Management of Persons Living with HIV: 2026

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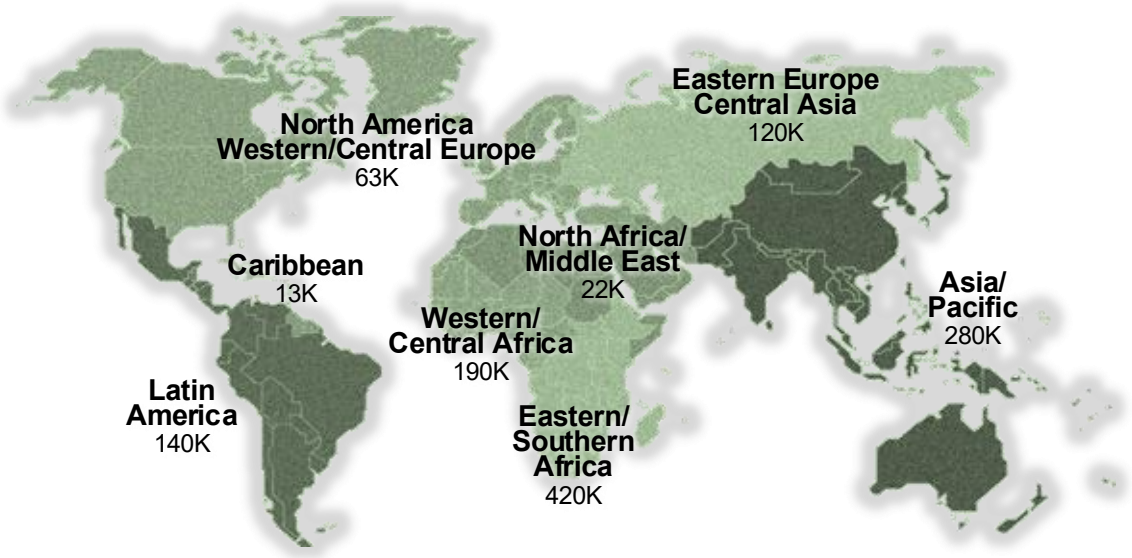
Disclosures

Research support: Gilead, ViiV
Consultant: Gilead, ViiV, Merck

Outline

- HIV Epidemiology
- Ending AIDS Epidemic
- HIV Prevention
- STI Prevention
- HIV Treatment: Including the use of long-acting therapy
- Healthy living with HIV: Vaccination, cancer, screening and beyond
- Healthy aging with HIV: Addressing comorbid conditions in PLWH

Estimated New HIV Diagnoses 2025
1.2 Million (0.95-1.7 million)



HIV Diagnoses/Day*

3288	World	<548
89	United States	<9

Today

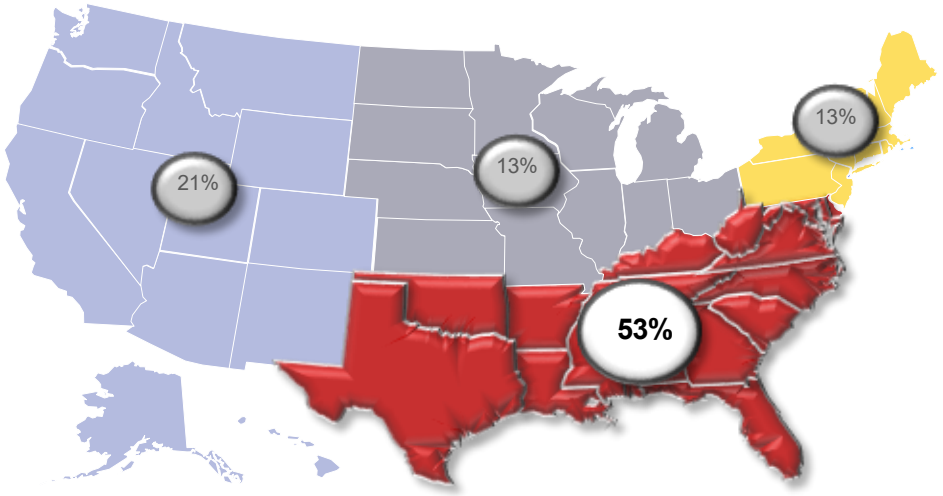
2030 Goal

*Estimated based on annual numbers.

UNAIDS. https://www.unaids.org/en/resources/fact-sheet. Published July 2026.
CDC. https://www.cdc.gov/hiv-data/initiatives/. Published May 7, 2026.

New Diagnoses (2025)
(n=32,574)

2030 Goal: <10K

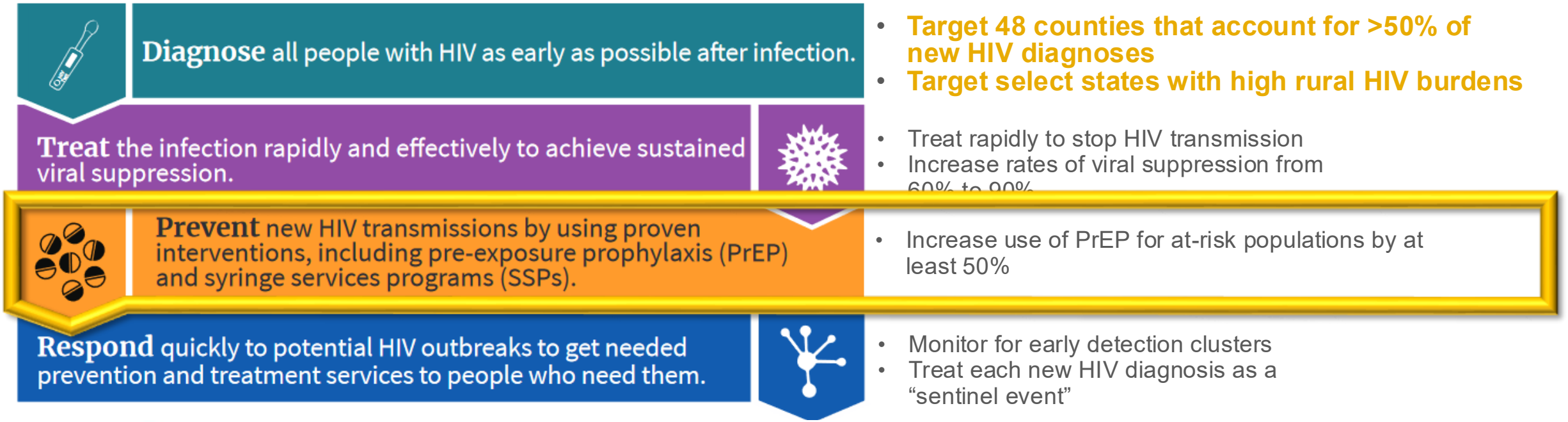


Inequities of Note

Race/ethnicity	Transmission	Age (years)
Black (39%)	MSM (66%)	25-44 (59%)
Hispanic (32%)	Other (34%)	≥45 (24%)
White (23%)		13-24 (17%)

CDC. https://www.cdc.gov/hiv-data/initiatives/. Published May 7, 2026.
CDC. https://www.cdc.gov/nchhstp/director-letters/new-injectable-hiv-prep%20.html. Published September 2025.
AIDsVu. 2025 National PrEP Data. Accessed September 2026.

Key Steps to Ending the HIV Epidemic in the United States

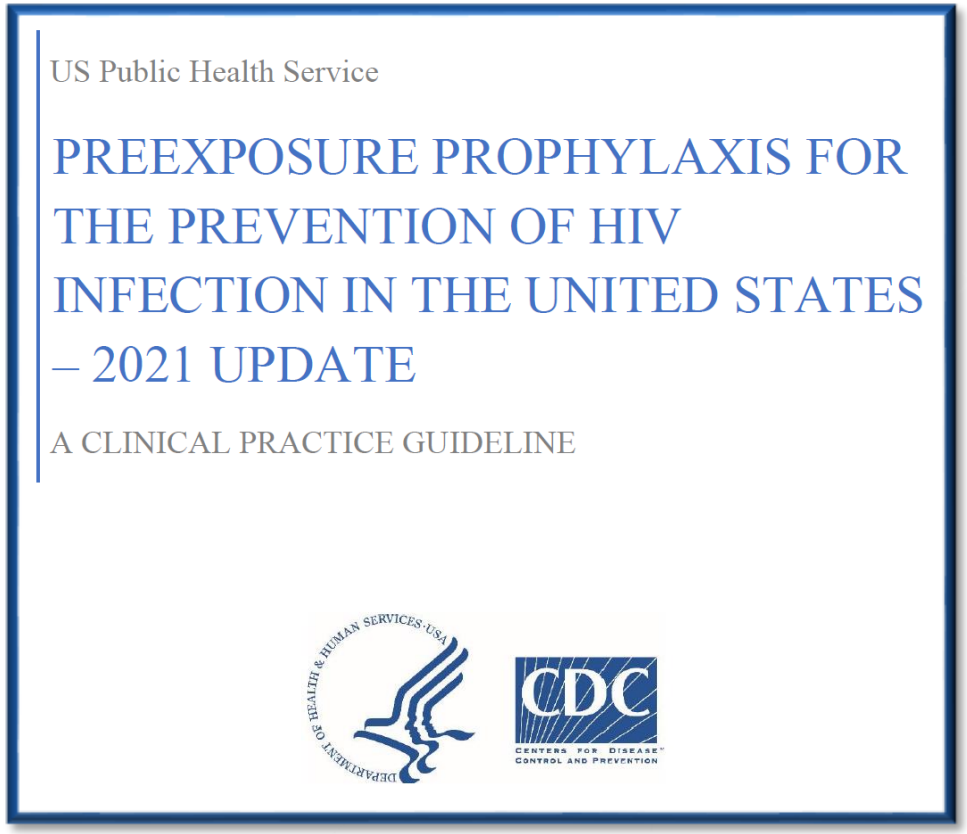


Ending the HIV Epidemic

Overall Goal: Decrease the number of new HIV diagnoses to 9,588 by 2025 and 3,000 by 2030.

DHHS, 2021. *HIV National Strategic Plan for the United States: A Roadmap to End the Epidemic 2021-2025*. https://files.hiv.gov/s3fs-public/HIV-National-Strategic-Plan-2021-2025.pdf.
Harris NS, et al. *MMWR Morb Mortal Wkly Rep*. 2019;68:1117-1123.

Who Is at Substantial Risk of Acquiring HIV Infection?



- Sexually active adults and adolescents who had anal or vaginal sex in the past 6 months **AND** any of the following
  - Sexually active partner with HIV (especially if partner has an unknown or detectable VL
  - Bacterial STI in past 6 months
  - History of inconsistent or no condom use with sexual partner(s)
- PWID
  - Partner with HIV **OR** sharing injection equipment

CDC. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf. Published December 2021.
Gandhi RT, et al. JAMA. 2023;329:63-84.

