
25-34	2,208	31%	11,326	36%	184,584	35%
35-44	2,243	31%	10,043	32%	156,123	29%
≥ 45	2,125	30%	7,945	25%	144,210	27%

	Lenacapavir		Cabotegravir		Oral PrEP	
	n	%	n	%	n	%
Copay						
<\$100	5,897	95%	20,792	95%	500,178	99%
>\$100	325	5%	902	5%	4858	1%
Insurance						
Commercial	4030	57%	21,782	68%	391,552	74%
Medicaid	1,961	28%	7,563	24%	60,919	11%
Other	1,138	16%	2,500	8%	78,197	15%

Conclusions

Long-acting injectable PrEP medications are a small share of US PrEP use

LEN use has grown faster than CAB use during a similar release stage

Inequity in LEN provision by race/ethnicity and age mirrors inequity seen in more established modalities

Differences by insurance type, and high copay levels, indicate insurance-related barriers may impede uptake

New interventions and policies are needed to make it easier to access injectable PrEP

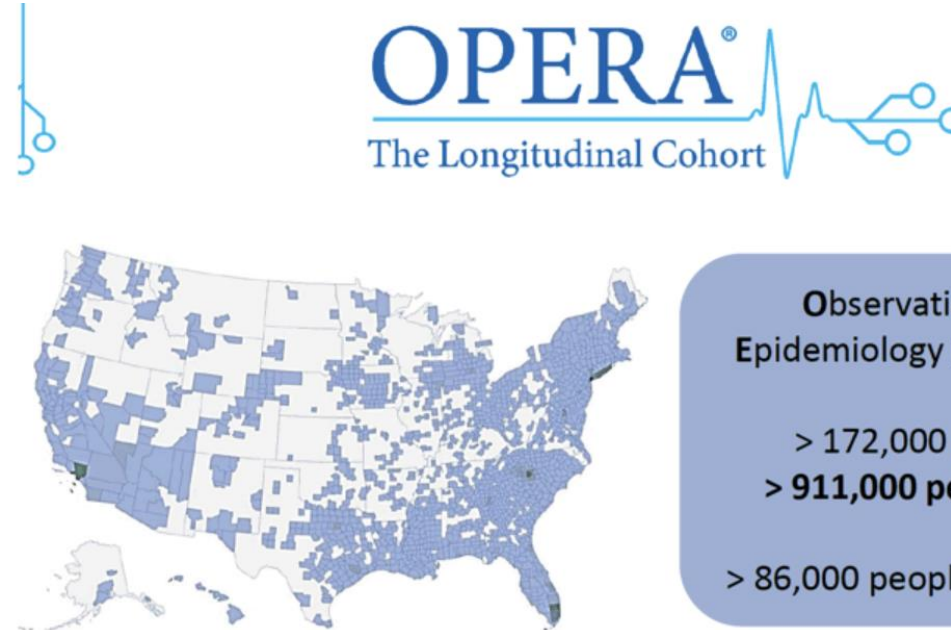
The screenshot shows the 'PrEP Locator' app interface. At the top, it says 'Find Your Clinic' and 'EMORY UNIVERSITY'. Below this, a prompt asks the user to 'Enter your ZIP code or share your location to find a PrEP clinic near you'. A search bar contains 'San Joan, Puerto Rico'. Below the search bar is a blue button labeled 'Use My Location'. Underneath are several filter buttons: '+ Injectable PrEP', '+ PrEP for uninsured', '+ Prescribed online', '+ Same-day oral PrEP start', '+ Accepts walk-ins', '+ Avg. wait time < 3 days', '+ Doxy-PEP', and '+ PrEP financial navigation'. At the bottom, there are links for 'Clear Filters' and 'Explain Filters'.

CAB PrEP in Women - OPERA Cohort^{USA}

Laura Armas-Kolostroubis, AHF, Dallas, TX, USA

Moving to long-acting PrEP

No HIV acquisitions among women on cabotegravir long-acting injectable PrEP despite mostly short injection delays in the US OPERA Cohort



Observational Pharmaco-
Epidemiology Research & Analysis

> 172,000 people with HIV
> 911,000 people without HIV

> 86,000 people ever received PrEP

Inclusion criteria

- ♦ Cisgender or transgender women
- ♦ ≥18 years old
- ♦ ≥1 CAB LA PrEP injection between 21 December 2021 and 31 December 2024

Follow-up through the 1st of:

- ♦ Loss to follow-up (12 months after last clinical encounter)
- ♦ Death
- ♦ Study end (30 April 2025)

1. PrEP use among women

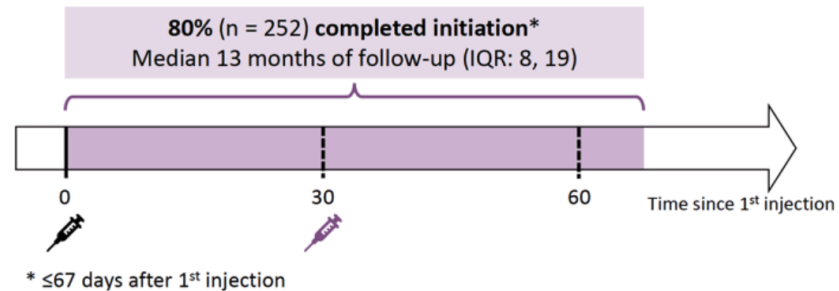
5,330 women started PrEP
(Dec 2021-2024)*



- CAB LA: 315 women (6%)
- TDF/FTC: 4,252 women (80%)
- TAF/FTC: 763 women (14%)

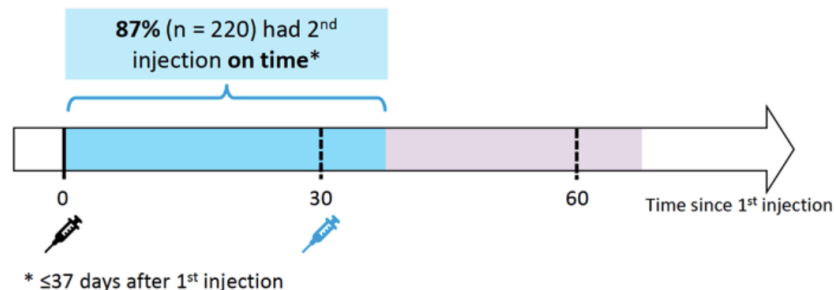
Complete initiation

Among 315 women initiating CAB LA PrEP



Timing of initiation injections

Among 252 women with complete initiation

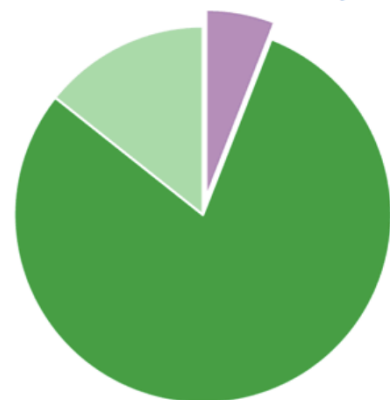


Characteristics at PrEP start

	Women on CAB LA PrEP N = 315	Women on Oral PrEP N = 5,015
Age, median (IQR)	28 (23, 37)	29 (24, 37)
Black race, n (%)	135 (43)	2,123 (42)
Transgender, n (%)	102 (32)	938 (19)
BMI ≥30 kg/m ² , n (%)	130 (43)	814 (35)
Medicaid recipient, n (%)	118 (38)	409 (8)
HIV tests in past 2 weeks, n (%)	263 (84)	4,167 (83)

1. PrEP use among women

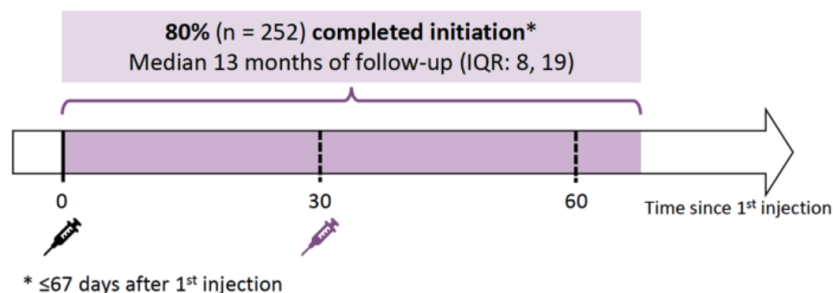
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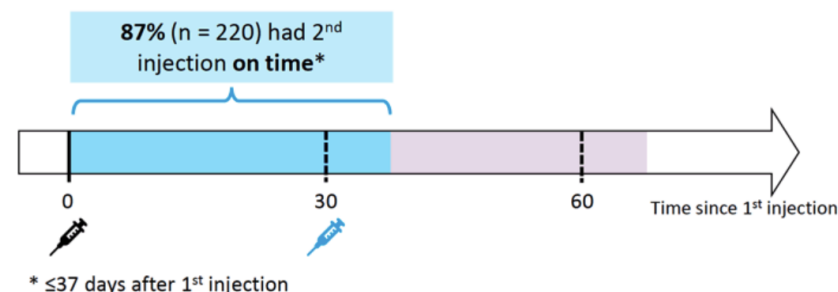
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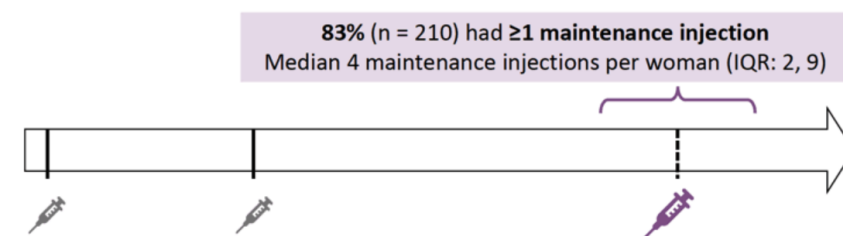


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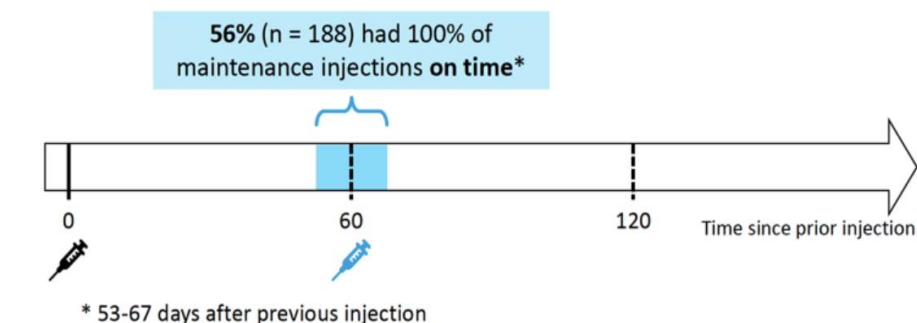
Maintenance injections

Among 252 women with complete initiation



Timing of maintenance injections

Among 210 women with ≥1 maintenance injection





Timing of late maintenance injections

Among 92 women with ≥ 1 late maintenance injection

89% (n = 82) had ≥ 1 **short delay**
not requiring reinitiation*



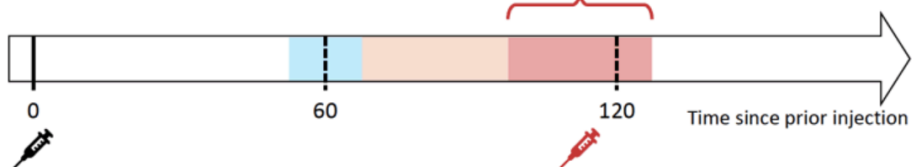
* 68-97 days after previous injection



Timing of late maintenance injections

Among 92 women with ≥ 1 late maintenance injection

15% (n = 14) had ≥ 1 **long delay**
requiring reinitiation*



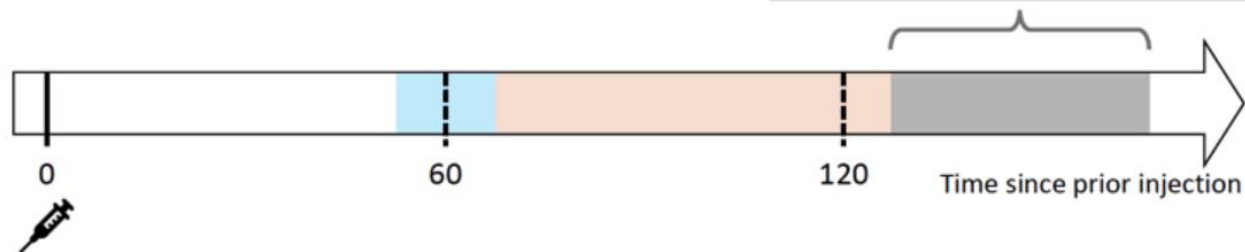
* 98-127 days after previous injection



Discontinuation

Among 210 women with ≥ 1 maintenance injection

38% (n = 80) **discontinued***



* >127 days without injection, corresponding to 2 missed injections

What did you find?

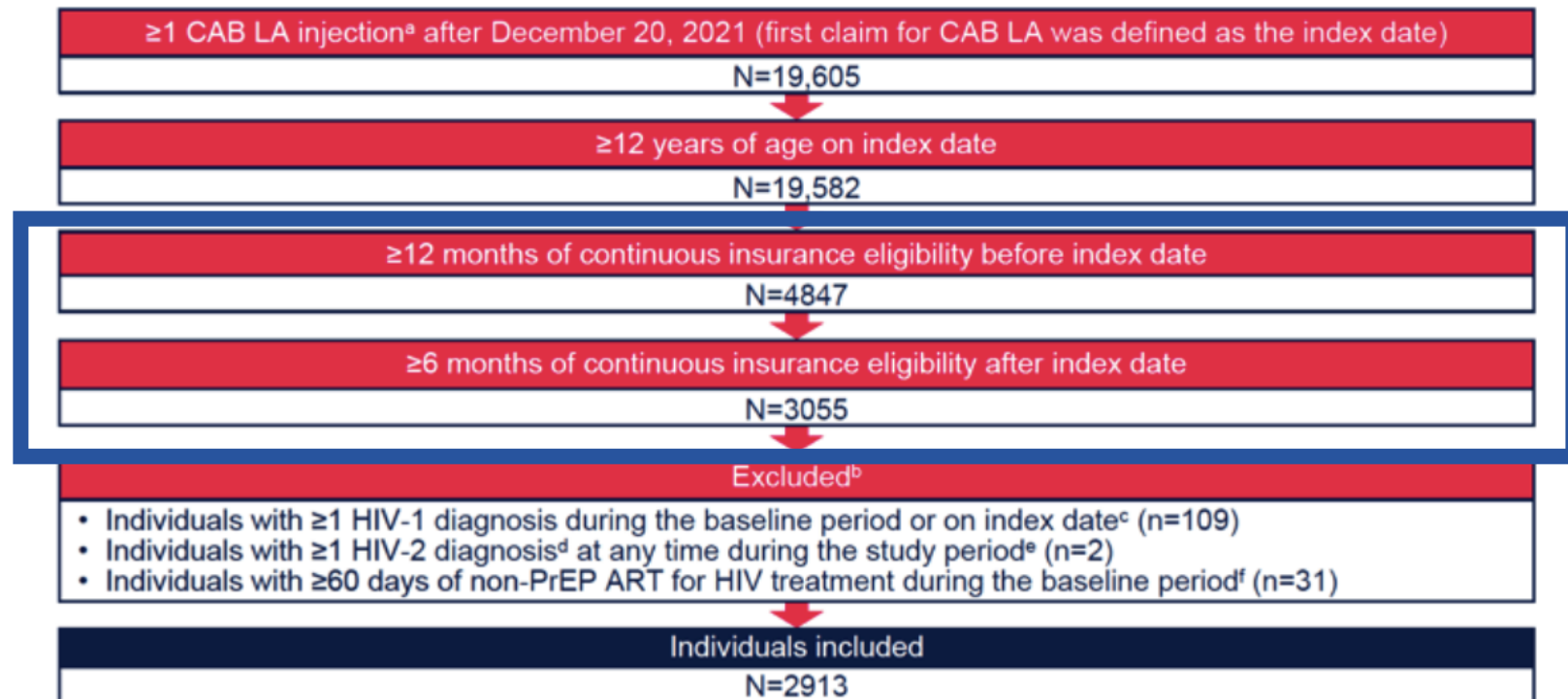
- ◆ CAB LA PrEP was highly effective in routine care, with no HIV acquisitions observed among women over a median of 13 months of follow-up, despite 44% of women receiving one or more late injection

CAB PrEP in stably insured USA

Real-world Utilization and Adherence of Cabotegravir Long-Acting for HIV Pre-exposure Prophylaxis in the United States: Updated Results From the PrEPFACTS Study Using Healthcare Administrative Claims Data

Gabrielle F. Herman,¹ Aimee A. Metzner,¹ Catherine Nguyen,² Farbod Alinezhad,³ Azeem Banatwala,² Dora Martinez,¹ Leili Young-Xu,³ Maral DerSarkissian²

Figure 2. Selection of Individuals Flowchart



Demographic Characteristics

- A total of 2913 individuals were included in this analysis (Table)
 - 60% of participants had commercial insurance, 36% had Medicaid, and 4% had Medicare
- Most (82%) individuals were male; race/ethnicity categories included White (31%), Black or African American (22%), and Hispanic or Latino (18%)

CAB LA Utilization

- Eligible individuals had a median (IQR) follow-up of 387 (279-560) days and 86% received >1 CAB LA injection
- The median (IQR) persistence among individuals who received >1 CAB LA injection was 577 (159-not reached) days (Figure 3)
- Persistence among individuals who received >1 CAB LA injection was 73% at 180 days and 61% at 360 days
- The median (IQR) number of injections was 6 (2-7) per individual per year

Figure 3. CAB LA Persistence Among Individuals With >1 Injection

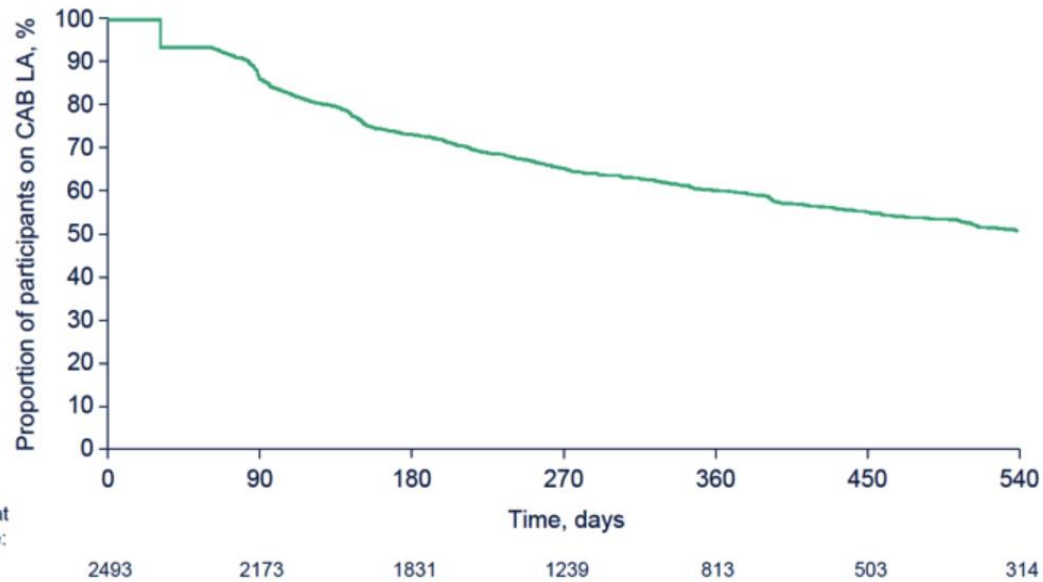
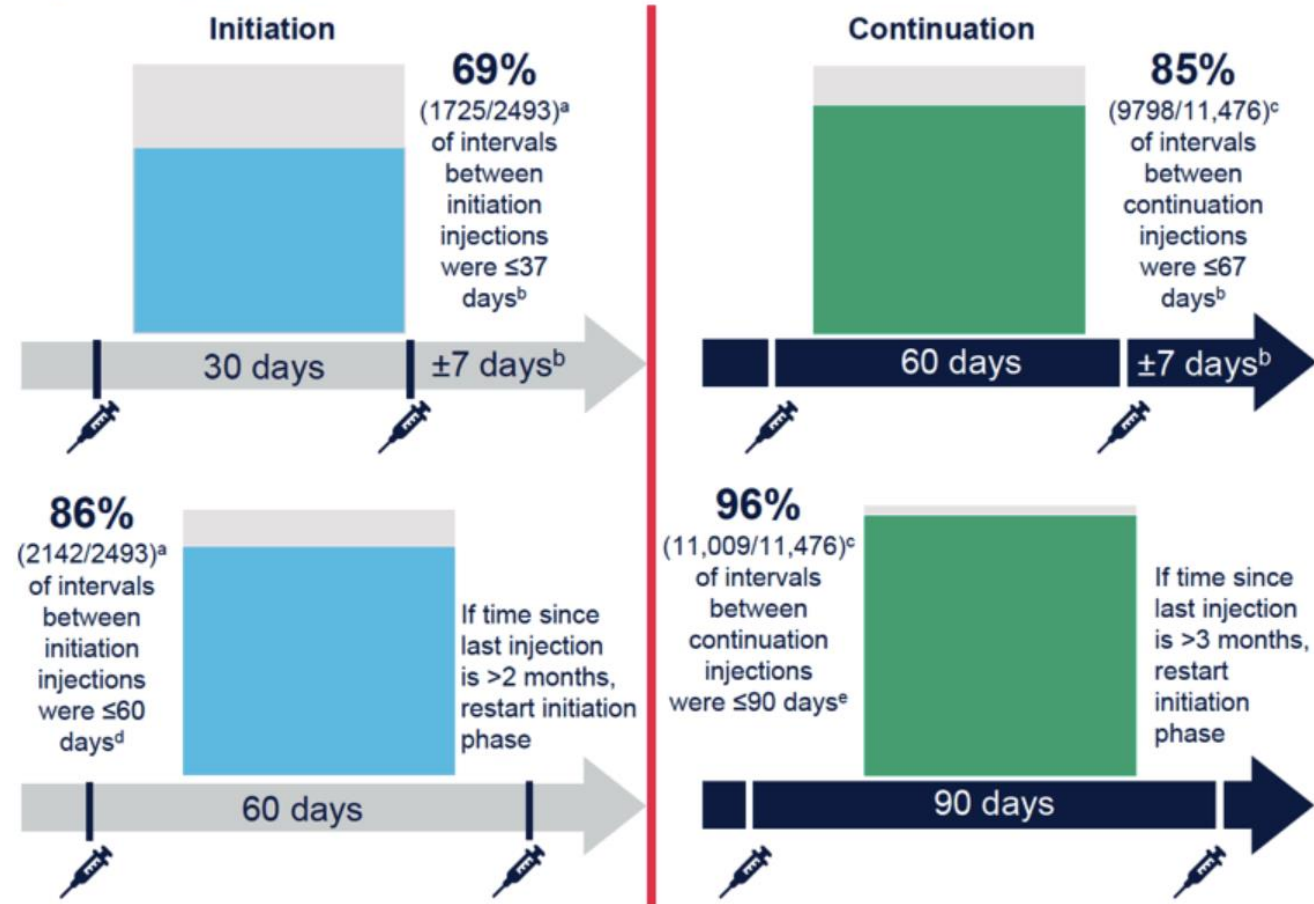


Figure 4. CAB LA Utilization



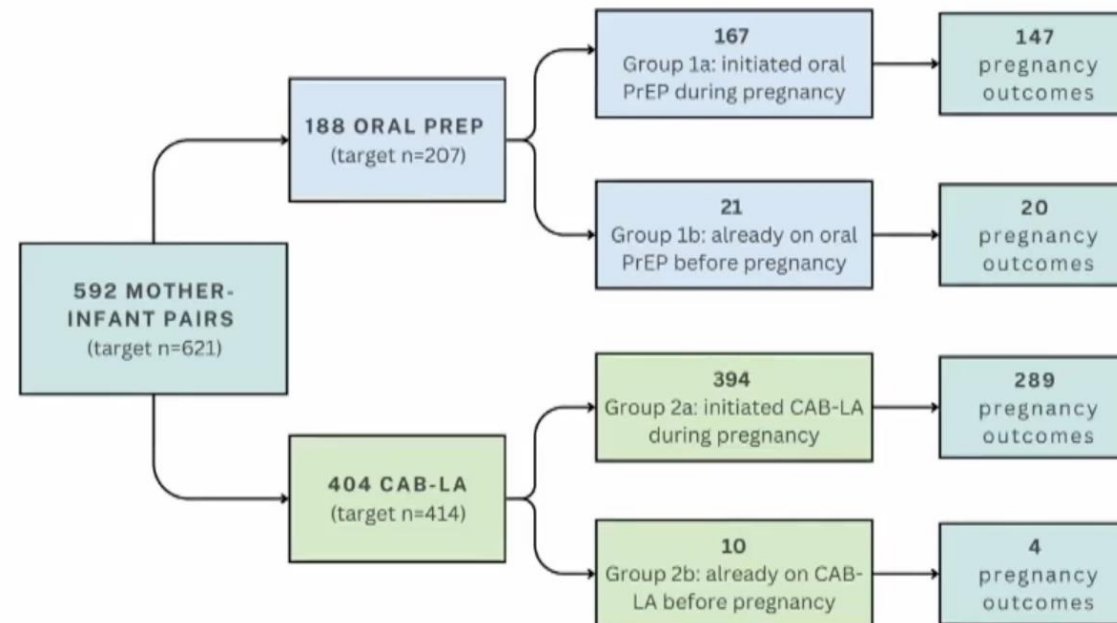
CAB PrEP in Pregnancy^{Malawi}

Interim Analysis of Adverse Pregnancy Outcomes with Injectable CAB-LA vs. Oral PrEP: Findings from the PrIMO Safety Cohort

Dr. Friday Saidi, MBBS MMED FCOG (ECSA)

Assistant Professor –OBGYN

UNC Project Malawi, University of North Carolina at



Primary Objective: Composite Adverse Pregnancy Outcomes

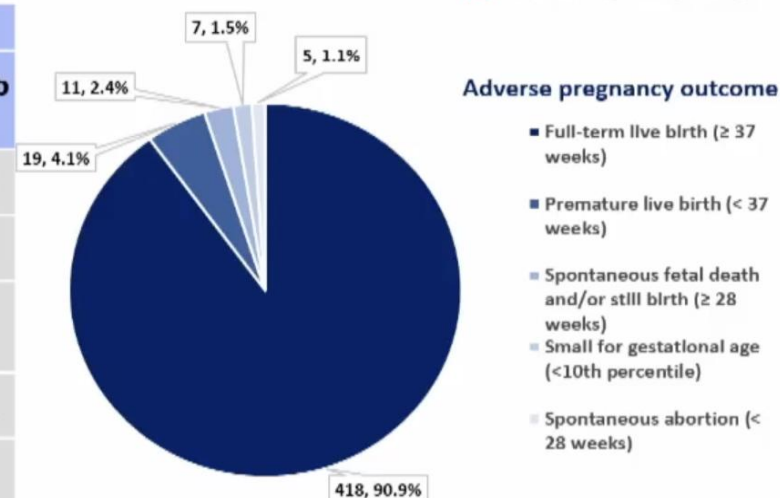
- ☐ **Spontaneous miscarriage** (<28 weeks gestation)
- ☐ **Stillbirth** (≥ 28 weeks gestation)
- ☐ **Spontaneous Preterm delivery** (<37 completed weeks' gestation)
- ☐ **Small for gestational age** (birth weight of less than 10th percentile for gestational age)

Pregnancy and birth outcomes



AIDS 2026

Outcomes by group	Oral PrEP		CAB-LA	
	Group 1a N = 147	Group 1b N = 20	Group 2a N = 289	Group 2b N = 4
Full-term live birth (≥ 37 weeks)	137 (93.2%)	17 (85%)	258 (89%)	3 (75%)
*Premature live birth (< 37 weeks)	4 (2.7%)	2 (10%)	16 (6%)	0 (0%)
Spontaneous fetal death/still birth (≥ 28 weeks)	1 (0.7%)	1 (5%)	9 (3%)	0 (0%)
Spontaneous abortion (< 28 weeks)	1 (0.7%)	0 (0%)	3 (1%)	1 (25%)
Small for gestational age (< 10 th percentile)	4 (2.7%)	0 (0%)	3 (1%)	0 (0%)



*Among the 22 pregnancies with preterm birth, four (18.2%) were twin gestations (two in each study group). Most preterm births (19/22, 86.4%) occurred following spontaneous labour (5 oral PrEP; 13 CAB-LA), whereas three (13.6%) followed induced labour, all of which occurred in the CAB-LA group.

	Adverse Pregnancy Outcome		Unadjusted RR (95% CI)	p-value	Adjusted RR (95% CI)	p-value
	No N (%)	Yes N (%)				
Oral PrEP	154 (92)	13 (8)	—	—	—	—
CAB-LA	264 (90)	29 (10)	1.27 (0.68, 2.53)	0.50	1.42 (0.72, 3.03)	0.30

CI = Confidence Interval, RR = Risk Ratio

RR and 95% CIs were estimated using modified Poisson regression with robust standard errors.

The adjusted model included PrEP duration, gestational age at enrollment, gravida, parity, education level, marital status, number of sexual partners, partner HIV status, occupation, and total earnings.

The risk of adverse pregnancy outcomes was slightly higher among those on CAB-LA (Groups 2a and 2b) compared to oral PrEP (Groups 1a and 1b) but neither association was statistically significant.

CAB vs LEN PrEP ISR – CLARITY Study

Presence, Severity, Interference With Usual and Daily Life Activities and Bothersomeness of Injection Site Reactions With Cabotegravir vs Lenacapavir: Insights From Participant Reported Outcomes in the CLARITY Study

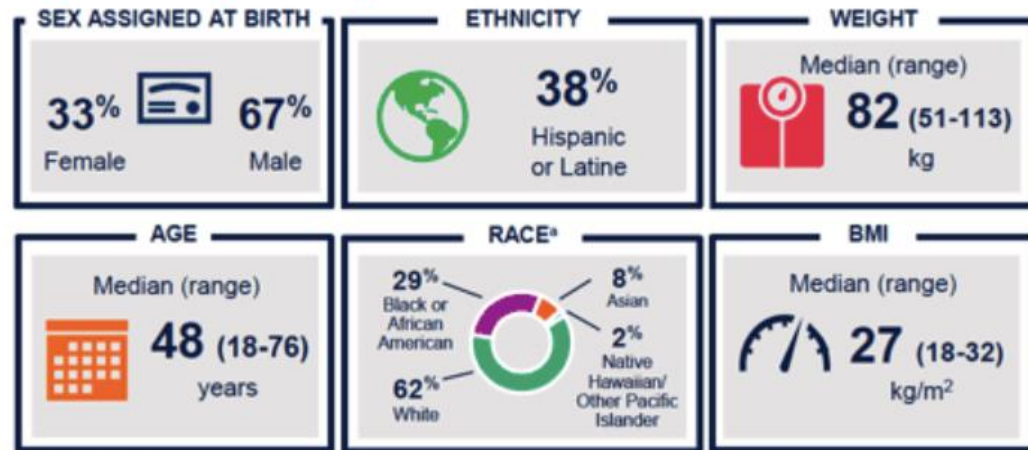
Laure Dupont-Benjamin,¹ Christina Donatti,² Dainielle Fox,³ Justine Boles,² Emilie Elliot,⁴ Apinya Vutikullird,⁵ Amber Mottola,⁵ Kim Fletcher,⁶ Kehui Wang,⁷ Suryakant Somvanshi,⁸ Richard Grove,⁶ Nanlesta Pilgrim,³ Piotr Budnik,² Jean van Wyk,² Harmony P. Garges,⁷ Kimberley Brown³

Participant and Provider Experiences With Long-Acting Cabotegravir vs Lenacapavir Injections: Results From the CLARITY Study

Katherine L. Nelson,¹ Laure Dupont-Benjamin,² Justine Boles,³ Emilie Elliot,⁴ Dainielle Fox,¹ Apinya Vutikullird,⁵ Amber Mottola,⁵ Kim Fletcher,⁶ Kehui Wang,⁷ Suryakant Somvanshi,⁸ Richard Grove,⁶ Rebecca Borsi,¹ Nanlesta Pilgrim,¹ Piotr Budnik,³ Jean van Wyk,³ Harmony P. Garges,⁷ Kimberley Brown¹

¹ViiV Healthcare, Durham, NC, USA; ²ViiV Healthcare, Rueil-Malmaison, France; ³ViiV Healthcare, London, UK; ⁴ViiV Healthcare, Madrid, Spain; ⁵Ark Clinical Research, Long Beach, CA, USA; ⁶GSK, London, UK; ⁷GSK, Durham, NC, USA; ⁸GSK, GCC, Bengaluru, India

Figure 2. Key Participant Baseline Characteristics



^aPercentages add up to over 100% due to rounding of individual categories.

Figure 1. Study Design

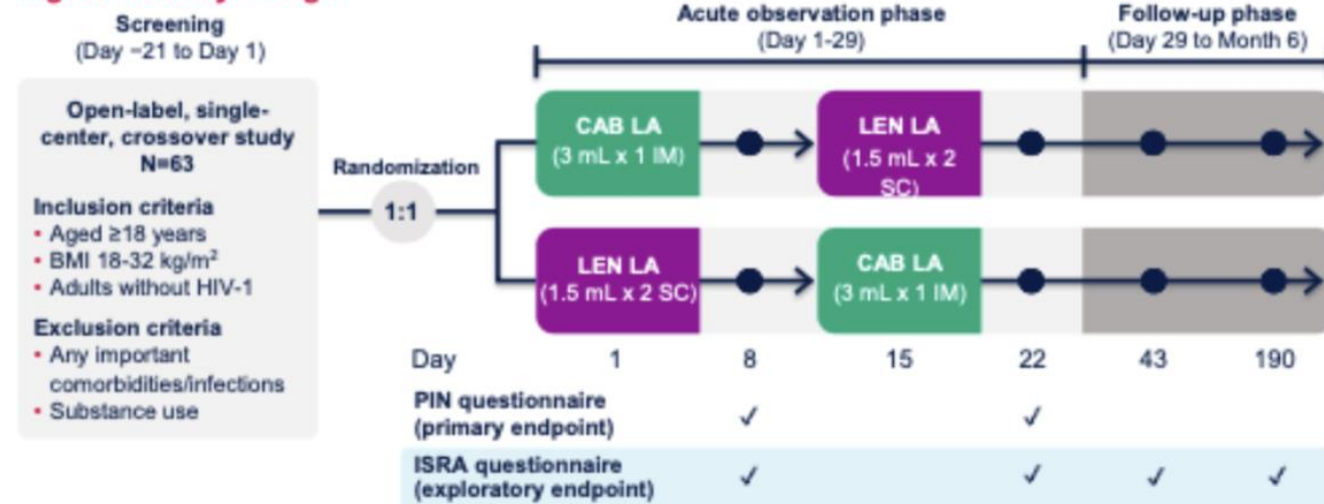


Figure 3. Participant ISRA Responses for Being Bothered by ISRs^a

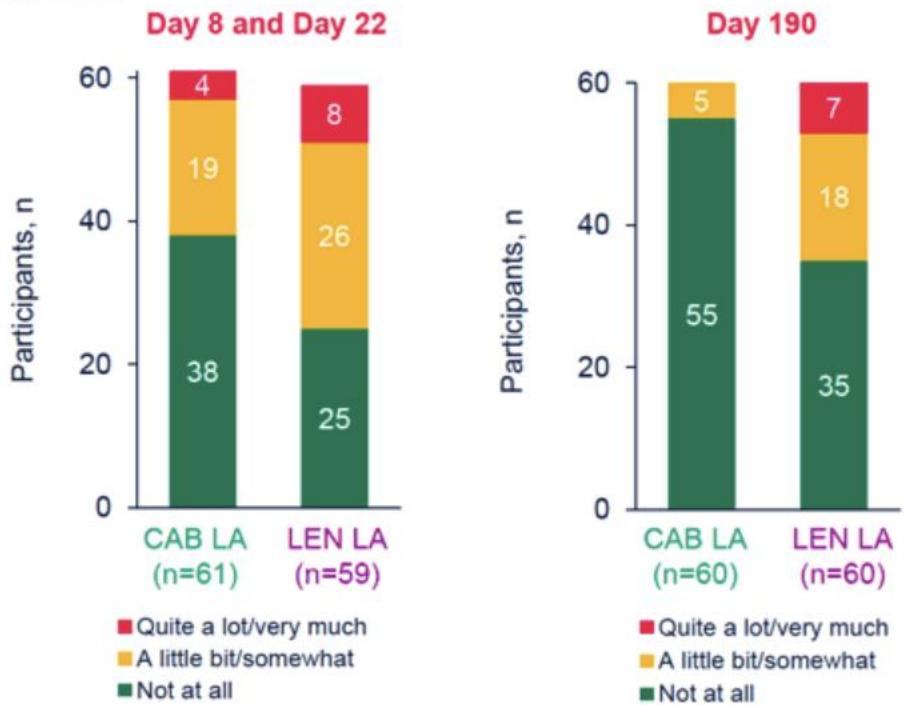
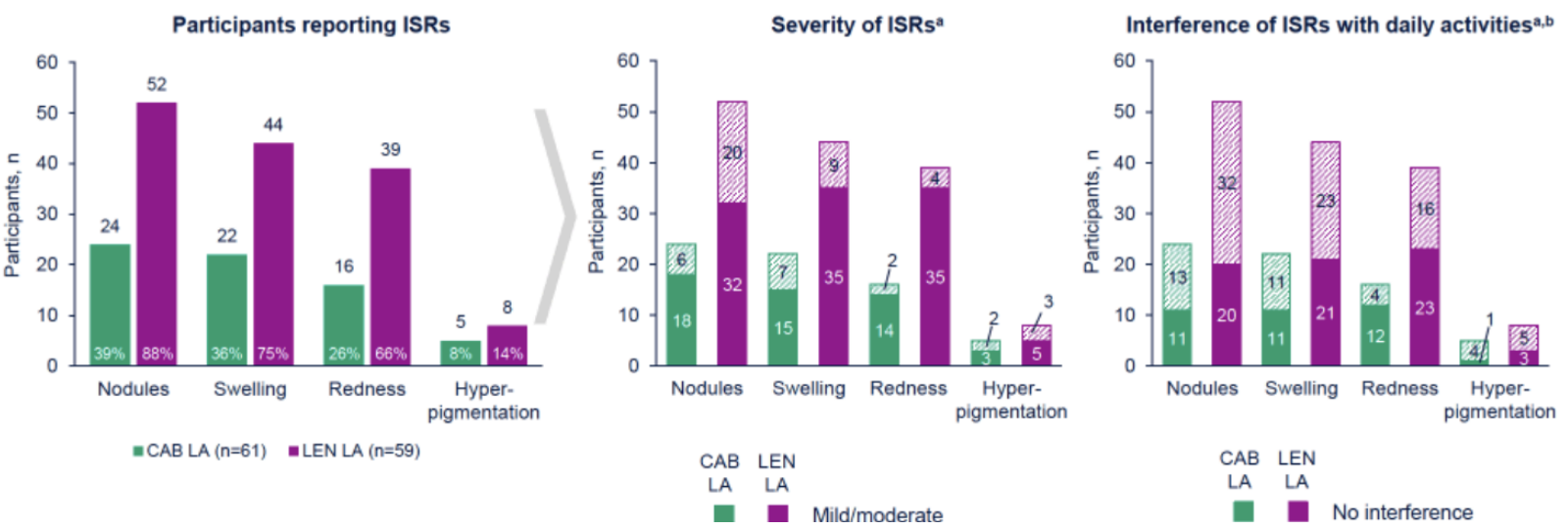


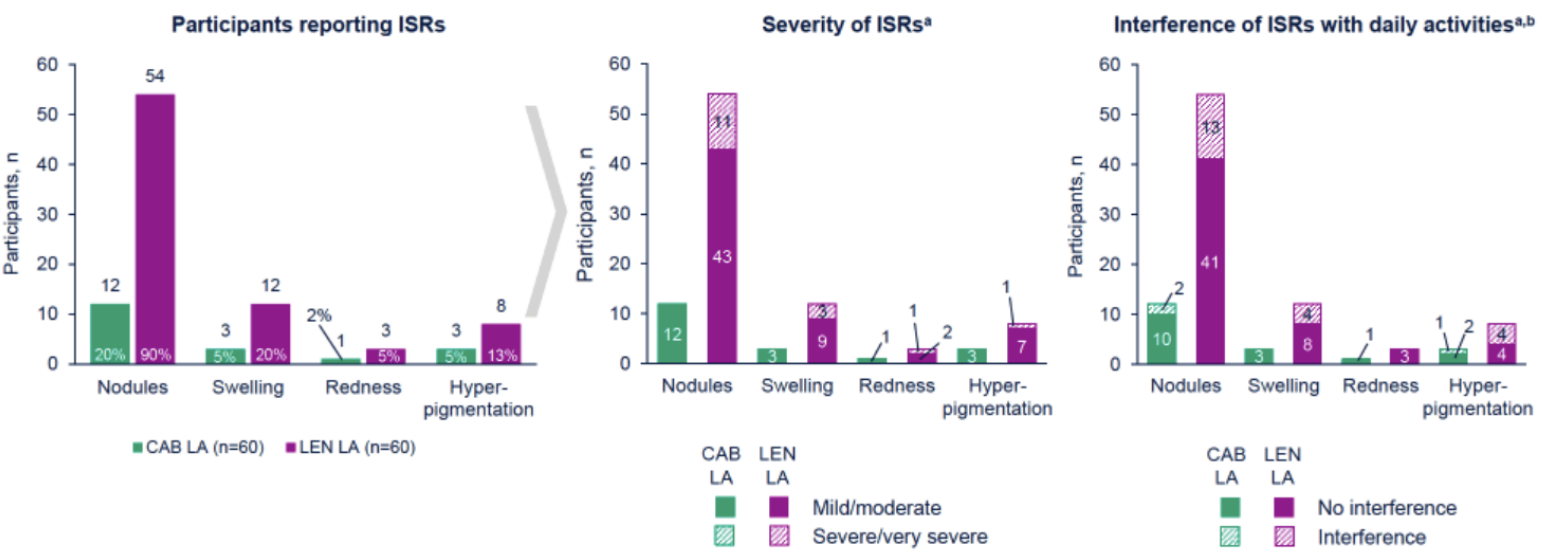
Figure 4. Participant ISRA Responses at Days 8 and 22