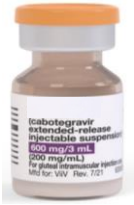
PrEP Options (2026)

	Oral Options			Long-Acting Injectable Options	
	F/TDF		F/TAF	Cabotegravir	Lenacapavir
	Daily	On-Demand	Daily	Every 2 Months	Every 6 Months
MSM	FDA On-Label Guideline Recommended (DHHS, IAS-USA, WHO)	FDA Off-Label Guideline Recommended (IAS-USA, WHO)	FDA On-Label Guideline Recommended (DHHS, IAS-USA, WHO)	FDA On-Label* Guideline Recommended (DHHS, IAS-USA, WHO)	FDA On-Label* Guideline Recommended (IAS-USA, WHO)
Transgender women		FDA Off-Label Not Recommended			
Heterosexual men					
Heterosexual women			FDA Off-Label Not Recommended		
Transgender men					

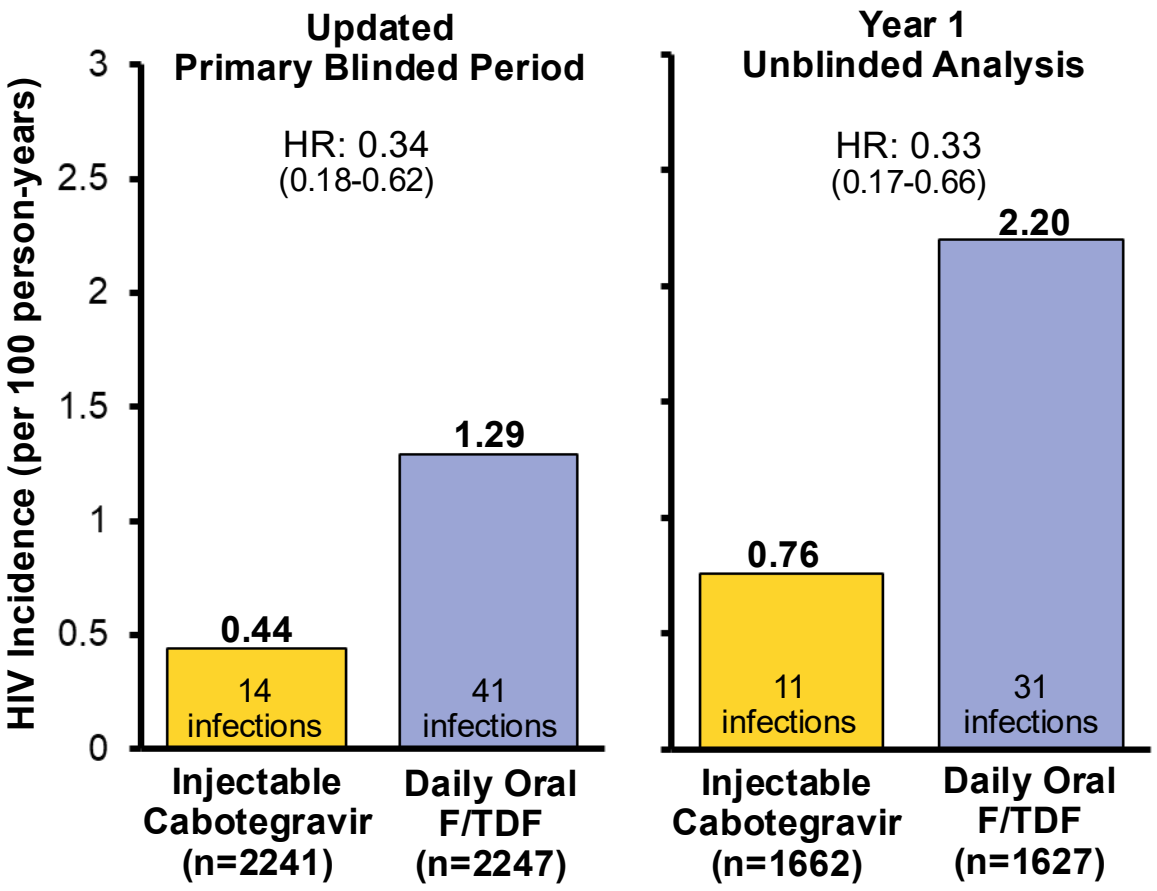
PWID: assess and consider sexual risk.
CDC indicates that PWID are likely to benefit from any FDA-approved PrEP option with or without a sexual risk indication.
*Except pregnancy: insufficient human data to adequately assess a drug-associated risk of birth defects and miscarriage.

CDC. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf. Published December 2021.
Gandhi RT, et al. *JAMA.* 2025;333:609-628.
WHO. https://www.who.int/publications/i/item/9789240111608. Published July 2025.

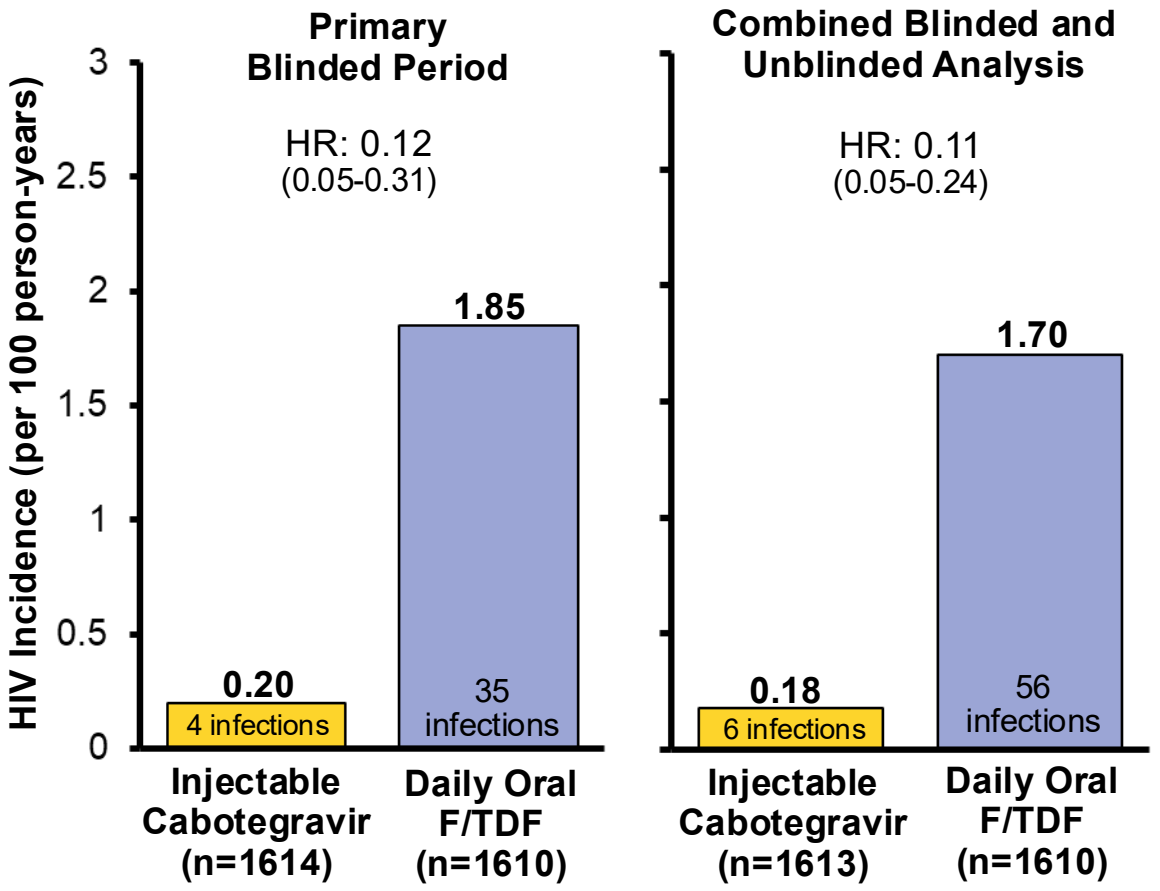
HPTN 083 and HPTN 084 Infection Rate



HPTN 083 (MSM/TGW)



HPTN 084 (Cisgender Women)



Landovitz RJ, et al. *N Engl J Med*. 2021;385:595-608.
Delany-Moretlwe S, et al. *Lancet*. 2022;399:1779-1789.
Delany-Moretlwe S, et al. *J Int AIDS Soc*. 2022;25(suppl 3):227-228. Abstract OALBX0107.

Real-World Use of Long-Acting Cabotegravir for PrEP: EHR Data

Kaiser Permanente
(2021-2024; n=23,311)

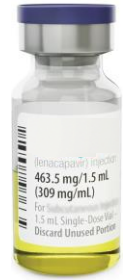
- Long-acting cabotegravir (n=180)
- Key results (cabotegravir)
  - On-time/early/late injections: 87%/4%/10%
  - Persistence at 12 months: 75%
  - Remained on/discontinued cabotegravir: 83%/17%
  - No HIV seroconversions (97 person-years of follow-up)

Trio Health Cohort
(2021-2024; n=526)

- Long-acting cabotegravir (n=526)
- Key results (cabotegravir)
  - Remained on/discontinued cabotegravir: 83%/17%
  - No HIV seroconversions (median follow-up: 7 months)
  - Delayed/missed injections: 33%/3%
  - Discontinuations due to injection site reactions (n=3)

Traeger MW, et al. *JAIDS.* 2026;101:812-818
Ramgopal M, et al. *Open Forum Infect Dis.* 2025;12(suppl 1):S101-S102. Abstract 505.

PURPOSE 1 and PURPOSE 2: Study Designs

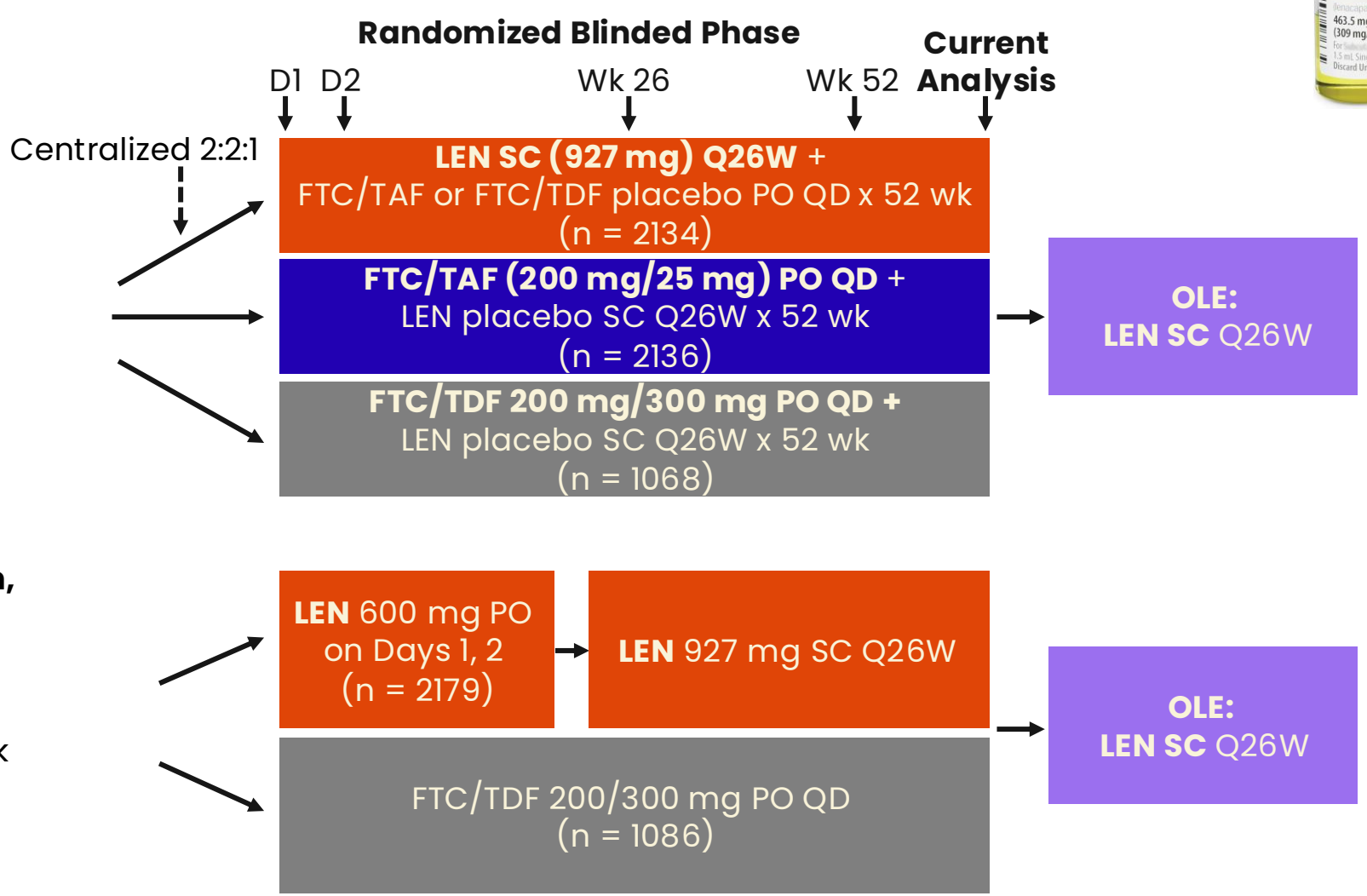


PURPOSE 1

Cisgender women aged 16-25 yr; sexually active with cisgender men and >1 vaginal intercourse within last 3 mo (not pregnant); unknown HIV status; no prior HIV testing or PrEP/PEP use in last 3 mo; ≥35 kg body weight; eGFR ≥60 mL/min
(N = 5345)