Day 190

- At Day 190 (6 months after injection), only 20% (12/60) of participants continued to report nodules after the CAB LA injection vs 90% (54/60) after LEN LA injections (Figure 5)
- No CAB LA-associated ISRs were reported to be severe, while 11/54 (20%) of LEN LA-associated nodules were reported as severe
- Overall, findings through 6 months post injection demonstrate that CAB LA is associated with a lower and less persistent ISR burden than LEN LA, including lower severity

Figure 5. Participant ISRA Responses on Day 190



IMPACT OF ISRs ON PARTICIPANTS

7
Days After
Injection

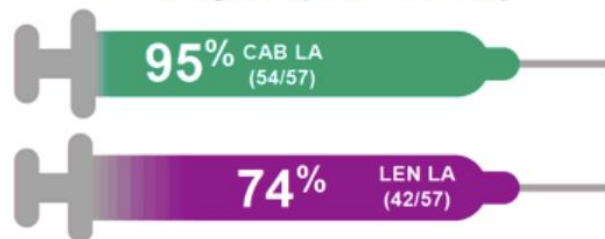
Day
43

Month
6

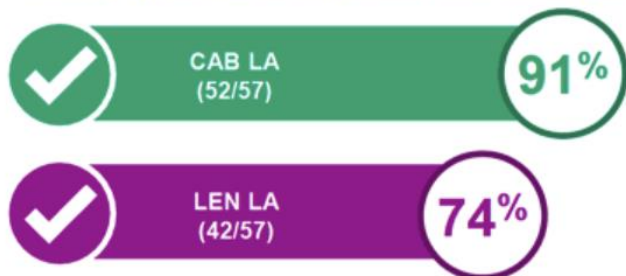
I felt comfortable during the injection process



Receiving the injection was easy



I had a good overall experience with the injection



Day 8 or Day 22 Visit Outcomes

- Participants self-reported less noticeable ISRs with CAB LA injections, and lower negative impacts on self-perception and social activities, compared with LEN LA

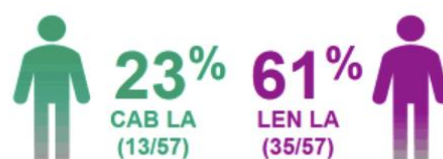
Day 43 Visit Outcomes

- More participants described ISRs with CAB LA (76%, 45/59) as "very acceptable or totally acceptable" at Day 43, vs LEN LA (44%, 26/59)

Month 6 Visit Outcomes

- Participants continued to describe ISRs as "very acceptable or totally acceptable" with CAB LA (70%, 42/60) vs LEN LA (37%, 22/60)

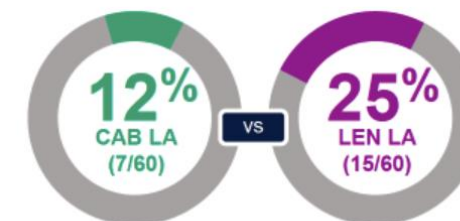
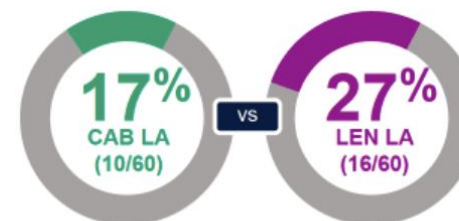
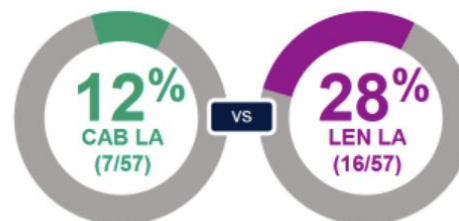
I find the ISRs on my body noticeable^a



I have concerns about how the injection would fit into my daily life^b



I have avoided social activities^c because of visible ISRs



I have avoided intimacy with a regular partner due to ISRs



LEN PrEP: PURPOSE 1&2 ISRs

Favorable Tolerability of Lenacapavir for PrEP Administered at Participant-Chosen Anatomic Sites in PURPOSE 1 and PURPOSE 2

Carlos Brites¹, Marcelo H Losso², Jorge Gallardo-Cartagena³, Pedro Cahn⁴, Jesse Clark⁵, Olivia Van Gerwen⁶, Ishana Harkoo⁷, Cheryl Louw⁸, Noah Kiwanuka⁹, Jenna Yager¹⁰, Pamela Wong¹⁰, Christoph C Carter¹⁰, Moupali Das¹⁰, Flavia Matovu Kiweewa¹¹

Figure 1. PURPOSE 1 and PURPOSE 2 Study Designs^{1,2}

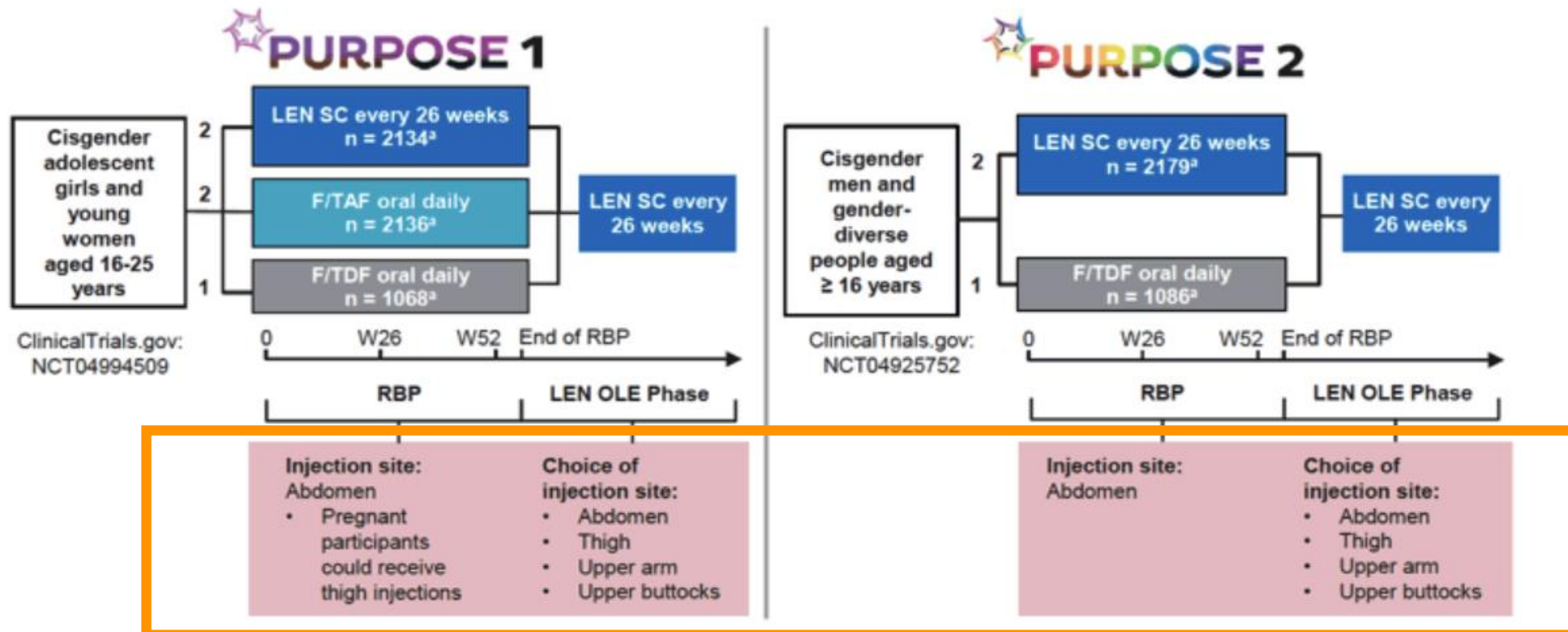


Figure 2. Percentage of Participants Experiencing ISRs by Injection Site

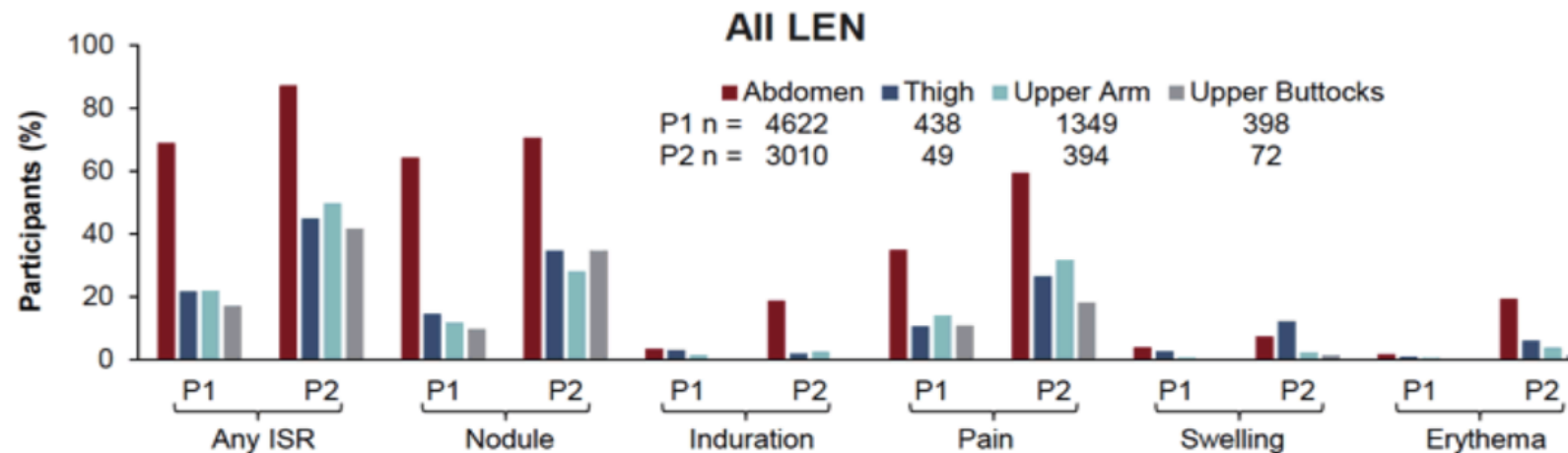


Table 2. Duration and Resolution of ISRs

 PURPOSE 1	Abdomen		Thigh	Upper Arm	Upper Buttocks	 PURPOSE 2	Abdomen		Thigh	Upper Arm	Upper Buttocks
	All LEN (n = 4622)	LEN Switch Group (n = 2482)	All LEN (n = 438)	All LEN (n = 1349)	All LEN (n = 398)		All LEN (n = 3010)	LEN Switch Group (n = 827)	All LEN (n = 49)	All LEN (n = 394)	All LEN (n = 72)
Total injections	28,891	11,082	1113	3298	895	Total injections	19,706	3113	109	846	145
Nodules, n (%)	11,899 (41.2)	4723 (42.6)	108 (9.7)	268 (8.1)	74 (8.3)	Nodules, n (%)	10,430 (52.9)	1839 (59.1)	35 (32.1)	213 (25.2)	44 (30.3)
Resolved, n (%) ^a	7326 (61.6)	2275 (48.2)	57 (52.8)	80 (29.9)	19 (25.7)	Resolved, n (%) ^a	6201 (59.5)	597 (32.5)	10 (28.6)	98 (46.0)	11 (25.0)
Median (Q1, Q3) days to resolution ^b	260 (151, 364)	182 (91, 275)	90 (80, 174)	91 (72, 142)	90 (86, 97)	Median (Q1, Q3) days to resolution ^b	270 (176, 367)	183 (106, 273)	116 (82, 178)	85 (32, 96)	182 (168, 184)
Indurations, n (%)	276 (1.0)	79 (0.7)	22 (2.0)	30 (0.9)	2 (0.2)	Indurations, n (%)	2025 (10.3)	398 (12.8)	1 (0.9)	15 (1.8)	0
Resolved, n (%) ^a	213 (77.2)	47 (59.5)	13 (59.1)	25 (83.3)	1 (50.0)	Resolved, n (%) ^a	1641 (81.0)	288 (72.4)	1 (100)	12 (80.0)	N/A
Median (Q1, Q3) days to resolution ^b	87 (15, 262)	53 (17, 233)	15 (11, 49)	29 (10, 55)	95	Median (Q1, Q3) days to resolution ^b	85 (7, 191)	11 (6, 115)	93	22 (3, 95)	N/A

- Injection site reactions (ISRs) were less frequent with LEN injections administered in the thigh, upper arm, and upper buttocks compared with the abdomen
- Nodules and indurations occurring after thigh, upper arm, or upper buttock injections resolved more quickly than those occurring after abdomen administration

HIV PrEP: What do people want?

Perceptions, Preferences, and Unmet Need for PrEP: Results from a Multi-Country Survey

Julia Charbonnier¹, Nomfundo Eland², Robin Barkins³, Xavier Guillaume⁴, Amina Omri⁴, Alexanne Morillo⁴, Coline Lestriez⁴, Joshua Gruber⁵, Kristin Baker⁶, Keshia O'Reilly⁵, Brett Shannon⁵, Cub Barrett⁵, Larkin Callaghan⁵, Maureen Owino⁶

- PrEP has been around a long time, but uptake and use is suboptimal
- As PrEP evolves important to take stock of potential user preferences
- Online survey of people who can benefit from PrEP in US, Canada, UK, S Africa

Table 1. Key Population Characteristics by PrEP Use

Key population, n (%)	All participants N=1262 (100)	Current PrEP user n=477 (38)	Former PrEP user n=149 (12)	PrEP-naïve n=636 (50)
Gender identity				
Cis women	648 (51)	189 (40)	84 (56)	375 (59)
Transgender/non-binary	102 (8)	27 (6)	17 (11)	38 (9)
Sexual orientation and ethnicity				
MSM	339 (27)	206 (43)	43 (29)	90 (14)
BIPOC	321 (25)	124 (26)	31 (21)	166 (26)
BIPOC MSM	126 (10)	86 (18)	17 (11)	23 (4)
Sociodemographic characteristics				
Migrant	180 (14)	95 (20)	17 (11)	68 (11)
Low income or underinsured	577 (46)	97 (20)	86 (58)	394 (62)
Age groups				
Young adults (<25 years)	129 (10)	31 (7)	28 (19)	70 (11)
Older adults (>50 years)	136 (11)	18 (4)	5 (3)	113 (18)

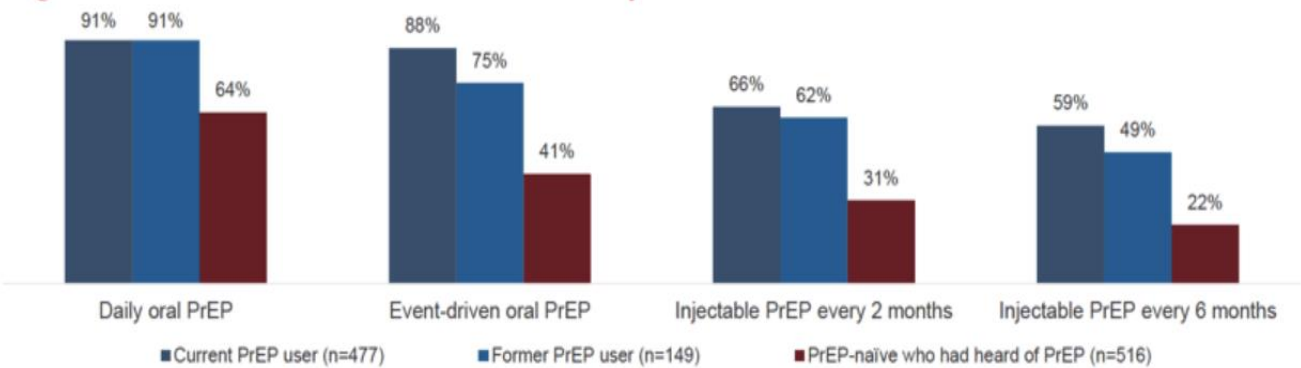
BIPOC, black, indigenous and people of color; MSM, men who have sex with men; PrEP, pre-exposure prophylaxis.

Awareness of PrEP

- In the overall study population, 10% of participants reported no prior awareness of PrEP
- Lack of awareness was highest in Canada and the UK (14% each), compared with the US (7%) and South Africa (6%)
- Among PrEP-naïve individuals, 81% had heard of PrEP, while 19% were unaware of PrEP
 - Familiarity with PrEP medication options was lower among PrEP-naïve participants who had heard of PrEP, compared with current or former PrEP users, particularly for injectable modalities (Figure 1)

Results

Figure 1. Awareness of PrEP Medication Options



Participants preferred PrEP options that minimize side effects, maintain effectiveness, and reduce dosing frequency

- Weekly oral and 6-monthly injectable PrEP options were associated with greater comfort than daily oral, event-driven, and 2-monthly injectable modalities

Figure 3. A) Barriers to PrEP Uptake Among PrEP-Naïve Individuals (n=516)^a and B) Reasons for Discontinuation Among Former PrEP Users (n=149)

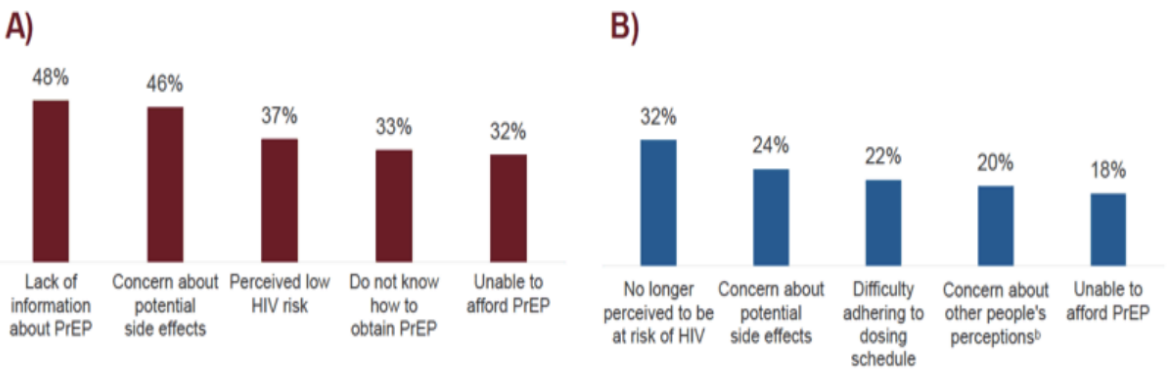
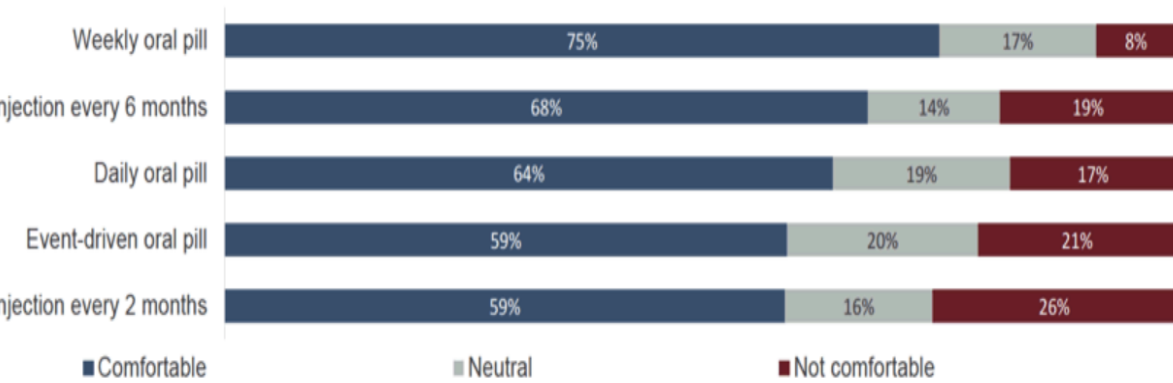


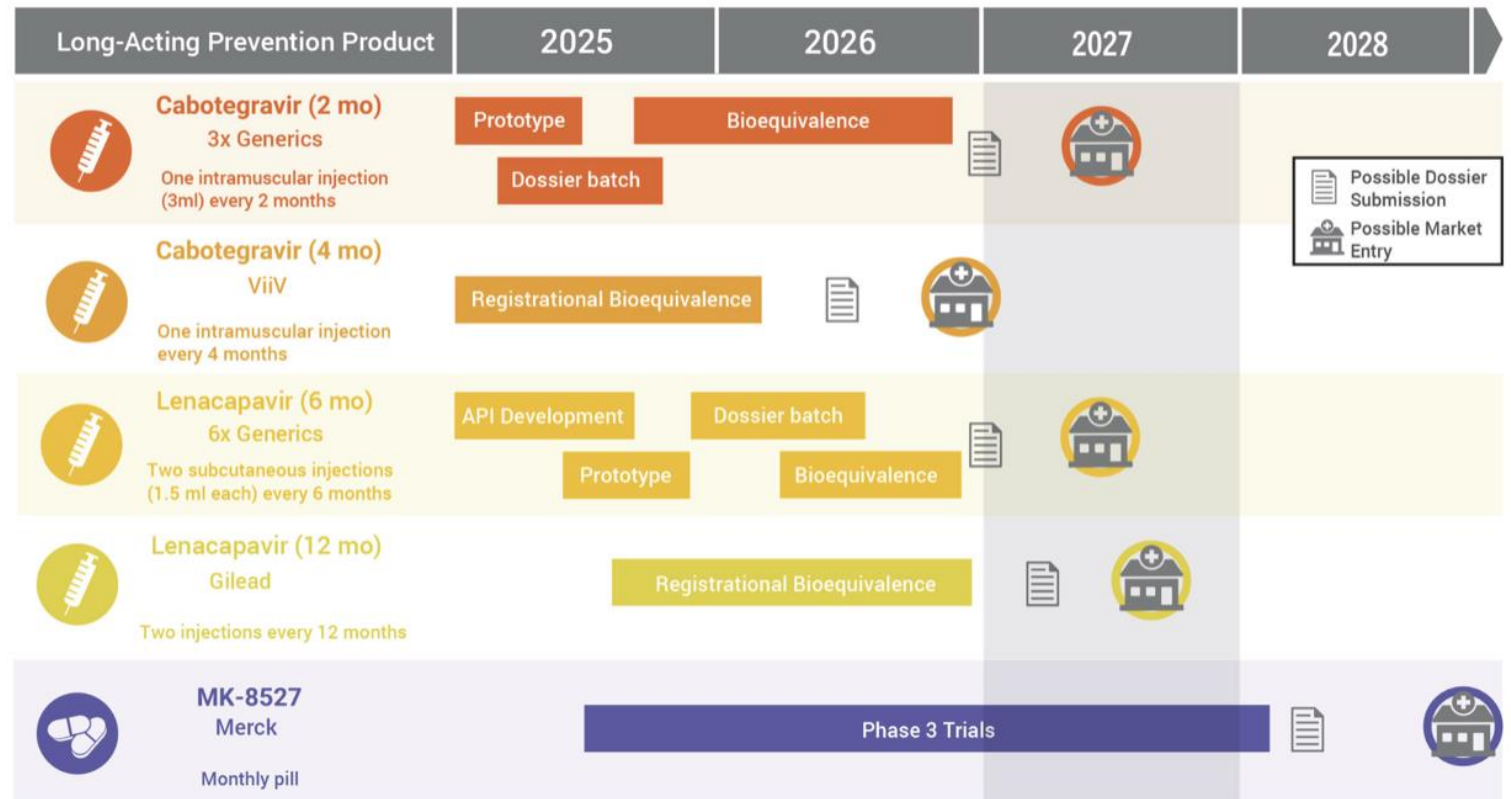
Figure 4. Reported Comfort Levels Across PrEP Modalities



PrEP Pipeline

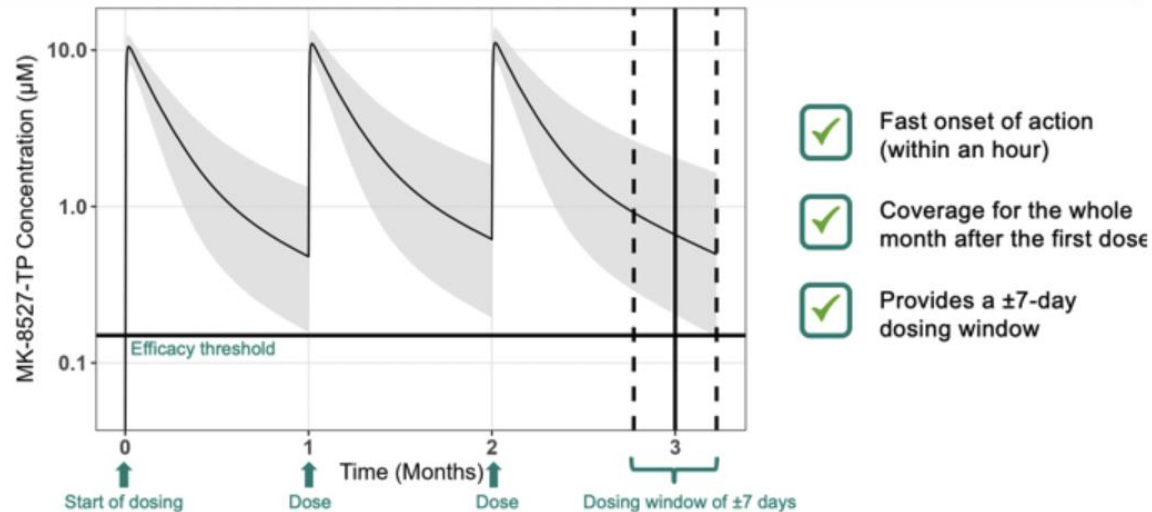
- Every 12-month lenacapavir IM
- Monthly oral MK-8527
- Broadly neutralizing antibodies
- Tenofovir rectal douche
- Implants?

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

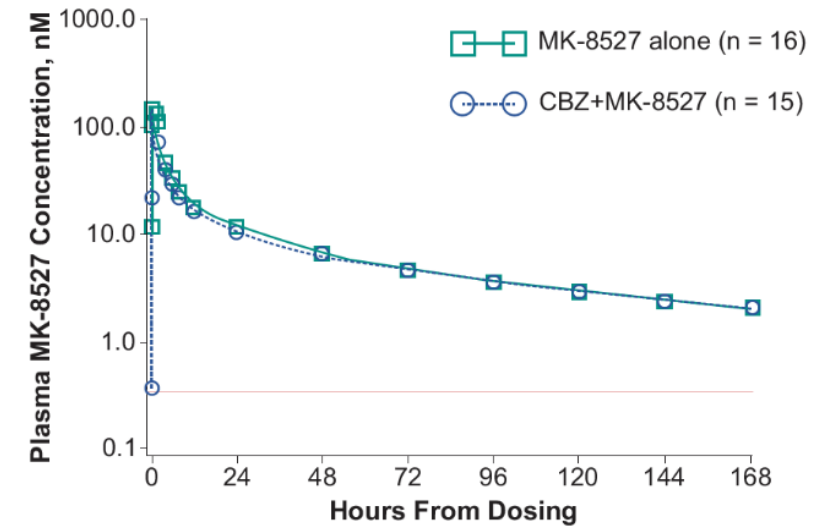


MK-8527^{NRTTI} (Alimatravir)– Monthly Oral PrEP

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



Month = 31 days. Bands represent fifth and 95th PI.
PI, prediction interval; PK, pharmacokinetics; qm, once-monthly; TP, triphosphate.



MK-8527 Phase 3 Program for PrEP



DOXYPEP - Australia

Substantial population-level reductions in syphilis and chlamydia among gay and bisexual men after introduction of doxyPEP guidance in Australia

Burnet
reach for the many

Michael Traeger, Burnet Institute

Jason Asselin, Htein Linn Aung, Allison Carter, Anna Wilkinson, Vincent Cornelisse, Dash Heath-Paynter, Eric Chow, Jason Ong, Rick Varma, Daniel Vujcich, Caroline Tng, Jenny McCloskey, Tom Rees, Brendan Quinn, Bridget Haire, Margaret Hellard, Rebecca Guy & Mark Stoové

Cohort & analysis

Clinical services: High caseload general practices & sexual health clinics

Cohort: Gay and bisexual men attending ACCESS clinics

Study period: 1st January 2022 – 31st December 2025 (4 years)

Outcomes:

- Syphilis (newly identified case of infectious syphilis)
- Chlamydia (positive NAAT)
- Gonorrhoea (positive NAAT or culture)



Data Source

- Surveillance network established >10 years ago
- >100 services with national representation
- High coverage of PrEP users and PLHIV
- Specialised data extraction software
- Linkage allows for individual-level, longitudinal monitoring over time and across clinics
- Linked data includes all test events, prescriptions and STI history



*Australian Collaboration for Coordinated
Enhanced Sentinel Surveillance of Blood-borne
Viruses and Sexually Transmitted Infections*



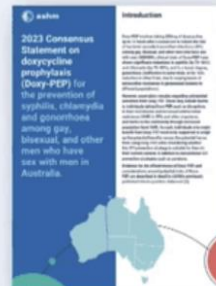
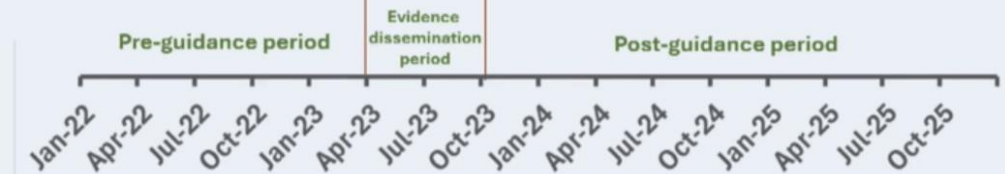
Time-series interruptions

Interruption 1: April 2023

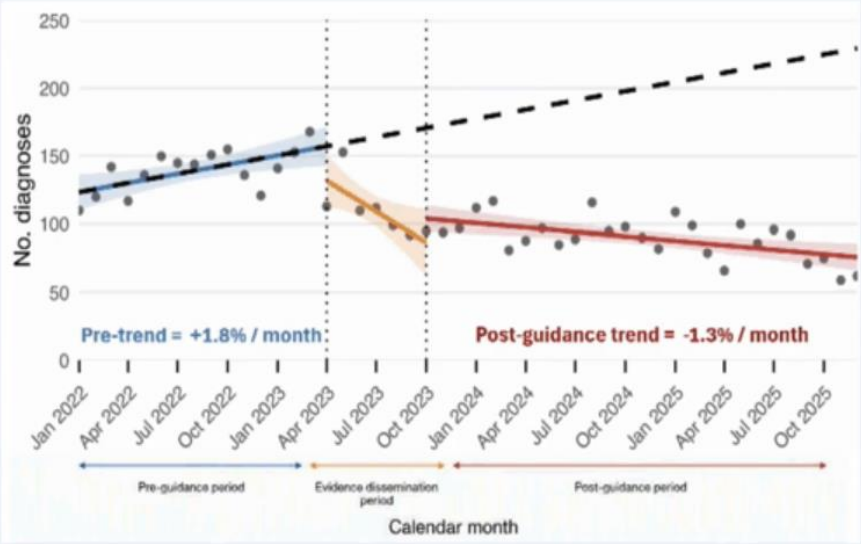
- Release of Australian interim position statement on DoxyPEP
- Publication of US DOXYPEP study in NEJM (Leutkemeyer et al)
- Community & clinician health promotion

Interruption 2: October 2023

- Release of Australian DoxyPEP Consensus Statement
- First prescribing recommendations for gay and bisexual men

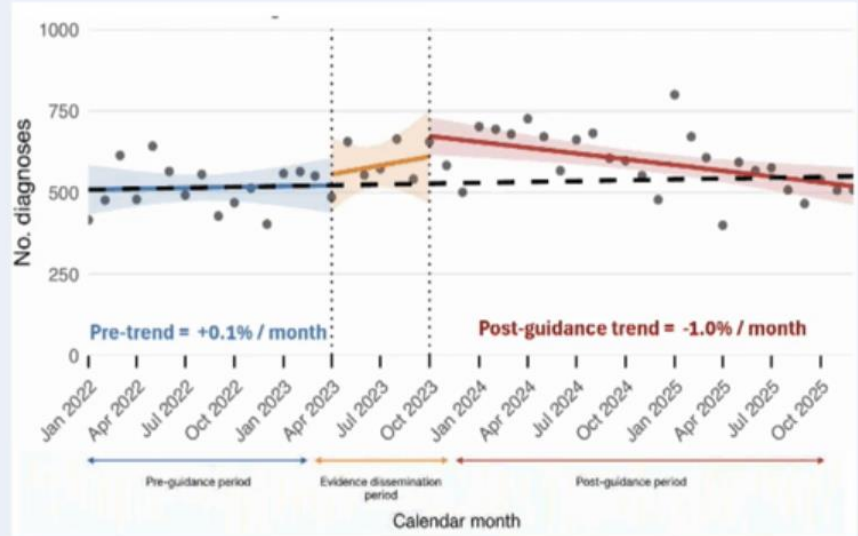


Syphilis diagnoses



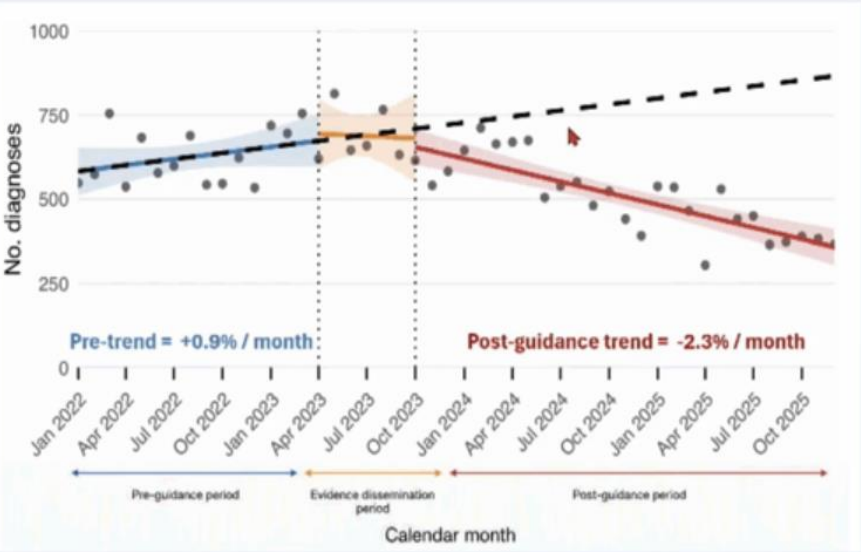
Estimated
2,973 fewer
diagnoses than
expected under the
pre-guidance trend
(55% reduction)

Gonorrhoea diagnoses



Estimated
1,556 more
diagnoses than
expected under the
pre-guidance trend
(11% increase)
(not-significant)

Chlamydia diagnoses



Estimated
7,604 fewer
diagnoses than
expected under the
pre-guidance trend
(36% reduction)

DOXYPEP - US^{NC}

Emily D Niehaus, MD MPH, Duke University



DoxyPEP: Delivering on its promise

Real-world effectiveness of doxycycline post- exposure prophylaxis (DoxyPEP) for STI prevention in a southern U.S. HIV/PrEP clinic



AIDS 2026

Methods

Population: Clients prescribed DoxyPEP from 1/1/22 – 12/31/25

Data: Duke Health electronic medical records

Exposure: individual-level DoxyPEP initiation

Outcomes:

- Incidence of gonorrhea, chlamydia, and syphilis diagnoses
 - Pre- & post-DoxyPEP incidence rates and crude incidence rate ratios (IRR)
- Quarterly incidence trends relative to DoxyPEP initiation
- Quarterly proportion receiving gonorrhea/chlamydia testing

Variable	N=380
Age, years (median, IQR)	36 (29-46)
Chart reviewed gender identity/sexual orientation	
Man who has sex with men	361 (95%)
Transgender woman	9 (2.4%)
Assigned female at birth	3 (0.8%)
Heterosexual cisgender man	7 (1.8%)
Race	
Black or African-American	177 (50%)
White	140 (40%)
All other races	34 (10%)
Hispanic ethnicity	
Insurance type	38 (11%)
Medicaid	46 (12%)
Medicare	25 (7%)
Private	261 (69%)
Self-pay	45 (12%)

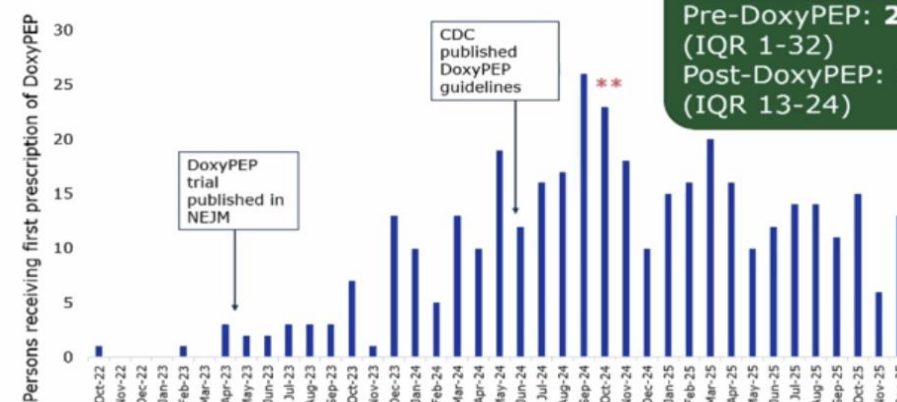
51% PWH
49% on PrEP

36% had a bacterial
STI in 12 months
before DoxyPEP was
prescribed.
46% of PWH, 26% of
PrEP users



AIDS 2026

DoxyPEP prescribing over time

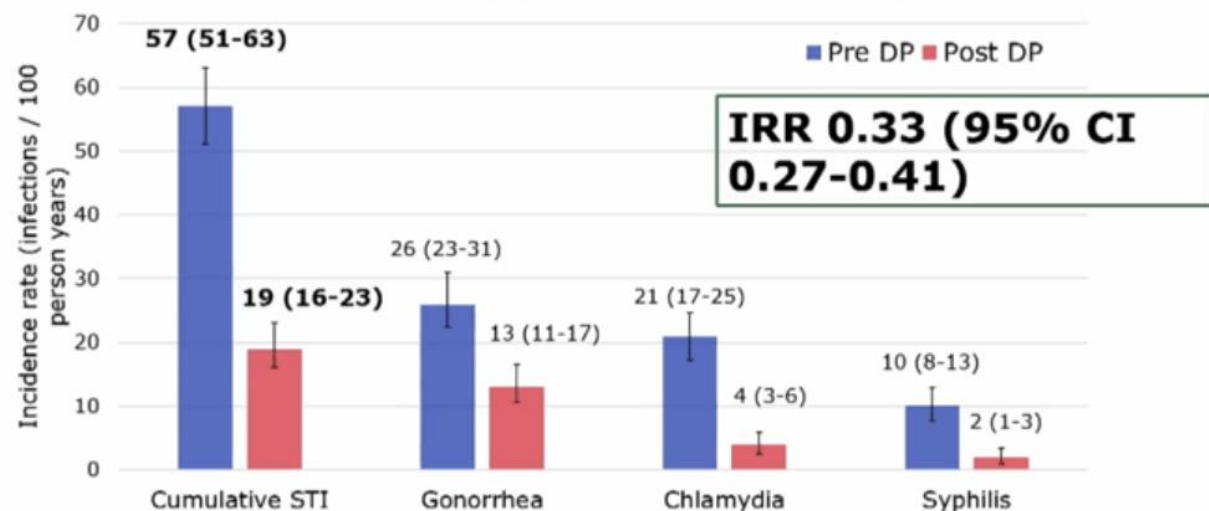


Median follow-up
Pre-DoxyPEP: 22 mo
(IQR 1-32)
Post-DoxyPEP: 19 mo
(IQR 13-24)



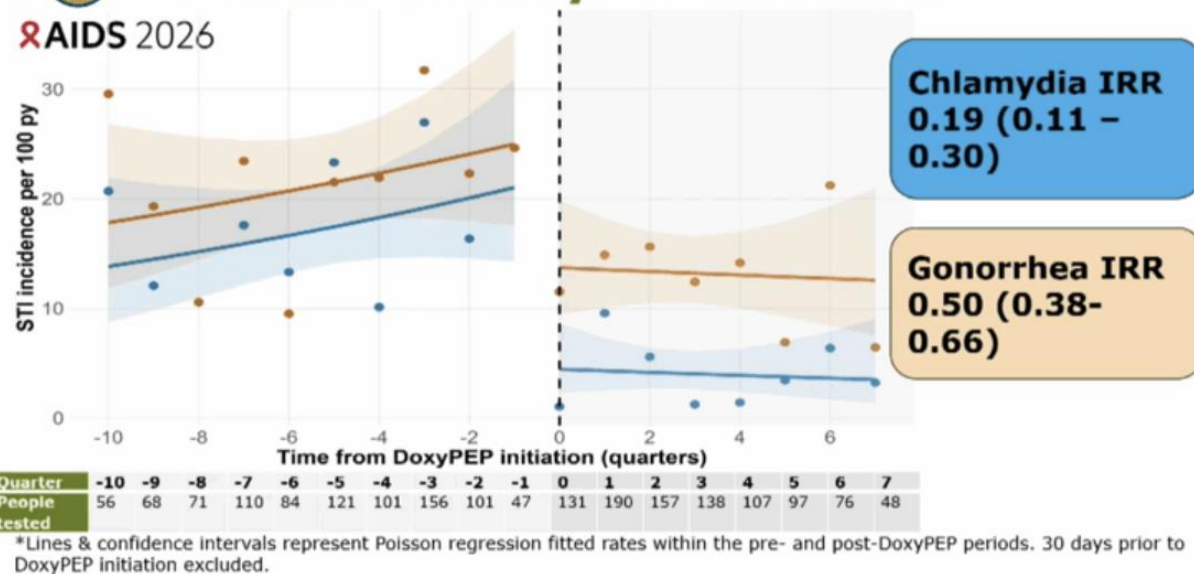
AIDS 2026

STI incidence rate was significantly lower in post- DoxyPEP period



AIDS 2026

Gonorrhea & chlamydia incidence relative to DoxyPEP initiation



- STI incidence was 67% lower after DoxyPEP initiation than prior.
- Similar relative reductions in STI incidence were observed regardless of history of STI in the last 12 months.
- STI testing patterns remained largely unchanged after DoxyPEP.

DOXYPEP – Modelling

Impact of doxy-PEP on sexually transmitted infections diagnoses and antibiotic use among men who have sex with men and trans women on PrEP in Brazil: a modelling study

M. Secco Torres da Silva¹, R. Ismério Moreira¹, I. Costa Leite², M. Cunha², M. Benedetti¹, A. Farias³, T. Silva Torres¹, C. Coutinho¹, B. Hoagland¹, V. Gonçalves Veloso¹, B. Grinsztejn¹

IDS 2026 Methods

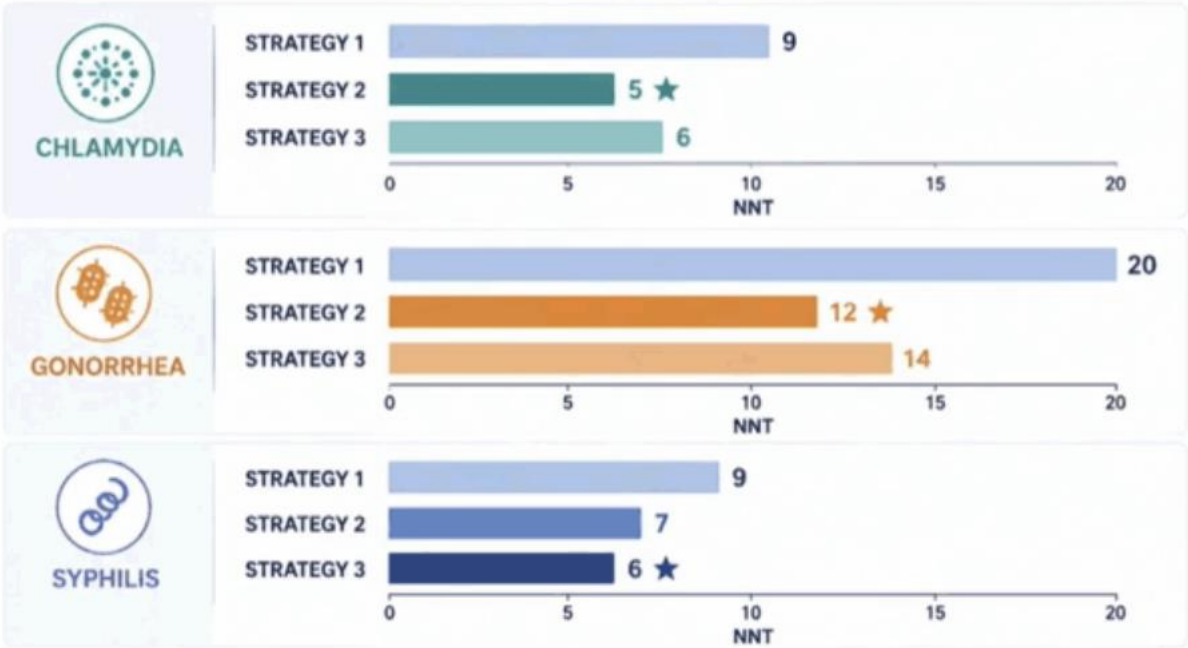
We used STI incidence data from Brazilian participants enrolled in the ImPrEP study to model the number of STI diagnoses that could be averted among MSM and TGW on PrEP in Brazil under three different doxy-PEP prescribing strategies:

- **(S1)** doxy-PEP initiation at PrEP enrollment regardless of STI testing results;
- **(S2)** doxy-PEP initiation after any positive STI test during PrEP follow-up;
- **(S3)** doxy-PEP initiation if any positive STI test at PrEP enrollment.

	Strategy 1	Strategy 2	Strategy 3
Number of participants receiving doxy-PEP	3,447 (100%)	1,473 (42.7%)	812 (28.7%)
Number of incident STI	2,035	2,035	2,035
Number of averted STI	1,617	894	583
Percentage of avertable STI	79.4%	43.9%	28.6%

2026

NNT by prescribing strategy



Antibiotic consumption

People on PrEP in Brazil by July 2026: 159,000

	Strategy 1	Strategy 2	Strategy 3
Number of people receiving doxy-PEP considering an uptake of 75% (x10 ³)	113.2	48.4	26.6
Doxy-PEP consumption (DDD)	452,763	193,478	106,656
Avoided antibiotic for chlamydia treatment (DDD)	7336	5643	2592
Avoided antibiotic for gonorrhea treatment (DDD)	118	84	40
Avoided antibiotic for syphilis treatment (DDD)	699	384	247
Total avoided antibiotic (DDD), monthly	8153	6111	2879
Monthly net doses variation (DDD)	444,610	187,367	103,777

↓ 58% ↓ 77%



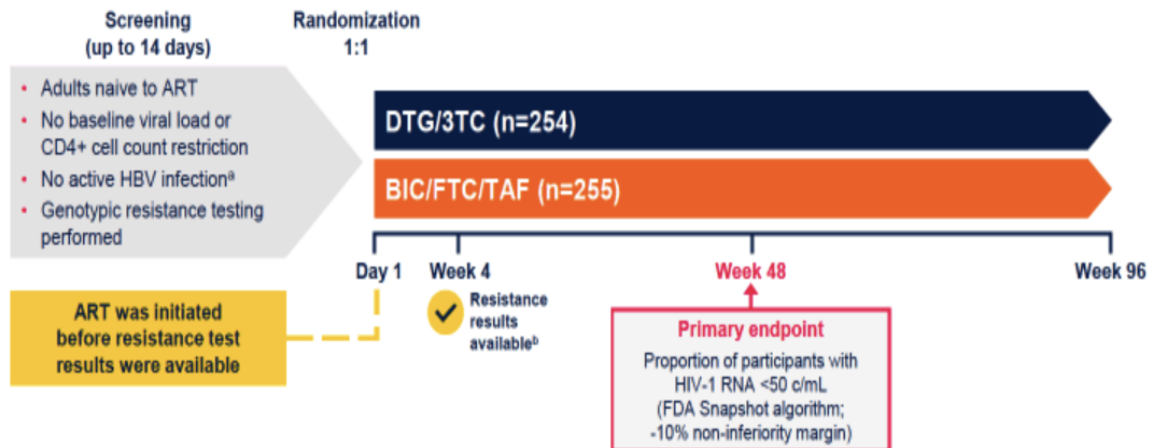
TREATMENT

DTG/3TC v BFTAF as 1st Line ART – VOGUE Trial

In VOGUE: DTG/3TC Demonstrates Non-Inferior Efficacy to BIC/FTC/TAF as First-Line Treatment

Jade Ghosn,^{1,2} Federico Pulido,³ Gustavo D. Lopardo,⁴ Anita Olczak,⁵ Diego Ripamonti,⁶ Charlotte Martin,⁷ Orlando Paredes Ceballos,⁸ Hartmut Stocker,^{9,10} Maria Josefina Mendez Vasquez,¹¹ Hiroyuki Gatanaga,¹² Simeon Metallidis,¹³ Daniel Elbirt,¹⁴ Gary Whitlock,¹⁵ José Ignacio Mateo González,¹⁶ Perry Mohammed,¹⁷ Kehui Wang,¹⁸ Ruolan Wang,¹⁹ Adelaide Jewell,¹⁷ Emilie Elliot,²⁰ Riya Moodley,¹⁷ Bryn Jones,¹⁷ Michelle Kisare,¹⁷ Piotr Budnik,¹⁷ Jean van Wyk,¹⁷ for the VOGUE study group

Phase 3b, randomized, open-label, non-inferiority study (NCT05979311)



- Randomization was stratified by plasma HIV-1 RNA (< vs ≥100,000 c/mL) and CD4+ cell count (< vs ≥200 cells/mm³)

Countries: Argentina, Belgium, Denmark, France, Germany, Greece, Ireland, Israel, Italy, Japan, Mexico, Poland, Portugal, Spain, Sweden, Switzerland, and United Kingdom.

VOGUE Study Population

See Poster WEPEB094 for additional data

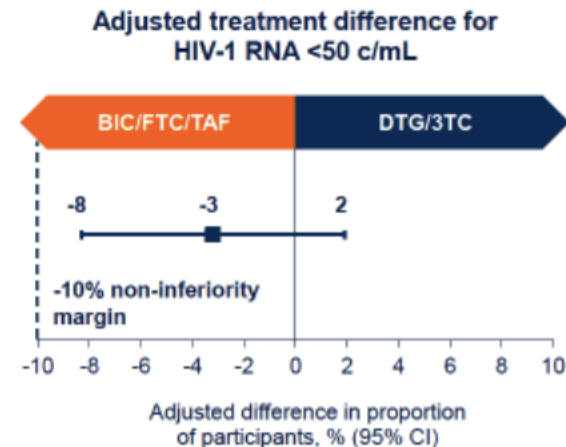
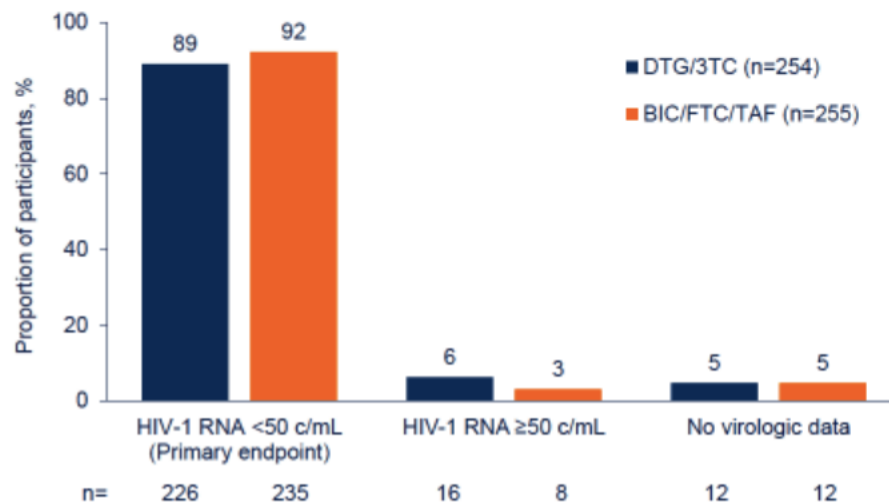


Parameter	DTG/3TC (n=254)	BIC/FTC/TAF (n=255)	Total (N=509)
Age, median (range), y	33 (18-73)	33 (18-84)	33 (18-84)
Sex assigned at birth, female, n (%)	41 (16)	38 (15)	79 (16)
Race (self-reported), n (%)			
White	211 (83)	212 (83)	423 (83)
Black or African American	24 (9)	20 (8)	44 (9)
Asian	14 (6)	12 (5)	26 (5)
Other ^a	5 (2)	11 (4)	16 (3)
Ethnicity (self-reported), Hispanic or Latino, n (%)	100 (39)	97 (38)	197 (39)
Plasma HIV-1 RNA, median (IQR), log ₁₀ c/mL	4.98 (4.40-5.56)	4.92 (4.39-5.45)	4.94 (4.40-5.46)
≥100,000 c/mL, n (%)	126 (50)	113 (44)	239 (47)
≥500,000 c/mL, n (%)	45 (18)	38 (15)	83 (16)
CD4+ cell count, median (IQR), cells/mm ³	375 (267-548)	372 (257-529)	373 (264-535)
<200 cells/mm ³ , n (%)	40 (16)	39 (15)	79 (16)
Time from screening to treatment initiation, median (IQR), d	10 (8-14)	10 (8-14)	10 (8-14)

- 0.4% (2/548) of screened individuals were excluded due to active hepatitis B virus infection
- 1 participant in each treatment group with baseline M184V achieved HIV-1 RNA <50 c/mL at Week 4 and discontinued study treatment per protocol

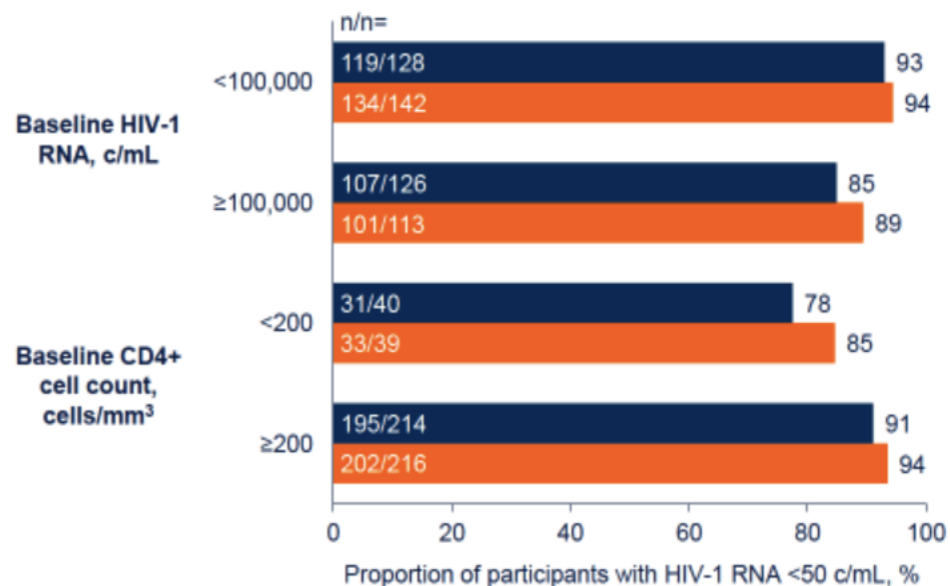
^aAmerican Indian or Alaska Native (DTG/3TC, n=1; BIC/FTC/TAF, n=4), Native Hawaiian or other Pacific Islander (DTG/3TC, n=3; BIC/FTC/TAF, n=5), or unknown race (DTG/3TC, n=1; BIC/FTC/TAF, n=2).

Snapshot outcomes at Week 48



- Most instances of Snapshot HIV-1 RNA ≥50 c/mL were viral load blips <200 c/mL after prior suppression to <50 c/mL, and participants continued on study^a

HIV-1 RNA <50 c/mL



- CVW was defined as 2 consecutive plasma HIV-1 RNA measurements meeting protocol-defined criteria for either virologic non-response or virologic rebound (≥200 c/mL)

Outcome, n (%)	DTG/3TC (n=254)	BIC/FTC/TAF (n=255)
CVW by Week 48	7 (3)	7 (3)
Virologic non-response	0	1
Virologic rebound	7	6
Treatment-emergent resistance^{a,b}	0	0

- No drug-related SAEs or fatal SAEs occurred in the study
- No new HBV infections or reactivations were observed
- Mean change in weight from baseline to Week 48 was +3.6 kg for DTG/3TC and +4.0 kg for BIC/FTC/TAF

DOR/3TC/TDF v DTG/FTC/TAF as 1st Line ART – Opti-DOR Trial^S Africa

Initial HIV-1 therapy for adults at high risk of treatment-associated weight gain: The Opti-DOR randomized clinical trial

Joana Woods¹, Limakatso Lebina², Karlien Moller¹, Godspower Akpomemie¹, Simiso Sokhela¹, Ncomeka Manentsa¹, Ngundu Behumuma², Andrew Hill³, WD Francois Venter¹

Study design



Eligibility

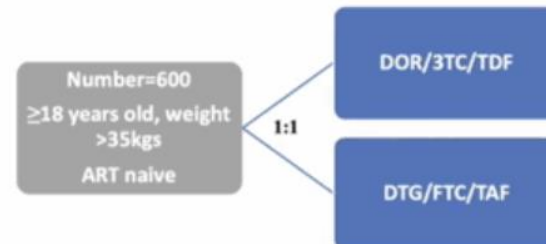
Inclusions: Adults, ART naïve, HIV-1 RNA >500 copies/mL, no baseline high-level DOR resistance

Key exclusions: active TB, eGFR <60 mL/min, significant hepatic disease, contraindicated medicines, pregnant/breastfeeding

Study design

Open-label, randomized, phase 3b trial

Protocol amendment removed BMI ≥25 kg/m² eligibility once weight endpoints were powered



Screen	Baseline	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	EOS
-60 to -1	Day 0	Week 4	Week 12	Week 24	Week 36	Week 48	Week 60	Week 72	Week 84	Week 96

Randomization.

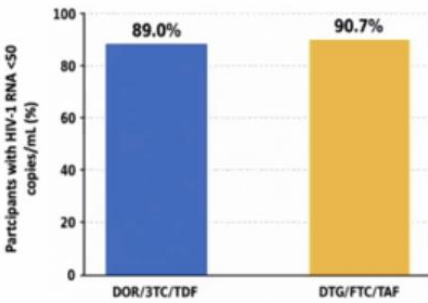
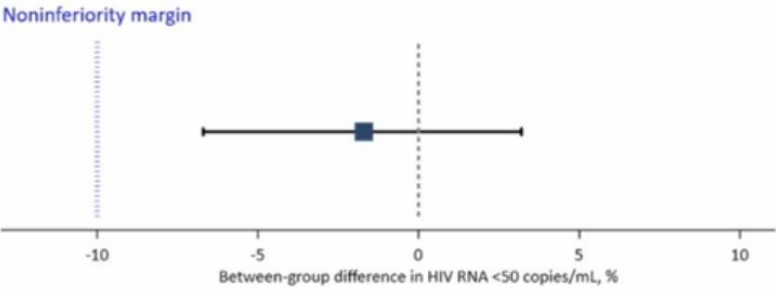
Primary end point

Characteristic	DOR/3TC/TDF (n=299)	DTG/FTC/TAF (n=301)
Age, median (IQR), years	34 (28–40)	34 (28–41)
Female sex, No. (%)	207 (69.2%)	206 (68.4%)
Black African, No. (%)	297 (99.3%)	300 (99.7%)
Median HIV-1 RNA, log ₁₀ copies/mL	4.3 (3.7–4.8)	4.4 (3.9–4.8)
HIV-1 RNA >100,000 copies/mL	52 (17.4%)	57 (18.9%)
Median CD4 count, cells/μL	322 (177–486)	324 (199–523)
CD4 <200 cells/μL	88 (29.4%)	76 (25.3%)
Median body weight, kg	75.0 (66.2–83.9)	74.8 (66.0–85.5)
Median BMI, kg/m ²	27.7 (25.2–31.8)	27.8 (25.0–31.7)
Obese (BMI ≥30 kg/m ²)	102 (34.1%)	102 (33.9%)

Primary outcome: noninferior viral suppression at Week 48 (NI met)



ITT: -1.7 percentage (95% CI: -6.6 to 3.1) NI margin: -10 percentage



Virological failure and resistance



- Protocol-defined failure* 9 vs 6 (DOR/3TC/TDF vs DTG/FTC/TAF). TOT ~25weeks per arm.
- DOR resistance 7/9 failures (high-level emergent resistance), predominant adherence issues, no OIs
- No INSTI/NRTI resistance in DTG/FTC/TAF arm

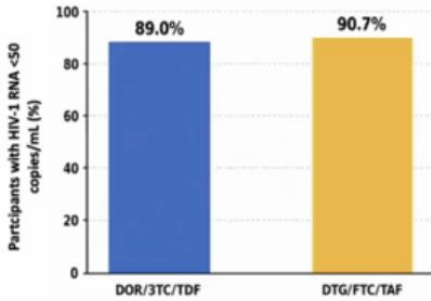
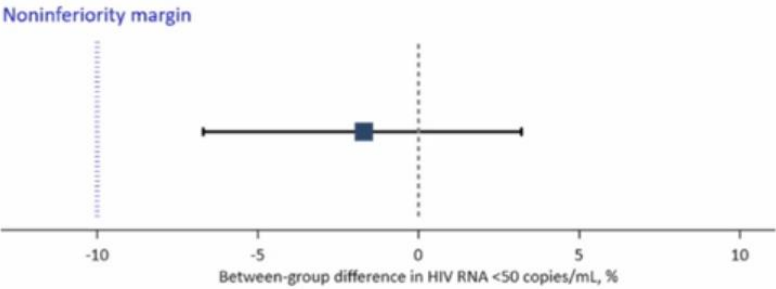
Emergent NRTI resistance	Emergent NNRTI resistance	HIV-1 subtype	Baseline CD4	Baseline VL	VL at Failure	Virological suppression achieved (Week)
K65R, M184MIV	V106M, V108I, E138A, M230	C	33	84 431	31 625	Changed to TLD Wk 48- suppressed by Wk 60
K65R	V106M, E138EK, F227L	C	11	300 706	352 299	Changed to TLD at Wk 36- suppressed by Wk 48
K65R,Y115F	V106M, Y181C, H221HY, F227L	C	30	213 324	214 042	Changed to TLD at Wk 36- suppressed Wk48
K70KQ, M184V	Y188L, P225PH	C	100	6 139	19 166	Changed to TLD Wk 48- suppressed by Wk 60
K65R	V106M	C	52	197 504	2 369	Changed to TLD at Wk 60- suppressed at Wk 72
K65R, S68N,M184V	V106M, E138K, F227L	C	14	43 471	23 331	LTFU
K65R	V106M, E138A, E227I	C	7	54 582	1 806	Changed to TLD at Wk 36- suppressed by Wk 48

* 2 x HIV-1 RNA ≥1000 copies/mL from week 24 or 2 consecutive HIV-1 RNA ≥200 copies/mL at week 48

Primary outcome: noninferior viral suppression at Week 48 (NI met)



ITT: -1.7 percentage (95% CI: -6.6 to 3.1) NI margin: -10 percentage



Virological failure and resistance

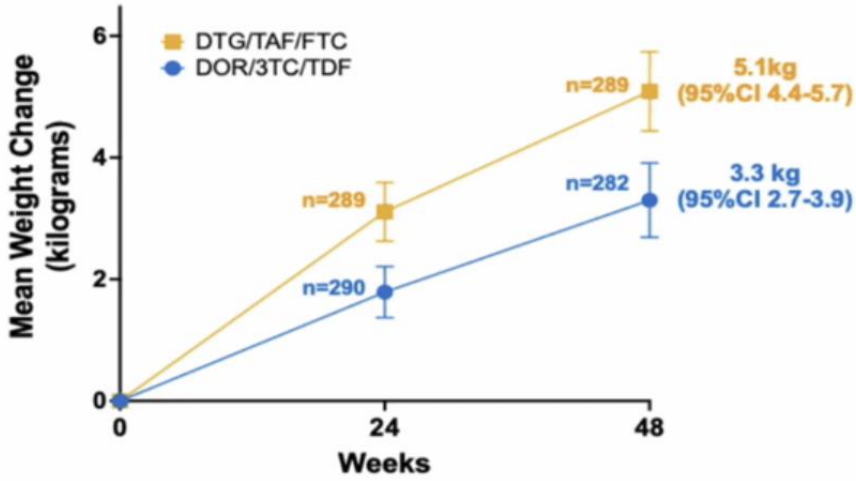


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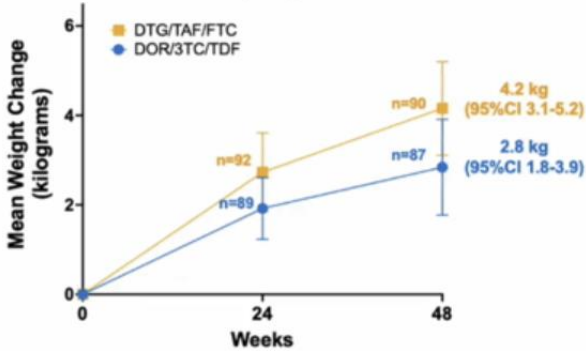
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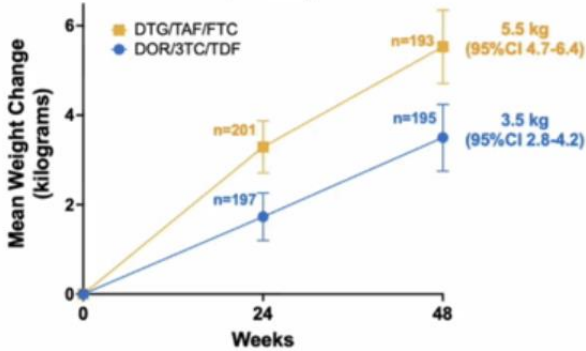
Mean Weight Change (Total Cohort)



Mean Weight Change (Men)



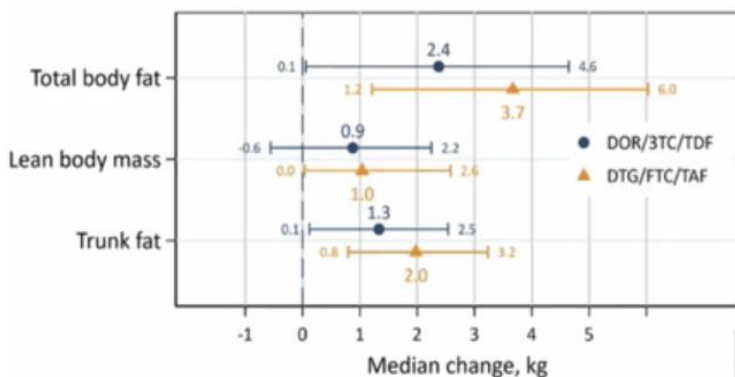
Mean Weight Change (Women)



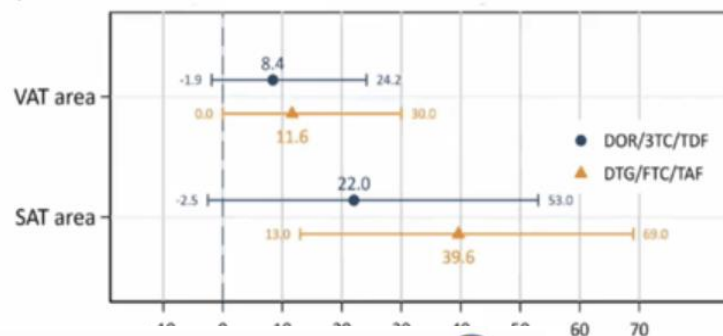
Linear Regression:
-DOR/3TC/TDF was associated with 1.92 kg less weight gain (95% CI, -2.78 to -1.07; P<0.001)
-Female sex, lower CD4 and higher VL independently associated

BMI change (difference -0.7 kg/m² ; 95% CI -1.2, -0.4)

Weight changes: DXA body composition



Values are median (IQR), error bars represent interquartile range



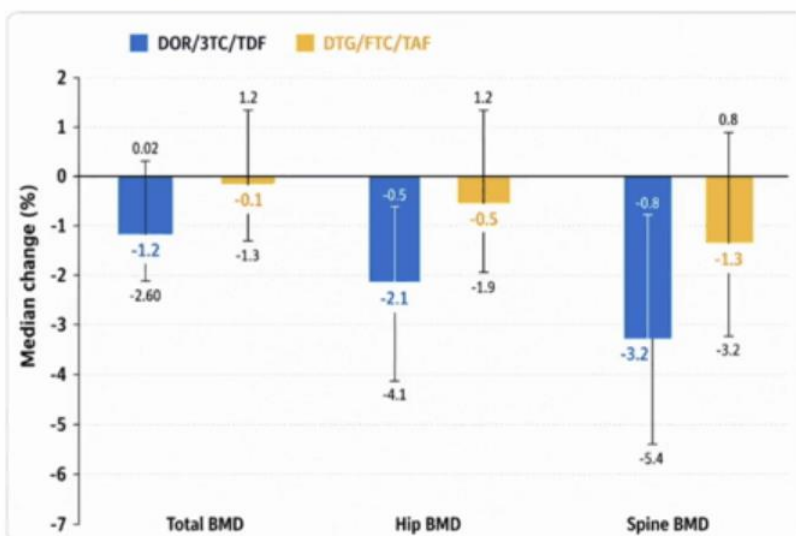
Metabolic outcomes: lipids, glycemic markers and blood pressure

Lipid measure	DOR/3TC/TDF change	DTG/FTC/TAF change	P value
Total cholesterol, mmol/L	-0.1	+0.2	<0.001
LDL cholesterol, mmol/L	-0.1	+0.1	<0.001
HDL cholesterol, mmol/L	+0.1	+0.2	0.014
Triglycerides, mmol/L	-0.1	-0.1	0.004
Total:HDL ratio	-0.4	-0.2	0.008

Other cardiometabolic outcomes

- Minimal changes in fasting glucose, HbA1c, fasting insulin and HOMA-IR over time, no difference between arms
- Blood pressure was similar between arms

Secondary outcomes: bone



Moderate impact on spine and hip BMD - favoring TAF.

Similar to other trial data (eg. ADVANCE-same population)

Metabolic and safety trade-offs: balanced regimen decision

Favored DOR/3TC/TDF

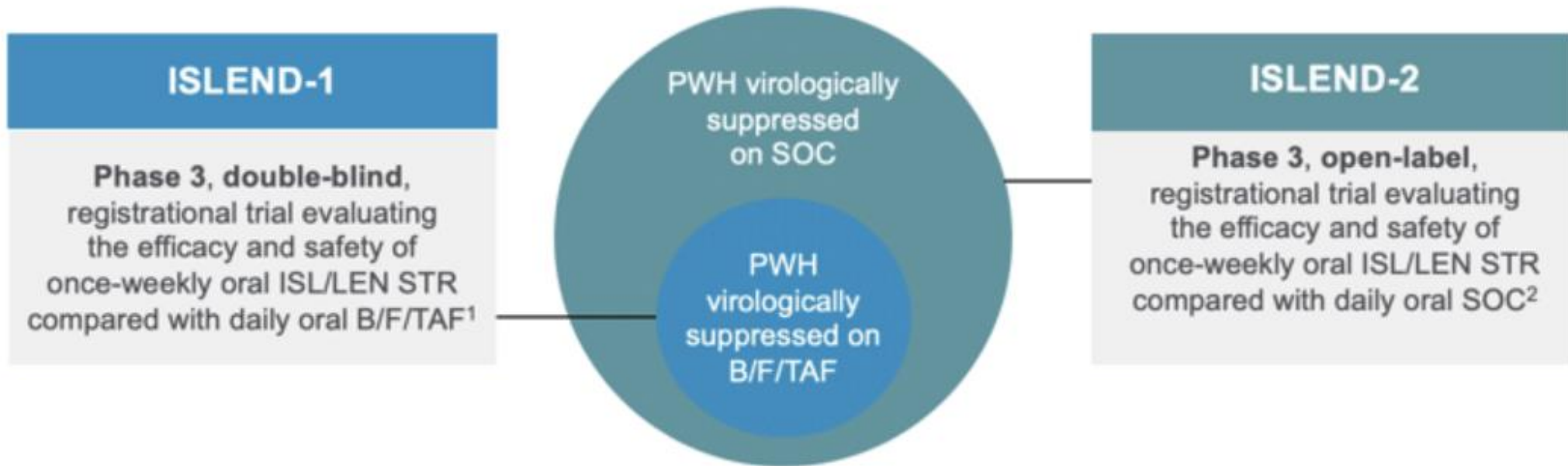
- Less median weight gain: 3.0 vs 5.0 kg, greater benefit in women
- Lower $\geq 5\%$ weight gain: 41.1% vs 56.8%
- Lower VAT accumulation
- More favorable lipid trajectories

Favored DTG/FTC/TAF

- No emergent INSTI resistance observed
- Avoids DOR resistance risk after failure
- Lower hip/spine BMD loss

ISL/LEN Phase 3 Development Program

PWH With Virologic Suppression



ISL/LEN Weekly Oral ART – ISLEND-1

Once-Weekly Oral Islatravir/Lenacapavir (ISL/LEN) Versus Daily Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF) in Virologically Suppressed Adults With HIV-1: Week 48 Results of the ISLEND-1 Phase 3 Trial

Jürgen K Rockstroh¹, Moti N Ramgopal², Adrian Curran Fabregas³, Malcolm Hedgcock⁴, Kimberly A Workowski⁵, Sylvie Ronot-Bregigeon⁶, Isabel Cassetti⁷, Cynthia Brinson⁸, Samir K Gupta⁹, Chien-Ching Hung¹⁰, Mark O'Reilly¹¹, Jihad Slim¹², Hiroyuki Gatanaga¹³, Peter Shalit¹⁴, Shan-Yu Liu¹⁵, Stephanie O Klopfer¹⁶, Fadi Shihadeh¹⁵, Nidhi Patel¹⁶, Renée-Claude Mercier¹⁵, Melissa Shaughnessy¹⁵, Hadas Dvory-Sobol¹⁵, Devi SenGupta¹⁵, Cyril Llamoso¹⁶, Martin S Rhee¹⁵, Chloe Orkin¹⁷ for the ISLEND-1 Study Team

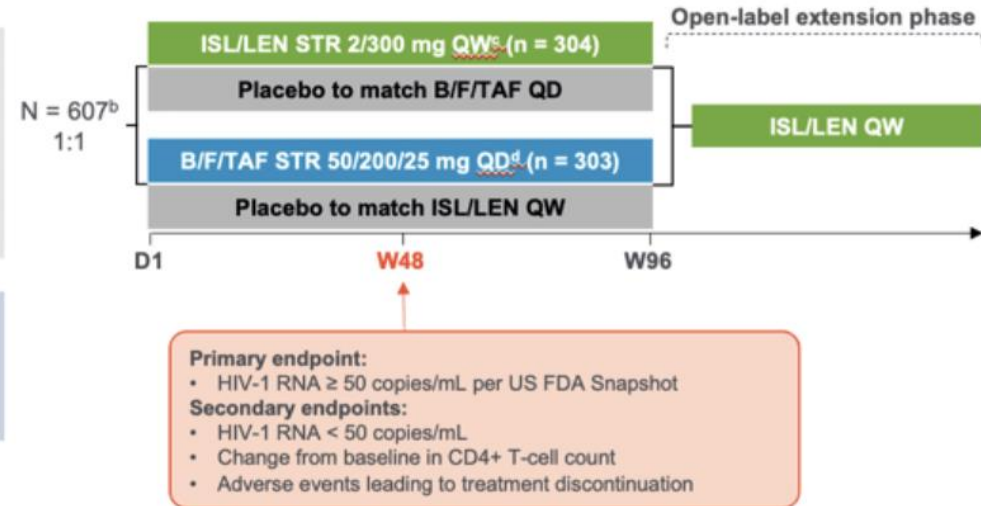
ISLEND-1: Phase 3, double-blind, active-controlled noninferiority study in virologically suppressed PWH

Eligibility criteria:

- Age ≥ 18 years
- HIV-1 RNA < 50 copies/mL for ≥ 6 months on B/F/TAF
- No prior exposure to ISL or LEN
- No history of virologic failure
- No HBV infection^a

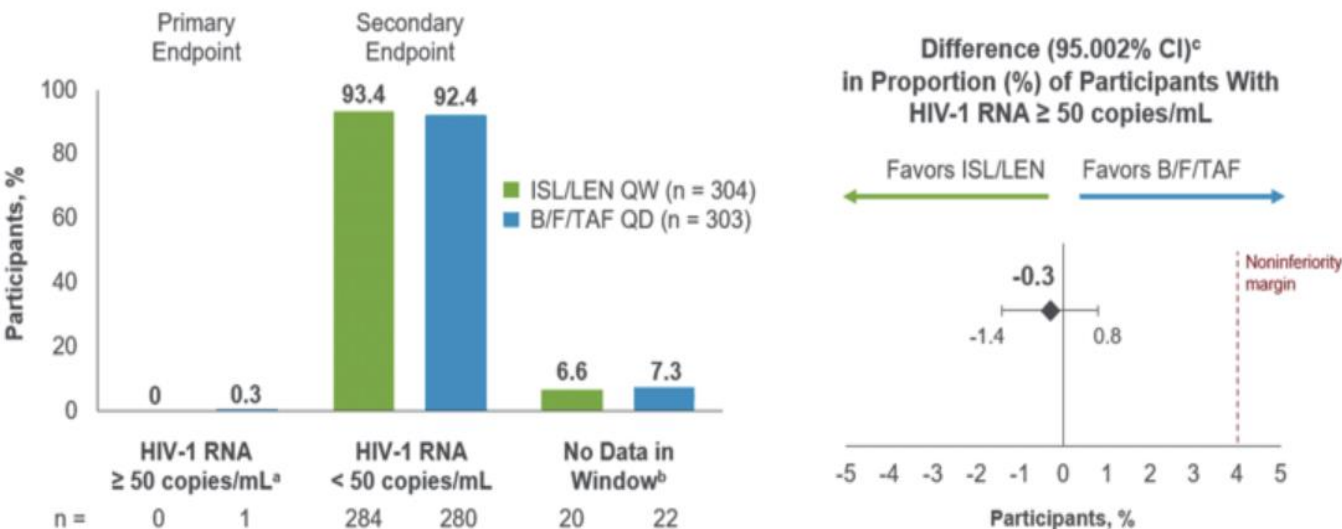
Stratification:

- Region (US vs non-US)
- CD4+ T-cell count (< 200, 200 to < 350, 350 to < 500, and ≥ 500 cells/ μ L)



	ISL/LEN QW (n = 304)	B/F/TAF QD (n = 303)
Age, years, median (IQR)	49 (38–60)	48 (38–60)
Age ≥ 50 years, n (%)	151 (50)	143 (47)
Age ≥ 65 years, n (%)	52 (17)	40 (13)
Assigned female at birth, n (%)	67 (22)	58 (19)
Gender identity, n (%)		
Cisgender man or woman	299 (98)	296 (98)
Transgender, gender nonbinary, or gender nonconforming	5 (2)	7 (2)
Race, n (%) ^a		
White	148 (49)	128 (42)
Black	89 (29)	100 (33)
Asian	32 (11)	33 (11)
Other ^b	20 (7)	25 (8)
Ethnicity: Hispanic, or Latine, n (%) ^a	73 (24)	87 (29)
BMI, kg/m ² , mean (SD)	28.3 (6.4)	28.0 (6.4)
Body weight, kg, mean (SD)	84.8 (19.3)	83.2 (17.5)
CD4+ T-cell count, cells/ μ L, mean (SD)	739 (289.2)	745 (319.3)
≥ 500 cells/ μ L, n (%)	241 (79)	240 (79)

Virologic Outcomes (FDA Snapshot) at Week 48



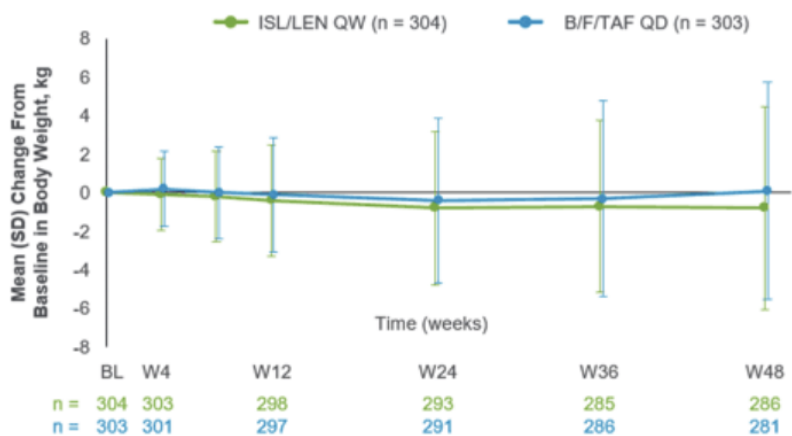
- Efficacy of once-weekly oral ISL / LEN was noninferior to that of once-daily B/F/TAF
- No emergent resistance to ISL or LEN was detected through Week 48

Safety Profile Overview

Participants, n (%)	ISL/LEN QW (n = 304)	B/F/TAF QD (n = 303)
Any AE	241 (79)	238 (79)
Grade ≥ 3	22 (7)	22 (7)
Treatment-related AEs	41 (13)	40 (13)
Most common treatment-related AEs (≥ 2% in the ISL/LEN group)		
Nausea	9 (3)	10 (3)
Headache	9 (3)	8 (3)
Dizziness	6 (2)	0
Serious AEs	16 (5)	14 (5)
AEs leading to study drug discontinuation ^a	6 (2)	5 (2)
Deaths	0	0

- There was one treatment-related serious AE: maculopapular rash (Grade 3) in an individual with prior history of asthma and drug hypersensitivity
- One participant (unvaccinated) discontinued treatment due to an AE of hepatitis B (Grade 2)

Change From Baseline in Body Weight Through Week 48



ISL/LEN Weekly Oral ART – ISLEND-2

Once-Weekly Oral Islatravir/Lenacapavir (ISL/LEN) Versus Daily Standard-of-Care (SOC) Therapy in Virologically Suppressed Adults With HIV-1: Week 48 Results of the ISLEND-2 Phase 3 Trial

Amy E Colson¹, Princy N Kumar², Peter J Ruane³, Ploenchana Chetchotisakd⁴, Winai Ratanasuwan⁵, Afaaf Liberty⁶, Ronald G Nahass⁷, Alejandro Arenas-Pinto⁸, Frank A Post⁹, David A Baker¹⁰, Pedro Cahn¹¹, Eveline Hofmann¹², Dai Watanabe¹³, Po-Liang Lu¹⁴, Anna H E Roukens¹⁵, Milosz Parczewski¹⁶, Hongyuan Wang¹⁷, Ke Chen¹⁸, Fadi Shihadeh¹⁷, Melissa Shaughnessy¹⁸, Hadas Dvory-Sobol¹⁷, Devi SenGupta¹⁷, Cyril Llamoso¹⁸, Martin S Rhee¹⁷, Onyema Ogbuagu¹⁹ for the ISLEND-2 Study Team