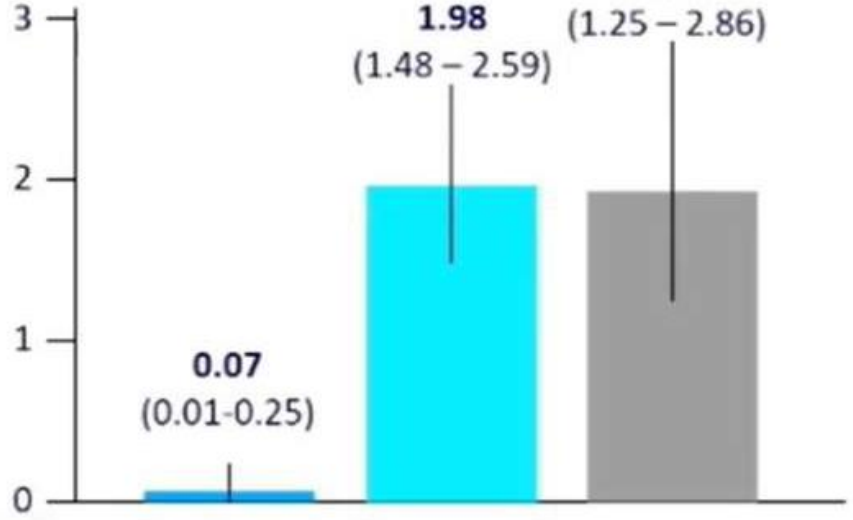
PURPOSE 2

Cisgender men, transgender women, transgender men, and gender nonbinary people with unknown HIV status; aged ≥16 yr; sexually active with ≥1 partner who is assigned male sex at birth within last 12 mo and 1 risk factor; no prior HIV testing or oral PrEP/PEP use in last 3 mo; no prior LA PrEP use
(N = 3271)



Ndlovu N, et al. CROI 2026, Abst 128; Cantas Lucio VD, et al. CROI 2026, Abst 129

PURPOSE 1
HIV Incidence per 100 PY (95% CI)
End of randomized blinded phase

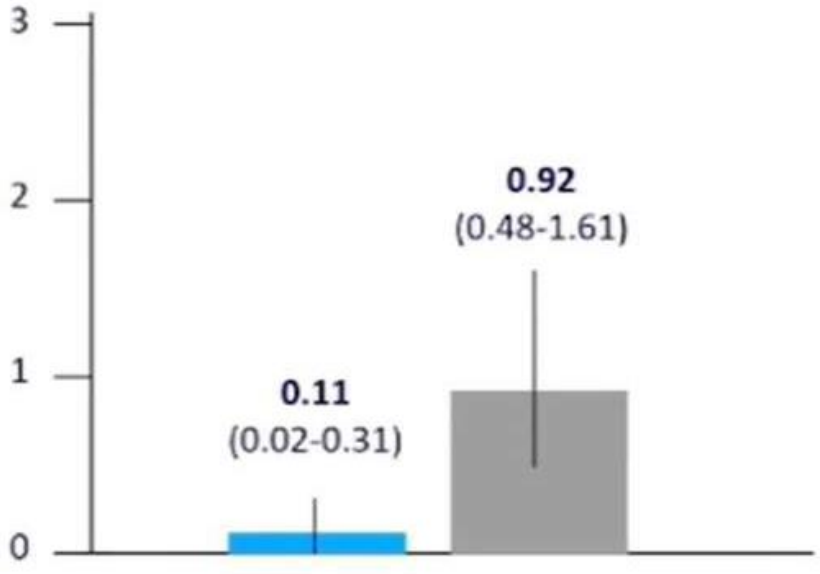


No. Participants:	2134	2136	1068
HIV acquisition:	2	52	25
PY of follow-up:	2953	2630	1291
	LEN SC	**TAF/FTC**	**TDF/FTC**

HIV infections at Primary Analysis: **0** **39** **16**

Participant A: Ab/Ag+ wk 52 (78 c/mL), all doses on time with good levels
Participant B: discontinued LEN >450 days before infection on oral Prep

PURPOSE 2
HIV Incidence per 100 PY (95% CI)
End of randomized blinded phase



No. Participants:	2179	1086
HIV acquisition:	3	12
PY of follow-up:	2843	1305
	LEN SC	**TDF/FTC**

HIV infections at Primary Analysis: **2** **9**

Participant 1, 2 and 3: Ab/Ag+ wks 13, 26 and 52
Participant 4: Ab/Ag+ 52 wks (RNA 2,020,000 c/mL
All without missed doses and with adequate levels

Future LA CAB PrEP options

Cabotegravir

EXTEND 4M
(1600 mg/3-mL im)
Phase 2b study
Single injection every 4 months
Results expected: 9/2026

Lenacapavir

sNDA
(Submitted: 6/15/2026)
Once-weekly 300-mg oral tablet
Supported by results from PURPOSE 1/2
FDA action date: 2/27/2027

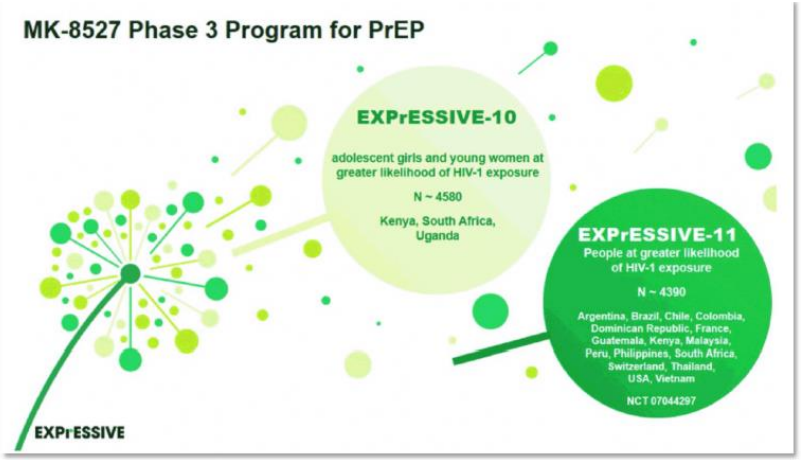
PURPOSE 365
(3000-mg im qyearly)
Phase 3 study
Diverse population of people who would benefit from PrEP
Primary objectives
Safey, tolerability, and pharmacokinetics

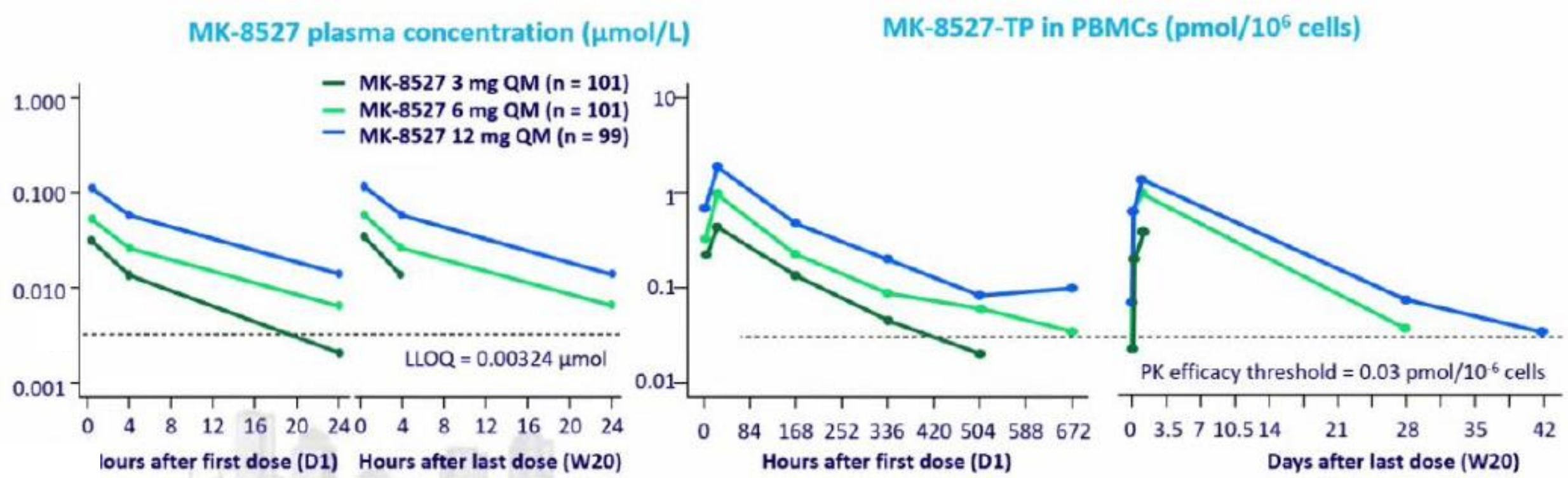
Alimatravir
(formerly MK-8527)

EXPrESSIVE-10 and -11
(NRTTI)
International phase 3 studies
Once-monthly oral tablet
Comparator: F/TDF
Diverse population of people who would benefit from PrEP
Estimated completion: mid/late 2027

Acuipil C et al. AIDS 2026. Abstract WEPEB096.
Jogiraju V, et al. *Lancet.* 2025;405:1147-1154.
Arens Y, et al. *Curr Opin HIV AIDS.* 2025;20:39-47.
Hughes E, et al. *Top Antivir Med.* 2026;34:353. Abstract 996.
NCT06741397. ClinicalTrials.gov.