ISLEND-2: Phase 3, open-label, active-controlled noninferiority study in virologically suppressed PWH

Eligibility criteria:

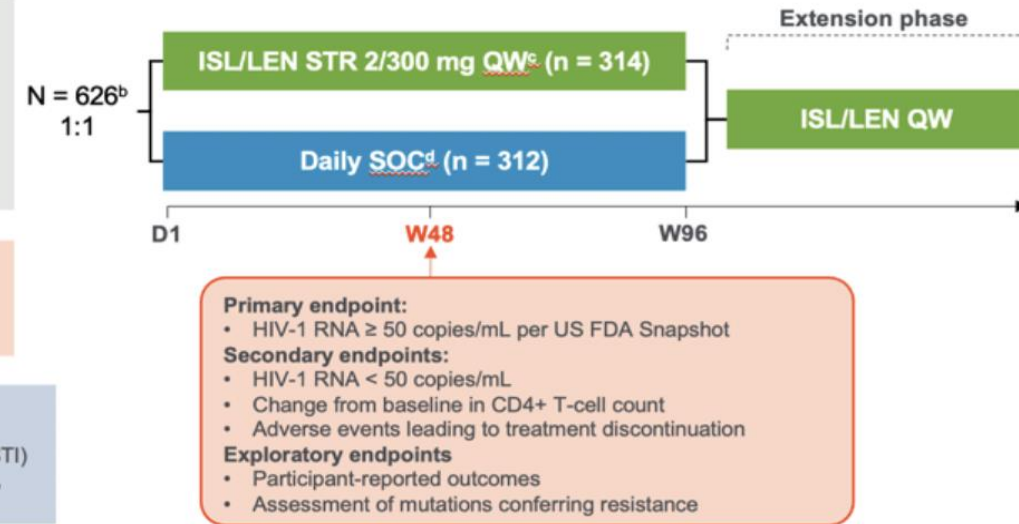
- Age ≥ 18 years
- HIV-1 RNA < 50 copies/mL for ≥ 6 months on daily oral SOC
- No prior exposure to ISL or LEN
- No history of virologic failure
- No HBV infection^a

SOC:

- INSTI + 1 or 2 NRTIs
- bPI + 2 NRTIs
- NNRTI + 2 NRTIs

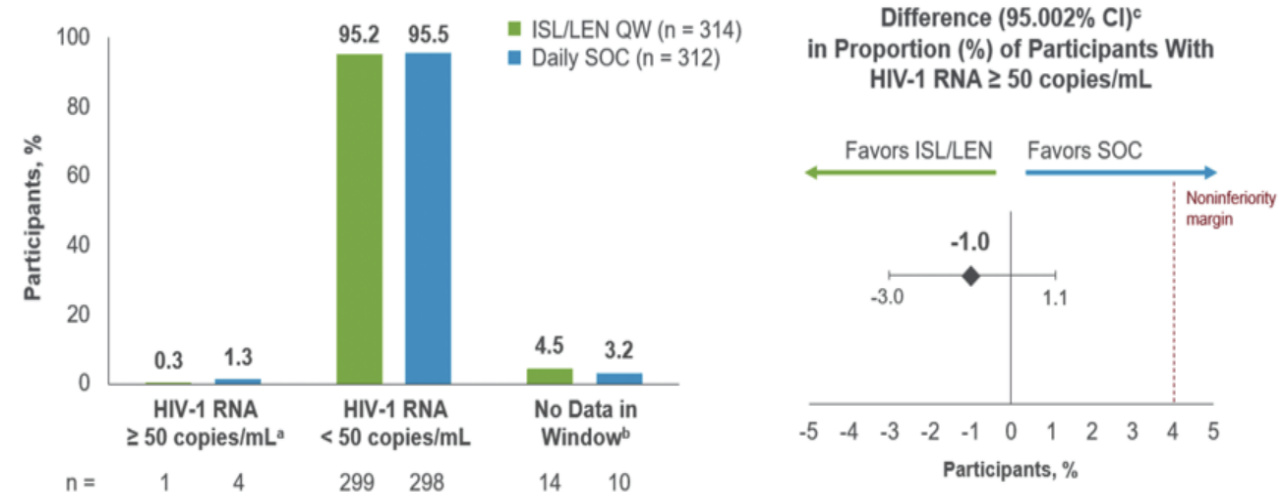
Stratification:

- Region (US vs non-US)
- Antiretroviral class (NNRTI, PI, and INSTI)
- CD4+ T-cell count (< 200, 200 to < 350, 350 to < 500, and ≥ 500 cells/μL)



	ISL/LEN QW (n = 314)	Daily SOC (n = 312)	Total (N = 626)
Age, years, median (IQR)	52 (42–60)	53 (43–61)	52 (42–60)
Age ≥ 65 years, n (%)	47 (15)	42 (13)	89 (14)
Assigned female at birth, n (%)	105 (33)	106 (34)	211 (34)
Race, n (%)^a			
White	130 (41)	134 (43)	264 (42)
Black	94 (30)	99 (32)	193 (31)
Asian	61 (19)	58 (19)	119 (19)
Other ^b	17 (5)	10 (3)	27 (4)
Ethnicity: Hispanic or Latine, n (%)^a	62 (20)	61 (20)	123 (20)
Antiretroviral medication class, n (%)			
INSTI	245 (78)	233 (75)	478 (76)
NNRTI	43 (14)	52 (17)	95 (15)
PI	26 (8)	27 (9)	53 (8)
Daily single-tablet regimen, n (%)	277 (88)	275 (88)	552 (88)
CD4+ T-cell count, cells/μL, mean (SD)	795 (346.4)	761 (319.0)	778 (333.2)
Lymphocyte count × 10³ cells/μL, mean (SD)	1.99 (0.63)	1.94 (0.62)	1.96 (0.62)
BMI, kg/m², median (IQR)	27.0 (23.9, 30.7)	26.7 (23.9, 30.5)	26.9 (23.9, 30.6)

Virologic Outcomes (FDA Snapshot) at Week 48



- Efficacy of once-weekly oral ISL/LEN was noninferior to that of daily SOC
- Participants in both treatment groups maintained high rates of virologic suppression
- No emergent resistance to ISL or LEN was detected through Week 48

Safety Profile Overview

Participants, n (%)	ISL/LEN QW (n = 314)	Daily SOC (n = 312)
Any AE	249 (79)	241 (77)
Grade ≥ 3	24 (8)	28 (9)
Treatment-related AEs	58 (18)	1 (< 1)
Grade ≥ 3	0	0
Most common ($\geq 2\%$ in the ISL/LEN group)		
Headache	15 (5)	0
Diarrhea	10 (3)	0
Nausea	9 (3)	0
Serious AEs	22 (7)	27 (9)
Treatment related ^a	1 (< 1)	0
AEs leading to study drug discontinuation^b	2 (1)	1 (< 1)
Deaths^c	1 (< 1)	2 (1)

- Body weight remained stable throughout 48 weeks in both treatment groups, with a mean (SD) change from baseline of 0.1 (4.74) kg in the ISL/LEN group and -0.3 (4.12) kg in the SOC group

ISL/ULO weekly oral ART

Randomized, Active-Controlled, Phase 2b Study Evaluating Efficacy and Safety of Switch to Islatravir (ISL) 2 mg With Ulonivirine (ULO) 200 mg Once Weekly in Virologically Suppressed Adults Living With HIV-1

Anne F. Luetkemeyer,¹ Mark Bloch,² Anita Scribner,³ Federico Hineostroza,⁴ Princy Kumar,⁵ Gary Sinclair,⁶ Cornelius Van Dam,⁷ Javier Morales-Ramirez,⁸ Martin Gubler,⁹ Uche Okoro,¹⁰ Yavun Xu,¹⁰ Kim Beckey,¹⁰ Luisa M. Stamm,¹⁰ Randolph P. Matthews,¹⁰ Mengchun Li¹⁰

- ISL is a potent NRTTI that blocks reverse transcriptase through multiple mechanisms, including inhibition of translocation and delayed chain termination^{3,4}
 - QW ISL 2 mg is predicted to exceed PK thresholds for full inhibitory activity against M184I/V variants (ie, trough ISL-triphosphate concentrations remain >5-fold above the inhibitory quotient)^{5,6}
- ULO is an investigational NNRTI with potent activity across HIV-1 subtypes and <5-fold shifts in IC₅₀ against common NNRTI resistance-associated mutations^{7,8}
- ISL/ULO is a potential long-acting, oral, 2-drug regimen active against HIV-1 variants with common RAMs
 - ISL and ULO have complementary antiviral resistance profiles and pharmacokinetics that support QW dosing⁸⁻¹¹
 - PK/PD modeling suggests that ISL 2 mg with ULO 200 mg QW can effectively treat HIV-1¹²
 - The 2-mg dose of ISL has not shown any lymphocytopenia signal in clinical trials to date

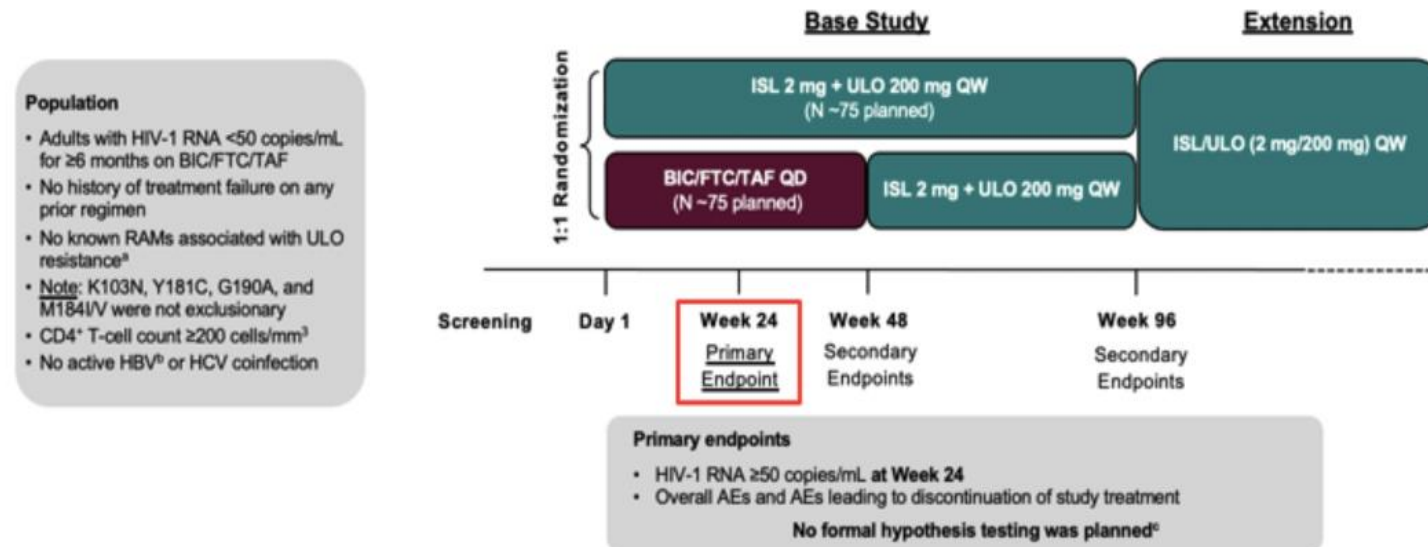
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Study Design

MK-8591B-060: Randomized, Open-Label, Phase 2b Study Comparing Efficacy and Safety of Switching to ISL+ULO QW vs Continuing BIC/FTC/TAF QD in Virologically Suppressed Adults Living With HIV-1 (NCT068910

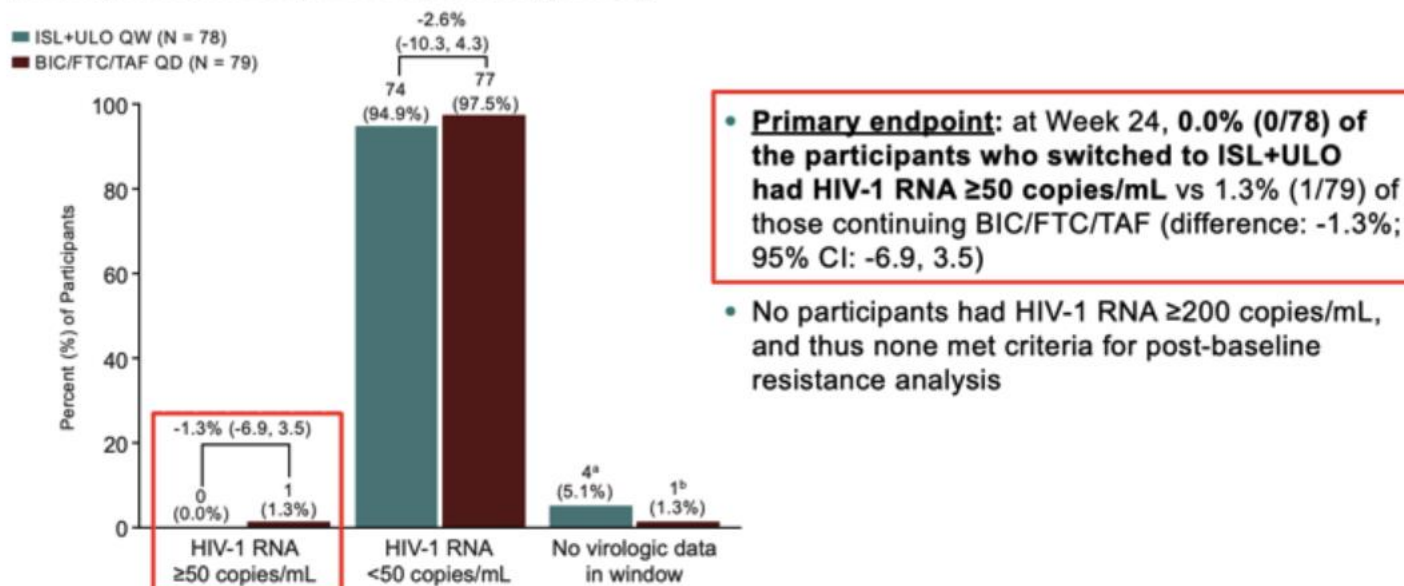


Characteristic	ISL+ULO QW N = 78	BIC/FTC/TAF QD N = 79	Total N = 157
Female sex at birth, n (%)	16 (20.5)	26 (32.9)	42 (26.8)
Gender identity, n (%):			
Cisgender man	62 (79.5)	50 (63.3)	112 (71.3)
Cisgender woman	16 (20.5)	26 (32.9)	42 (26.8)
Transgender woman	0 (0.0)	3 (3.8)	3 (1.9)
Age (years), median (IQR)	48.5 (38 – 56)	48.0 (41 – 57)	48.0 (39 – 57)
≥ 50 years old, n (%)	35 (44.9)	36 (45.6)	71 (45.2)
Race, n (%):			
White	43 (55.1)	43 (54.4)	86 (54.8)
Black/African-American	23 (29.5)	27 (34.2)	50 (31.8)
Asian	4 (5.1)	6 (7.6)	10 (6.4)
Multi-racial/Other/Unknown	8 (10.3)	3 (3.8)	11 (7.0)
Hispanic or Latino, n (%)	20 (25.6)	18 (22.8)	38 (24.2)
CD4 ⁺ T-cell counts			
CD4 ⁺ T-cell count (cells/mm ³), median (IQR)	783.5 (627 – 990)	840.0 (676 – 1122)	810.0 (655 – 1016)
CD4 ⁺ T-cell count ≥ 350 cells/mm ³ , n (%)	76 (97.4)	78 (98.7)	154 (98.1)
Prior ART			
Duration of all prior ART (years), median (IQR)	10.2 (4.5 – 17.5)	11.5 (6.1 – 17.8)	10.6 (5.4 – 17.8)
Duration of prior BIC/FTC/TAF (years), median (IQR)	4.5 (2.0 – 5.9)	4.0 (2.1 – 6.1)	4.3 (2.1 – 6.0)
Hepatitis B serology ^a			
HBcAb-positive <u>and</u> HBsAb-positive, n (%)	16 (20.5)	17 (21.5)	33 (21.0)
HBcAb-negative <u>and</u> HBsAb-positive, n (%)	46 (59.0)	35 (44.3)	81 (51.6)
HBcAb-negative <u>and</u> HBsAb-negative, ^b n (%)	15 (19.2)	24 (30.4)	39 (24.8)

• The study enrolled in the USA (including Puerto Rico; 69.4% of participants in total), Australia (17.8%), and Switzerland (12.7%)

Efficacy of ISL+ULO was Comparable to BIC/FTC/TAF at Week 24

Virologic outcomes (FDA snapshot approach)



AE Profiles of ISL+ULO and BIC/FTC/TAF Were Generally Comparable Through Week 24

Participants with..., n (%)	ISL+ULO QW N = 78	BIC/FTC/TAF QD N = 79	Treatment Difference (95% CI)
One or more AEs	43 (55.1)	44 (55.7)	-0.6 (-16.0, 14.9)
Drug-related ^a AEs	10 (12.8) ^b	0 (0.0)	12.8 (7.1, 22.1)
Grade 3 or 4 AEs	3 (3.8)	5 (6.3)	-2.5 (-10.7, 5.3)
Drug-related ^a Grade 3 or 4 AEs	0 (0.0)	0 (0.0)	0.0 (-4.7, 4.7)
Serious AEs	3 (3.8) ^c	0 (0.0)	3.8 (-0.9, 10.7)
Drug-related ^a serious AEs	0 (0.0)	0 (0.0)	0.0 (-4.7, 4.7)
AEs leading to discontinuation of study treatment	1 (1.3)	0 (0.0)	1.3 (-3.4, 6.9)
Grade 3 or 4 laboratory abnormalities ^d	9 (11.6)	19 (28.2)	-12.5 (-24.6, -0.5)

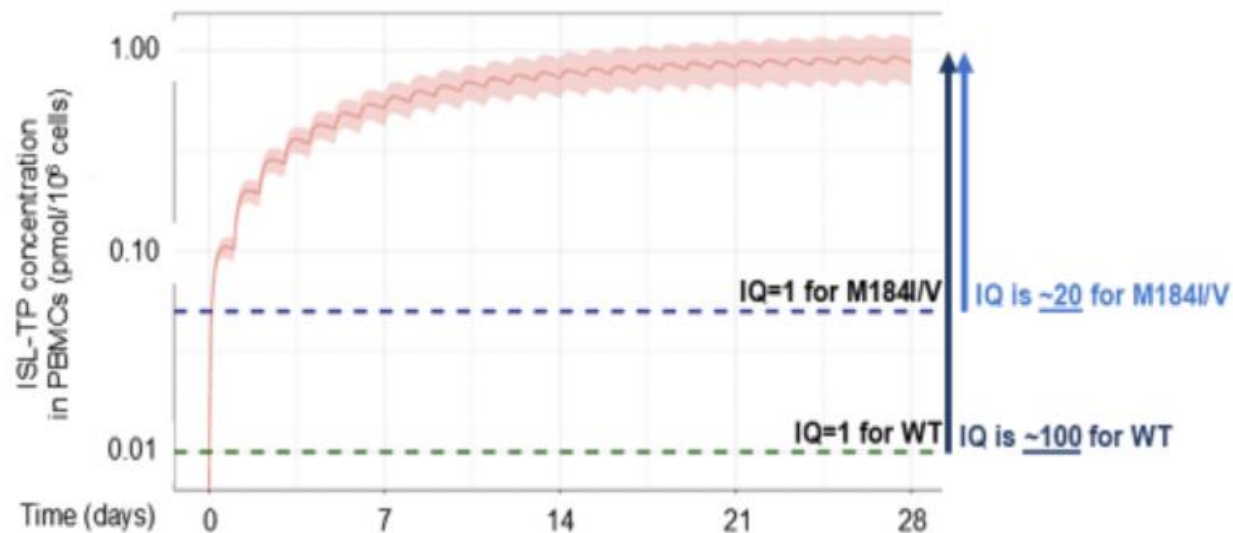
- All ISL+ULO QW drug-related AEs were Grade 1 or 2; the only drug-related AE in >1 participant was 'dizziness' (n=2, 2.6%)
- The higher rate of drug-related AEs with ISL+ULO is not unexpected due to the open-label switch design
- 1 participant discontinued ISL+ULO due to Grade 2 'skin reaction' (drug related, per site investigator) at Week 16; the participant previously had a similar skin reaction with efavirenz
- There were no HBV reactivations or new infections
- Changes in mean body weight from baseline at Week 24 were not clinically meaningful (ie, less than 0.5 kg change in each group)

DOR/ISL – Baseline Proviral DNA Resistance

Switching to Doravirine/Islatravir (100 mg/0.25 mg)
Once Daily Maintained Viral Suppression at Week 96 in
the Presence of Baseline NNRTI Resistance-Associated
Mutations and/or M184I/V in Proviral DNA

Tracy L. Diamond, Uchechukwu Nwoke, Monica Fuszard, Chenguang Zhang, Stephanie O. Klopfer, Mengchun Li, Wayne Greaves, Jason Kim, Michelle C. Fox, Ernest Asante-Appiah

- ISL is a potent nucleoside reverse transcriptase translocation inhibitor (NRTTI) with activity against wild-type (WT) HIV and variants with NRTI RAMs including M184I/V
 - Simulation of the pharmacologically active ISL-triphosphate (TP) concentration-time profile shows an inhibitory quotient (IQ) of 100 and 20 for wild-type (WT) HIV and M184I/V, respectively, with ISL 0.25 mg once daily¹



$$IQ = C_{\text{trough}}/IC_{50}$$

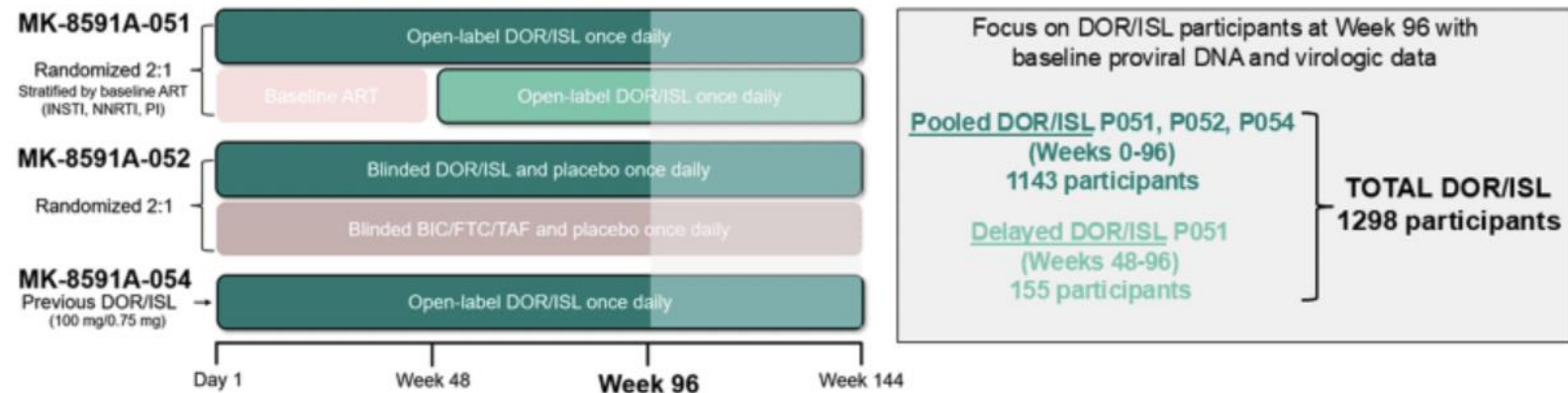
¹Pham M, et al. ID Week 2025.

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Once Daily Maintained Viral Suppression at Week 96 in
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DOR/ISL (100 mg/0.25 mg) Phase 3 Studies in Virologically Suppressed Adults (HIV-1 RNA <50 copies/mL)



Eligibility based on medical history and available records

- No history of treatment failure on any regimen
- No documented resistance to DOR: V106A/M, V108I, Y188L, H221Y, P225H, F227C/L, M230I/L, L234I, P236L, or Y318F

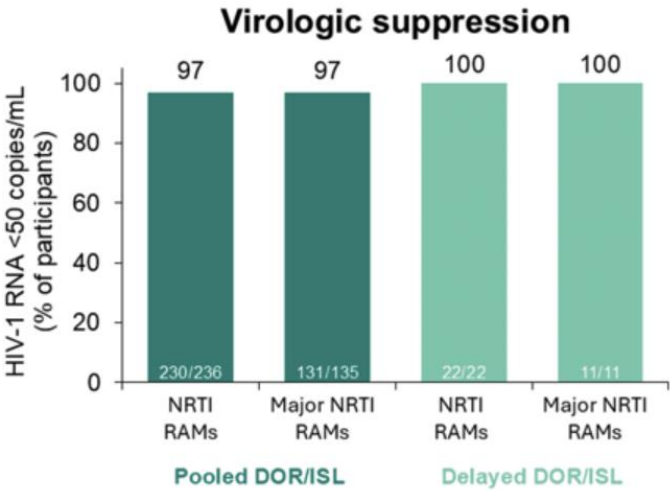
Baseline resistance testing was performed retrospectively on proviral DNA by GenoSure Archive® assay (Monogram Biosciences) using whole blood samples collected on Day 1

High Rates of Virologic Suppression Maintained at Week 96 in the Presence of Baseline **NRTI** RAMs in Proviral DNA

RAMs	Prevalence		Total Prevalence (N=1298)
	Participants (n)		
	Pooled DOR/ISL	Delayed DOR/ISL	
NRTI	236	22	20%
Major NRTI	135	11	11%

Most prevalent major NRTI RAMs detected

- M184I/V – 70 (5.4%)
- D67N – 23 (1.8%)
- K70E/R – 30 (2.3%)
- A62V – 21 (1.6%)
- M41L – 26 (2.0%)
- T215F/Y – 19 (1.5%)

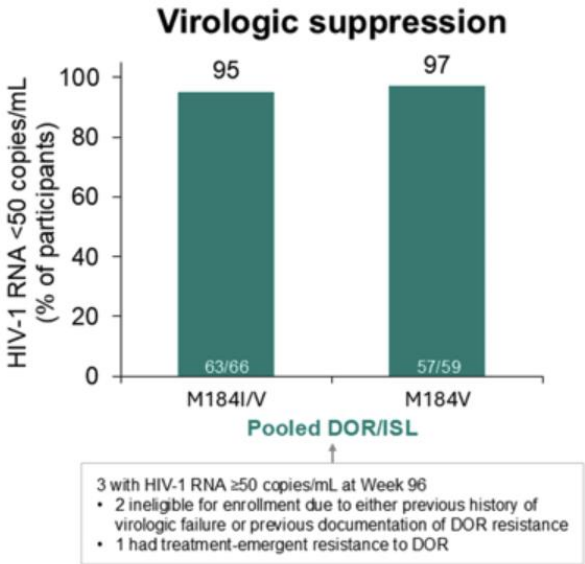


NRTI RAMs: M41L, E44D, A62V, K65E/N/R, D67N, T69D/N, 69ins, K70E/R, L74V, V75I, F77L, Y115F, F116Y, V118I, Q151M, M184I/V, L210W, T215A/C/D/E/F/G/H/I/L/N/S/V/Y, K219E/N/Q/R
Major NRTI RAMs: M41L, A62V, K65E/N/R, D67N, 69ins, K70E/R, L74V, V75I, F77L, Y115F, F116Y, Q151M, M184I/V, L210W, T215F/Y, K219E/Q

High Rates of Virologic Suppression Maintained at Week 96 in the Presence of Baseline **M184I/V** in Proviral DNA

RAMs	Prevalence		Total Prevalence (N=1298)
	Participants (n)		
	Pooled DOR/ISL	Delayed DOR/ISL	
M184I/V	66	4	5%
M184V	59	4	5%

90% (63/70) of M184I/V was M184V

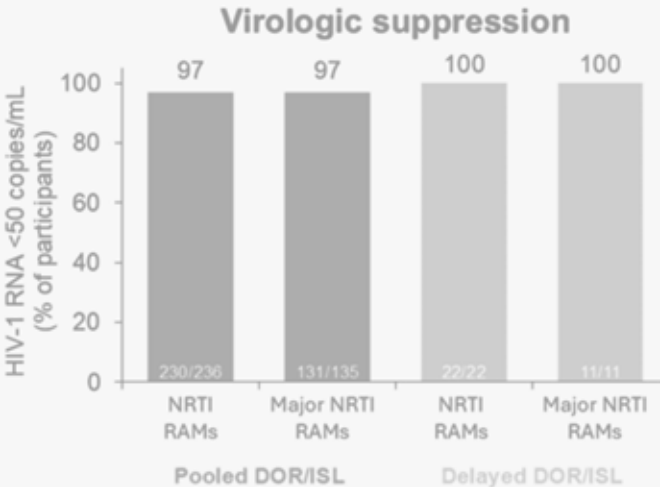


High Rates of Virologic Suppression Maintained at Week 96 in the Presence of Baseline **NRTI** RAMs in Proviral DNA

RAMs	Participants (n)		Total Prevalence (N=1298)
	Pooled DOR/ISL	Delayed DOR/ISL	
NRTI	236	22	20%
Major NRTI	135	11	11%

Most prevalent major NRTI RAMs detected

- M184I/V – 70 (5.4%)
- D67N – 23 (1.8%)
- K70E/R – 30 (2.3%)
- A62V – 21 (1.6%)
- M41L – 26 (2.0%)
- T215F/Y – 19 (1.5%)

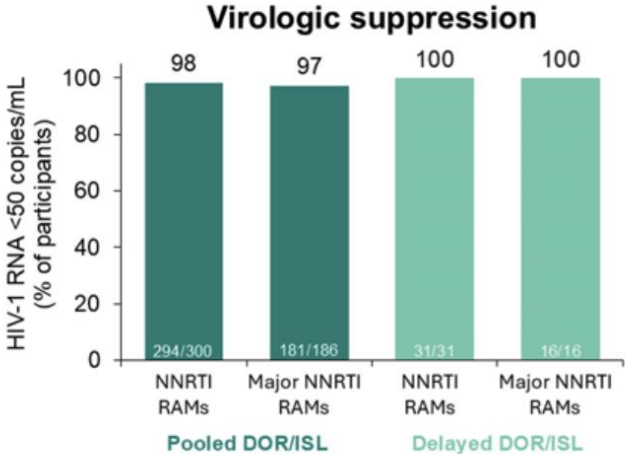


High Rates of Virologic Suppression Maintained at Week 96 in the Presence of Baseline **NNRTI** RAMs in Proviral DNA

RAMs	Participants (n)		Total Prevalence (N=1298)
	Pooled DOR/ISL	Delayed DOR/ISL	
NNRTI	300	31	26%
Major NNRTI	186	16	16%

Most prevalent major NNRTI RAMs detected

- K103N/S – 86 (6.6%)
- E138A/G/K/Q/R – 82 (6.3%)
- G190A/S – 16 (1.2%)
- Y181C/I/V – 11 (0.8%)

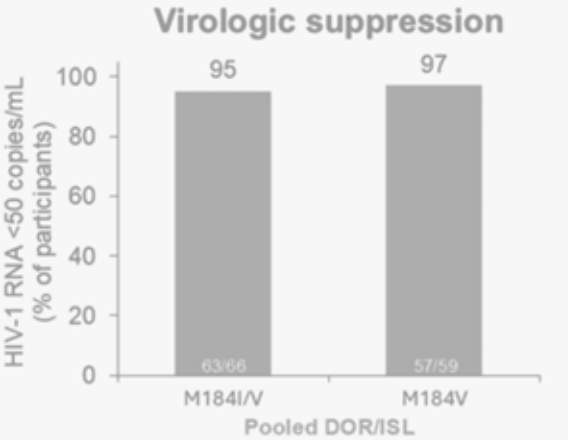


NNRTI RAMs: V90I, A98G, L100I, K101E/H/P, K103N/R/S, V106A/I/M/T, V108I, E138A/G/K/Q/R, V179D/F/I/T, Y181C/I/V, Y188C/H/L, G190A/E/S, H221Y, P225H, F227C/H/I/L/R/V, M230I/L, L234I, P236L, Y318F
Major NNRTI RAMs: L100I, K101E/P, K103N/S, V106A/M, V108I, E138A/G/K/Q/R, Y181C/I/V, Y188C/H/L, G190A/S, F227C/I/L/R/V, M230I/L, Y318F

High Rates of Virologic Suppression Maintained at Week 96 in the Presence of Baseline **M184I/V** in Proviral DNA

RAMs	Participants (n)		Total Prevalence (N=1298)
	Pooled DOR/ISL	Delayed DOR/ISL	
M184I/V	66	4	5%
M184V	59	4	5%

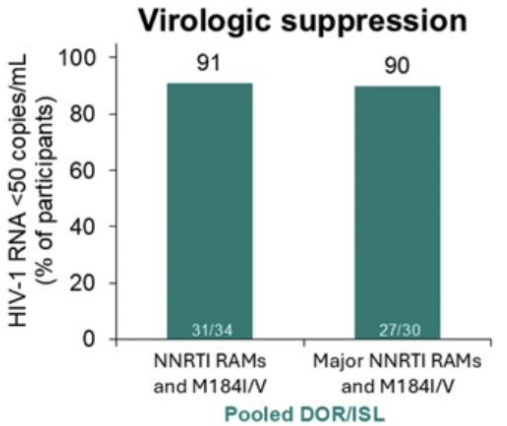
90% (63/70) of M184I/V was M184V



3 with HIV-1 RNA ≥50 copies/mL at Week 96
• 2 ineligible for enrollment due to either previous history of virologic failure or previous documentation of DOR resistance
• 1 had treatment-emergent resistance to DOR

High Rates of virologic Suppression Maintained at Week 96 in the Presence of Baseline **NNRTI** RAMs and **M184I/V** in Proviral DNA

RAMs	Participants (n)		Total Prevalence (N=1298)
	Pooled DOR/ISL	Delayed DOR/ISL	
NNRTI and M184I/V	34	1	3%
Major NNRTI and M184I/V	30	1	2%



3 with HIV-1 RNA ≥50 copies/mL at Week 96
• 2 ineligible for enrollment due to either previous history of virologic failure or previous documentation of DOR resistance
• 1 had treatment-emergent resistance to DOR

BIC/LEN – ARTISTRY-1 Trial

Baseline and Week 48 Resistance Analyses in the Phase 3 ARTISTRY-1 Study Evaluating the Bictegravir/Lenacapavir Single-Tablet Regimen

Nicolas Margot¹, Nina Pennetzdorfer², Vidula Naik³, Jairo M Montezuma-Rusca⁴, Peter Sklar⁵, Christian Callebaut⁶

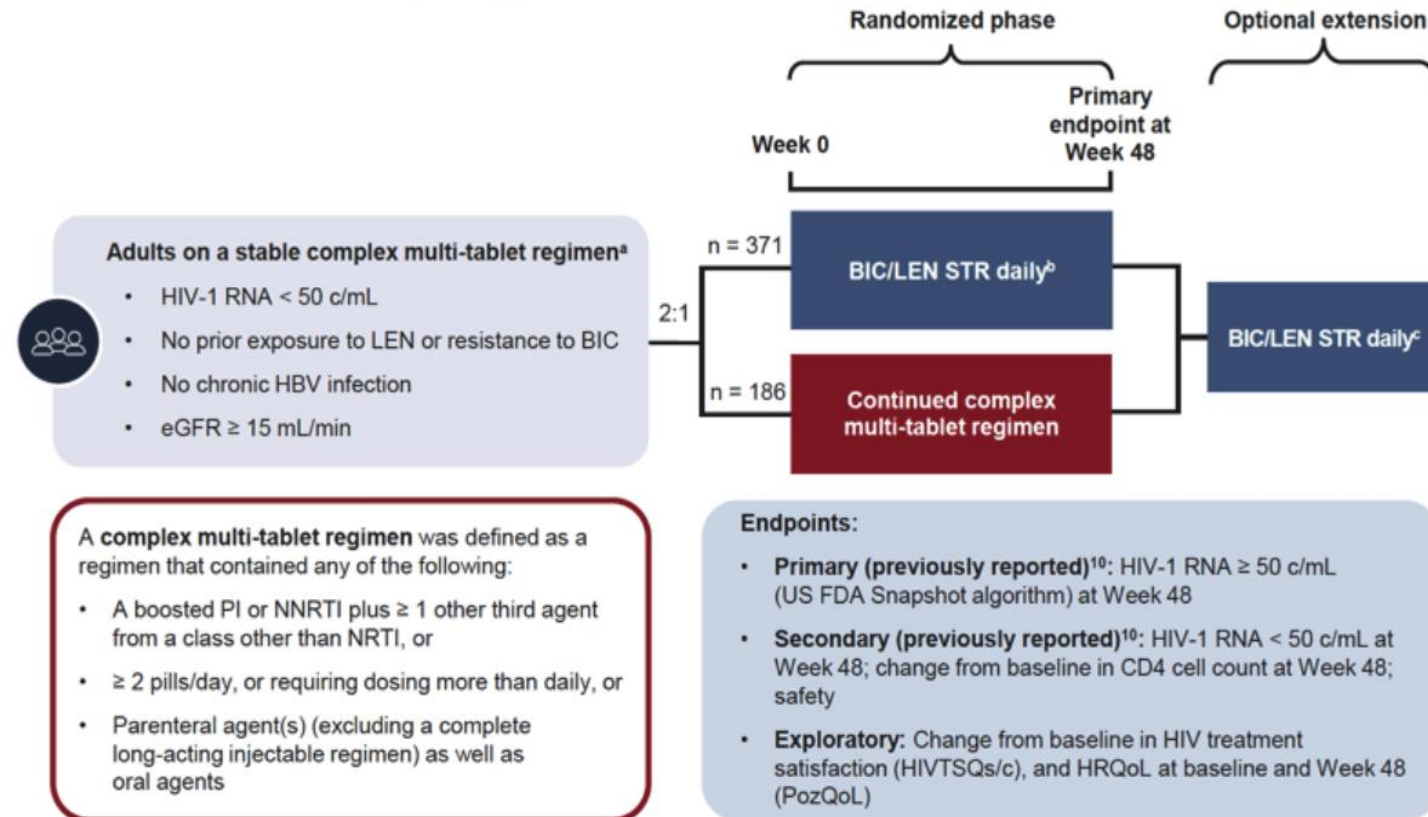
Metabolic Changes at 48 Weeks in People With HIV and Virologic Suppression Switching to Single-Tablet Bictegravir/Lenacapavir From Complex Antiretroviral Regimens: Results From the Phase 3 ARTISTRY-1 Trial

Isabel L Cassetti¹, Peter J Ruane², Thomas Lutz³, José I Bernardino⁴, Valérie Pourcher⁵, Xu Zhang⁶, Peter Sklar⁶, Jairo M Montezuma-Rusca⁸, Karam Mounzer⁷

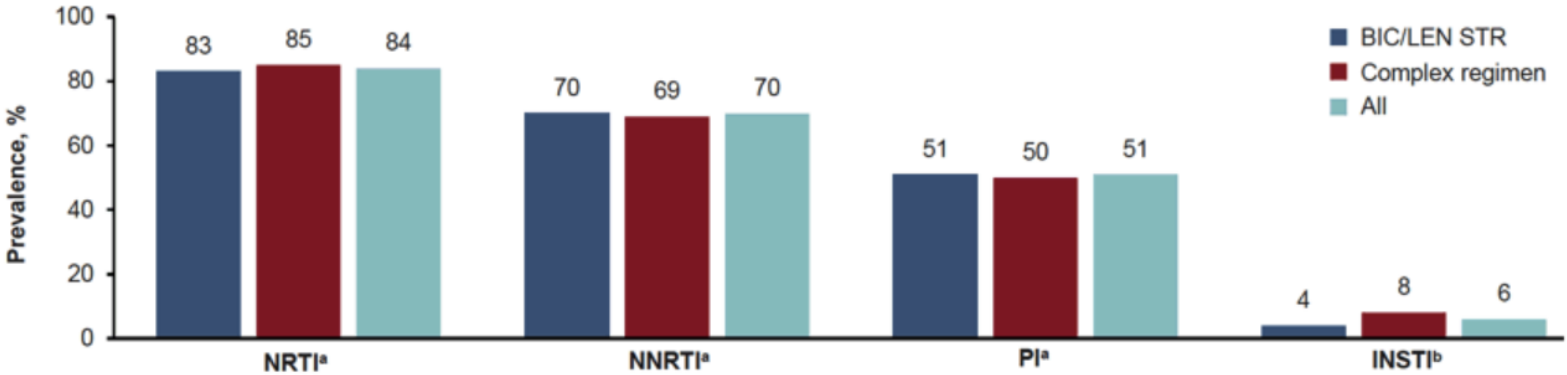
Increased Treatment Satisfaction and Maintained Health-Related Quality of Life Among People With HIV Switching to a Bictegravir/Lenacapavir Single-Tablet Regimen From Complex Regimens: Results From the Phase 3 ARTISTRY-1 Trial

Chloe Orkin¹, Andrea Antinori², Christian Hoffmann³, Manuel Pardo⁴, Isabel Cassetti⁵, Po-Liang Lu⁶, Andrew Carr⁷, Jose I Bernardino⁸, Saied Shahrzad⁹, Caroline Burk⁹, Ying Guo⁹, Jairo M Montezuma-Rusca⁹, Peter Sklar⁹, Kwanza Price⁹, Benoit Trottier¹⁰