PK of Q month MK-8527 (NRTTI): Phase 2 study in low risk adults

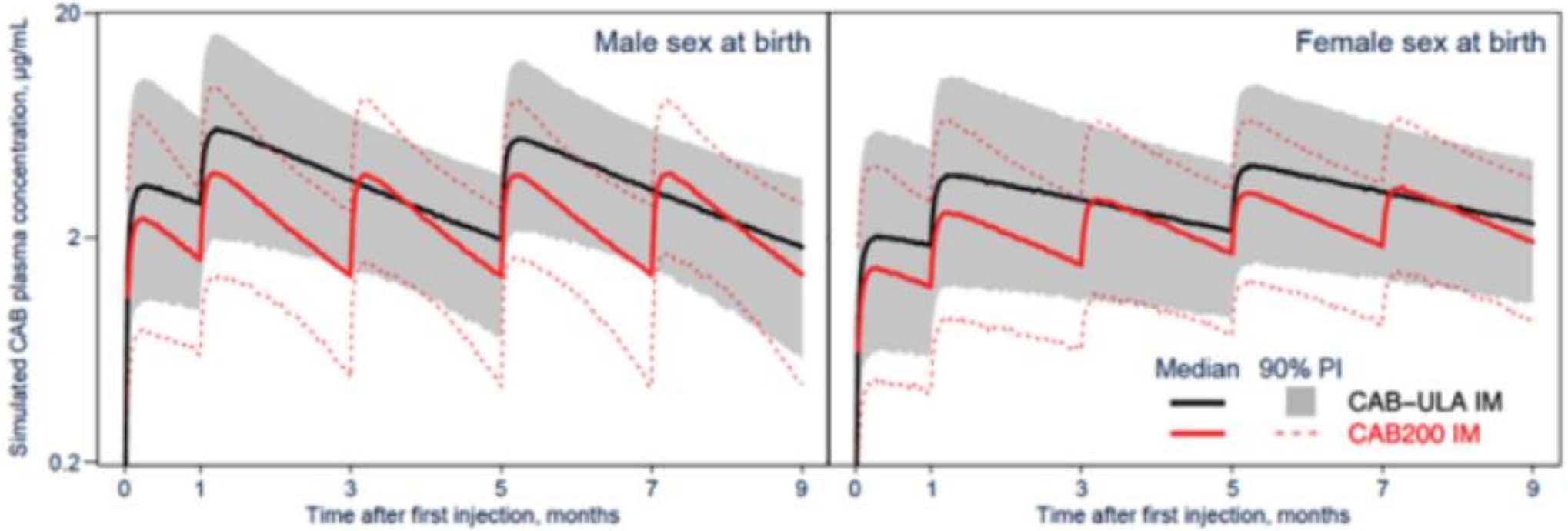




Mayer K, et al. IAS 2025; Abst. OA50106LB

CAB-Ultra long acting (q4 months)

- PK simulations[a] predict a CAB-ULA IM dose interval of ≥4 months achieves higher exposure than approved CAB200 IM at intervals of 2 months
- CAB-ULA IM $t_{1/2}$ was predicted to be >2x the $t_{1/2}$ of CAB200 IM

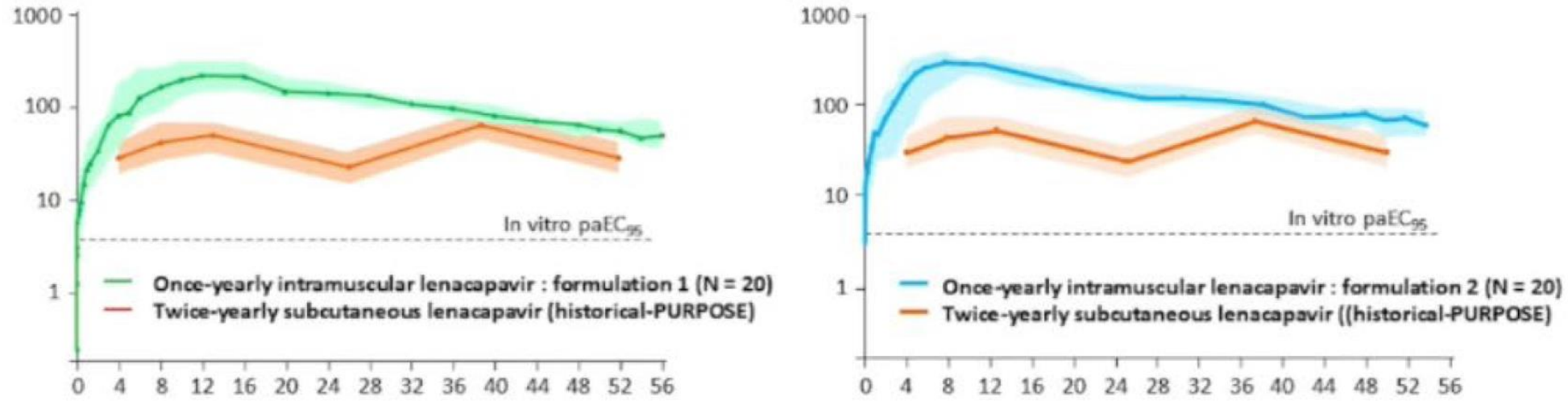


CAB, cabotegravir; IM, intramuscular; PI, prediction interval; PK, pharmacokinetics; Q4M, every 4 months; SC, subcutaneous; $t_{1/2}$, terminal half-life; ULA, ultra-long-acting. [a]1600-mg (3-mL) CAB-ULA per injection.

Han K, et al. CROI 2024

Lenacapavir IM once-yearly

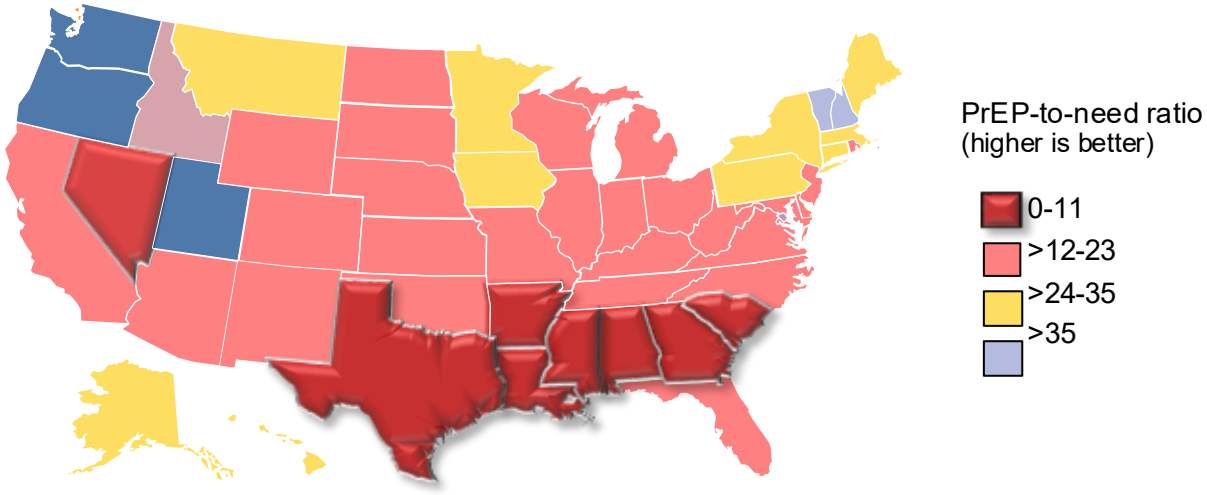
- Phase 1, open-label in participants without HIV
- PK, safety and tolerability of 2 LEN free acid formulations administered by 2 ventrogluteal IM injections as a single 5000 mg dose (formulation 1 with 5% w/w ethanol, formulation 2 with 10% w/w ethanol)

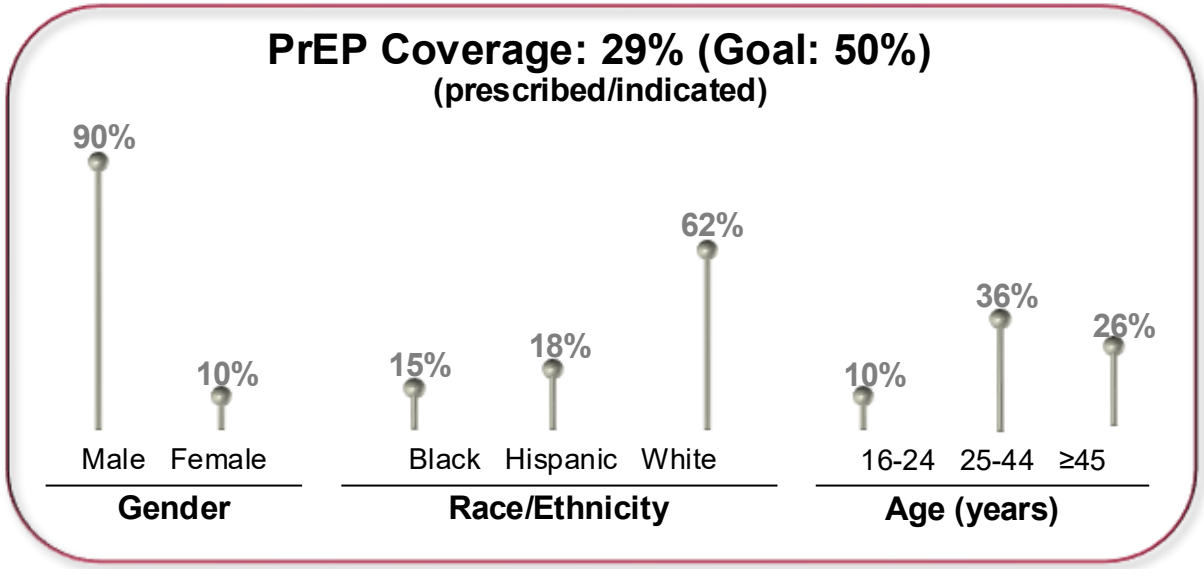


- Injection site pain :16 (80%) given formulation 1, 15 (75%) formuation
- ISR generally mild, resolved within 1 week and reduced by pretreatment with ice

Jogiraju V, et al. CROI 2025, Abst 154, and Lancet online 11 March 2025

PrEP-to-Need Ratio (2025)





CDC. https://www.cdc.gov/hiv-data/initiatives/. Published May 7, 2026.
CDC. https://www.cdc.gov/nchhstp/director-letters/new-injectable-hiv-prep%20.html. Published September 2025.
AIDsVu. 2025 National PrEP Data. Accessed September 2026.

PrEP Uptake: Barriers and Potential Solutions

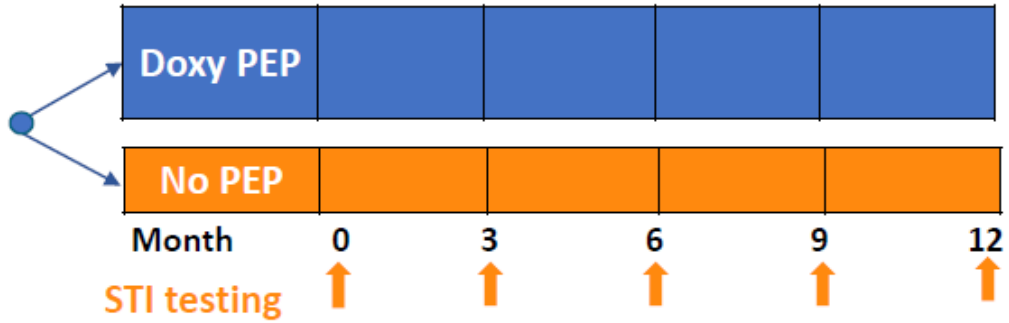
Key Barriers	Potential Solutions
Limited awareness of PrEP	Education (patient/provider) Communication between providers
Low-risk perception	Education (patient/provider)
Stigma	Increase cultural understanding Improve communication/understanding between patient and provider
Provider bias and mistrust of healthcare system	Education (patient/provider) Address systemic biases (eg, education, advocacy, and diverse healthcare professional staff)
Limited access to medical care	Education (patient/provider) Extending access to PrEP Technological alternatives (eg, telemedicine) Address competing priorities (eg, food, shelter, safety, other healthcare, childcare)
Financial barrier	Awareness/guidance of financial aid options
Concern about side effects	Education (patient/provider)

Mayer KH, et al. *Adv Ther.* 2020;37:1778-1811.
Magnus M, et al. *J Med Access.* 2023;Dec 6.;7:27550834231214958.

Preventing STIs: DoxyPEP

Intervention: Open label doxycycline 200 mg as PEP within 72 hours after condomless sexual contact, max 200mg /daily

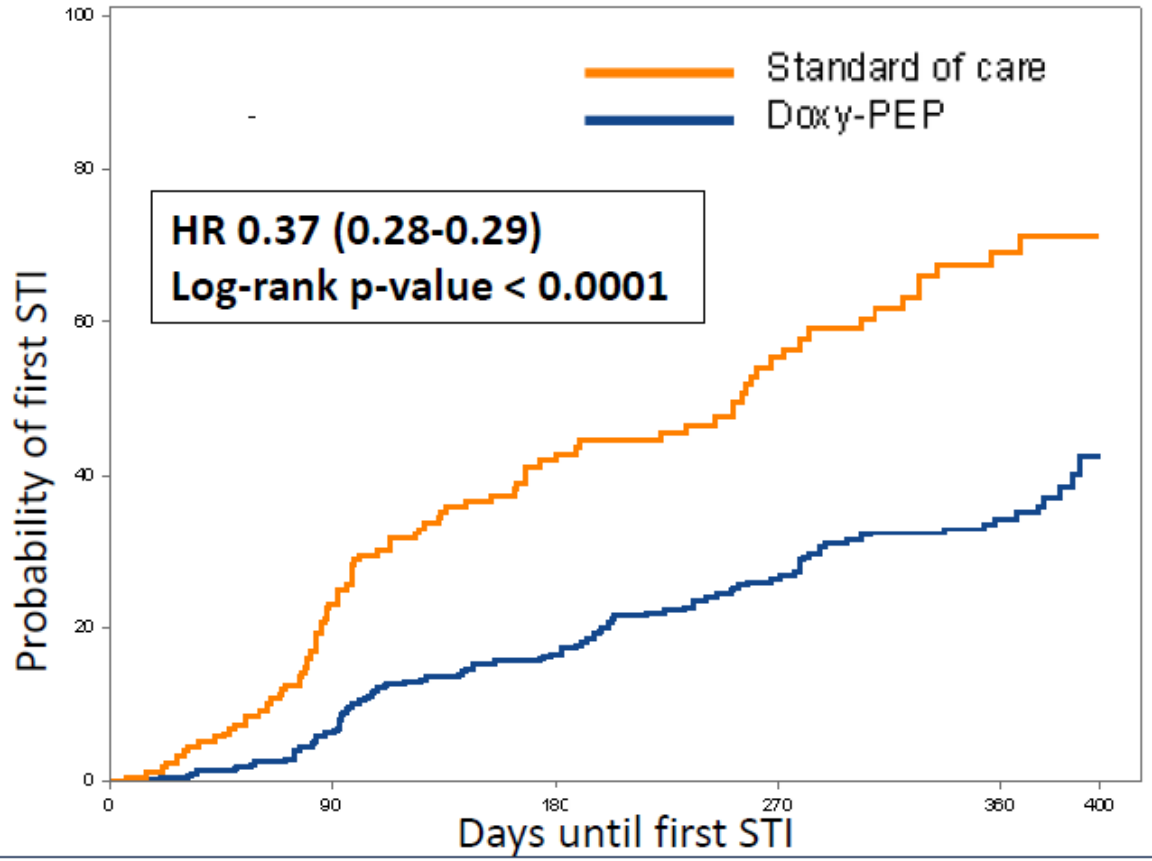
MSM & TW living with HIV *or* *2:1 randomization* without HIV on PrEP



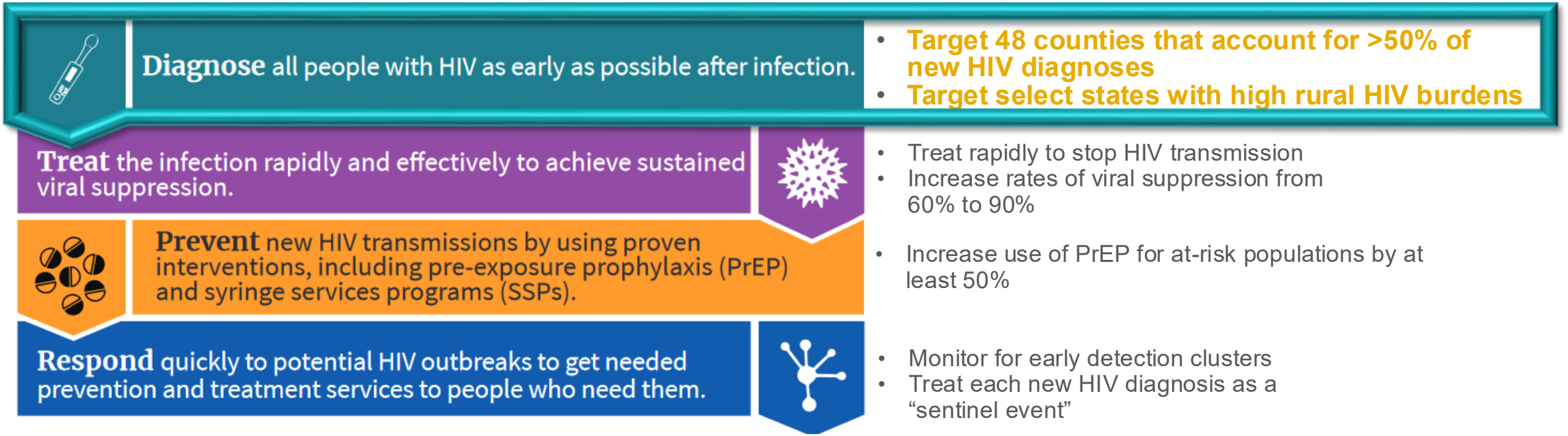
DoxyPEP Results

- Overall 65% ↓ reduction in bacterial STIs each quarter
- ≈ 80% ↓ chlamydia & syphilis
- ≈ 50% ↓ gonorrhea
- Effectiveness independent of HIV serostatus

DOXYPEP



Key Steps to Ending the HIV Epidemic in the United States



Ending the HIV Epidemic

Overall Goal: Decrease the number of new HIV diagnoses to 9,588 by 2025 and 3,000 by 2030.

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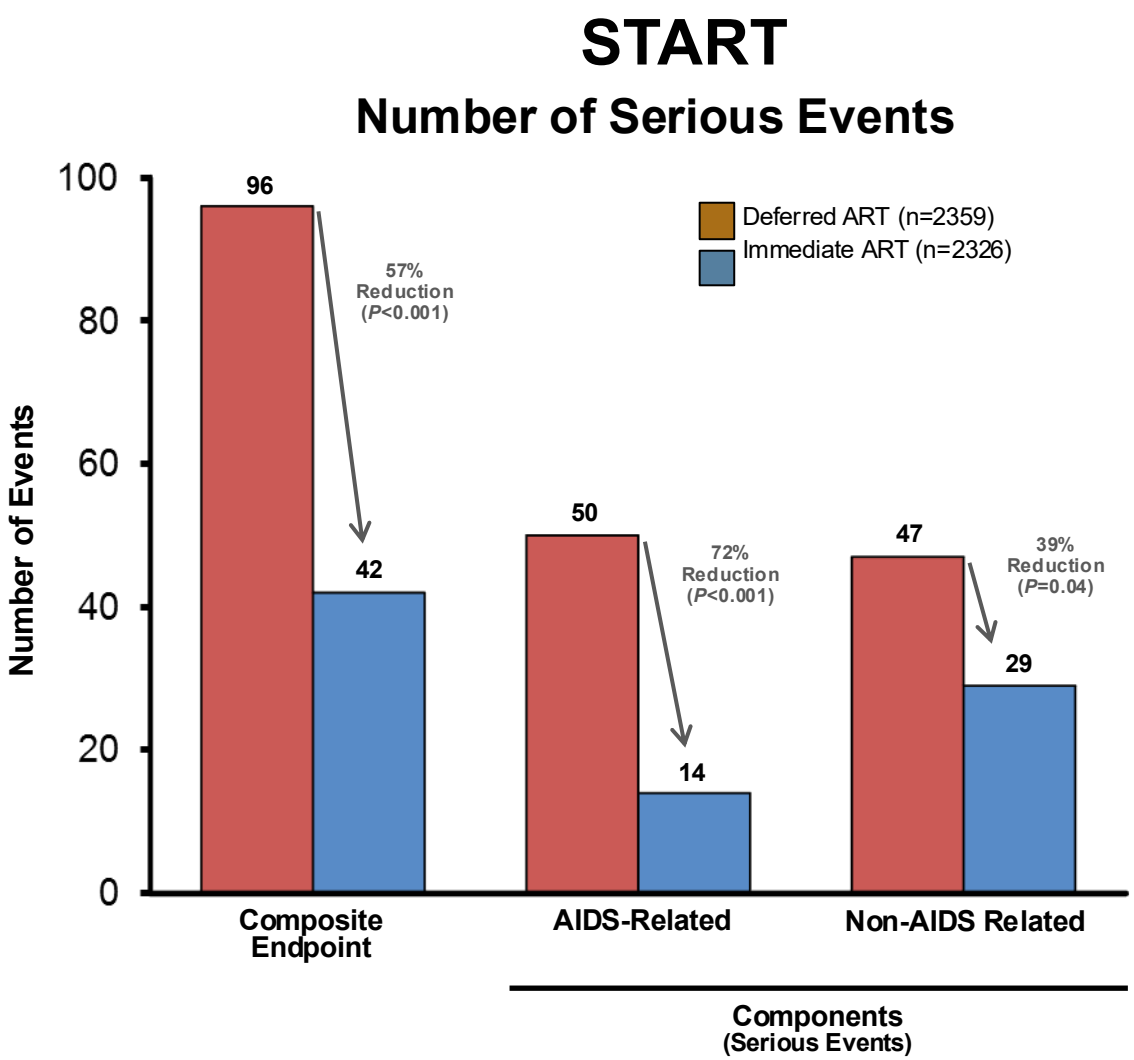
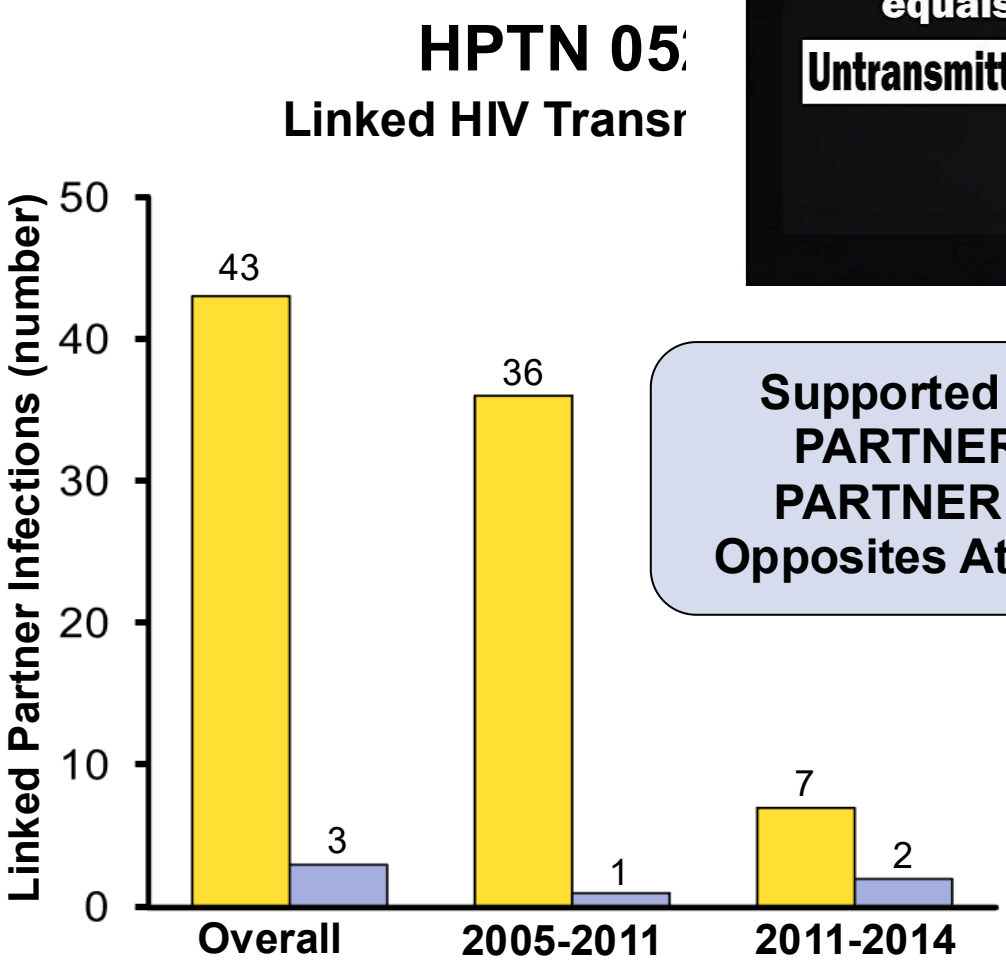
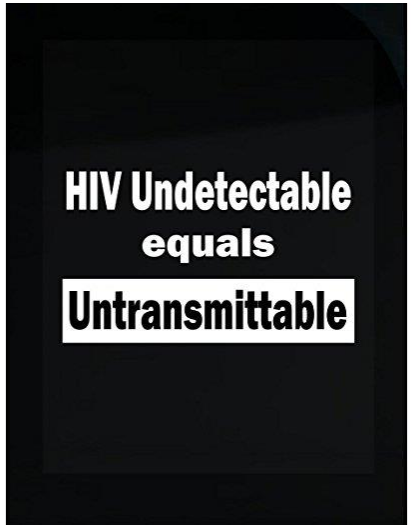
Harris NS, et al. *MMWR Morb Mortal Wkly Rep*. 2019;68:1117-1123.