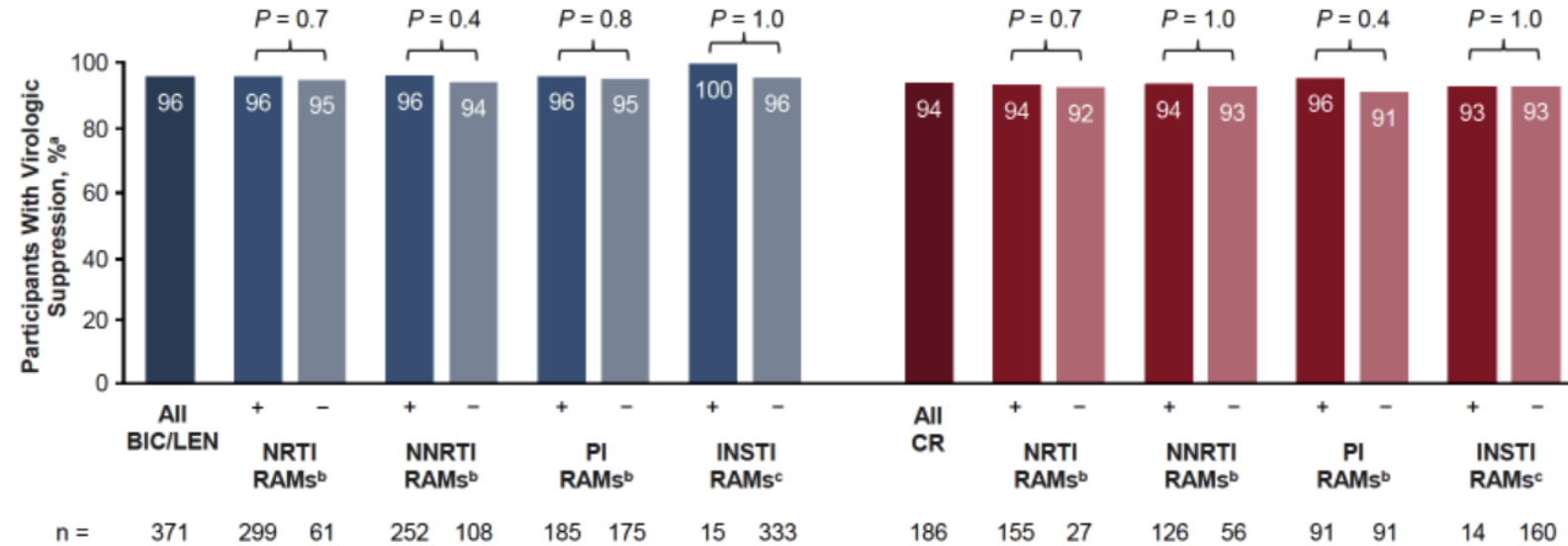
Phase 3 ARTISTRY-1 Study Design



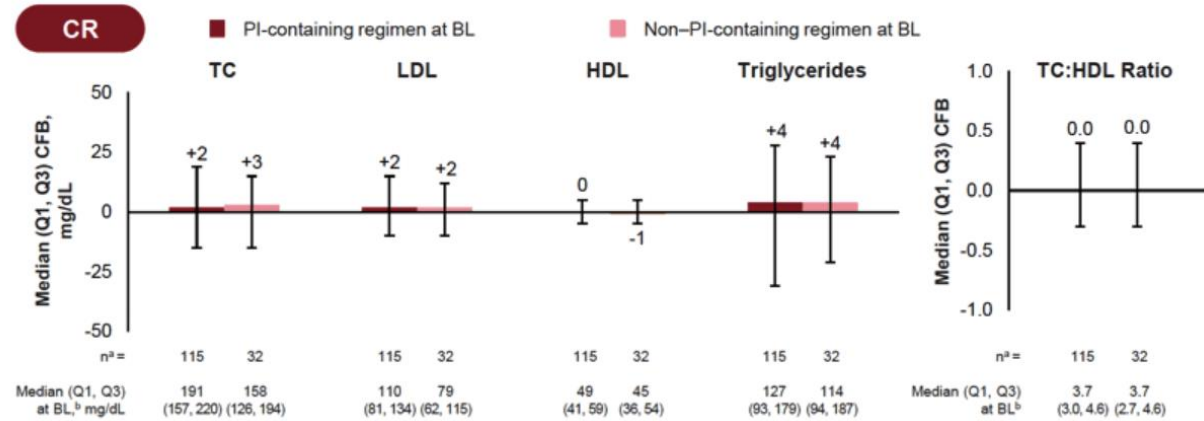
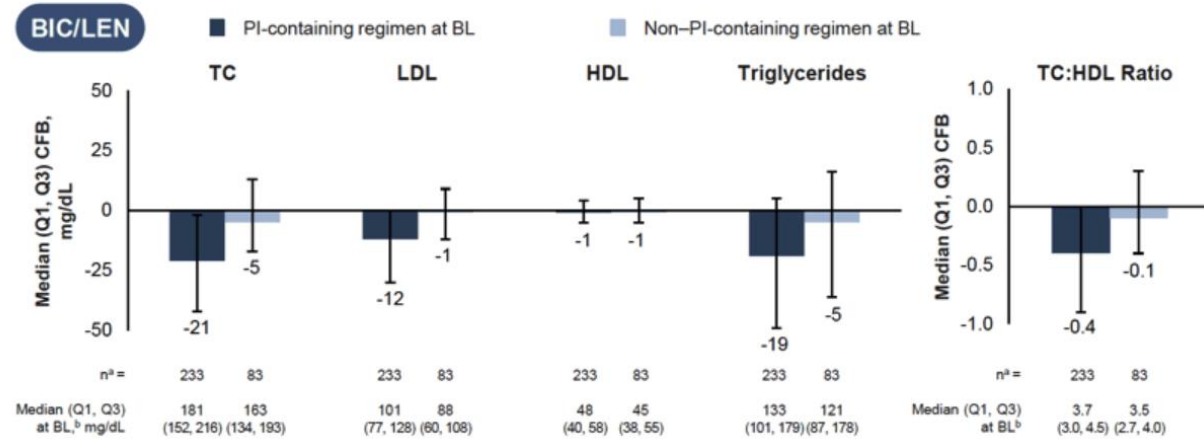
Baseline Pre-Existing Resistance Mutations per Treatment Group



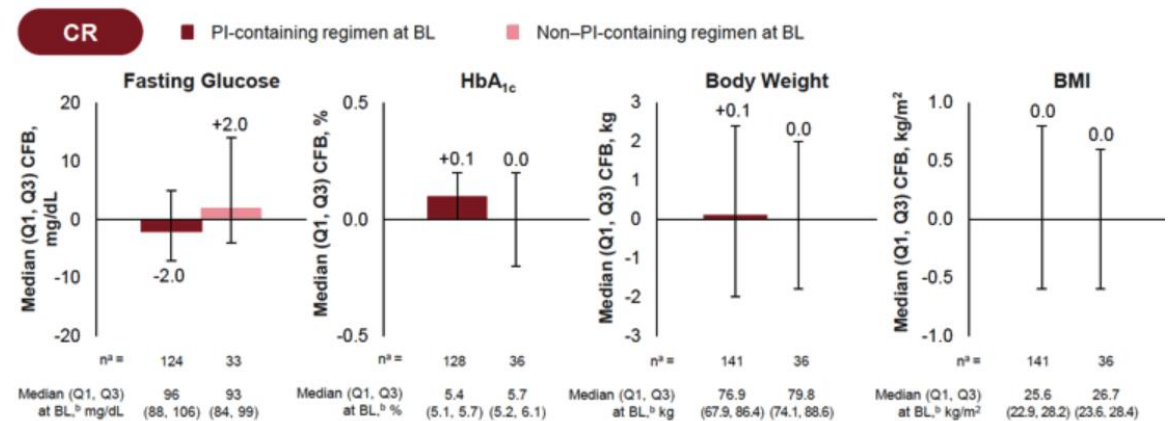
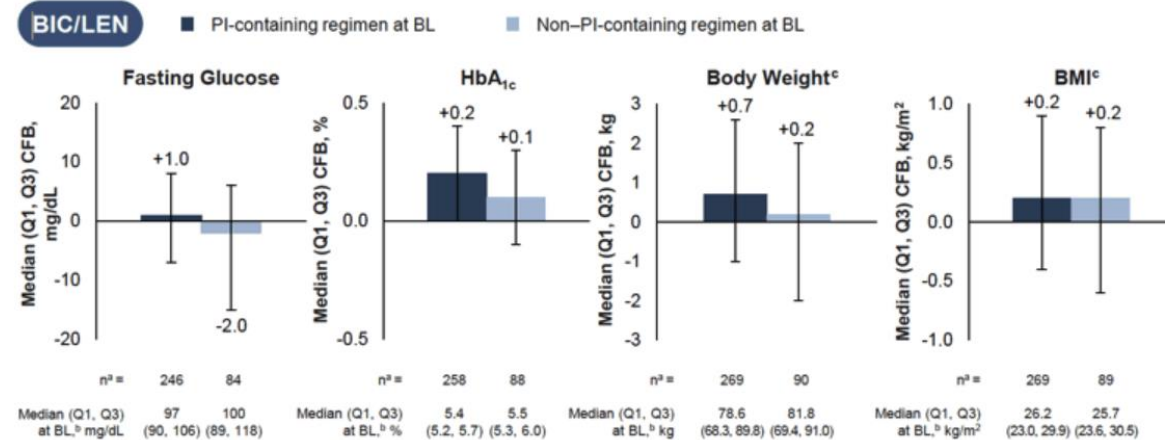
Response to Treatment per Baseline RAM Category



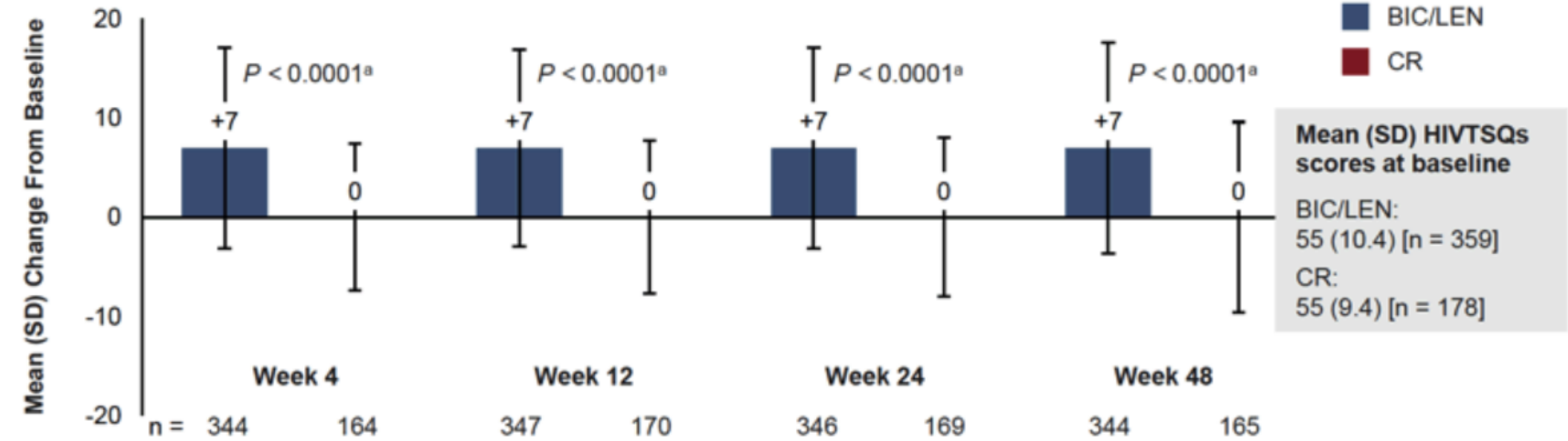
Absolute Change From Baseline in Fasting Lipid Parameters at Week 48



Absolute Change From Baseline in Cardiometabolic Parameters at Week 48



Change in HIVTSQs Total Scores From Baseline Through Week 48



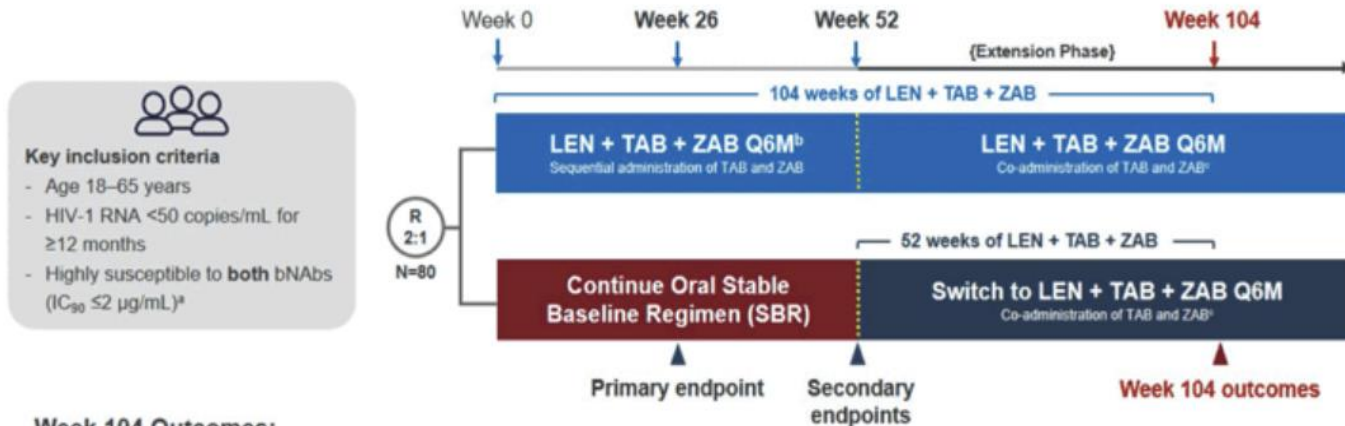
More LEN+bNAbs (TAB+ZAB) – 104 Weeks

Efficacy and Safety of Twice-Yearly Lenacapavir, Teropavimab, and Zinlirvimab as an HIV-1 Treatment for Up to 104 Weeks

James H. McMahon^{*1}, Joseph Eron², Aditya Gaur³, Edwin DeJesus⁴, David A. Baker⁵, Cynthia Brinson⁶, Paul Cook⁷, Gordon Crofoot⁸, Joel Gallant⁹, Mehri S. McKellar¹⁰, Hui Liu¹¹, Nan Zhang¹¹, Kwad Mponponsuo¹¹, Sean E. Collins¹¹, Onyema Ogbuagu¹²

Phase 2 Study Design

— Randomized, open-label, active-controlled, multicenter study (NCT05729568)

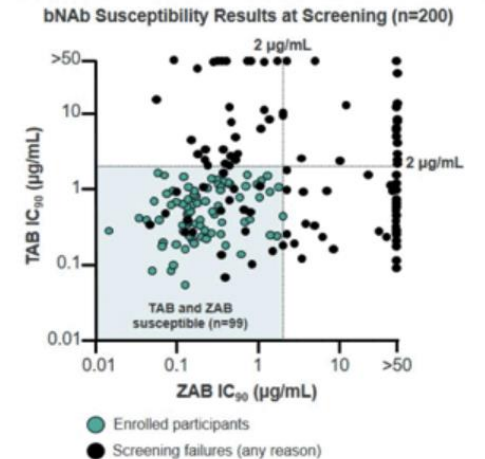
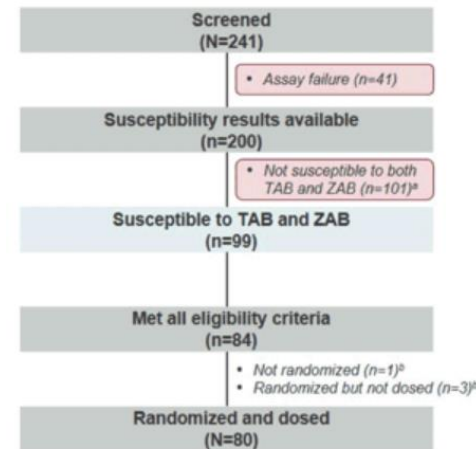


Week 104 Outcomes:

- HIV-1 RNA <50 copies/mL and ≥50 copies/mL by missing=excluded (M=E) analysis
- Change from baseline in CD4+ T-cell count; safety (adverse events); pharmacokinetics of LEN + TAB + ZAB; anti-drug antibodies (ADAs)

Screening bNAb Susceptibility

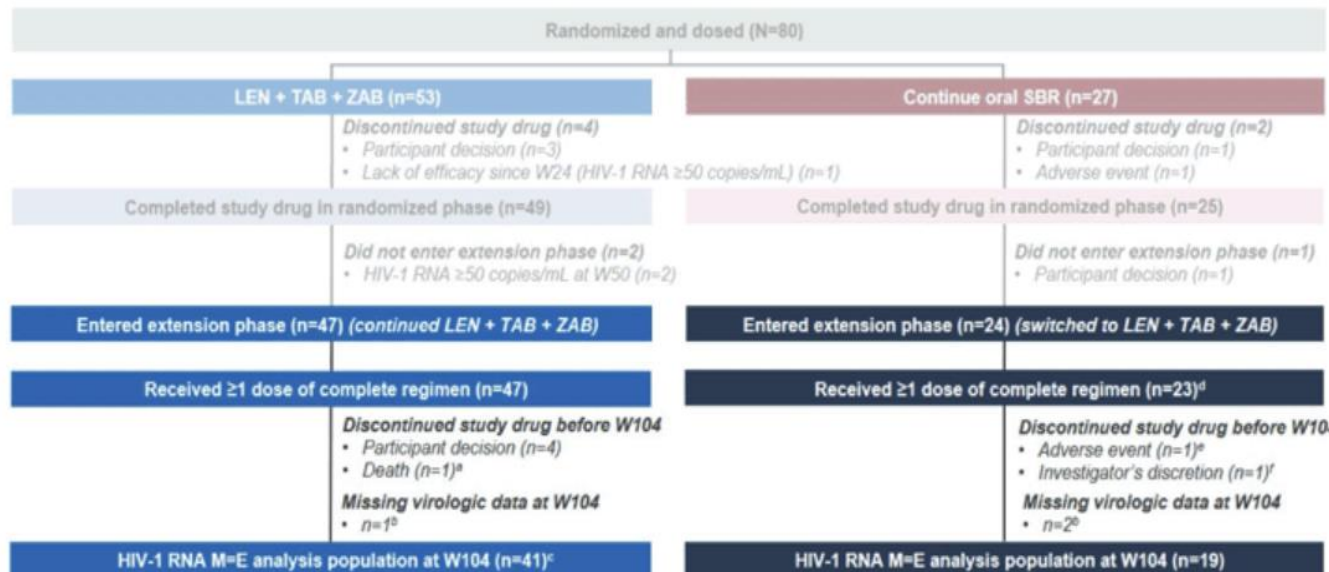
— The screening population included participants from both the SBR and LEN + TAB + ZAB group:



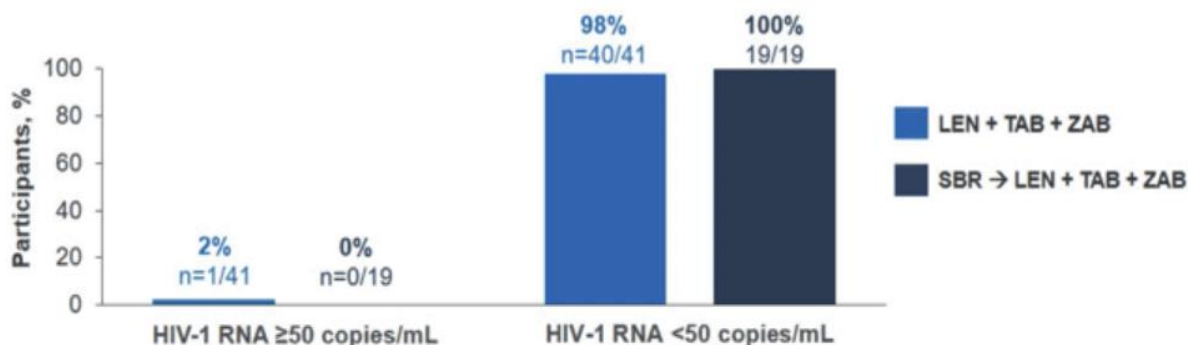
^aSusceptibility: TAB only: 47 (24%); ZAB only: 31 (16%); neither: 23 (12%). ^bParticipant decision.

bNAb, broadly neutralizing antibody; IC₉₀, 90% inhibitory concentration; LEN, lenacapavir; SBR, stable baseline regimen; TAB, teropavimab; ZAB, zinlirvimab.

Participant Disposition



Week 104 Virologic Outcomes (Missing=Excluded)

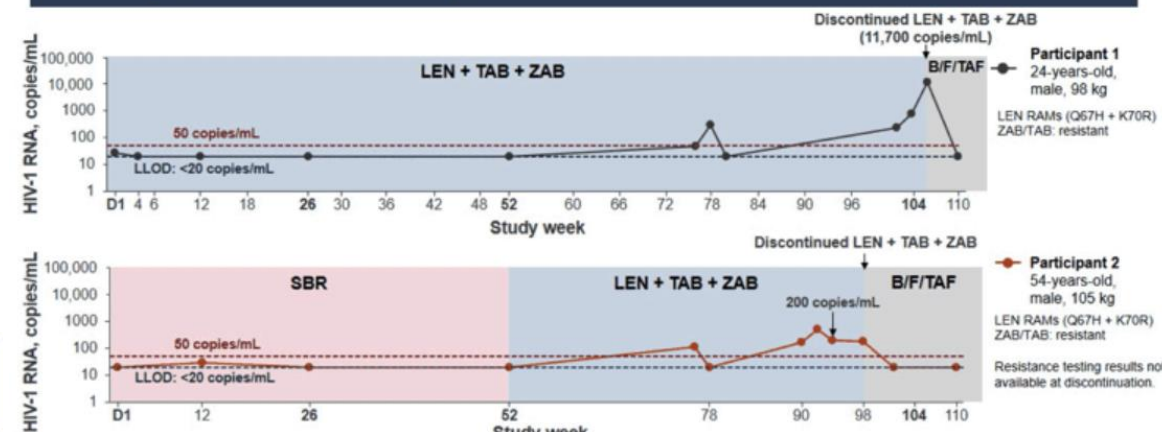


- One participant in the LEN + TAB + ZAB group met criteria for confirmed virologic rebound at Week 104 and discontinued due to lack of efficacy
- One participant in the SBR → LEN + TAB + ZAB group met criteria for confirmed virologic rebound at Week 90
 - Discontinued study treatment prior to Week 104 (investigator's discretion): Week 104 data are 'missing' and excluded from M=E analysis

Median (IQR) CD4+ T-cell count changes from baseline at Week 104:

- +34 (-71 to 111) cells/ μ L in the LEN + TAB + ZAB group
- 38 (-159 to +40) cells/ μ L in the SBR → LEN + TAB + ZAB group

Participants with Virologic Rebound



- PK of TAB and ZAB were consistent with the median of the respective group, trough LEN concentrations were below the median, but within the range observed in this and prior studies with LEN¹⁻³
- No ADAs to TAB or ZAB were detected in either participant

LEN + TAB + ZAB administration timepoints are indicated in bold.
ADA, antidrug antibody; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; LEN, lenacapavir; LLOD, lower limit of detection; PK, pharmacokinetics; RAM, resistance-associated mutation; SBR, stable baseline regimen; TAB, tenofovir; ZAB, zidovudine.

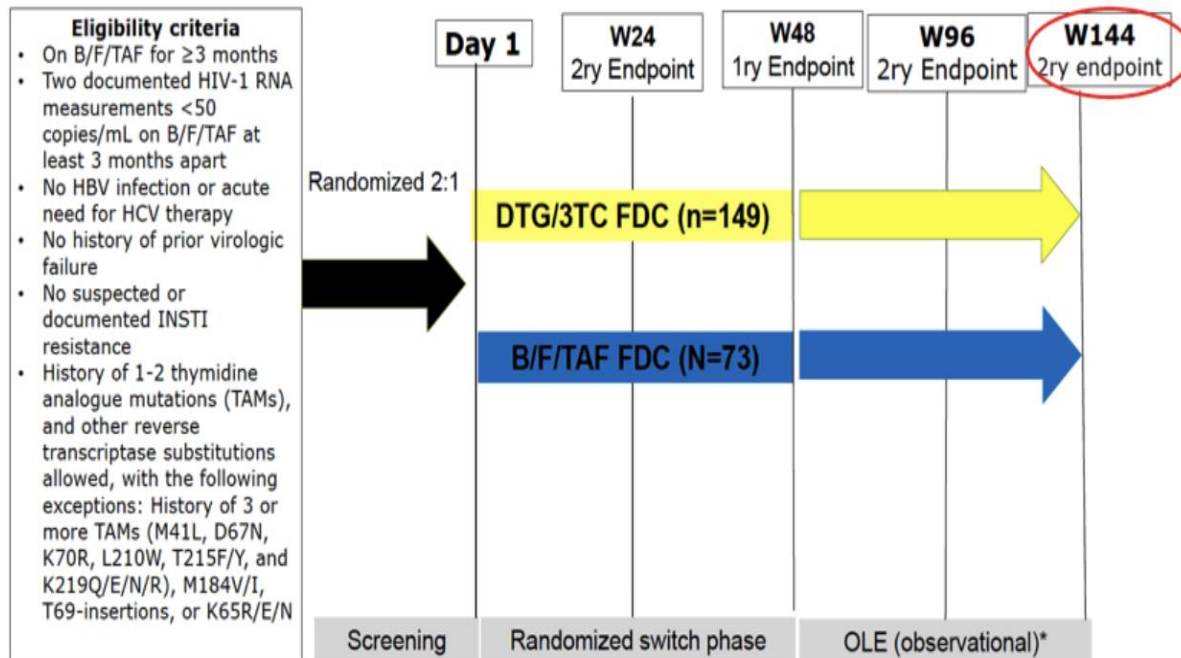
1. Ogburn O, et al. *Lancet Microbe* 2026;7(3): 101283. 2. Eron JJ, et al. *Lancet HIV* 2024;11(3):e146-e155. 3. Kelley CF, et al. *N Engl J Med* 2025; 392:1261-1276.

DTG/3TC v BFTAF as Switch ART – DYAD Trial^{week 144}

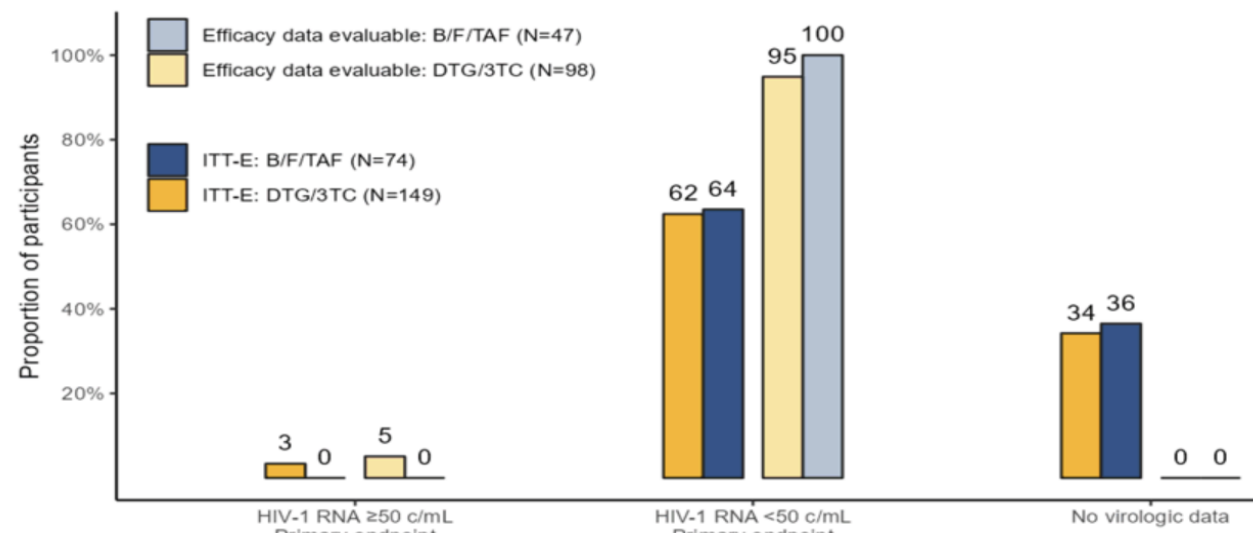
Long-term efficacy, safety and persistence of dolutegravir/lamivudine vs. bicitegravir/emtricitabine/tenofovir alafenamide among virologically suppressed adults-results from the 144-week observational extension phase of the DYAD study

Charlotte-Paige Rolle MD MPH^{1,2}, Jamie Castano MA¹, Vu Nguyen MS¹, Federico Hineostroza MD^{1,3}, Edwin DeJesus MD^{1,3}

DYAD (NCT04585737) was an open-label randomized clinical trial of virologically suppressed adults



Characteristic	DTG/3TC N=149	B/F/TAF N=73
Age		
Median (range), y	49 (24-73)	51 (20-73)
Age ≥50 y, n (%)	74 (50)	44 (60)
Sex		
Female, n (%)	24 (16)	12 (16)
Race		
Caucasian, n (%)	102 (68)	54 (74)
Black, n (%)	44 (30)	18 (25)
Asian, n (%)	1 (1)	0 (0)
Other, n (%)	2 (1)	1 (1)
Ethnicity		
Hispanic/Latino, n (%)	43 (29)	22 (30)
Not Hispanic/Latino, n (%)	106 (71)	51 (70)
BMI, median (range)	29.8 (18.8-56.6)	29.5 (20-49.8)
Weight, median (range), kg	90.4 (53.1-171.9)	88.5 (59.1-123.5)
CD4+ cell count, median (range) cells/mm³	720.5 (214-1479)	734.5 (151-1573)
CD4+ cell count		
≥350 cells/mm ³ , n (%)	139 (93)	70 (96)
<350 cells/mm ³ , n (%)	10 (7)	3 (4)
Duration of HIV infection, median (range), years	13 (1-36)	14 (1-36)
Duration of ART prior to Day 1, median (range), years	12 (1-32)	9.5 (1-27)
Number of ART regimens prior to Day 1	3 (1-9)	3 (1-10)
Current Insurance Coverage		
Private, n (%)	132 (89)	59 (81)
Medicaid, n (%)	5 (3)	2 (3)
Medicare, n (%)	12 (8)	10 (13)
Ryan White, n (%)	0 (0)	2 (3)
Baseline genotype available, n (%)	60 (40)	37 (51)
NRTI Resistance, n (%)	3 (2)	6 (8)
NNRTI Resistance, n (%)	16 (11)	13 (18)
PI Resistance, n (%)	27 (18)	16 (22)
INSTI Resistance, n (%)	1 (1)	2 (3)

Figure 1. Virologic outcomes at Week 144 by FDA Snapshot Analysis**Table 5.** Mean change from baseline in renal and metabolic parameters at Week 144

Parameter and Timepoint	DTG/3TC N=149	B/F/TAF N=73	Between group difference (95% CI)	P-value
Creatinine, mg/dL Week 144 Change (Mean $\pm$ SD)	0.03 $\pm$ 0.13	0.04 $\pm$ 0.13	-0.01 (-0.06 ; 0.04)	0.652
eGFR, mL/min Week 144 Change (Mean $\pm$ SD)	-3.84 $\pm$ 12.95	0.51 $\pm$ 15.2	-4.35 (-9.47 ; 0.78)	0.095
Total Cholesterol, mg/dL Week 144 Change (Mean $\pm$ SD)	-9.2 $\pm$ 34.23	-3.02 $\pm$ 27.73	-6.18 (-17.31 ; 4.96)	0.274
LDL Cholesterol, mg/dL Week 144 Change (Mean $\pm$ SD)	-8.39 $\pm$ 31.27	-5.22 $\pm$ 21.58	-3.17 (-12.7 ; 6.35)	0.511
HDL Cholesterol, mg/dL Week 144 Change (Mean $\pm$ SD)	-0.06 $\pm$ 7.07	0.18 $\pm$ 9.33	-0.24 (-3.42 ; 2.94)	0.881
Triglycerides, mg/dL Week 144 Change (Mean $\pm$ SD)	-3.12 $\pm$ 84.9	13.38 $\pm$ 81.63	-16.5 (-47.07 ; 14.07)	0.287
Total Cholesterol:HDL ratio Week 144 Change (Mean $\pm$ SD)	-0.3 $\pm$ 0.92	-0.22 $\pm$ 0.77	-0.08 (-0.47 ; 0.31)	0.692
Weight, kg Week 144 Change (Mean $\pm$ SD)	-1.67 $\pm$ 6.73	-1.85 $\pm$ 7.66	0.18 (-2.48 ; 2.84)	0.895
BMI, kg/m² Week 144 Change (Mean $\pm$ SD)	-0.97 $\pm$ 2.51	-1.11 $\pm$ 2.54	0.14 (-0.78 ; 1.05)	0.766

Abbreviations. B, bictegravir; F, emtricitabine; TAF, tenofovir alafenamide; DTG, dolutegravir; 3TC, lamivudine; CI, confidence interval; SD, standard deviation

At Week 144, no significant differences in mean change from baseline in creatinine, lipid parameters, weight, and BMI were observed between treatment groups.

CAB/RPV v TLD in Virologically Suppressed Adolescents – LATA Trial

Every-8-weeks injectable cabotegravir and rilpivirine is superior to daily oral tenofovir disoproxil fumarate/ lamivudine/ dolutegravir in adolescents living with HIV in sub-Saharan Africa: LATA 96-week results

Mutsa Bwakura-Dangarembizi*, Elizabeth Chappell, Adeodata R. Kekitlinwa, Cissy Kityo, Abraham Siika, Mo Archary, Lungile Jalta, Hilda A Mujuru, Louis Diana Anena, Shamim Nakabuye, Cecilia Killa, Rosie Mngqibisa, George Akabwai, Henry Mugerwa, Simon Walker, Janet Seeley, David Burger, Anas Omar, Alasdair Bamford, Annabelle South, Hanh Nguyen, Carlo Giaquinto, Ben Spittle, Deborah Ford, Sarah Pett, on behalf of the LATA trial team

*University of Zimbabwe Clinical Research Centre, Harare, Zimbabwe

Study design: open-label non-inferiority (NI) RCT comparing Q8W LAI CAB/RPV (**LAI**) vs. daily oral TLD (**control**)

Inclusion criteria: Adolescents aged 12-19 years living with HIV-1, on ART ≥ 1 year, ≥ 35 kg, HBsAg negative, no history of treatment failure, virologically suppressed (< 50 copies/mL) for 12 months

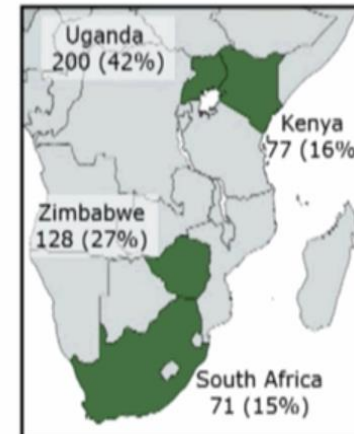
Follow-up: Until last participant reached 96 weeks, VL testing 24-weekly

Primary endpoint: Confirmed viral rebound (2 consecutive HIV-1 RNA ≥ 50 copies/mL), any time through week 96

➤ NI margin and significance level depended on the event rate in the control arm¹

Baseline characteristics

476 participants enrolled: 235 **LAI**, 241 **control**

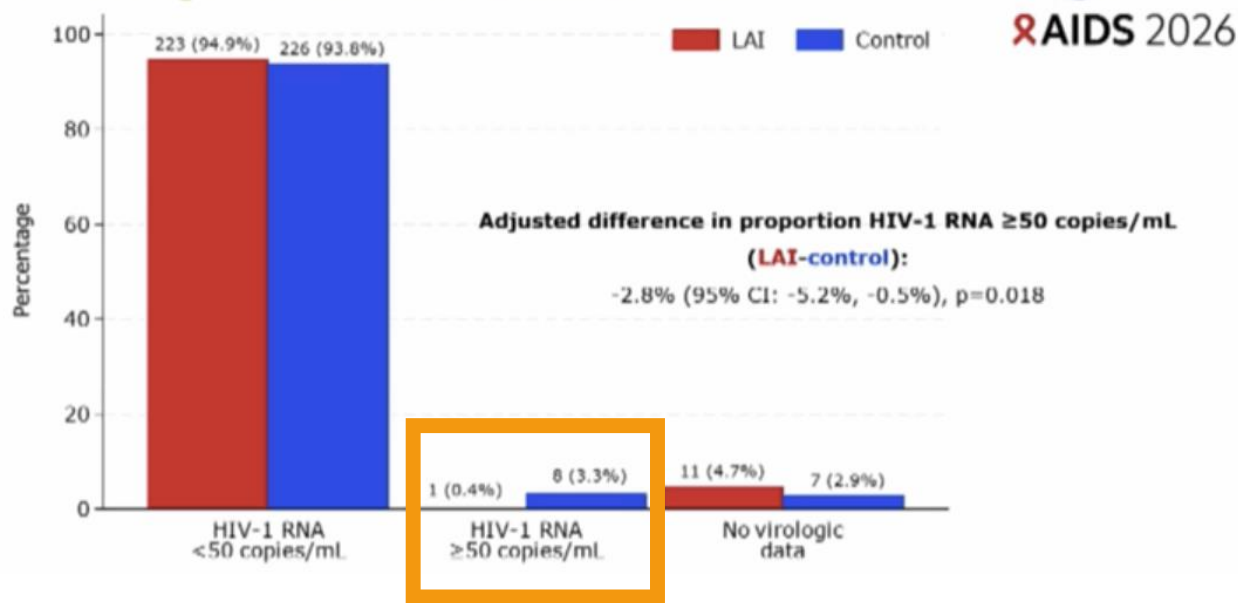


At baseline, % or median (range):

- **Age:** 16.5 years (12.0, 19.99)
- **Sex:** 54% female
- **Mode of HIV acquisition:** 98% vertical
- **BMI:** 19.6 kg/m² (14.2, 39.9)
- **Years on ART:** 11.7 years (1.4, 18.9)
- **Previous ART:** 99.6% DTG, 83% NNRTI
- 40% chose **optional CAB/RPV Oral Lead In** (LAI arm only)

All characteristics were well balanced across arms

FDA snapshot at week 96

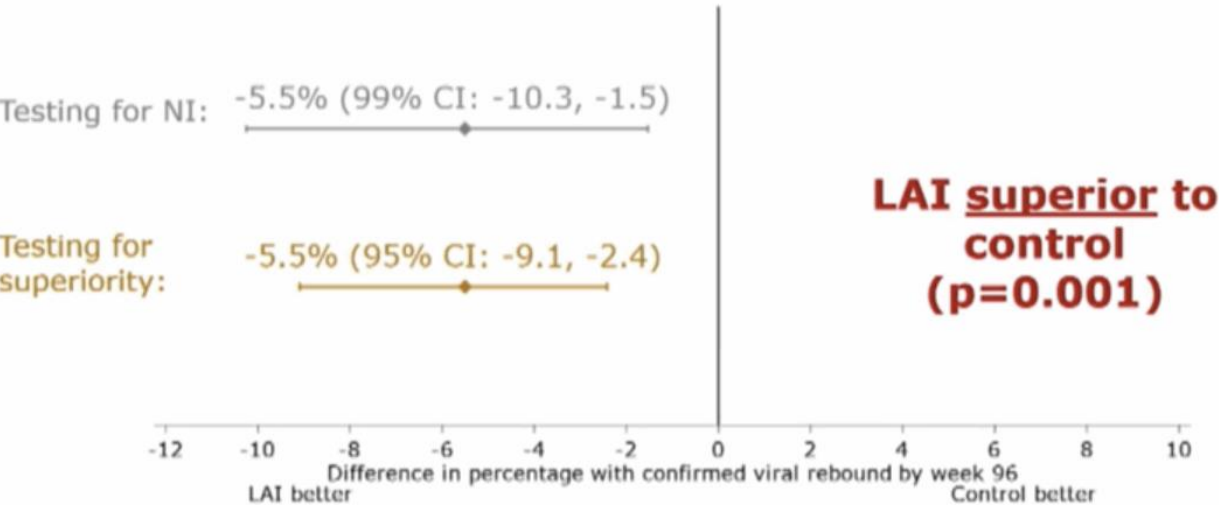


Major resistance mutations at confirmed viral rebound

	LAI (N=2)	Control (N=8)
INSTI	1	0
NRTI	0	1
NNRTI	1	2
PI	0	0

Primary outcome: ITT results

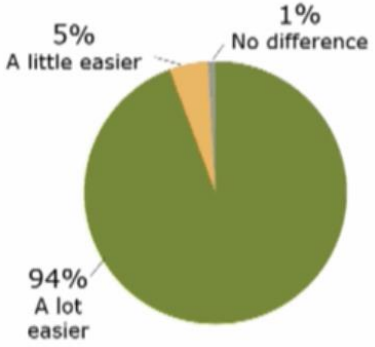
2 (0.9%) **LAI** vs. 15 (6.4%) **control** had confirmed viral rebound



Acceptability

99% of participants (in both **LAI** and **control**) reported that taking HIV medication had not been a burden and had not made it difficult to live a normal life

Those on **LAI** were asked:
"How does receiving injections of HIV medication make things for you compared to taking your medicines every day?"