ART: When to Start

When to Start







Supported by PARTNER, PARTNER 2, Opposites Attract

Lundgren JD, et al. NEJM 2015; 373:795-807; Cohen M ,et al. NEJM 2016; 375:830-839

Current Recommendations for Same-Day ART

DHHS[1]	Recommended	
	WHO[2]	IAS-USA[3]
▪ Recommend initiating ART at time of diagnosis (when possible), or soon afterwards (AII)	▪ Recommended where feasible	▪ Start ART as soon as possible, including immediately after diagnosis, if patient is ready

- No randomized data outside of RLS showing improved retention in care or outcomes beyond time to viral suppression
- Can be resource intensive, including staff and drug availability
- Rationale for immediate ART in resourced setting is to increase uptake of ART, decrease time required to link to care and viral suppression, and improve rate of suppression
- **Risk of immediate ART is likely to be very low**

1. DHHS ART Guidelines, Https://clinicalinfo.hiv.gov/en/guidelines/ September 2024; 2. WHO Guidelines. July 2019. 3. Gandi RT, et al. JAMA. 2022.

ART: What to Start

First-Line regimens

Preferred Regimen for most patients

- Bictegravir/Emtricitabine/Tenofovir alafenamide (B/F/TAF)
- Dolutegravir (DTG) + Tenofovir alafenamide/emtricitabine (TAF/FTC)
- Dolutegravir/lamivudine (DTG/3TC)*

Preferred regimen for most pregnant patients

- DTG + TDF (or TAF)/FTC
- Bictegravir/Emtricitabine/Tenofovir alafenamide (B/F/TAF)

LA Cabotegravir PrEP in previous 12 months

- Darunavir/cobicistat (or ritonavir if pregnant) + TDF (or TAF)/FTC (pending INSTI resistance results)

*Only if no HBV and resistance genotype available

ART Switch

ARV Switch: The Why and How in Clinical Practice

Why

- Optimization in suppressed patients
  - Simplify regimen (# and frequency)
  - Tolerability
  - Co-morbidity
  - Drug-drug, drug-food interactions
  - Pregnancy
  - Cost
- Virologic failure (VL repeatedly >200 c/mL despite good adherence)

How

- Maintain or achieve viral suppression to avoid resistance
- Need to consider
  - Previous ART
  - Previous/current resistance
  - Likelihood of adherence
  - Drug-drug or drug-food
  - Comorbid conditions

•DHHS ART Guidelines, Https://clinicalinfo.hiv.gov/en/guidelines/ September 2024

Considerations When Switching Regimens in Virologically Suppressed Patients (Optimization)

Drug Resistance

- Review ART history
- Review all resistance test results (old and new)
- Consider switch only if new regimen is likely to maintain suppression
- Within-class switches usually maintain virologic suppression if no resistance to drugs in that class
- Caution when switching from high barrier regimen (e.g., boosted PI) to low barrier regimen (e.g., NNRTI) if any underlying resistance
- Consider expert consultant if underlying resistance

Safety

Review ART history for intolerance

- Must be HLA-B*5701 negative if considering ABC
- Consider drug–drug interactions with comedications

Comorbidity

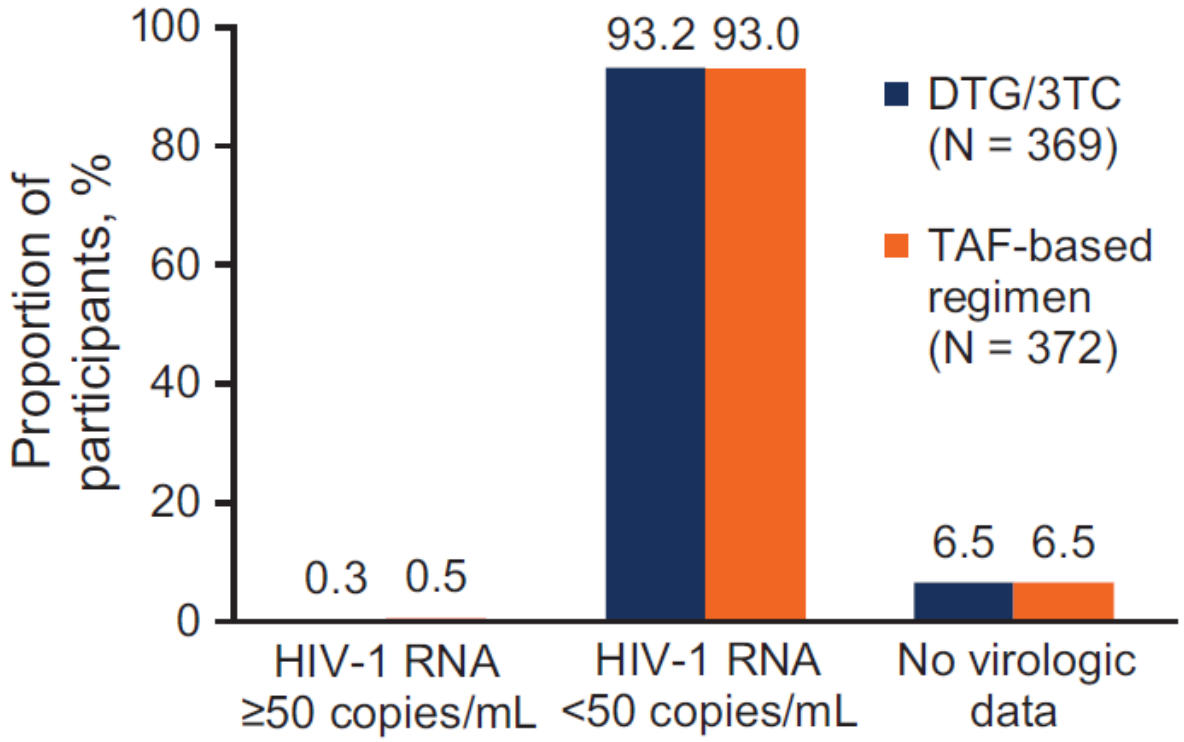
- HBV coinfection
- Cardiovascular disease or risk
- Renal function
- Bone mineral density
- Pregnancy
- Other coinfections

DHHS ART Guidelines, Https://clinicalinfo.hiv.gov/en/guidelines/ September 2024

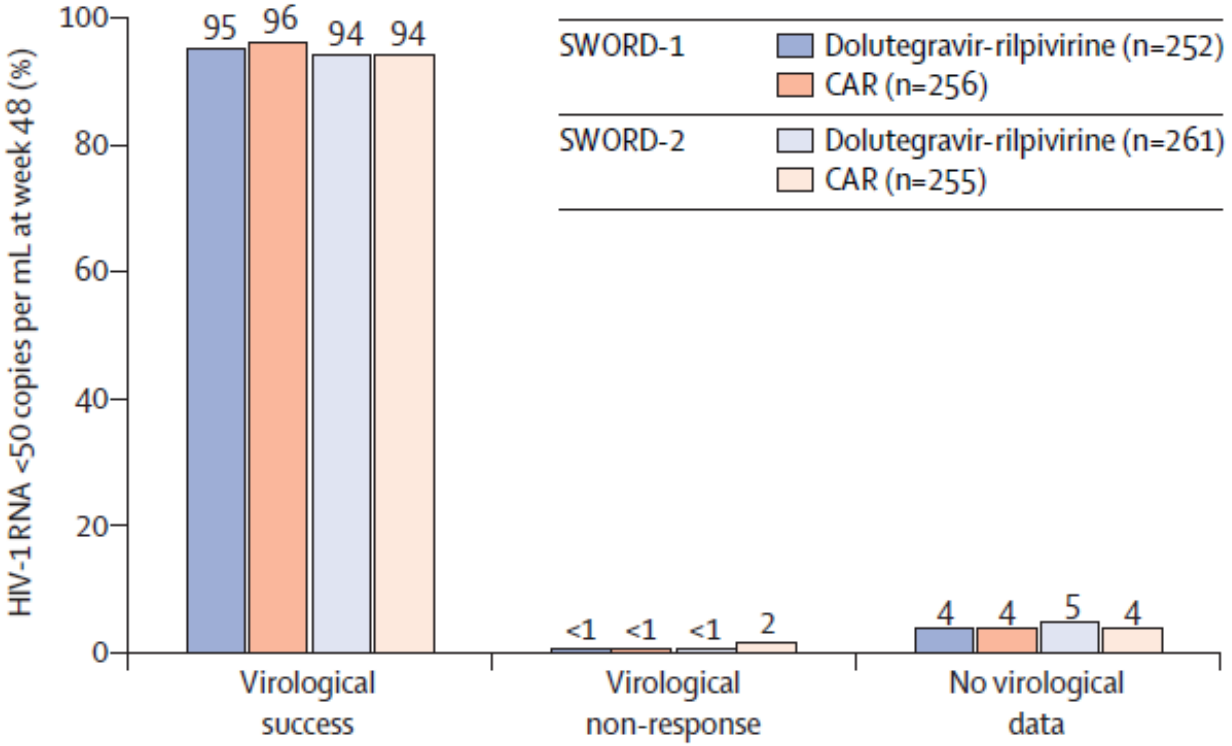
ART: Switch in those with no underlying resistance