ART Adherence – Barriers and Facilitators

Community HERO Treatment Survey: Stigma and Barriers to and Facilitators of Treatment Adherence Across a Global Population of People With HIV

Xavier Guillaume¹, Marcel Dams², Nomfundo Eland³, Maureen Owino⁴, Carlos Saucedo⁵, Yun-Chung Lu⁶,
Josep Mallolas⁷⁻⁹, Amina Omri¹, Alissar Moussallem¹, Larkin Callaghan¹⁰, Michael Bogart¹⁰, Neia Prata Menezes¹⁰, Connie Kim¹⁰

Participant Demographic and Clinical Characteristics

- A total of 2532 PWH have participated in the survey to date; demographic and clinical characteristics are summarised in **Table 1**
 - Most (2355/2532 [93%]) participants were currently receiving treatment, with the majority receiving an STR (1731/2345 [74%])

Table 1. Participant Demographic and Clinical Characteristics

Characteristic	Participants (N = 2532)
Age, y, mean (SD)	42.1 (12.0)
Sex assigned at birth, n (%)	
Male	1938 (77)
Female	588 (23)
Prefer not to answer	6 (<1)
Country/region, n (%)	
United States	402 (16)
Japan	250 (10)
Mexico	250 (10)
United Kingdom	213 (8)
Taiwan	208 (8)
South Africa	205 (8)
Italy	203 (8)
Spain	201 (8)
Canada	200 (8)
France	200 (8)
Germany	200 (8)

Methods

- This ongoing, multinational, observational, cross-sectional study consisted of a quantitative, 45-minute online survey; results presented in this poster reflect data collected from May 2024 to May 2025
 - Participant recruitment was conducted via a multimodal approach, including HIV communities and databases; referrals from HIV advocacy groups, physicians, and other PWH; and social media targeting
 - The survey was codeveloped by investigators and community advocates representing the survey countries/regions (Canada, France, Germany, Italy, Japan, Mexico, South Africa, Spain, Taiwan, the United Kingdom, and the United States) and was translated into local languages
- Eligible participants were ≥18 years of age, had a self-reported diagnosis of HIV, resided in 1 of the survey countries/regions, and could complete the survey in 1 of the local languages

Subpopulation, n (%) ^a	
MSM	1416 (56)
Older adults (≥50 y of age)	706 (28)
People who use drugs	616 (24)
Cisgender women	561 (22)
Migrants	268 (11)
Un-/underinsured	244 (10)
Black, Latinx, and other BIPOC MSM communities ^b	179 (7)
Transgender and nonbinary individuals	131 (5)
Young adults (18-24 y of age)	128 (5)

ART status, n (%)	
On ART, no history of treatment interruption	1789 (71)
On ART, with prior treatment interruption(s)	566 (22)
Previously on ART, not currently receiving treatment	79 (3)
No prior ART	98 (4)
Time since HIV diagnosis, y, median (IQR)	9.0 (4.0-18.0)
Time since HIV diagnosis, n (%)	
<5 y ago	711 (28)
≥5 y ago	1821 (72)
<10 y ago	1351 (53)
≥10 y ago	1181 (47)
Type of ART, n (%) ^{a,c}	n = 2345
Single-tablet regimen	1731 (74)
Multi-tablet regimen once daily	339 (14)
Multi-tablet regimen multiple times per day	75 (3)
Injections only	122 (5)
Injections and oral pills	78 (3)

Difficulty With Treatment Adherence

- Among participants currently receiving ART, 317/2345 (14%) reported difficulty with treatment adherence (Figure 1)
 - The proportion of participants reporting difficulty with treatment adherence varied by type of ART, ranging from 12% for those taking STRs to 20% for those taking MTRs multiple times per day

Figure 2. Stigma-Related Challenges Among Participants Currently Receiving Treatment^a and Among Participants Currently Receiving Treatment With and Without Adherence Difficulties

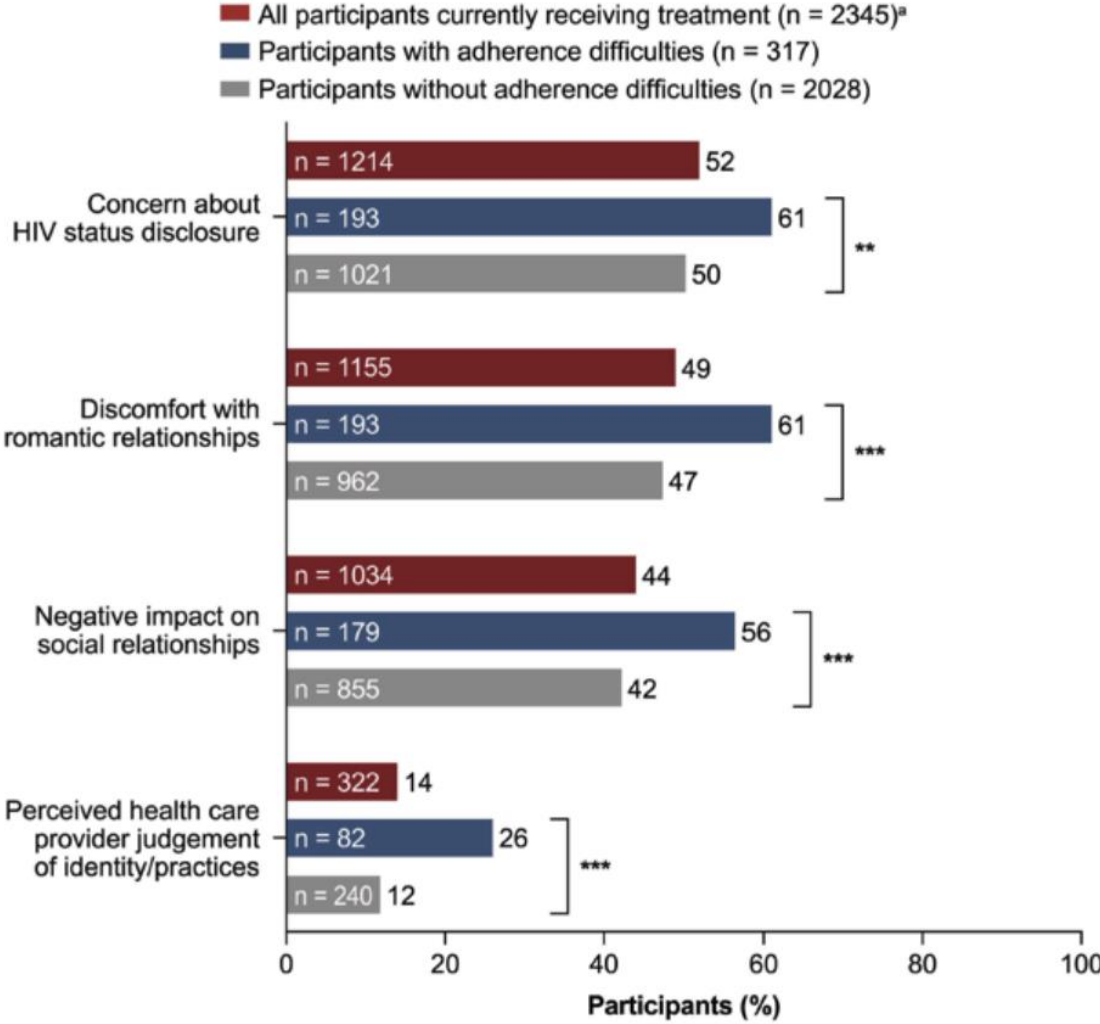


Figure 3. Barriers to Treatment Adherence Among Participants Currently Receiving Treatment With Adherence Difficulties, Overall and by Type of ART^{a,b}

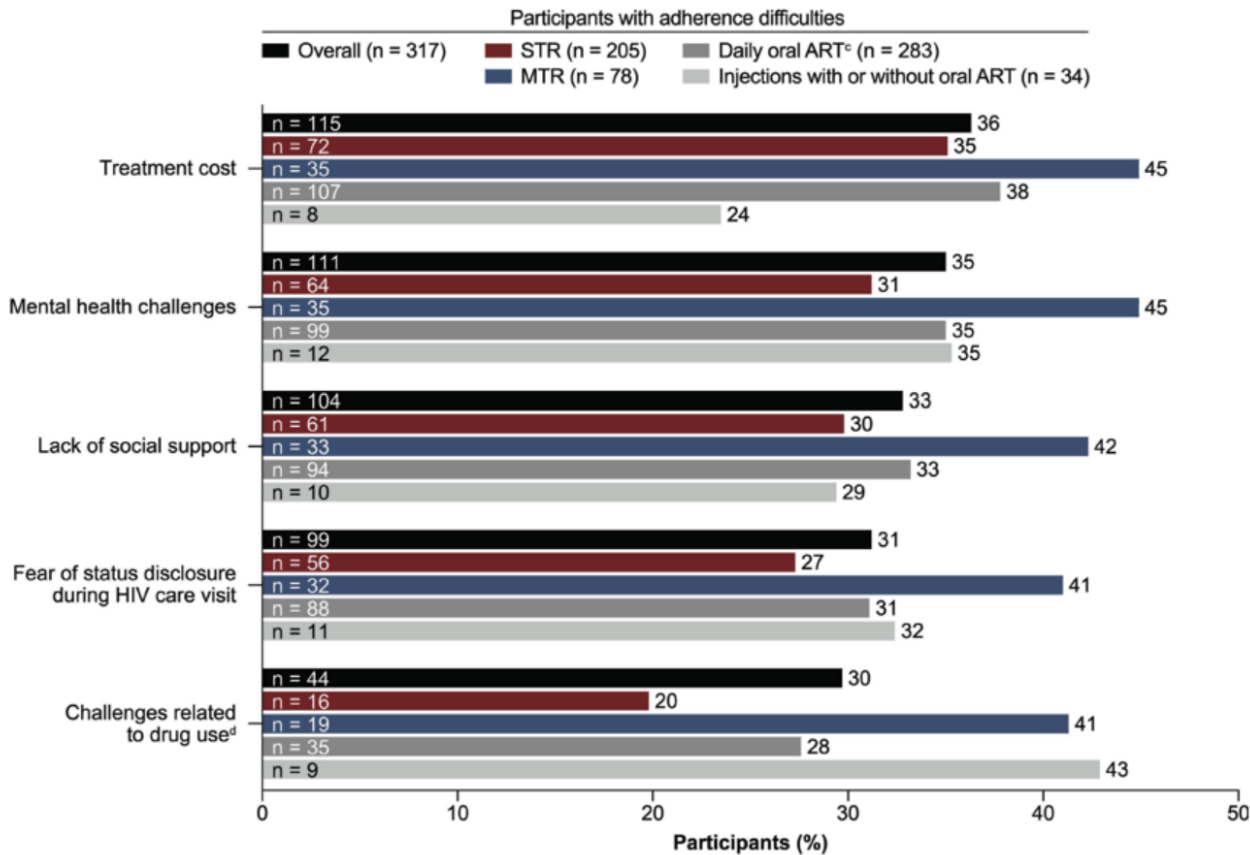
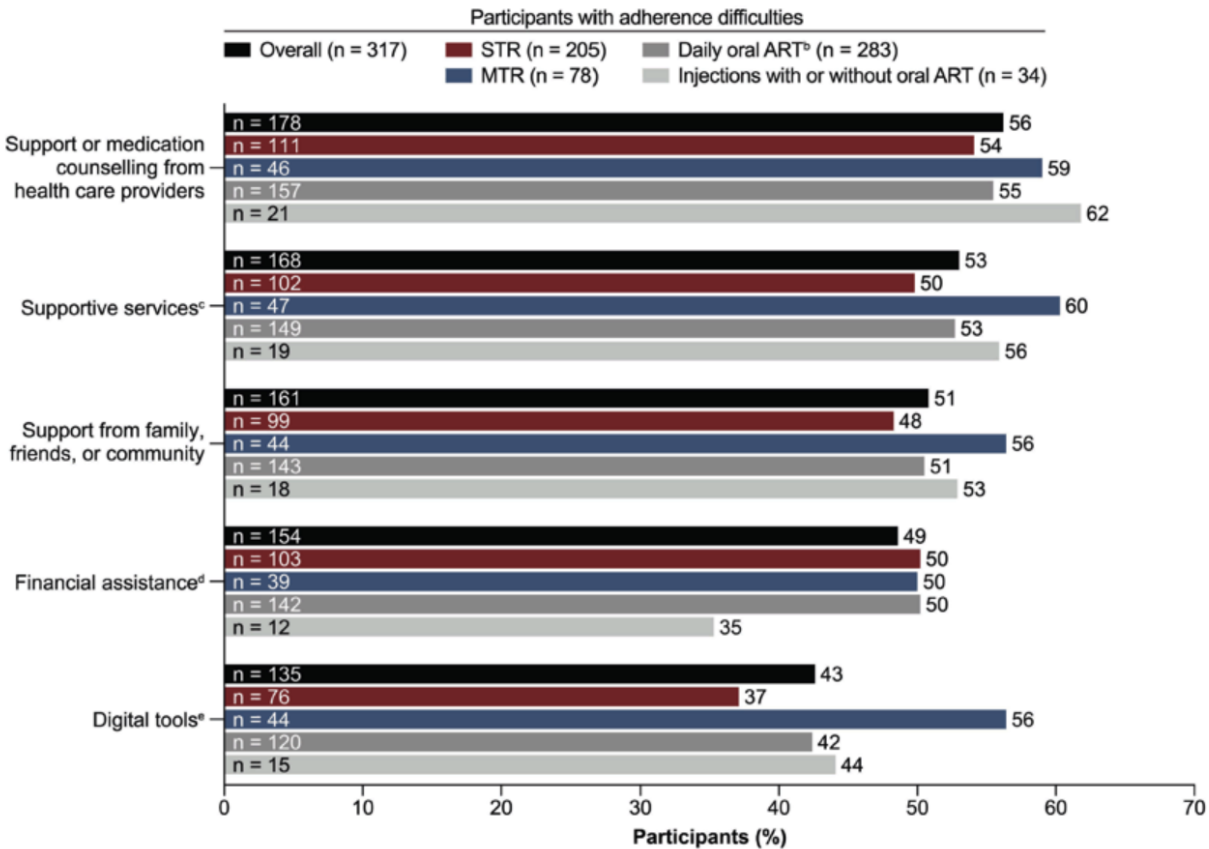


Figure 4. Facilitators of Treatment Adherence Among Participants Currently Receiving Treatment With Adherence Difficulties, Overall and by Type of ART^a



ART Pipeline

- Ultra-Long CAB^{INSTI}
 - 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
- Lotivibart (N6LS)^{bNAbs}
 - 3x per year infusion



Well-Being

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

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

CVD

ASCVD

Heart Failure

Sex*

☒ Male ☐ Female

Total Cholesterol (mg/dL)*

130-320

BMI (kg/m²)*

18.5-39.9

Lipid-lowering medication

Current use of statin medication to lower cholesterol

☒ No ☐ Yes

Age (years)*

30-79

HDL Cholesterol (mg/dL)*

20-100

Diabetes

Any history of diabetes.

☒ No ☐ Yes

Anti-hypertensive medication

Current use of any medication for hypertension

☒ No ☐ Yes

SBP (mmHg)*

90-200

eGFR (mL/min/1.73m²)*

15-140

Current Smoking

Any cigarette use within the last 30 days

☒ 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

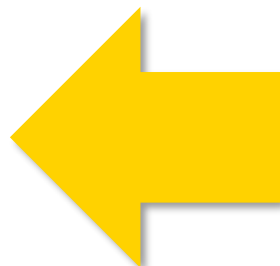
2026

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

- Start early
- Get low (LDL)
- Check $L_p(a)$



Lipid Lowering to Reduce ASCVD Risk

Screen
EARLIER



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

Check
REGULARLY



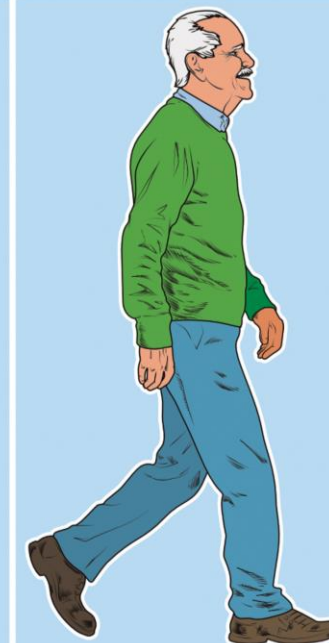
- Screen lipids again at age **19y**
- Recheck at least every **5y** and use PREVENT-ASCVD to identify risk

Aim for
LOWER LDL-C



- **<100 mg/dL** for PREVENT-ASCVD <10%
- **<70 mg/dL** for PREVENT-ASCVD $\geq 10\%$, 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

The F.D.A. Approves a New Pill to Slash Cholesterol Levels

The new pills can lower cholesterol levels far below what can be achieved with statins, clinical trials have shown.



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

FEBRUARY 5, 2026

VOL. 394 NO. 6

A Placebo-Controlled Trial of the Oral PCSK9 Inhibitor Enlicotide

Ann Marie Navar, M.D., Ph.D.,¹ Elina Mikhailova, M.D., Ph.D.,² Alberico L. Catapano, Ph.D.,^{3,4} Puja Banka, M.D.,⁵ Dirk J. Blom, M.D.,⁶ Alberto Cadena, M.D.,⁷ Susan Kourpanidis, M.S.,⁵ Norman E. Lepor, M.D.,^{8,9} Kazuhisa Tsukamoto, M.D., Ph.D.,¹⁰ Geraldine Mendizabal, M.D.,¹¹ Julio Nunez, M.D.,¹² Wenjuan Zhang, Ph.D.,¹³ Pengfei Zhu, D.Phil.,¹³ Min Zhuo, M.D., M.P.H.,⁵ and Christie M. Ballantyne, M.D.,¹⁴ for the CORALreef Lipids Investigators*

A Placebo-Controlled Trial of the Oral PCSK9 Inhibitor Enlicotide

A Research Summary based on Navar AM et al. | 10.1056/NEJMoa2511002 | Published on February 5, 2026

WHY WAS THE TRIAL DONE?

For patients with an elevated low-density lipoprotein (LDL) cholesterol level, PCSK9 inhibitors are an effective nonstatin therapy to lower LDL cholesterol, but current formulations are available only in an injectable form. The long-term efficacy and safety of an oral PCSK9 inhibitor are uncertain.

HOW WAS THE TRIAL CONDUCTED?

Adults who had a history of an atherosclerotic cardiovascular disease event with an LDL cholesterol level of 55 mg per deciliter or higher, as well as those who were at risk for a first event with an LDL cholesterol level of 70 mg per deciliter or higher, were randomly assigned in a 2:1 ratio to receive either once-daily oral enlicotide (20 mg) or placebo for 52 weeks. The primary end point was the mean percent change in LDL cholesterol levels at week 24.

TRIAL DESIGN

- Phase 3
- Double-blind
- Randomized
- Placebo-controlled
- Location: 168 sites in 14 countries

RESULTS

The mean percent change in LDL cholesterol levels at week 24 was significantly greater with enlicotide than with placebo (−57.1% vs. 3.0%). The incidence of adverse events did not appear to differ between the groups.

LIMITATIONS AND REMAINING QUESTIONS

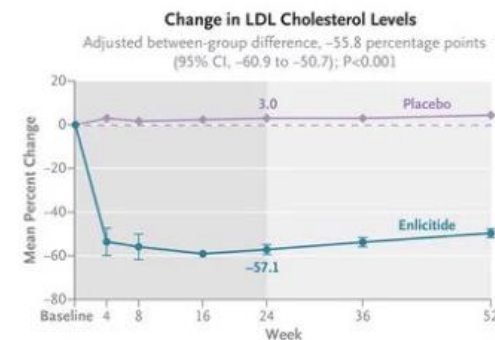
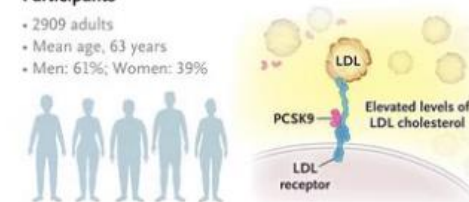
- The efficacy results reflect reductions in LDL cholesterol levels in the context of a clinical trial, not routine clinical practice.
- Although the trial follow-up was up to 52 weeks, patients receive lipid-lowering therapy for the prevention of atherosclerotic cardiovascular disease for years. The longer-term durability of the treatment effect, adherence, and effects on outcomes remains unknown.
- The trial was not powered to detect rare adverse events.

CONCLUSIONS

Among participants who had a history of or were at risk for a first atherosclerotic cardiovascular disease event, treatment with enlicotide resulted in lower LDL cholesterol levels than placebo at 24 weeks.

Participants

- 2909 adults
- Mean age, 63 years
- Men: 61%; Women: 39%



The New York Times

The F.D.A. Approves New Pill to Slash Cholesterol

The new pills can lower cholesterol levels more than achieved with statins, clinical trials show.

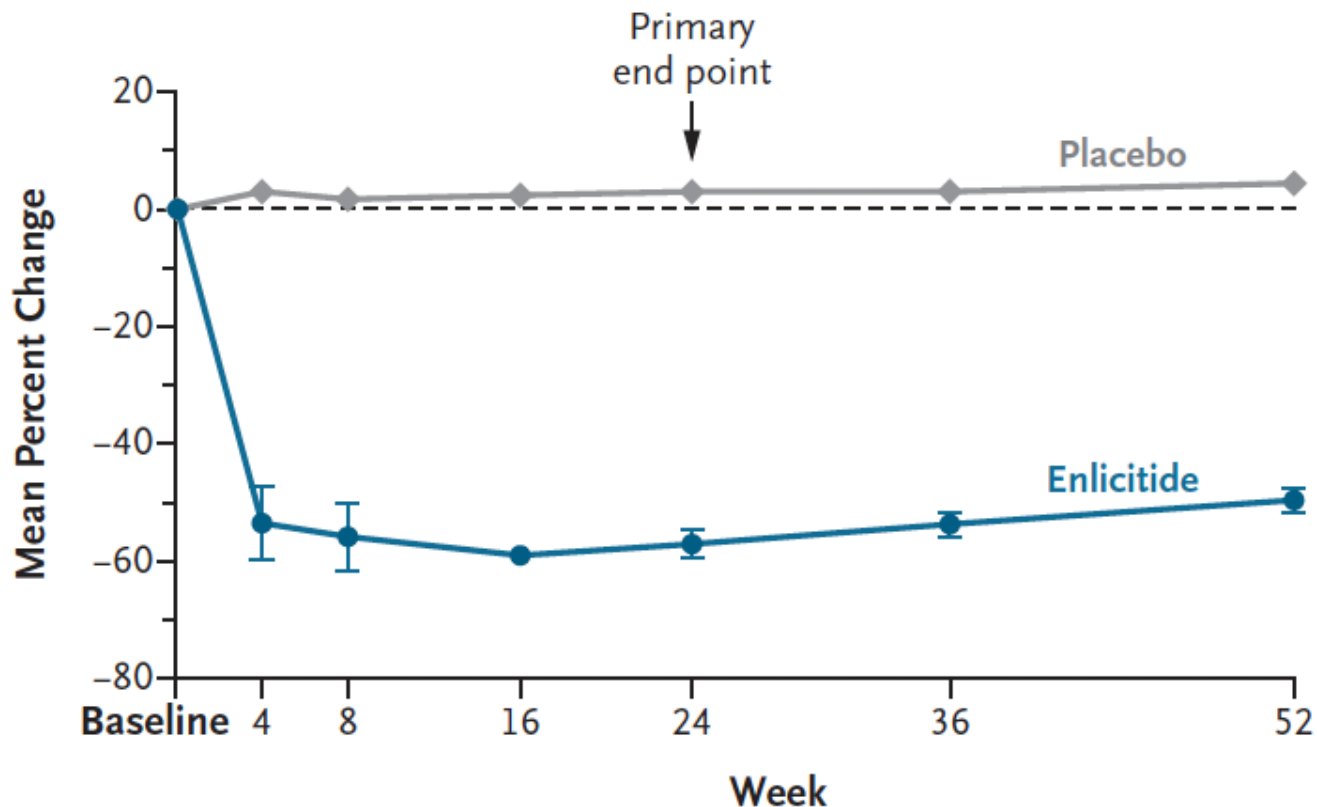
The NEW ENGLAND JOURNAL OF MEDICINE

ESTABLISHED IN 1812

A Placebo-Controlled Trial of the Oral PCSK9 Inhibitor Enlicitide

Ann Marie Navar, M.D., Ph.D.,¹ Elina M. Laitinen, M.D.,² Dirk J. Blom, M.D.,⁶ Alberto Cadena, M.D.,³ Kazuhisa Tsukamoto, M.D., Ph.D.,¹⁰ Gerardo Hernandez, M.D.,⁴ Pengfei Zhu, D.Phil.,¹³ Miriam S. Blaser, M.D.,⁵ for the ENLIGHTEN Investigators

A Change in LDL Cholesterol Levels



No. of Participants

Placebo	969	933	937	927	923	909	898
Enlicitide	1935	1836	1852	1824	1832	1798	1771

treatment with enlicitide resulted in lower LDL cholesterol levels than placebo at 24 weeks.

NEJM QUICK TAKE | EDITORIAL

THE NEW ENGLAND JOURNAL OF MEDICINE

A Placebo-Controlled Trial of the Oral PCSK9 Inhibitor Enlicitide

A Research Summary based on Navar AM et al. | 10.1056/NEJMoa2511002 | Published on February 5, 2026

Participants

- 2909 adults
- Mean age, 63 years
- Men: 61%; Women: 39%



Enlicitide
20 mg



N=1940

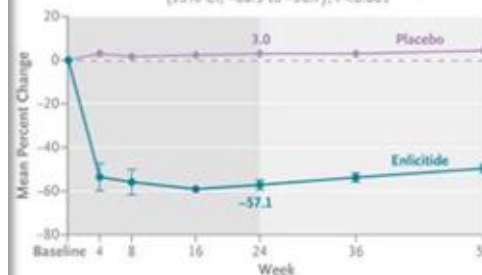
Placebo



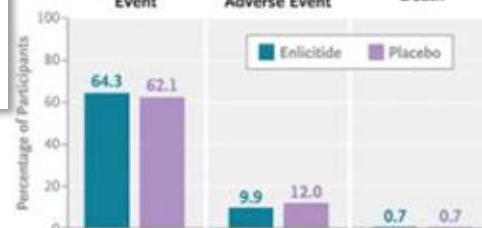
N=969

Change in LDL Cholesterol Levels

Adjusted between-group difference, -55.8 percentage points (95% CI, -60.9 to -50.7); P<0.001



Any Adverse Event Any Serious Adverse Event Death



Lancet Commission on Aging with HIV

The Lancet HIV Commission on ageing and HIV: a global perspective



Amy C Justice*, Keri N Althoff*, A Mark Clarfield, Brenda Crabtree Ramirez, Nathan Ford, Mary-Anne Hartley, Jepchirchir Kiplagat, Grace C Y Lui, Aggrey S Semeere, Marco Vitoria, Stephen Watiti, Tristan J Barber, Till W Barnighausen, Marta Boffito, Mark Brennan-Ing, Jessica Castilho, Stephen R Connor, Claudia Cortes, Giovanni Guaraldi, Meredith Greene, Beatriz Grinsztejn, Catherine Godfrey, Workegegnehu Hailu, Virgilio A Hernandez Ruiz, Javier Hourcade Bellocq, Vanessa Johnson, John Joska, Parastu Kasaie, Oageng Moseki, Nadia Naous, Joel Negin, Daniel Ochieng, Dorothy Onyango, Nicoletta Policek, Yvette Raphael, Julia Rohr, Anat Rosenthal, Enid J Schatz, Melissa C Schnure, Kailey R Seiler, Tinei Shamu, Mikaela Smit, Kristen A Stafford, Omar Sued, Andrew Tan, Jaques D du Toit, Sandra Wagner Cardoso

Executive summary

Global access to antiretroviral therapy (ART) for people living with HIV is a miracle of the modern era. Continued access to ART has extended the lives of millions of people living with HIV. At the same time, a growing number of people newly diagnosed with HIV are aged 50 years or older, and their treatment is often delayed. Older people at risk for HIV or living with HIV face unique challenges,

total population living with HIV. Assuming a continuation of current trends, the median age of adults with HIV is expected to increase to 50 years by 2040, with 20·2 million people with HIV being older than 50 years of age and accounting for 51% of all people living with HIV. Importantly, in 2040, 96% of people with HIV older than 50 years are forecast to reside in low-income and middle-income countries (LMICs).

Lancet HIV 2026; 13: e569–610
Published Online
July 27, 2026
[https://doi.org/10.1016/S2352-3018\(26\)00058-5](https://doi.org/10.1016/S2352-3018(26)00058-5)
See Comment pages
e518 and e520
For the French translation of the
executive summary see [Online](#)

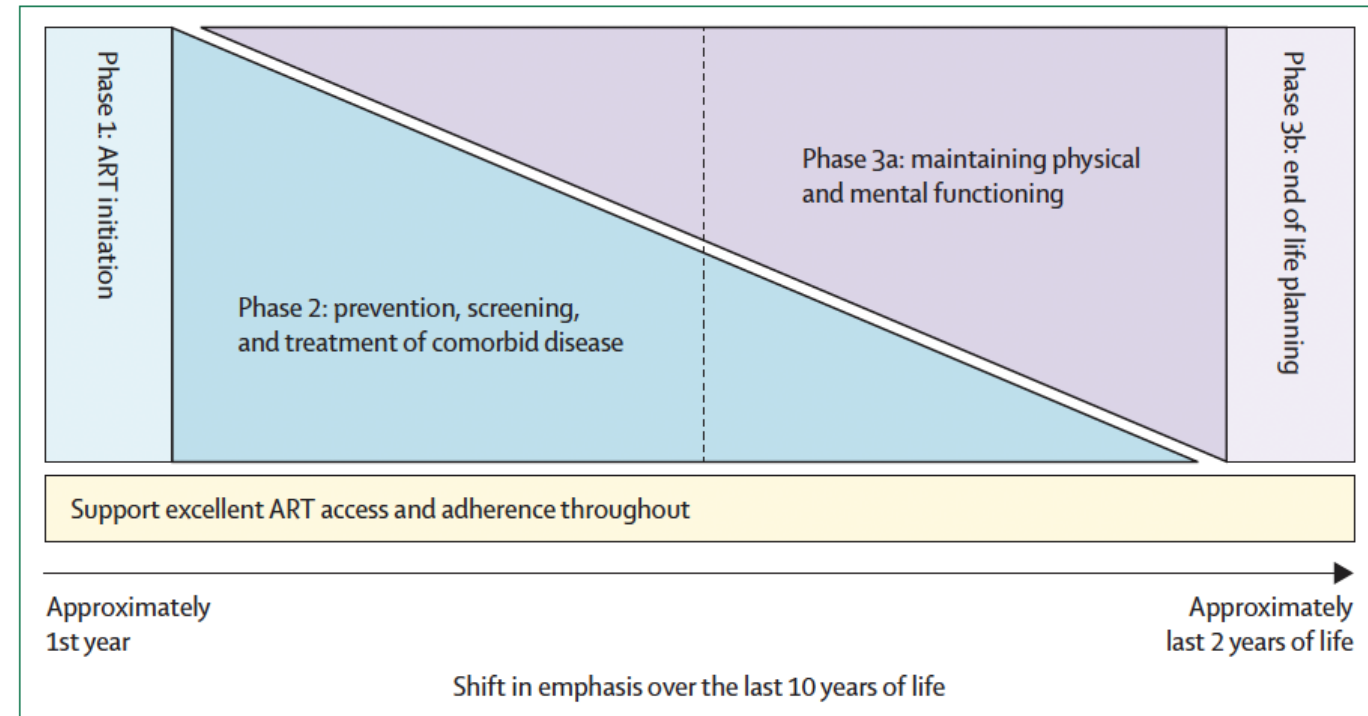


Figure 3: Phases of health care and their emphasis to optimise ageing with HIV

Definition and diagnostic criteria of clinical obesity

Executive summary

Current BMI-based measures of obesity can provide underestimate and overestimate adiposity and individual information about health at the population level, which undermines medically-sound thought to health care and policy. This Commission sought to define clinical obesity as a condition of illness that, akin to the notion of chronic disease and tissues. The specialties, directly results from other medical adiposity on the function of organs and tissues. A specific aim of the Commission was to establish objective criteria for disease diagnosis, aiding clinical decision making and prioritisation of therapeutic interventions and public health strategies. To this end, a group of 58 experts—representing multiple evidence specialties and countries—discussed development process and participated in a consensus development session. Among these commissioners was ensure consideration of patient perspectives. The Commission defines obesity as a condition characterised by excess adiposity and still without abnormal distribution or function of adipose tissue, and with causes that are multifactorial and still incompletely understood. We define clinical obesity as a chronic, systemic illness characterised by alterations in the function of tissues, organs, the entire individual, or a combination thereof, due to excess adiposity. Clinical obesity can lead to severe end-organ damage, causing life-altering and potentially life-threatening complications (eg, heart attack, stroke, and renal failure). We define preclinical obesity as a state of excess adiposity with a varying, but generally tissues and organs and a varying, but generally increased, risk of developing clinical obesity and several other non-communicable diseases (eg, type 2 diabetes, increased risk of developing clinical obesity and several other non-communicable diseases, certain types of mortality and cardiovascular disorders). Although the risk of mortality and obesity-associated diseases can rise as a continuum (moderately-associated levels of fat mass, we differentiate across increasing clinical and obesity-related purposes. We recommend that BMI should be used only as a surrogate (illness) for clinical and policy-related purposes, for measure of health risk at a population level, for epidemiological studies, or for screening purposes, rather than as an individual measure of health. Excess adiposity should be confirmed by either direct

[illegible]

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Defining Obesity

The Lancet Diabetes & Endocrinology Commission

Definition and diagnostic criteria of clinical obesity

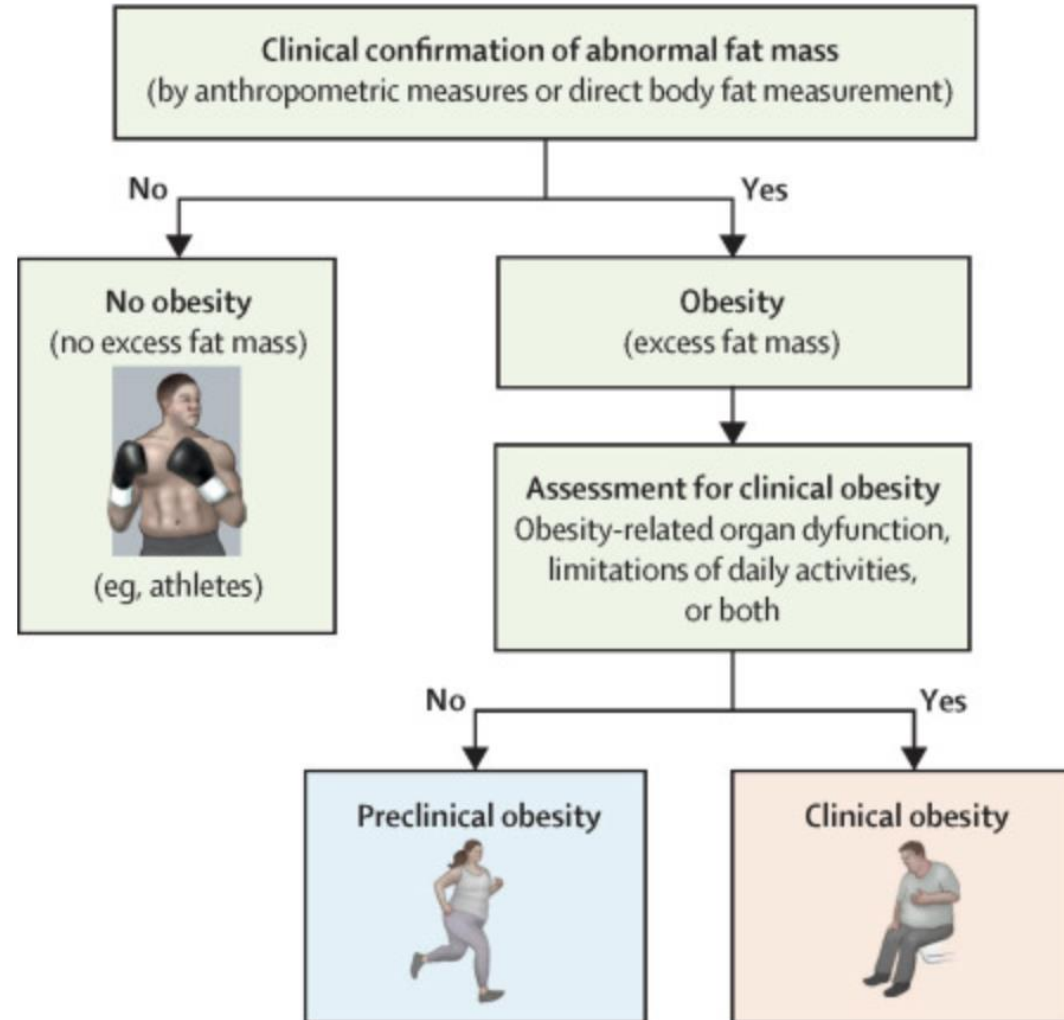
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Executive summary

Current BMI-based measures of obesity can both underestimate and overestimate adiposity and provide inadequate information about health at the individual level, which undermines medically-sound approaches to health care and policy. This Commission sought to define clinical obesity as a condition of excess to the notion of chronic disease in other medical specialties, directly results from the effect of excess adiposity on the function of organs and tissues. The specific aim of the Commission was to establish objective criteria for disease diagnosis, aiding clinical decision making and prioritisation of therapeutic interventions and public health strategies. To this end, a group of 58 experts—discussed available evidence and participated in a consensus development process. Among these commissioners were people with lived experience of obesity. The Commission defines obesity as a condition characterised by excess adiposity, with or without abnormal distribution or function of adipose tissue, and with causes that are multifactorial and still incompletely understood. We define clinical obesity as a chronic, systemic illness characterised by alterations in the function of tissues, organs, the entire individual, or a combination thereof, due to excess adiposity. Clinical obesity can lead to severe end-organ damage, causing life-altering and potentially life-threatening complications (eg, heart attack, stroke, and renal failure). We define preclinical obesity as a state of excess adiposity with preserved function of other tissues and organs and a varying, but generally increased, risk of developing clinical obesity and several other non-communicable diseases (eg, type 2 diabetes, cardiovascular disorders). Although the differentiation between preclinical and clinical obesity (ie, health vs illness) should be used only as a surrogate measure of health risk at a population level, for epidemiological studies, or for screening purposes, rather than as an individual measure of health. Excess adiposity should be confirmed by either direct measurement of body fat, where available, or at least one anthropometric criterion (eg, waist circumference, waist-to-hip ratio, or waist-to-height ratio) in addition to BMI, using validated methods and cutoff points appropriate to age, gender, and ethnicity. In people with very high BMI (ie, $>40 \text{ kg/m}^2$), however, excess adiposity can pragmatically be assumed, and no further confirmation is required. We also recommend that people with confirmed obesity status (ie, excess adiposity with or without abnormal organ or tissue function) should be assessed for clinical obesity. The diagnosis of clinical obesity requires one or both of the following main criteria: evidence of reduced organ or tissue function due to obesity (ie, signs, symptoms, or diagnostic tests showing abnormalities in the function of one or more tissue or organ system); or substantial, age-adjusted limitations of daily activities reflecting specific effect of obesity on mobility, other basic activities of daily living (eg, bathing, dressing, toileting, continence, and eating), or both. People with clinical obesity should receive timely, evidence-based treatment, with the aim to induce improvement of obesity and (possibly) of clinical manifestations of obesity and prevent progression to end-organ damage. People with preclinical obesity should undergo evidence-based health counselling, monitoring of their health status over time, and, when applicable, appropriate intervention to reduce risk of developing clinical obesity and other obesity-related diseases. Policy makers and health authorities should ensure adequate and equitable access to available evidence-based treatments for individuals with a chronic and potentially life-threatening illness. Public health strategies to reduce the incidence and prevalence of obesity at population levels must be based on current scientific evidence, rather than unproven assumptions that blame individual responsibility for the development of obesity. Weight-based bias and stigma are major obstacles in efforts to effectively prevent and treat obesity; health-care professionals and policy makers should issue proper training to address this important issue of obesity. All recommendations presented in this Commission have been agreed with the highest level of consensus among the commissioners (grade of

measurement of body fat, where available, or at least one anthropometric criterion (eg, waist circumference, waist-to-hip ratio, or waist-to-height ratio) in addition to BMI, using validated methods and cutoff points appropriate to age, gender, and ethnicity. In people with very high BMI (ie, $>40 \text{ kg/m}^2$), however, excess adiposity can pragmatically be assumed, and no further confirmation is required. We also recommend that people with confirmed obesity status (ie, excess adiposity with or without abnormal organ or tissue function) should be assessed for clinical obesity. The diagnosis of clinical obesity requires one or both of the following main criteria: evidence of reduced organ or tissue function due to obesity (ie, signs, symptoms, or diagnostic tests showing abnormalities in the function of one or more tissue or organ system); or substantial, age-adjusted limitations of daily activities reflecting specific effect of obesity on mobility, other basic activities of daily living (eg, bathing, dressing, toileting, continence, and eating), or both. People with clinical obesity should receive timely, evidence-based treatment, with the aim to induce improvement of obesity and (possibly) of clinical manifestations of obesity and prevent progression to end-organ damage. People with preclinical obesity should undergo evidence-based health counselling, monitoring of their health status over time, and, when applicable, appropriate intervention to reduce risk of developing clinical obesity and other obesity-related diseases. Policy makers and health authorities should ensure adequate and equitable access to available evidence-based treatments for individuals with a chronic and potentially life-threatening illness. Public health strategies to reduce the incidence and prevalence of obesity at population levels must be based on current scientific evidence, rather than unproven assumptions that blame individual responsibility for the development of obesity. Weight-based bias and stigma are major obstacles in efforts to effectively prevent and treat obesity; health-care professionals and policy makers should issue proper training to address this important issue of obesity. All recommendations presented in this Commission have been agreed with the highest level of consensus among the commissioners (grade of

Elevated body weight or BMI



Defining Obesity

The Lancet Diabetes & Endocrinology Commission

Definition and diagnostic criteria of clinical obesity

Francesco Rubino, David E Cummings, Robert H Eckel, Ricardo V Cohen, John P H Wilding, Wendy A Brown, Fatima Cody Stanford, Rachel L Batterham, I Sadaf Farooqi, Nathalie J Fargnoul-Lambert, Carol W Le Roux, Naveed Sattar, Louise A Baur, Katherine M Morrison, Anoop Misra, Takashi Kadowaki, Kwang Wei Tham, Priya Sumithran, W Timothy Garvey, John P Kirwan, José-Manuel Fernández-Real, Barbara E Corkey, Hermann Toplak, Alexander Kojouhar, Robert F Kushner, Francesco Branca, Jonathan Valabhji, Matthias Blüher, Stefan R Bornstein, Harvey J Grill, Eric Ravussin, Edward Galea, Noor B Al Busaidi, Nasreen F Alfaris, Ebaa Al Ozairi, Lena M S Carlsson, Karine Clément, Jean-Pierre Després, John B Dixon, Gauden Galea, Lee M Kaplan, Blandine Laferrère, Martine Laville, Soo Lim, Jesús R Luna Fuentes, Vicki M Mooney, Joseph Nadgrowski Jr, Agnieszka Uroń, Magdalena Olszanecka-Glinianowicz, An Pan, François Pattou, Philip R Schauer, Matthias H Tschöp, Maria T van der Merwe, Roberto Vettor, Geltrude Mingrone

Executive summary

Current BMI-based measures of obesity can both underestimate and overestimate adiposity and provide inadequate information about health at the individual level, which undermines medically-sound approaches to health care and policy. This Commission sought to define clinical obesity as a condition of illness that, akin to the notion of chronic disease in other medical specialties, directly results from the effect of excess adiposity on the function of organs and tissues. The specific aim of the Commission was to establish objective criteria for disease diagnosis, aiding clinical decision making and prioritisation of therapeutic interventions and public health strategies. To this end, a group of 58 experts—discussed available evidence and participated in a consensus development process. Among these commissioners were people with lived experience of obesity to ensure consideration of patients' perspectives. The Commission defines obesity as a condition characterised by excess adiposity and still as without abnormal distribution or function of adipose tissue, and with causes that are multifactorial and still incompletely understood. We define clinical obesity as a chronic, systemic illness characterised by alterations in the function of tissues, organs, the entire individual, or a combination thereof, due to excess adiposity. Clinical obesity can lead to severe end-organ damage, causing life-altering and potentially life-threatening complications (eg, heart attack, stroke, and renal failure). We define preclinical obesity as a state of excess adiposity with preserved function and several tissues and organs and a varying, but generally increased, risk of developing clinical obesity and several other non-communicable diseases (eg, type 2 diabetes, cardiovascular disorders). Although the differentiation between preclinical and clinical obesity (ie, health vs illness) should be used only as a surrogate measure of health risk at a population level, for epidemiological studies, or for screening purposes, rather than as an individual measure of health. Excess adiposity should be confirmed by either direct

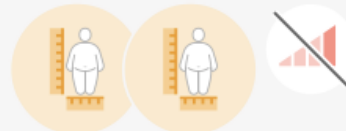
measurement of body fat, where available, or at least one anthropometric criterion (eg, waist circumference, waist-to-hip ratio, or waist-to-height ratio) in addition to BMI, using validated methods and cutoff points appropriate to age, gender, and ethnicity. In people with very high BMI (ie, $>40 \text{ kg/m}^2$), however, excess adiposity can pragmatically be assumed, and no further confirmation is required. We also recommend that people with or without abnormal organ or tissue adiposity should be assessed for clinical obesity. The diagnosis of clinical obesity requires one or both of the following main criteria: evidence of reduced organ or tissue function due to obesity (ie, signs, symptoms, or diagnostic tests showing abnormalities in the function of one or more tissue or organ system); or substantial age-adjusted limitations of daily activities, other than specific effect of obesity on mobility, toileting, activities of daily living (eg, bathing, dressing, continence, and eating), or both. People with clinical obesity should receive timely, evidence-based treatment, with the aim to induce improvement of obesity and (where possible) of clinical manifestations of obesity and prevent progression to end-organ damage. People with preclinical obesity should undergo evidence-based interventional treatment, monitoring of their health status over time, and, when applicable, appropriate intervention to reduce risk of developing clinical obesity and other obesity-related diseases. Policy makers and health authorities should ensure adequate and equitable access to available evidence-based treatments for individuals with a chronic and potentially life-threatening illness. Public health strategies to reduce the incidence and prevalence of obesity at population levels must be based on current scientific evidence. Weight-based assumptions that blame individual responsibility for the development of obesity, or unproven assumptions that health-care providers receive bias and stigma and treat obesity, should be effectively prevented and policy makers should issue proper training to address this important issue of obesity. All recommendations presented in this Commission have been agreed with the highest level of consensus among the commissioners (grade of

1 Excess body fat?

The first step in such a diagnosis is confirming excess body fat, which can be achieved via one of the following three criteria:



At least one measurement of body size and BMI



At least two measurements of body size, regardless of BMI



Direct body fat measurement, such as a DEXA scan

Measurements of body size

The commission defines three measurements of body size that can be used to confirm excess body fat:



Waist circumference
 $\geq 102 \text{ cm}$ for men*
 $\geq 88 \text{ cm}$ for women*



Waist-to-hip ratio
 >0.90 for men*
 >0.85 for women*



Waist-to-height ratio
 >0.50 for all*

Excess body fat can pragmatically be assumed if BMI is $>40 \text{ kg/m}^2$

Defining Obesity

Changing profiling of obesity under the new definition and its adverse complications with chronic conditions in people with HIV

Xueying Yang¹, Huiyi Xia, Fanghui Shi, Sharon Weissman, Hao Zhang, Xiaoming Li

¹ Department of Health Promotion, Education and Behavior, Arnold School of Public Health, University of South Carolina, Columbia, USA, 29208

Background

- People with HIV (PWH) have a higher prevalence of obesity than the general population.
- A recent Lancet Commission proposed a new obesity definition integrating Body Mass Index (BMI) with anthropometric measures, representing a paradigm shift in obesity classification.
- This study evaluated the association of obesity defined by the new Lancet Commission criteria with cardiovascular disease (CVD) and diabetes among PWH.