TANGO and SWORD Studies
Novel 2-drug regimens

TANGO



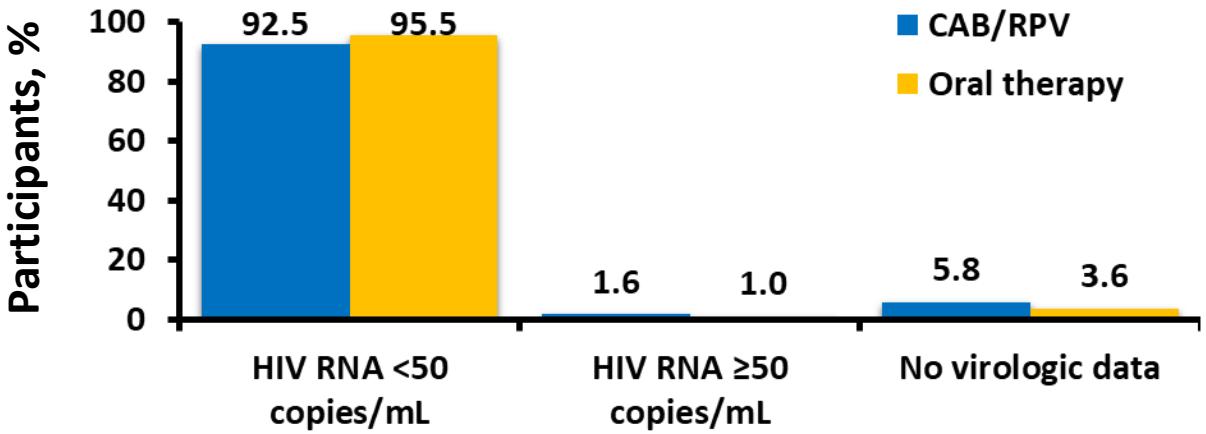
SWORD 1 and 2



Van Wyk J, et al. CID 2020; 71:1920-1929; . Llibre JM, et al. Lancet 2018; 391:839-849

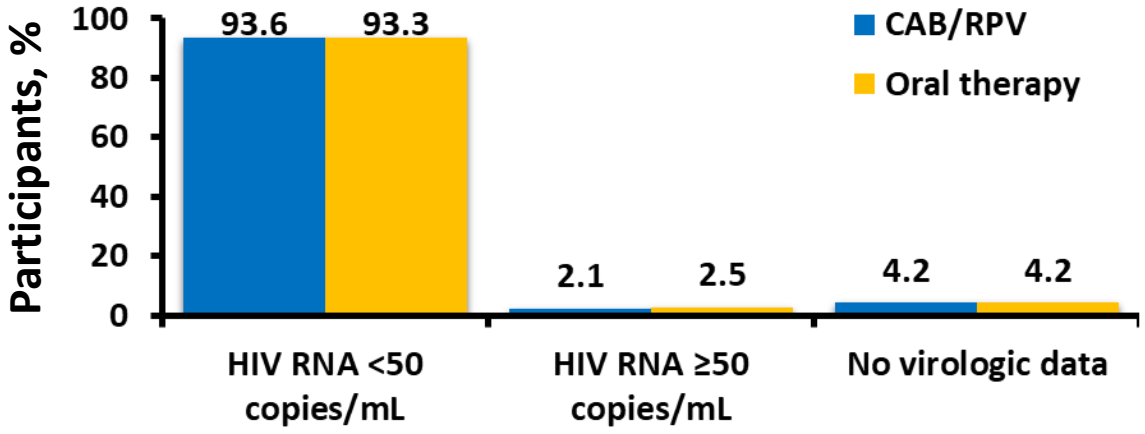
Long-Acting CAB/RPV vs Oral ART
ATLAS and FLAIR

LA CAB/RPV is noninferior to oral ART at 48 weeks in treatment-experienced patients[1,a]



Injection site reactions were seen in 81% of CAB/RPV group and decreased to 11% at week 48

LA CAB/RPV is noninferior to oral ART at 48 weeks in treatment-naïve patients[2,b]



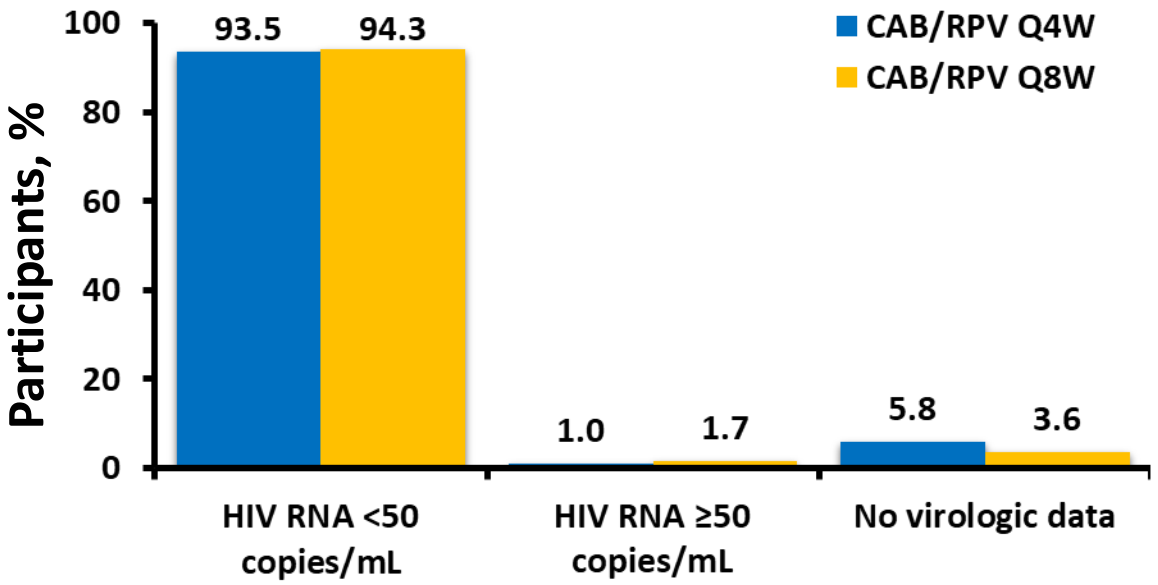
Injection site reactions were seen in 86% of CAB/RPV group and decreased to 20% at week 48

[a]N=618 adults with HIV who were virally suppressed for ≥6 months on standard oral ART regimens were randomly assigned to continue their current regimen or switch to oral CAB/RPV for 4 weeks followed by monthly IM injections of long-acting CAB/RPV for 52 weeks; [b]N=618 adults with HIV who had not previously received ART were given 20 weeks of DTG/ABC/3TC. Those who had HIV RNA <50 copies/mL after 16 weeks were randomly assigned to continue their current regimen or switch to oral CAB/RPV for 4 weeks followed by monthly IM injections of long-acting CAB/RPV for 48 weeks.

1. Swindells S, et al. *N Engl J Med*. 2020;382(12):1112-1123; 2. Orkin C, et al. *N Engl J Med*. 2020;382(12):1124-1135.

Long-Acting CAB/RPV Q4W vs Q8W
ATLAS-2M (at 48 wks)

CAB/RPV Q8W noninferior to Q4W



- Injection site reactions were rated as mild-to-moderate by 98% of participants experiencing them
  - Median duration of 3 days

LA CAB/RPV only indicated for those virologically suppressed: Limited data in those with poor adherence or viremia

Overton ET, et al. *Infect Chemother.* 2020;52(suppl):S378-S379.

Hsu RK et al. *Journal of the International AIDS Society* 2025, **28**:e70068
http://onlinelibrary.wiley.com/doi/10.1002/jia2.70068/full | https://doi.org/10.1002/jia2.70068

JIAS JOURNAL OF THE INTERNATIONAL AIDS SOCIETY

RESEARCH ARTICLE

Comparable real-world effectiveness between switches to cabotegravir + rilpivirine long-acting or modern daily oral regimens in the United States: an OPERA cohort study

Ricky K. Hsu[1,2], Michael G. Sension[3], Jennifer S. Fusco[4,§], Laurence Brunet[4], Quateka Cochran[5], Brooke Levis[4], Gayathri Sridhar[6], Vani Vannappagari[6], Jean Van Wyk[7], Michael B. Wohlfeiler[8] and Gregory P. Fusco[4]

[§]Corresponding author: Jennifer S. Fusco, Epividian, 150 Fayetteville Street Suite 2300, Raleigh, NC 27601, USA. (jennifer.fusco@epividian.com)

Table 3. Virologic outcomes among those with follow-up viral load

		CAB+RPV LA N = 1293	Oral ART N = 2523
	Number of VLs available over follow-up, median (IQR)	3.0 (2.0, 4.0)	3.0 (2.0, 5.0)
Last viral load	< 200 copies/ml, *n* (%)	1281 (99)	2431 (96)
	< 50 copies/ml, *n* (%)	1229 (95)	2298 (91)
CVF	*n* (%)	15 (1)	44 (2)
	Unadjusted odds ratio (95% CI)[a]	0.66 (0.35, 1.00)	Reference
	Adjusted odds ratio (95% CI)[a,b]	0.64 (0.40, 1.02)	Reference