Methods

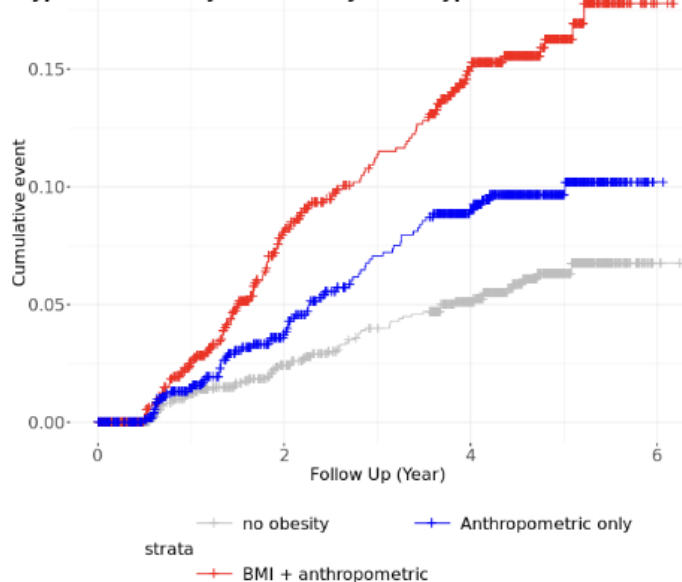
• Data Source

- Data were obtained from the All of Us Research Program. The analytic sample included 3,343 PWH for the diabetes analysis and 4,147 PWH for the CVD analysis.

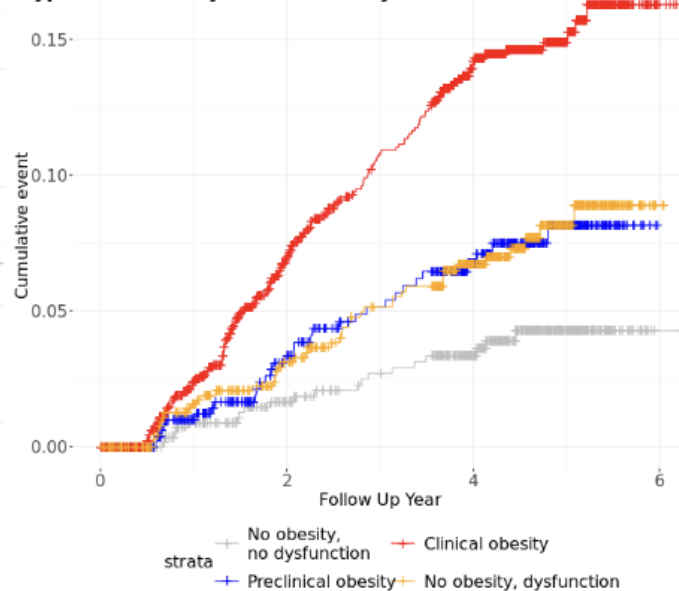
- Overall, 65.7% (2,900/4,414) PWH met the obesity criteria.
- Among participants with obesity, 53.3% (1,546/2,900) were classified as BMI-plus-anthropometric obesity and 46.7% (1,354/2,900) as anthropometric-only obesity.
- And 79.2% (2,296/2,900) PWH had clinical obesity and 20.8% (604/2,900) had preclinical obesity (Table 1).

	Obesity Category, N (%)				Obesity Phenotype, N (%)			Clinical Obesity Status, N (%)		
	Overall (N=4414)	Obesity absent (N=1514)	Obesity present (N=2900)	P	BMI-plus- anthropomet ric (N=1546)	Anthropomet ric-only (N=1354)	P	Preclinical Obesity (N=604)	Clinical Obesity (N=2296)	P
Baseline Age										
Mean (SD)	54.7 (12.2)	50.9 (12.9)	56.7 (11.4)	<0.001	54.8 (11.4)	58.9 (10.9)	<0.001	51.3 (12.7)	58.1 (10.6)	<0.001
Sex at birth										
Female	1373 (31.1%)	283 (18.7%)	1090 (37.6%)	<0.001	735 (47.5%)	355 (26.2%)	<0.001	212 (35.1%)	878 (38.2%)	0.170
Male	3041 (68.9%)	1231 (81.3%)	1810 (62.4%)		811 (52.5%)	999 (73.8%)		392 (64.9%)	1418 (61.8%)	
Race										
White	1045 (23.7%)	312 (20.6%)	733 (25.3%)	<0.001	341 (22.1%)	392 (29.0%)	<0.001	135 (22.4%)	598 (26.0%)	0.243
Black/African American	2247 (50.9%)	862 (56.9%)	1385 (47.8%)		829 (53.6%)	556 (41.1%)		303 (50.2%)	1082 (47.1%)	
Asian	27 (0.6%)	17 (1.1%)	10 (0.3%)		8 (0.5%)	2 (0.1%)		2 (0.3%)	8 (0.3%)	
American Indian/Alaska Native	72 (1.6%)	21 (1.4%)	51 (1.8%)		20 (1.3%)	31 (2.3%)		7 (1.2%)	44 (1.9%)	
Other/Unknow n	1023 (23.2%)	302 (19.9%)	721 (24.9%)		348 (22.5%)	373 (27.5%)		157 (26.0%)	564 (24.6%)	
Ethnicity										
Not Hispanic or Latino	3499 (79.3%)	1251 (82.6%)	2248 (77.5%)	<0.001	1230 (79.6%)	1018 (75.2%)	0.006	465 (77.0%)	1783 (77.7%)	0.767
Hispanic or Latino/Unknow n	915 (20.7%)	263 (17.4%)	652 (22.5%)		316 (20.4%)	336 (24.8%)		139 (23.0%)	513 (22.3%)	

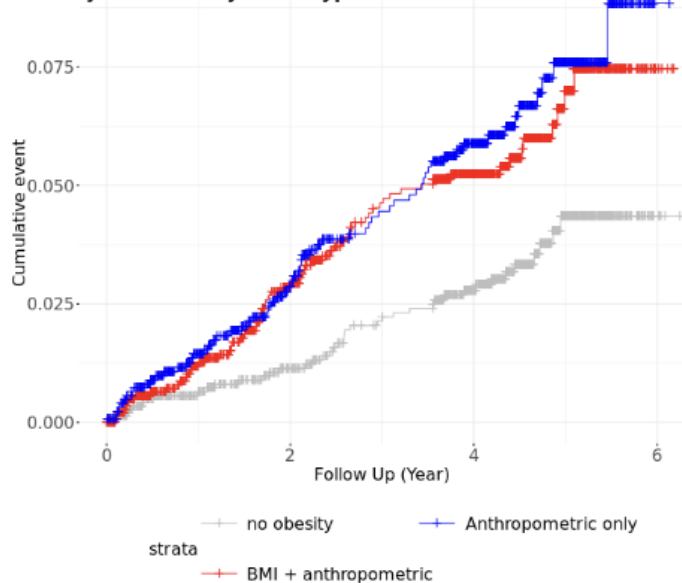
Type2 Diabetes By New Obesity Phenotype



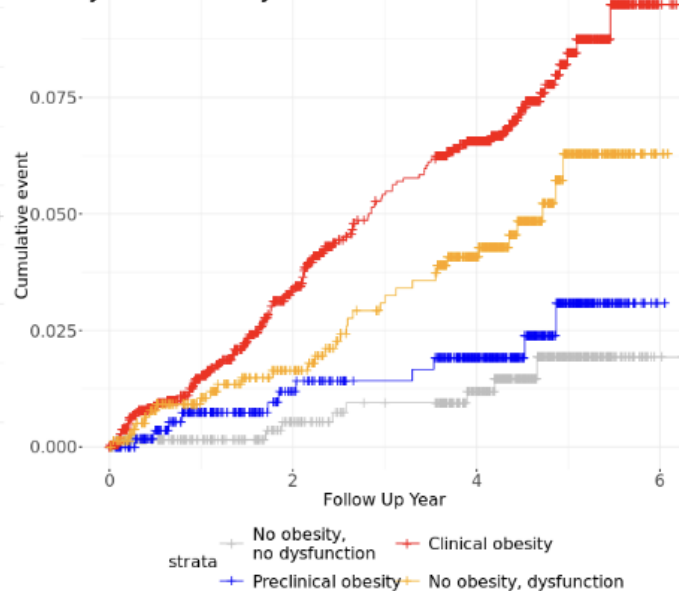
Type2 Diabetes By Clinical Obesity Status



CVD By New Obesity Phenotype



CVD By Clinical Obesity Status



Conclusion

- Adoption of the new definition of obesity among PWH substantially increased obesity prevalence, largely by identifying central adiposity.
- BMI-plus-anthropometric obesity was associated with both type 2 diabetes and CVD, whereas anthropometric-only obesity was associated only with CVD.
- Incorporating anthropometric measures into obesity assessment may improve cardiovascular risk stratification among PWH.

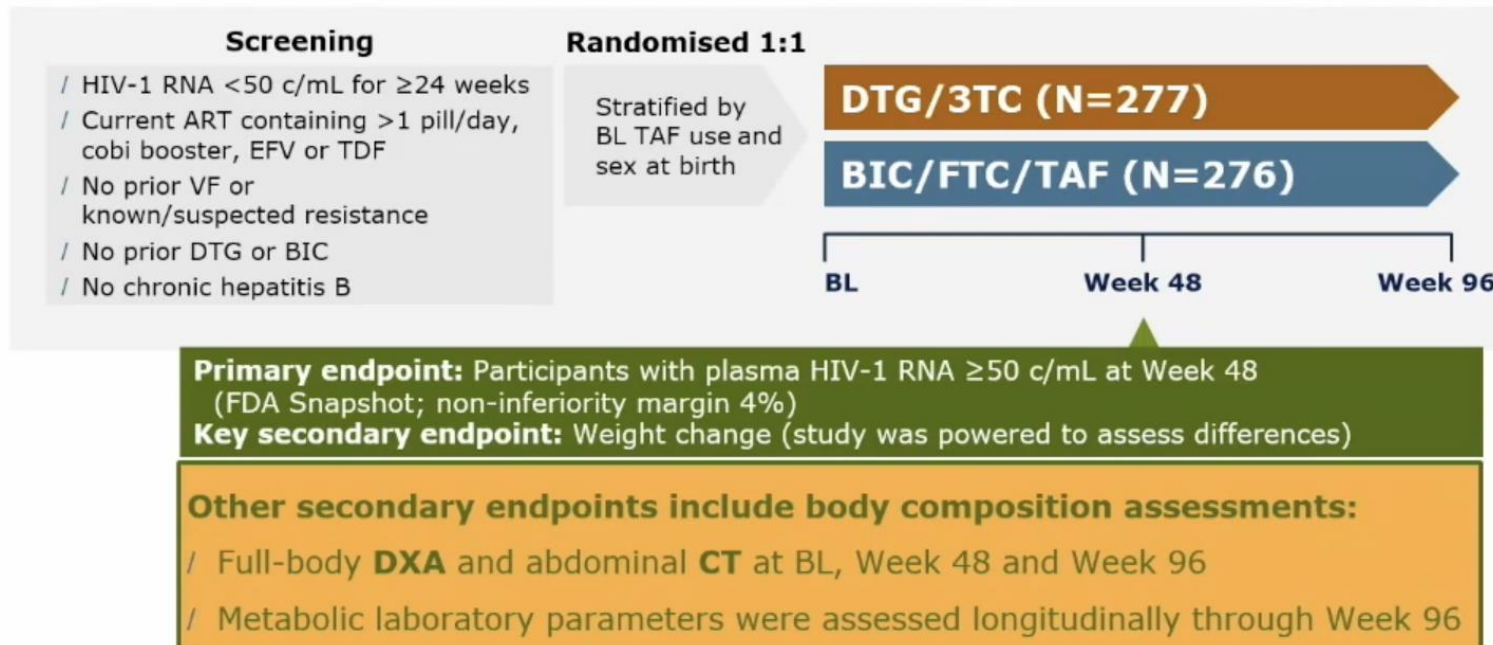
More Paso Doble

The body composition signature of switching to BIC/FTC/TAF or DTG/3TC over 96 weeks

Esteban MARTINEZ CHAMORRO, Spain

Week 96
body-
composition
substudy of
PASO DOBLE

Phase IV, open-label, multicentre, randomised clinical trial^{1,2}



30
sites
across
Spain

Collaborative study
between **Fundación
SEIMC-GESIDA** and
ViiV Healthcare

Key findings at Week 96³

- / DTG/3TC was **non-inferior** to BIC/FTC/TAF in maintaining **virologic suppression**
- / DTG/3TC was associated with less **weight gain*** and lower odds of **clinically meaningful[†]** weight gain versus BIC/FTC/TAF

Analysis population with DXA + abdominal CT:
At baseline: 498/553 (90.1%)

DTG/3TC n=250; BIC/FTC/TAF n=248

Included in the Week-96 analyses: 446/553 (80.7%)

DTG/3TC n=224; BIC/FTC/TAF n=222

Only participants with paired body-composition data included in longitudinal analyses

Adjusted by sex, age, race, baseline weight and baseline TAF use

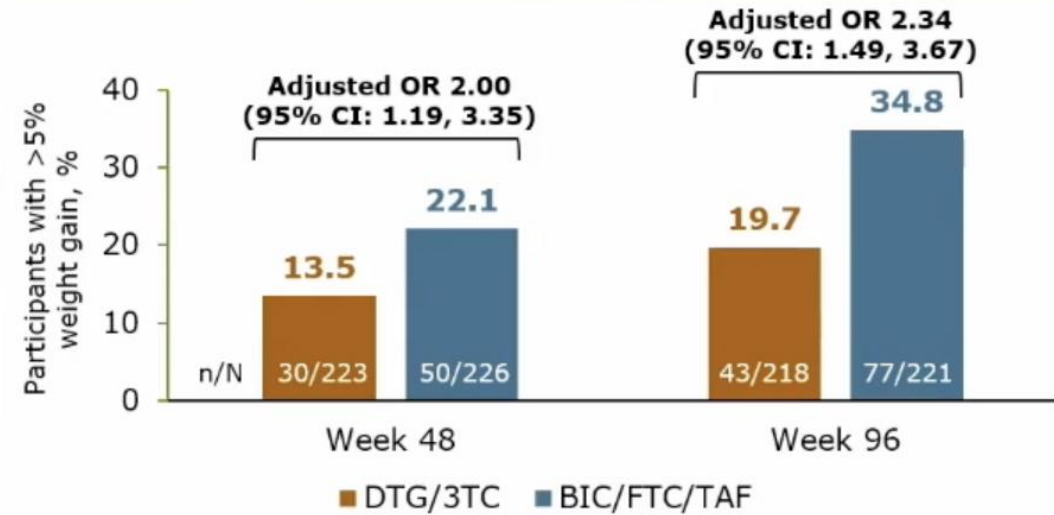
Baseline characteristics

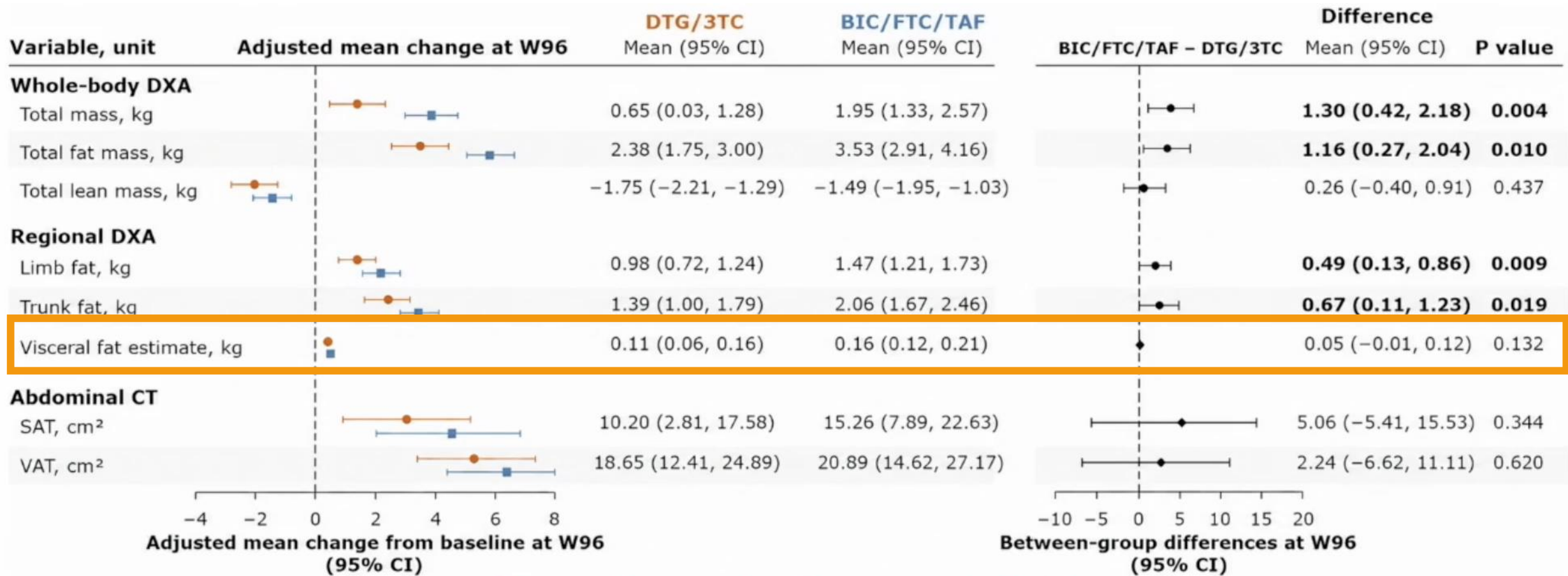
Median (IQR) or n (%)

Characteristic	DTG/3TC (N=250)	BIC/FTC/TAF (N=248)
Age (years)	49.1 (40.7–57.0)	50.8 (39.0–57.7)
Male sex at birth, n (%)	184 (73.6)	185 (74.6)
Weight (kg)	73.0 (64.0–84.0)	72.8 (63.0–82.0)
BMI (kg/m ²)	25.2 (22.4–28.4)	24.8 (22.1–28.0)
Obesity (≥30), n (%)	45 (18.0)	39 (15.7)
CD4 count (cells/mm ³)	716.8 (522.0–918.4)	677.2 (479.5–856.5)

Baseline characteristics balanced between arms

>5% weight gain in the body-composition substudy



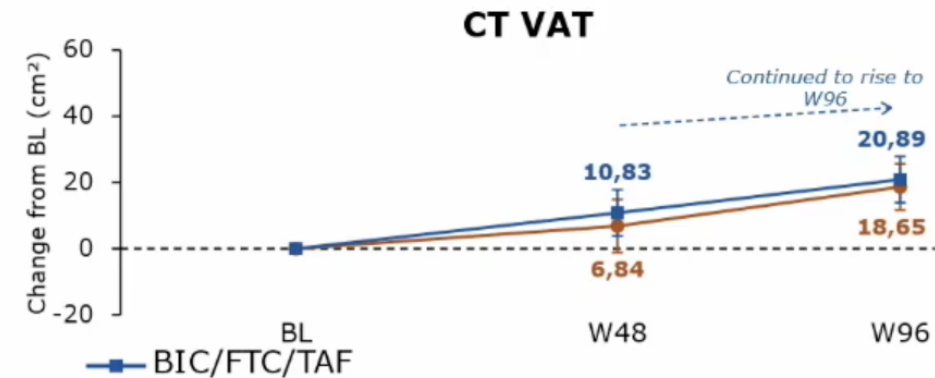
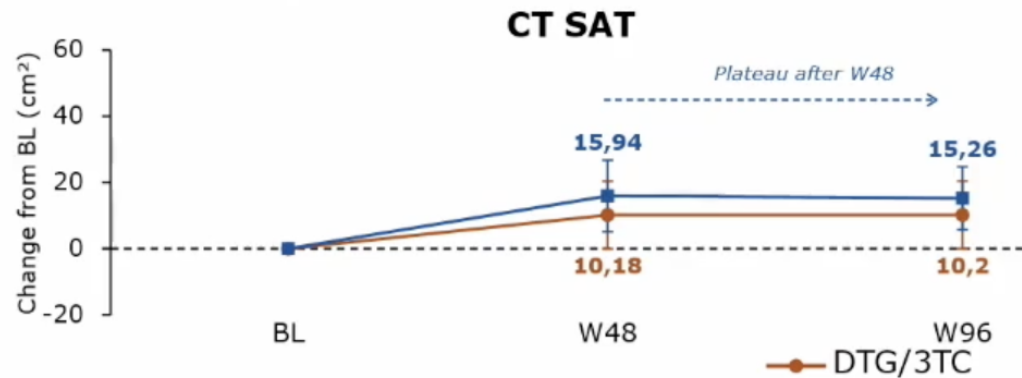
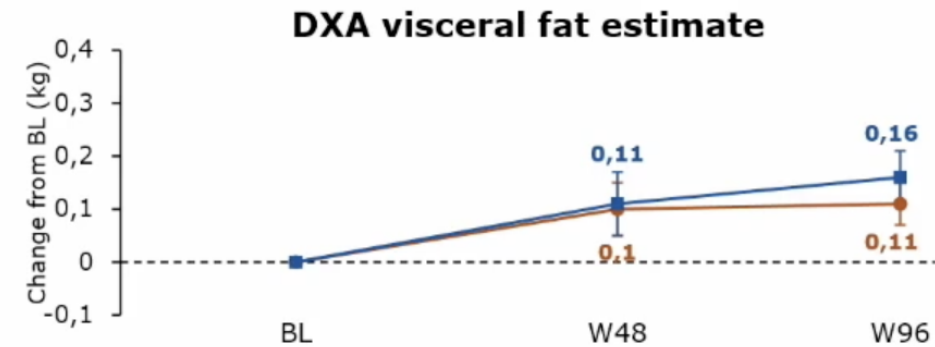
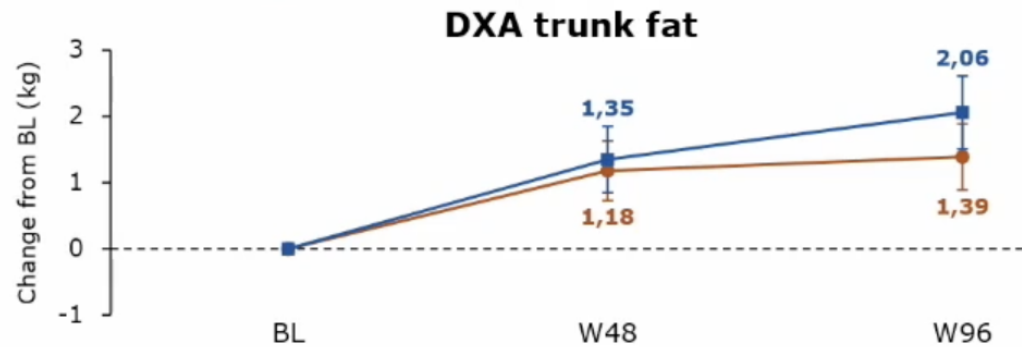


**Fat mass increased and lean mass declined;
between-arm differences were driven mainly by greater adipose gain with BIC/FTC/TAF**

Fat accumulation differed by compartment



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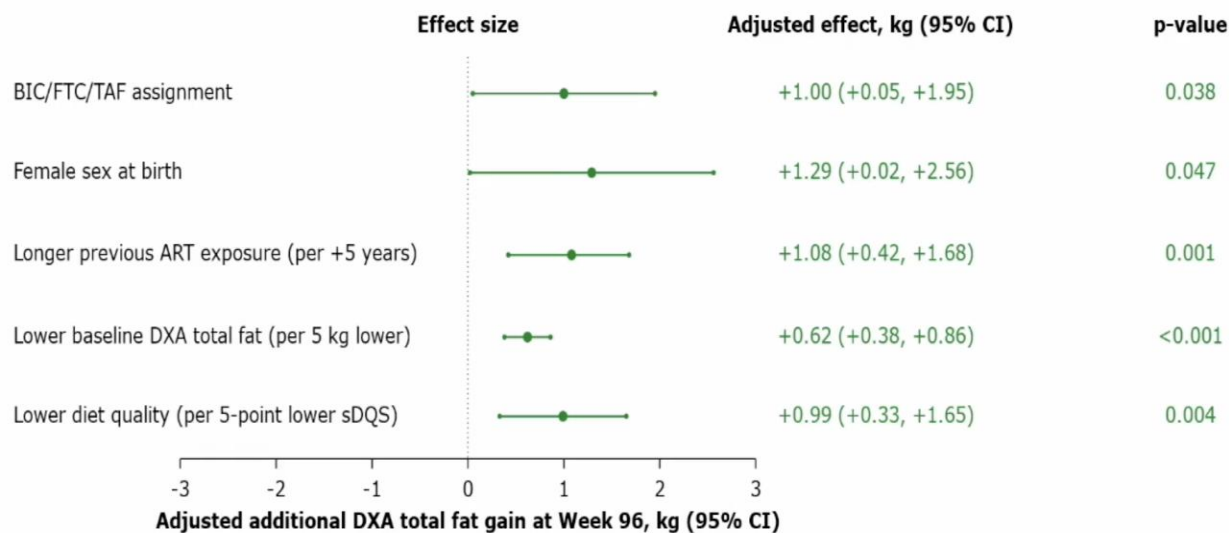
Central fat accrued with both regimens; subcutaneous expansion attenuated after Week 48, while central fat measures continued to increase through Week 96

Predictors of DXA total fat mass change

Week-96 multivariable model



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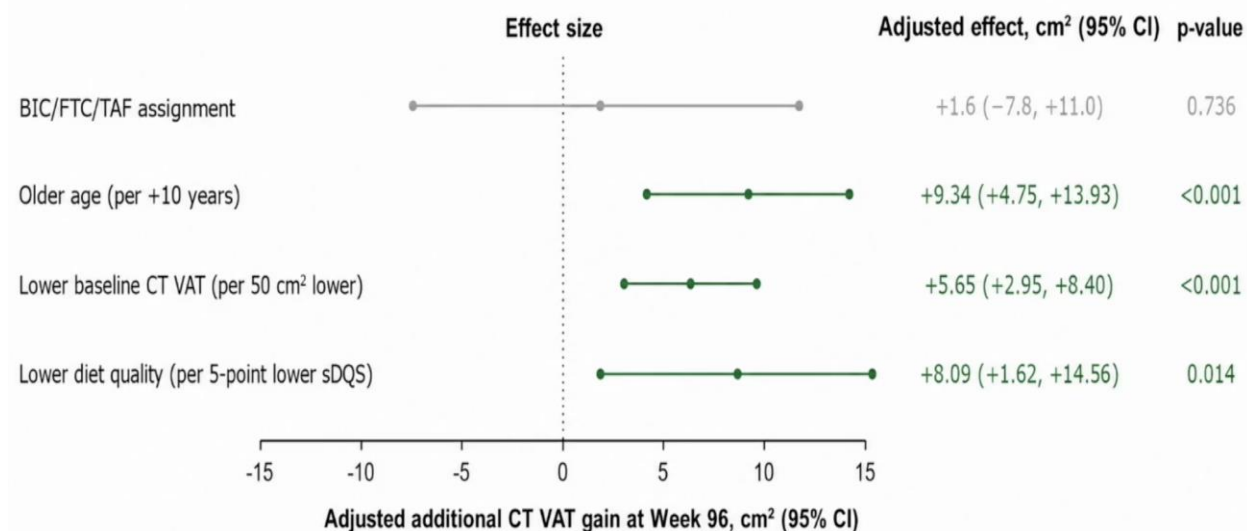
Greater fat gain reflected treatment assignment plus host, ART-history, and lifestyle factors

Predictors of CT VAT change

Week-96 multivariable model



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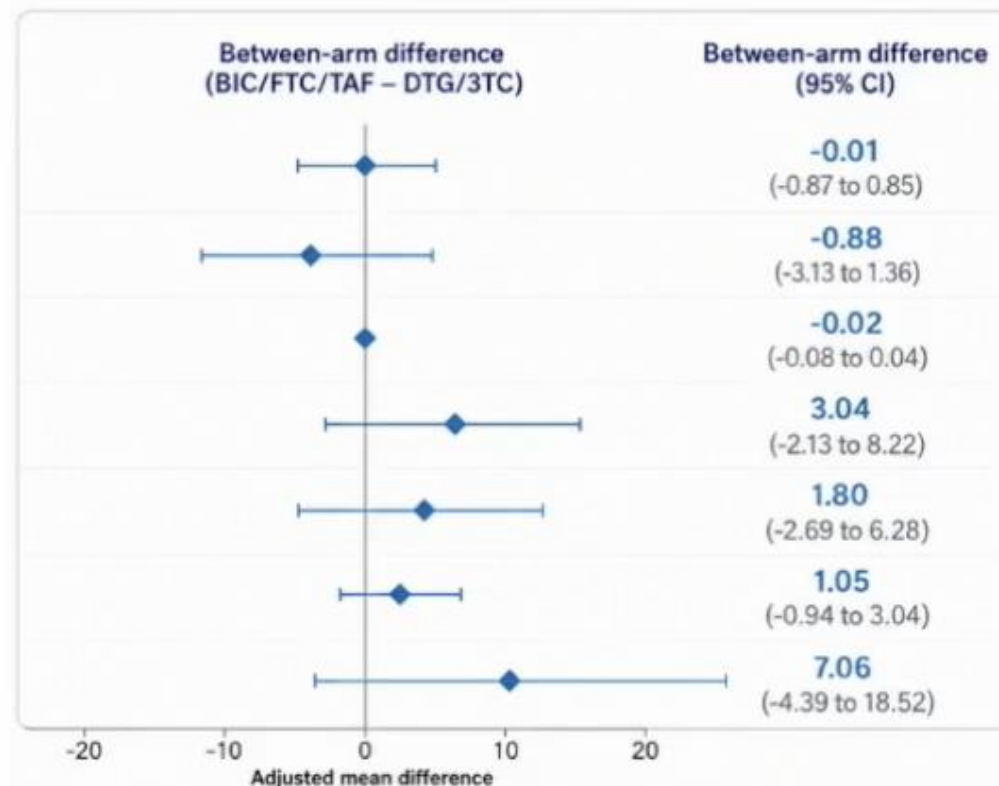
Greater CT VAT gain was independently associated with older age, lower baseline VAT, and lower diet quality; no independent treatment effect was observed

Metabolic changes at Week 96



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Parameter	DTG/3TC Adjusted mean change (95% CI)	BIC/FTC/TAF Adjusted mean change (95% CI)
HOMA-IR	-0.55 (-1.15, 0.06)	-0.56 (-1.17, 0.06)
Glucose (mg/dL)	-0.10 (-1.67, 1.47)	-0.98 (-2.59, 0.62)
HbA1c (%)	0.14 (0.09, 0.18)	0.12 (0.07, 0.16)
Total cholesterol (mg/dL)	-6.47 (-10.05, -2.89)	-3.43 (-7.16, 0.30)
LDL (mg/dL)	-2.29 (-5.38, 0.80)	-0.49 (-3.75, 2.76)
HDL (mg/dL)	-1.50 (-2.87, -0.13)	-0.45 (-1.89, 1.00)
Triglycerides (mg/dL)	-20.85 (-28.76, -12.95)	-13.79 (-22.05, -5.53)



Despite differences in adiposity, metabolic laboratory changes remained modest through Week 96, with no clear between-arm differences

Fractures and ART

Risk of fracture with contemporary antiretrovirals within the RESPOND Consortium

Bastian Neesgaard¹, Win Min Han², Jennifer Hoy³, Angela Öllinger⁴, Huldrych Günthard^{5,6}, Josip Begovac⁷, Ferdinand Wit^{8,9}, Clara Lehmann¹⁰, Charlotte Martin¹¹, Andrew Carr¹², Cristina Mussini¹³, Antonella Castagna¹⁴, Fiona Burns¹⁵, Alex Schneider¹⁶, Martin Gisinger¹⁷, János Szlavik¹⁸, Philip Tarr¹⁹, Lauren Greenberg¹, Nadine Jaschinski¹, Jean van Wyk²⁰, Megan Dunbar²¹, Lital Young²², Kathy Petoumenos² and Lene Ryom^{1,23,24} on behalf of RESPOND

RESULTS

- A total of 40,244 participants were included (Table 1)
- Participants who experienced a fracture were older, current smokers, and more likely to have a low BMI, chronic kidney disease, HCV, or a prior fracture
- During a median follow-up of 8.4 years (301,862 person-years of follow-up), 2155 participants experienced one or more fractures (2,544 fractures in total)
- Lower leg fractures were the most prevalent, accounting for 375 fractures (14.7%)

RESULTS

 of Infectious Diseases

- There were 555 (21.8%) fractures at locations associated with osteoporosis (fractures of the spine, lower arm/wrist and hip)
- Prior fractures were not associated with INSTI initiation but showed a small association with TAF initiation (OR 1.08; 95% CI 1.02–1.15).
- Smoking status was significantly associated with INSTI and TAF initiation (1.26; 1.23–1.3 and 1.16; 1.12–1.20); eGFR <60 was borderline significant for both initiating INSTIs and TAF (1.05; 1.00–1.11 and 1.01; 0.95–1.07)
- Age >40 years compared to older age groups was associated with a lower likelihood of initiating either an INSTI or TAF (global p <0.001 for both)
- Ever exposure to INSTIs or to TAF was associated with a small increased relative fracture risk (Figure 1)
- After excluding those with prior TDF use and censoring at TDF initiation, the associations were no longer statistically significant. Similar findings occurred when excluding prior PI/b exposure and censoring at PI/b initiation

HBV in a NJ HIV Clinic

Humberto R. Jimenez, Rutgers University

Spotlight on the liver

Evaluation of Hepatitis B Virus Epidemiology and Impact of Select Demographic Factors on Seroprevalence within an Urban Clinic in the US



Methods

Single-center, retrospective analysis

Inclusion criteria

- HIV Diagnosis (PWH)
- Age $\geq$ 18 yrs old
- $\geq$ 1 visit at our clinic between 08/2023 – 07/2024

Primary endpoint

- Proportion of patients that are immune to HBV

Secondary endpoints

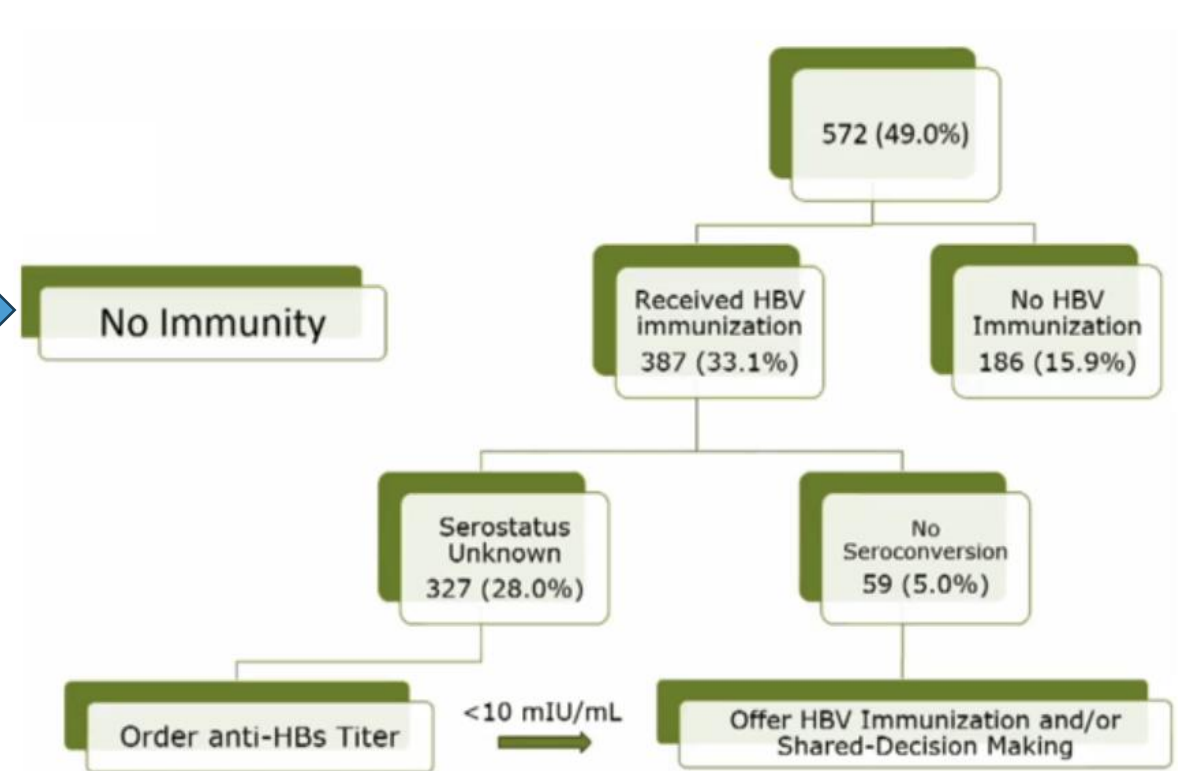
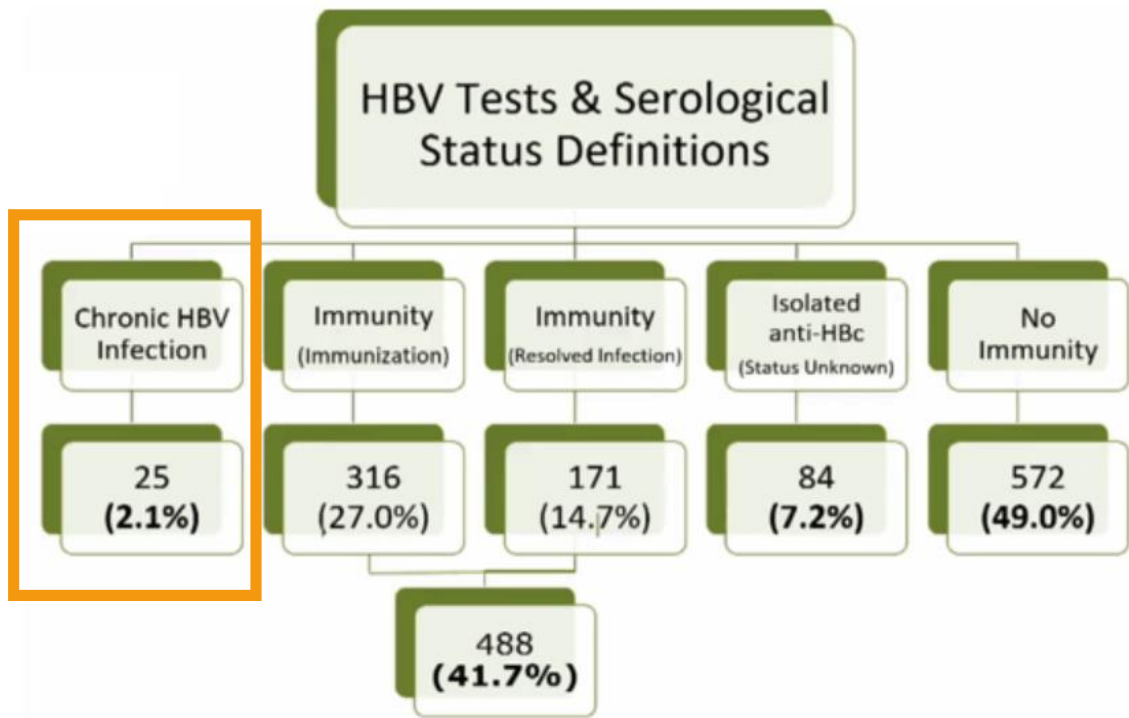
- Proportion of patients with:
 - Chronic HBV
 - Susceptibility to HBV
 - Isolated anti-HBc
 - TFFV-free regimens
- HBV serostatus by demographic and clinical characteristics

Baseline Characteristics



Demographics	Total (N=1168)
Age, years, mean (SD)	48.9 (14.4)
Gender	
Cisgender male	726 (62.1%)
Cisgender female	428 (36.6%)
Transgender female	16 (1.4%)
Years since HIV diagnosis (SD)	13.6 (9.9)
AIDS diagnosis	456 (39.0%)

Demographics	Total (N=1168)
Race/Ethnicity	
Hispanic/Latine	659 (56.3%)
Black, Non-Hispanic	433 (37.0%)
White, Non-Hispanic	70 (6.0%)
Asian	8 (0.7%)

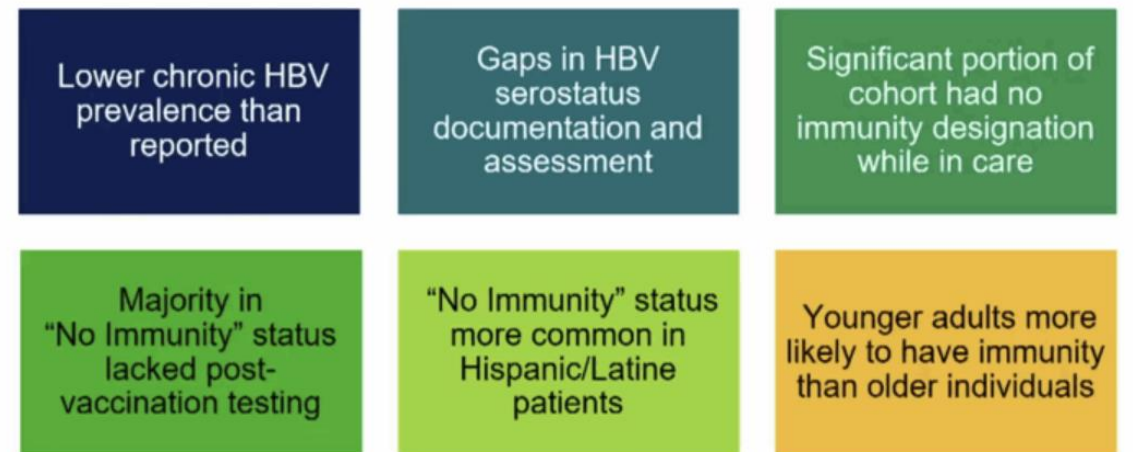


Baseline HBV Seroprevalence Based on Whether TFFV in Regimen

Characteristic	Overall (N=1168)	TFFV-Free Regimen (n=213)	TFFV-Containing Regimen (n=883)
HBV Seroprevalence			
Chronic HBV	25 (2.1%)	2 (0.9%)	22 (2.5%)
Immune	487 (41.7%)	99 (46.5%)	358 (40.5%)
Isolated Anti-HBc	84 (7.2%)	21 (9.9%)	56 (6.3%)
Not Immune	572 (49.0%)	91 (42.7%)	447 (50.6%)

Tact-statistic v2=8.54 n value 0.036

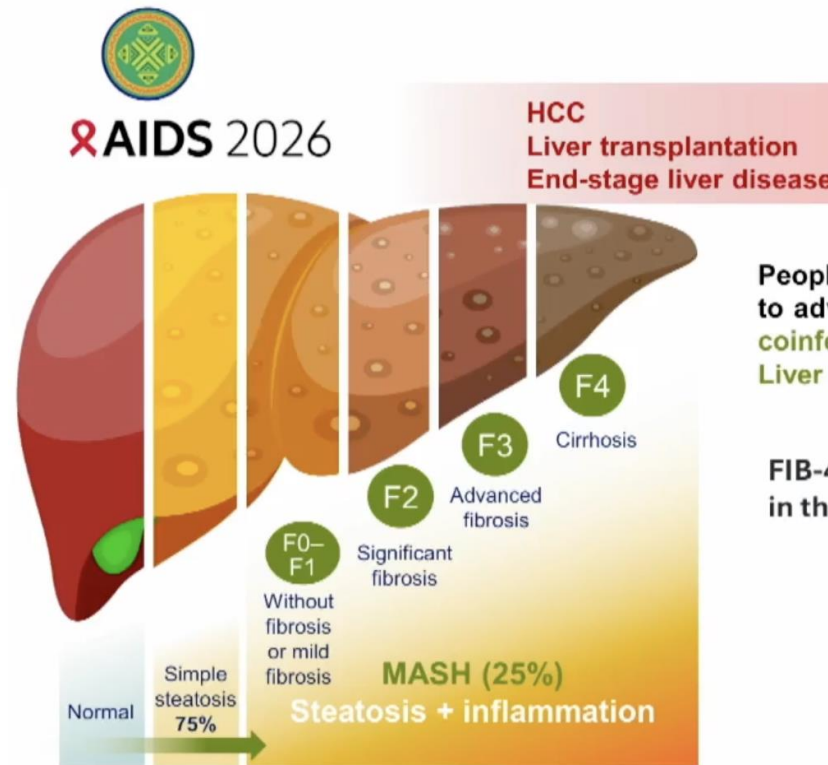
Discussion



Steatosis/Fibrosis Score

The **SAFE** (steatosis-associated fibrosis estimator) score predicts incidence of advanced liver fibrosis in people living with HIV: a prospective analysis from the PROSPEC-HIV cohort

Hugo PERAZZO



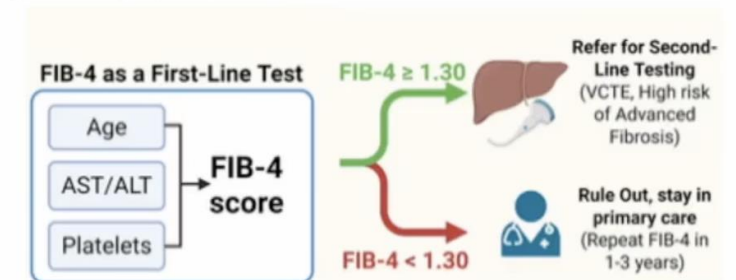
26-31 July • Rio de Janeiro, Brazil

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Background

People living with HIV (PLWH) can progress from normal liver to advanced fibrosis or cirrhosis mainly due to **viral hepatitis coinfection** and **Metabolic dysfunction-Associated Steatotic Liver Disease (MASLD)**

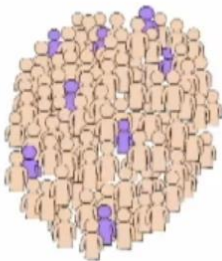
FIB-4 has been used as a first step to assess risk of fibrosis in the general population



Steatosis/Fibrosis Score



Large Cohort
Logistic Regression
Algorithms (GAM / RF / GBM)



Parameters

Age, BMI, type 2 diabetes, AST, ALT, globulin and platelet count

SAFE score

< 0: Low risk for significant fibrosis (F0-1)

0 to 99: Intermediate risk (potential F2 fibrosis)

≥ 100: High risk for significant fibrosis (F3/F4)

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Steatosis-Associated Fibrosis Estimator (SAFE) score

ORIGINAL ARTICLES: STEATOHEPATITIS

The steatosis-associated fibrosis estimator (SAFE) score: A tool to detect low-risk NAFLD in primary care

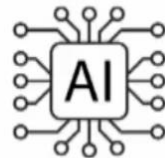
⑩ Sripongpun, Pimsiri^{1,2}; ⑩ Kim, W. Ray¹; ⑩ Mannalithara, Ajitha¹; Charu, Vivek^{3,7}; Vidovszky, Anna¹; Asch, Steven⁶; Desai, Manisha⁷; ⑩ Kim, Sun H.^{5,6}; ⑩ Kwong, Allison J.¹

Author Information

Hepatology 77(1):p 256-267, January 2023. | DOI: 10.1007/hep.32545

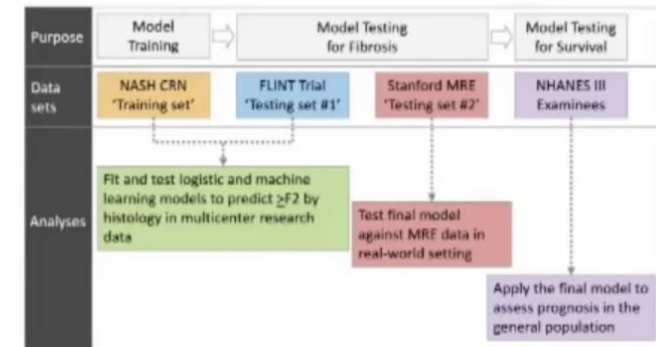
Model Training

**Machine Learning
Natural Language
Processing (NLP)**

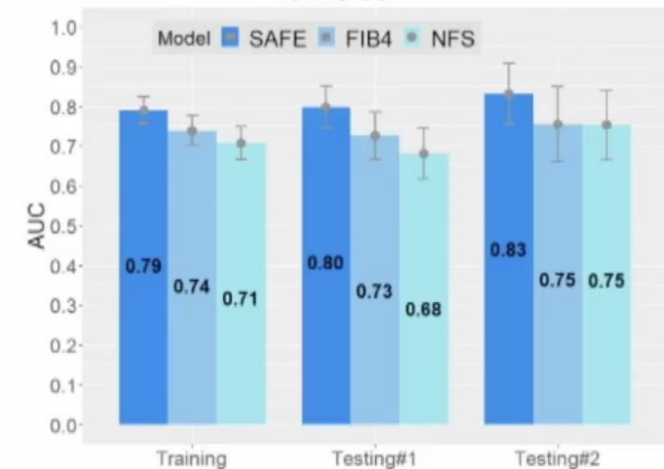


SCORE

Serological Biomarker that was developed with AI



AUROC





General Overview
N=744

52% Female
Age - median= 45 years
87% HIV mono-infection

55% BMI ≥ 25 Kg/m²
12% T2DM

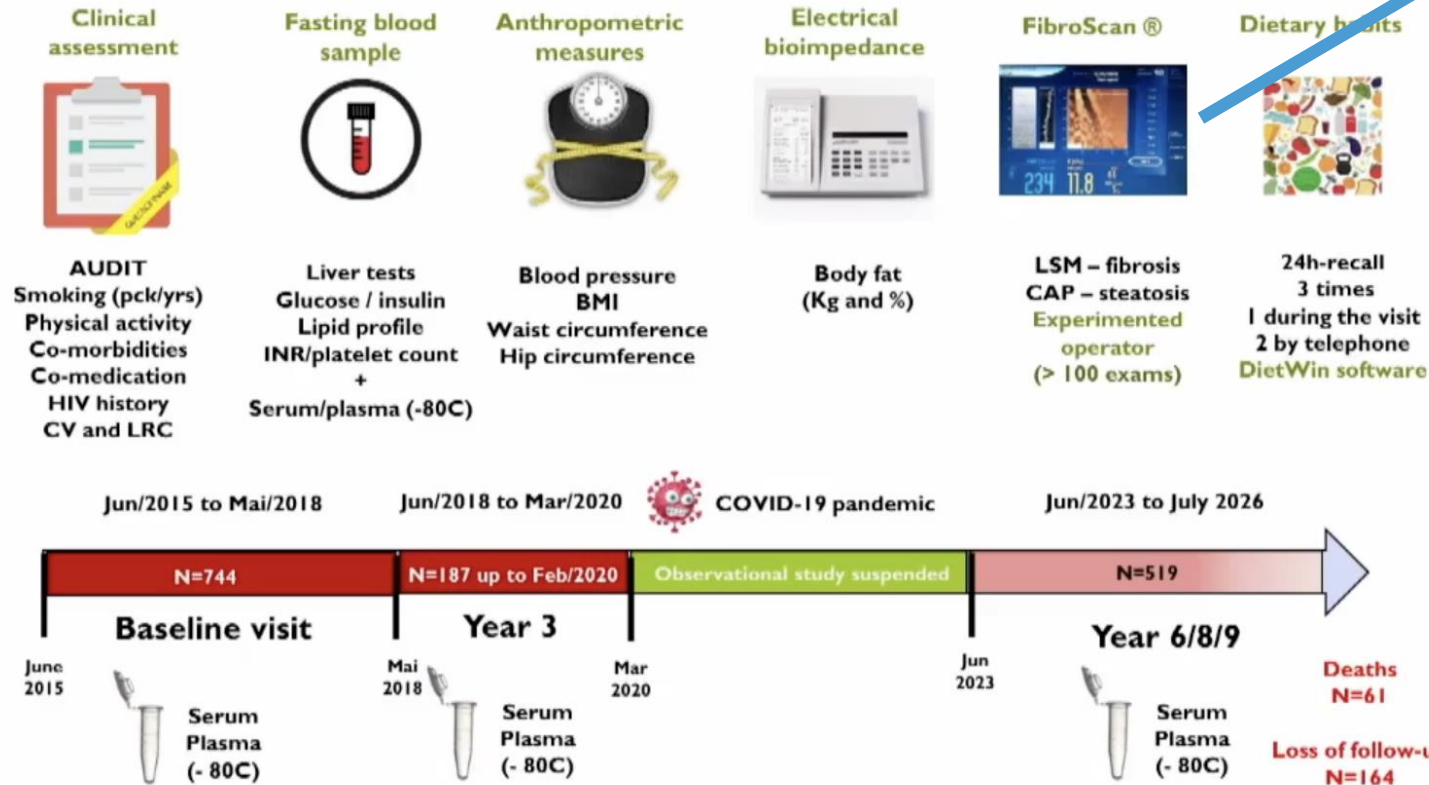
Duration of HIV infection
median=9.6 years

98% under c-ART

CD4 count
median=668 cells/mm³

87% undetectable VL

PROSPEC-HIV cohort (NCT02542020)



Primary Outcome

Development of advanced liver fibrosis

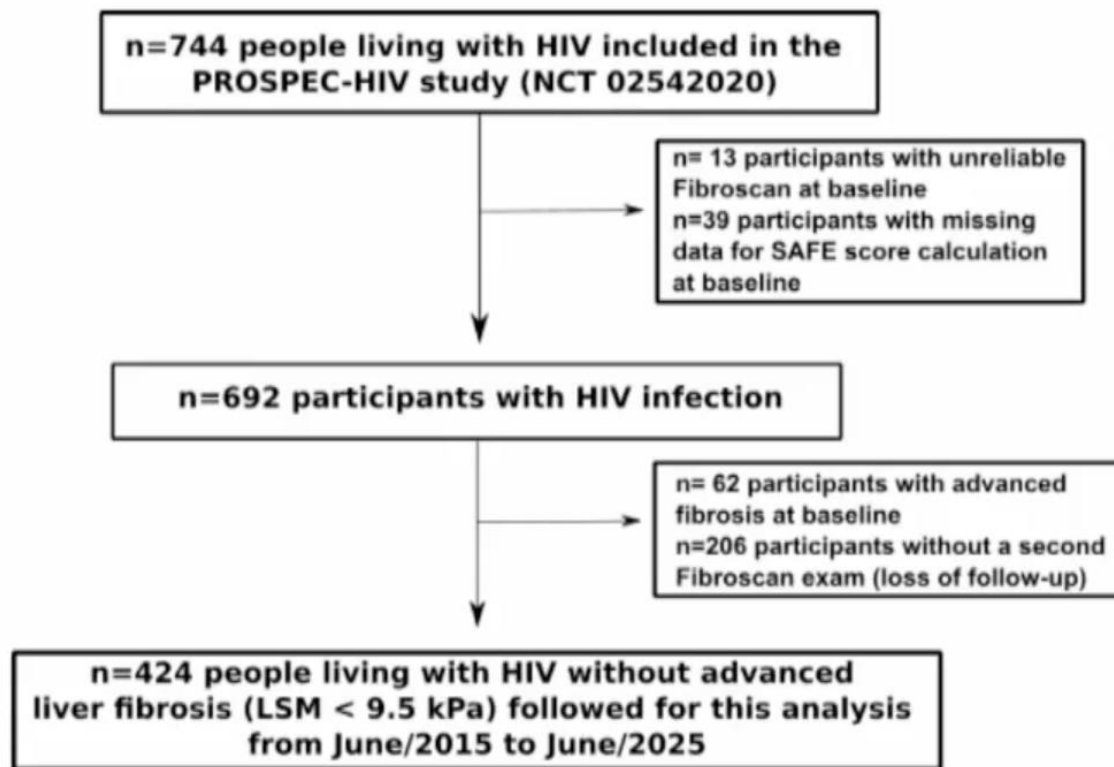


Fibroscan – experimented operator (> 100 exams)

Advanced fibrosis - LSM ≥ 9.5 kPa



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Results

Characteristics of participants (n=424)

Demographic characteristics	N=424
Female sex at birth	225 (53%)
Age, years	44 (36-52)
Etiology	
HIV-monoinfection	382 (90%)
Viral hepatitis coinfection	42 (10%)
Cardiometabolic risk factors	
BMI, Kg/m ² ^b	25.2 (22.7-28.9)
Obesity - BMI ≥ 30 Kg/m ²	79 (18%)
Type-2 diabetes ^a	41 (10%)
Hypertension ^a	140 (33%)
Hypertriglyceridemia ^a	155 (37%)
Metabolic dysfunction-Associated Steatotic Liver Disease (MASLD)	67 (16%)
Biochemistry	
ALT, UI/L	31 (23-43)
AST, UI/L	26 (20-34)
HIV history and c-ART data	
c-ART use	417 (98%)
Duration of c-ART, years	7.2 (3.5-13.4)
CD4 count, cells/mm ³	668 (457-898)
Undetectable HIV-RNA (< 100 copies/ml)	373 (88%)
SAFE score categories	
Low SAFE score (<0)	195 (46%)
Intermediate SAFE score (0-100)	163 (38%)
High SAFE score (>100)	66 (16%)

Median time of follow-up

8 years [IQR=6.8-8.7; range=3.0-9.8]

New cases of advanced fibrosis - LSM $\geq$ 9.5 kPa

N=28 participants developed advanced liver fibrosis

Incidence-rate = **8.8 events per-1,000-PY**

The incidence-rate was significantly higher in people with high-SAFE ($\geq$ 100) compared to those without (**19 vs 9 events per-1,000-PY**) - **RR=2.71 (95%CI, 1.23-5.99), p=0.01**



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AUROC

N=424

Outcome=Advanced fibrosis
(LSM $\geq$ 9.5 kPa)

The SAFE score had a better accuracy to predict incidence of advanced fibrosis compared to FIB-4 score

AIDS 2026 Cox proportional hazards models

SAFE score – 3 categories

	Crude HR (95%CI)	P value	Adjusted HR (95%CI)*	P value
SAFE score				
Low SAFE score (<0)	Reference		Reference	
Intermediate SAFE score (0-100)	2.45 (0.93-6.46)	0.070	2.26 (0.84-6.02)	0.105
High SAFE score (>100)	4.66 (1.68-13.1)	0.004	3.67 (1.25-10.8)	0.018

SAFE score & FIB-4 – Intermediate/High vs Low

	Crude HR (95%CI)	P value	Adjusted HR (95%CI)*	P value
SAFE score				
Low SAFE score (<0)	Reference		Reference	
Intermediate/High SAFE score ($\geq$ 0)	2.93 (1.87-7.23)	0.020	2.57 (1.02-6.49)	0.046
FIB-4				
Low FIB-4 (< 1.30)	Reference		Reference	
Intermediate/High FIB-4 ($\geq$ 1.30)	1.92 (0.85-4.36)	0.119	1.85 (0.80-4.25)	0.148

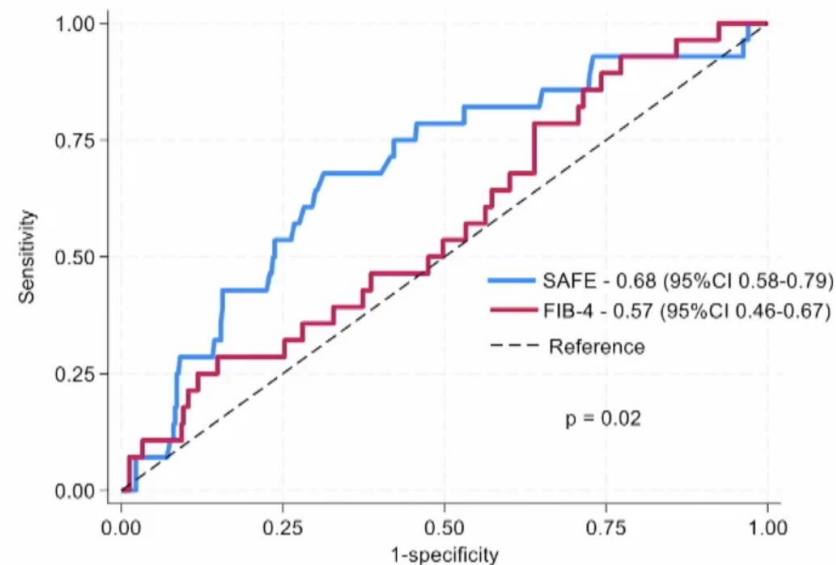
* Cox models were adjusted for MASLD (no vs yes) and Viral Hepatitis Coinfection (no vs yes)

Presence of MASLD was significantly associated with incident advanced fibrosis in all Models

26–31 July • Rio de Janeiro, Brazil

aids2026.org

AUROC for SAFE score compared to FIB-4 to predict incidence of advanced fibrosis (defined as LSM $\geq$ 9.5 kPa) in people with HIV infection (n=424) followed for a median time of 8 yrs (IQR, 6.8-8.7)





AIDS 2026

The SAFE-score formula:

$$\text{SAFE} = 2.97 * \text{age} + 5.99 * \text{BMI} (\text{BMI} > 40 \text{ was set to } 40) + 62.85 * \text{diabetes} (0 \text{ if absent, } 1 \text{ if present}) + 154.85 * \text{Ln}(\text{AST}) - 58.23 * \text{Ln}(\text{ALT}) + 195.48 * \text{Ln}(\text{globulin, g/dL}) - 141.61 * \text{Ln}(\text{platelets, } 10^9/\text{uL}) - 75.$$

The SAFE-score can be easily calculated using online tools:

Stanford University – Medical Calculators

Stanford University
Medical Calculators
Department of Medicine
Home

SAFE Calculator

Age	0	Years
BMI	0	kg/m ²
Diabetes	Yes <input checked="" type="button" value="No"/>	
AST	0	U/L
ALT	0	U/L
Globulin	0	g/dL
Platelets	0	x 10 ⁹ /L

SAFE: 0

Introduction: The SAFE (Steatosis-associated Fibrosis Estimator) score is a scoring system to categorize NAFLD patients by their risk of having significant liver fibrosis (stage 2 or higher) and long-term outcome.

<https://medcalculators.stanford.edu/safe>

MD Calc web-site

Steatosis-Associated Fibrosis Estimator (SAFE) Score

Estimates the risk of moderate to advanced liver fibrosis (stages 2 or higher) among patients with metabolic dysfunction-associated steatotic liver disease (MASLD).

When to Use
Pearls/Pitfalls
Why Use

Age		years
BMI	Norm: 20 - 25	kg/m ²
Diabetes	<input checked="" type="button" value="No"/> Yes	
AST	Norm: 10 - 40	U/L
ALT	Norm: 10 - 55	U/L
Albumin	Norm: 3.5 - 5.0	g/dL
Total protein	Norm: 6.0 - 8.5	g/dL
Platelets	Norm: 150 - 350	x 10 ⁹ /L

Result:
Please fill out required fields.

<https://www.mdcalc.com/calc/10613/steatosis-associated-fibrosis-estimator-SAFE-score>

Anal Cancer Risks in the ANCHOR Trial

INCIDENT ANAL CANCER DIAGNOSED DURING THE ANAL CANCER/HSIL OUTCOMES RESEARCH (ANCHOR) STUDY: A COLLECTIVE CASE REVIEW

H. Dunlevy ¹, J.M. Berry-Lawhorn ², N. Jay ², G. Ellsworth ³, J. Pugliese ², D. Kwon ⁴, J. Schouten ⁵, C. Conageski ¹, S. Goldstone ⁶, J. Palefsky ²

BACKGROUND

The ANCHOR study enrolled 4535 people with HIV 35 years and older who were randomized to either active monitoring (AM) or treatment of high-grade squamous intraepithelial lesions (HSIL) with a primary endpoint of progression to anal cancer. **Treatment reduced the risk of anal cancer by 57%.**

30 individuals with progression to cancer

Active monitoring: 21

Treatment: 9

We reviewed factors associated with progression to cancer.

Category	Variable	Cancer		Randomized, Non-cancer		UVA OR (95% CI)	p-value	MVA OR (95% CI)	p-value
		N	%	N	%				
		30	100	4505	100				
Age at screening	<50 years	7	23.3	1,907	42.3	ref			
	50 years and older	23	76.7	2,598	57.7	4.38 (1.28, 15)	0.0186	4.57 (1.3, 16.1)	0.0179
Sex	Male	26	86.7	3,794			1.00		
	Female	4	13.3	711					
DARE	Normal	14	46.7	4,036	89.6	ref			
	Abnormal	15	50.0	395	8.8	127.6 (17.2, 948.6)	<0.0001	88.8 (11.7, 671.8)	<0.0001
Smoking	Yes	23	76.7	2441	54.2		0.031		
	No	5	16.7	1510	33.5				
Nadir CD4	<200 cells/mm3	21	70.0	2,243	49.8		0.0483		
	200-500 cells/mm3	9	30.0	1,847	41.0				
	>500 cells/mm3	.	.	412	9.1				
CD4 Nadir (Log 10)	1 unit increase					0.38 (0.21, 0.66)	0.0008	0.53 (0.29, 0.98)	0.0427

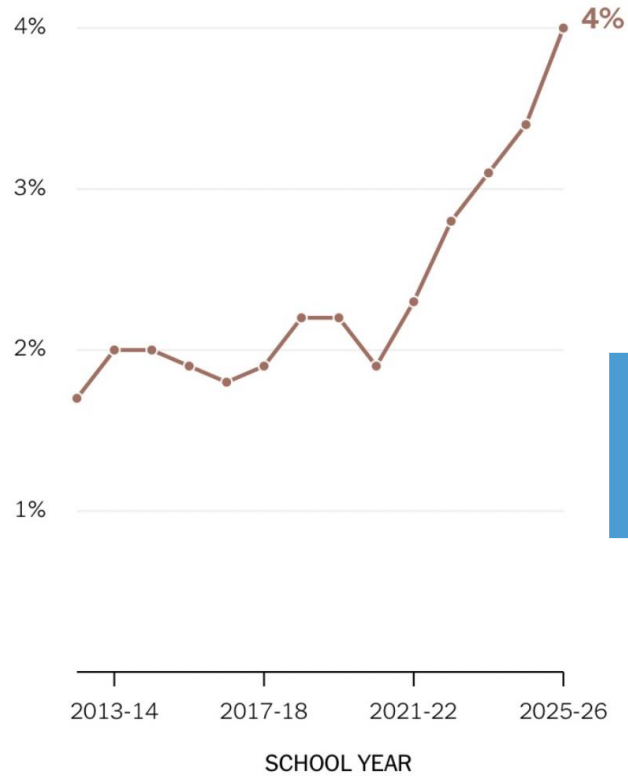
Compared to those with HSIL, those who developed cancer were more likely to be **OLDER, SMOKE, HAVE LOWER CD4 NADIR and HISTORY OF CONDYLOMA**



**TAKING
MATTERS INTO
YOUR OWN
HANDS**

Less vaccination = More preventable infections

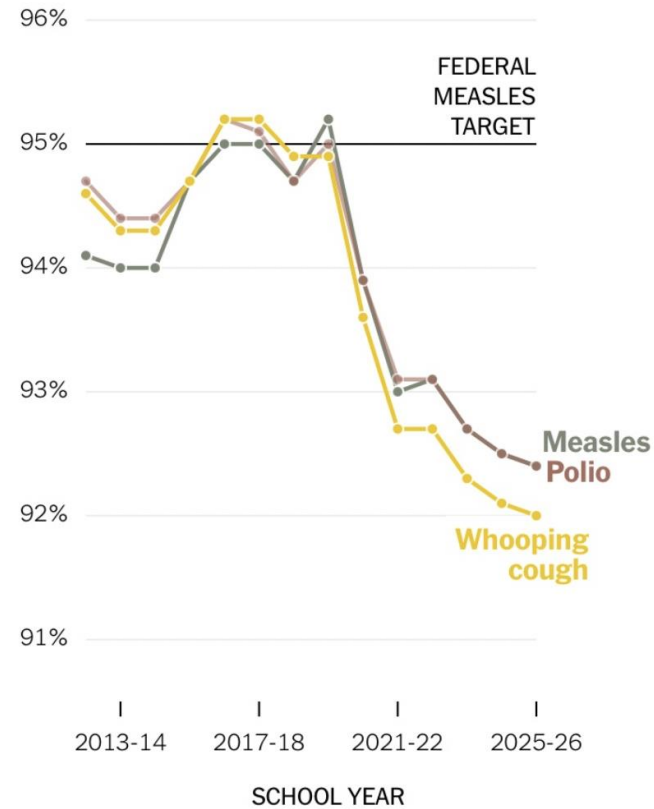
Share of U.S. kindergarteners with a nonmedical exemption



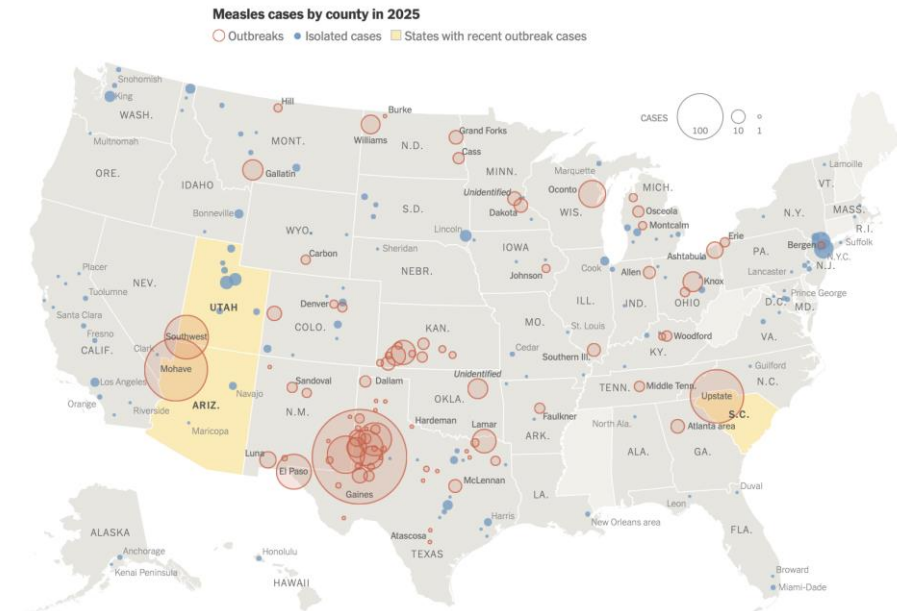
Source: Centers for Disease Control and Prevention



Share of U.S. kindergarteners vaccinated against...

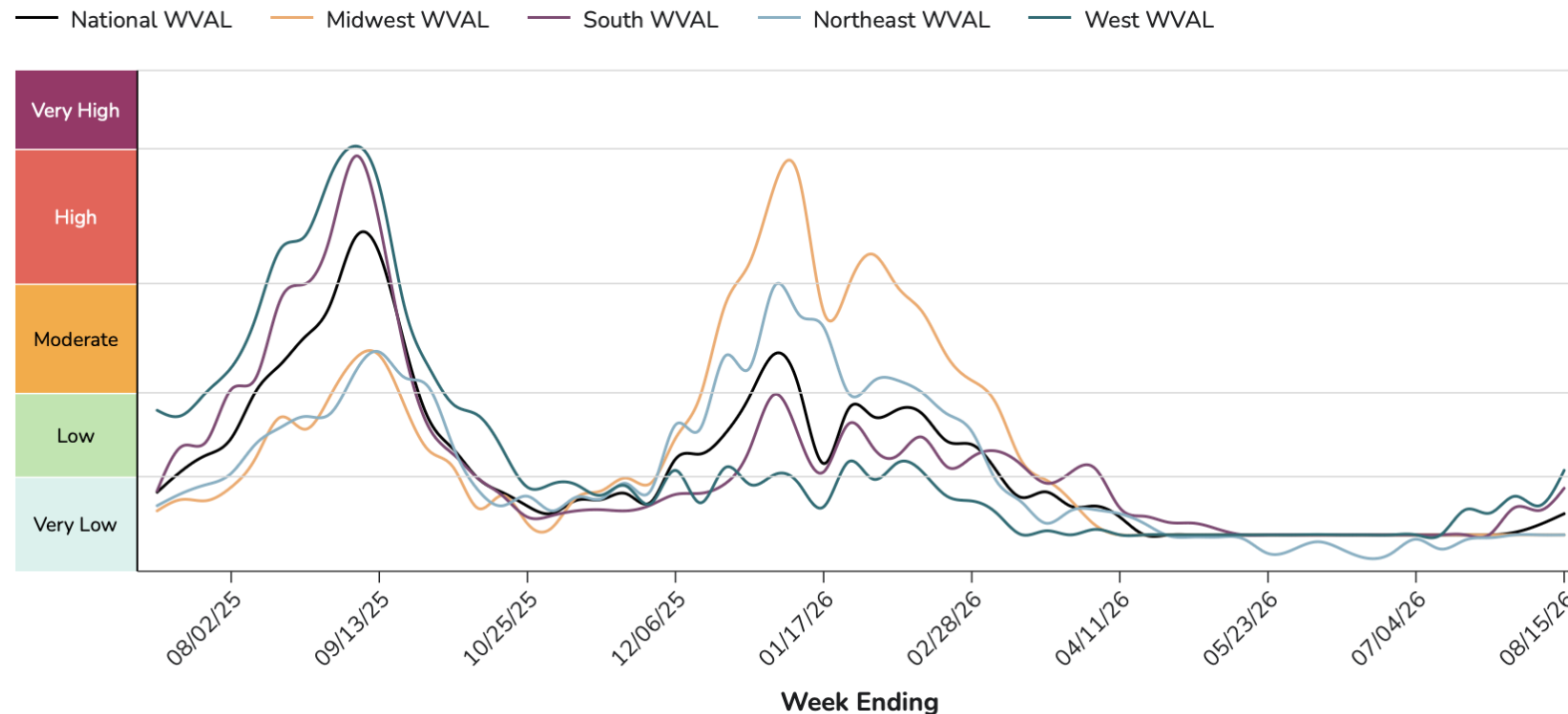


Source: Centers for Disease Control and Prevention The New York Times



Track COVID-19 - Wastewater

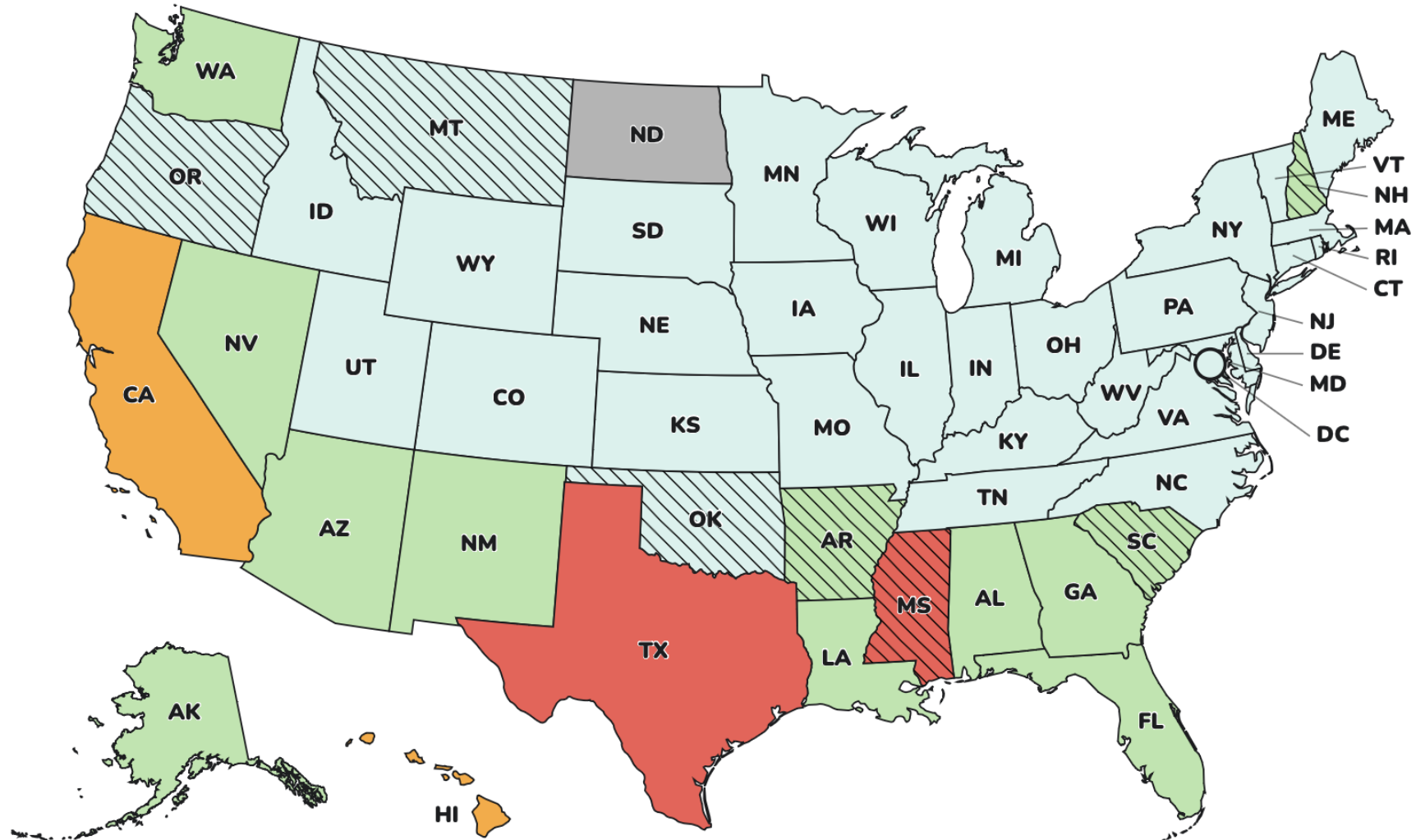
- Wastewater testing is most reliable way to track SARS-CoV-2 infections in US, regions, and states.
- Easy to find on CDC website along with flu and RSV:
 - <https://www.cdc.gov/wastewater/respiratory-viruses/national.html>



COVID-19 Wastewater Viral Activity Levels



⊘ Limited Coverage



Other matters that matter:

- **Get your human shots!**
 - Flu – mRNA!!
 - COVID-19 – New shots in Sept
 - RSV
- **Be a force for truth**
 - Resist nonsense
 - Control cynicism
 - Embrace logic



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