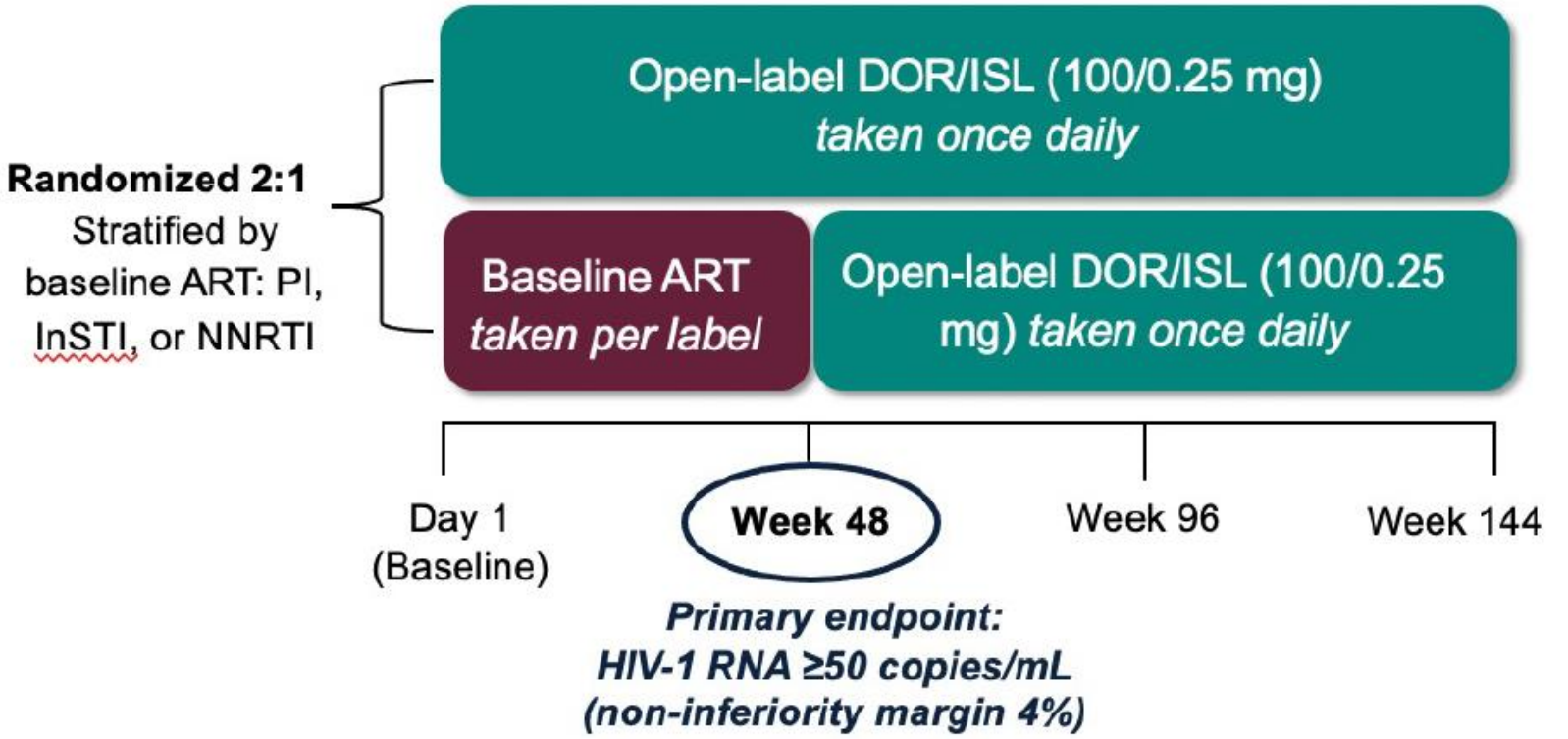
- Suppressed, treatment experienced adults (median 11 months f/u)
- 92% on second gen INSTI
- Persistence on regimen ~80% in both groups
- VF 1-2% in both groups

Switch to DOR/ISL (100/0.25 mg) QD from cART

Population

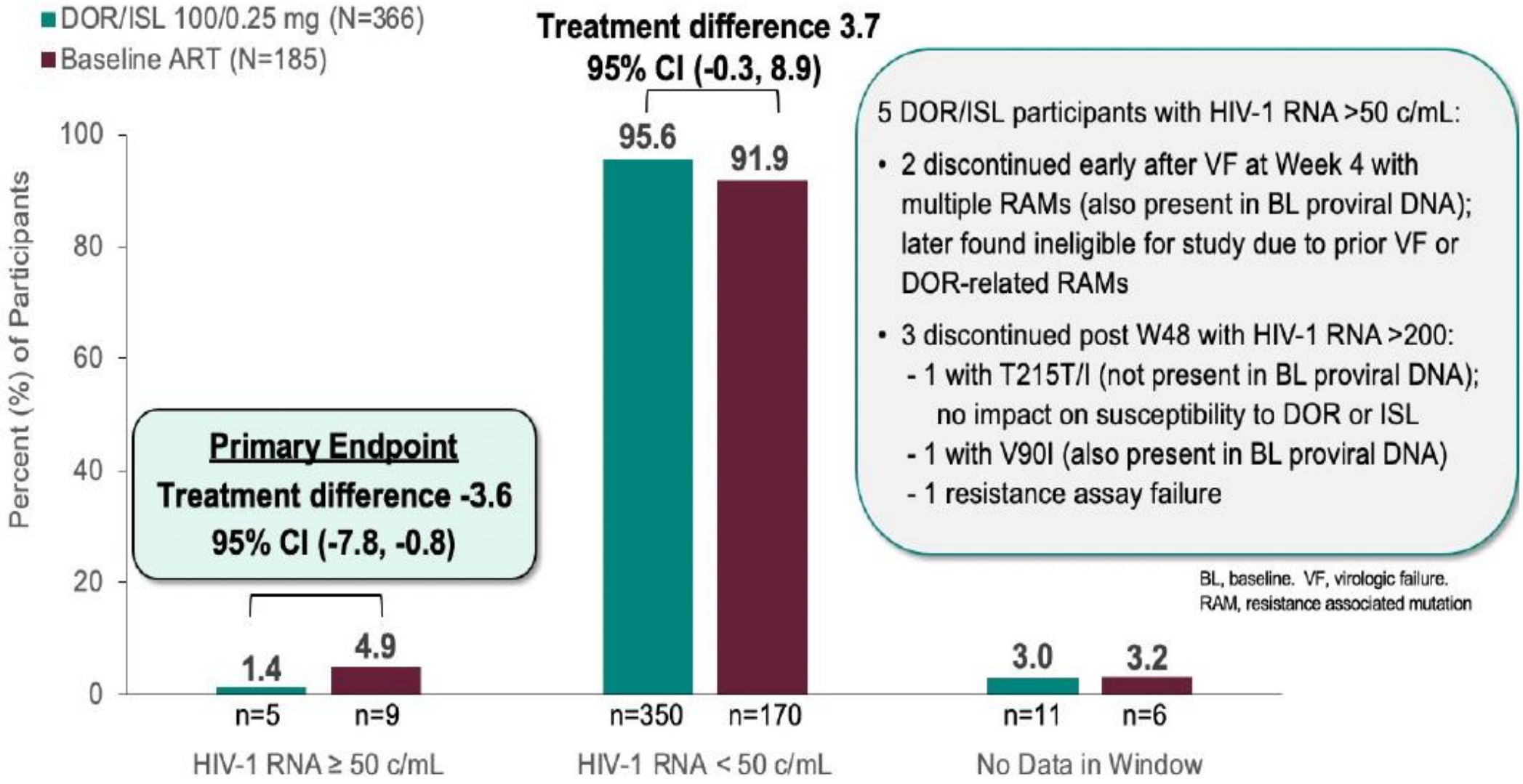
- Adults with HIV-1 RNA <50 copies/mL for ≥3 months on stable, oral 2- or 3-drug ART
- CD4 count ≥50 cells/mm^3 and total lymphocyte count ≥650 cells/mm^3
- No history of treatment failure on any regimen
- No known resistance to DOR*
- No active HBV infection

* V106A/M, V108I, Y188L, H221Y, P225H, F227C/L, M230I/L, L234I, P236L or Y318F



Discontinuation was required for confirmed decline in total lymphocytes (≥30% and to <1000 cells/mm^3) or in CD4 count (<350 cells/mm^3 from baseline ≥500, ≥30% and to <350 from baseline ≥350, or to <200 from baseline ≤349)

Orkin C, et al. Lancet 2026



No decline in total lymphocyte or CD4+ lymphocyte counts

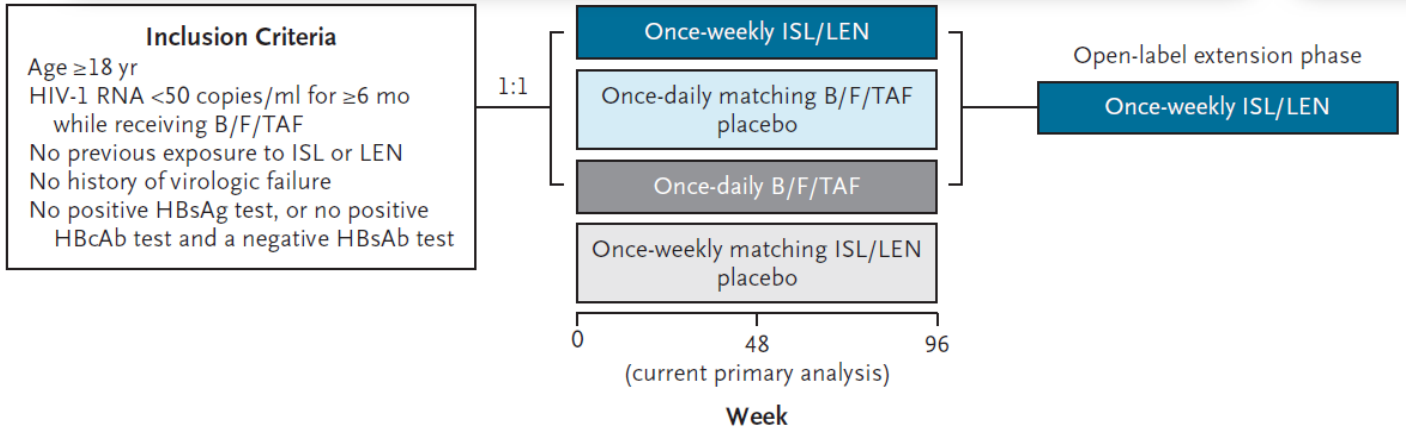
<u>Reminder</u>: ISL contraindicated with 3TC and FTC; potentially reduce intracellular ISL

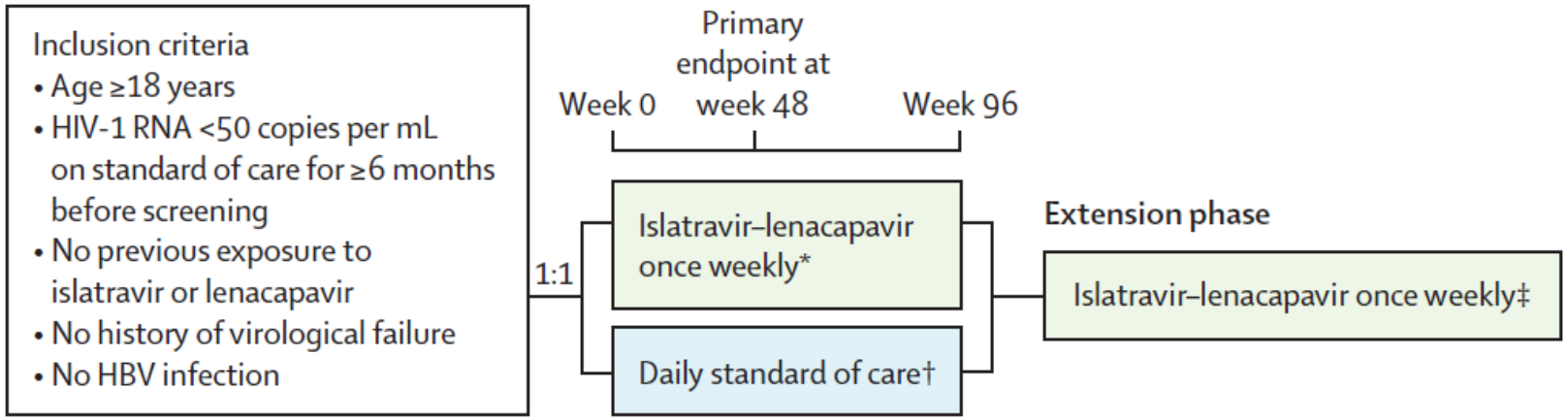
Phase 3 Trial of Weekly Oral Islatravir–Lenacapavir for HIV-1 Treatment

J.K. Rockstroh,[1] M.N. Ramgopal,[2] A. Curran Fàbregas,[3] M. Hedgcock,[4] K.A. Workowski,[5] S. Ronot-Bregigeon,[6] I. Cassetti,[7] C. Brinson,[8] S.K. Gupta,[9] C.-C. Hung,[10] M. O'Reilly,[11,12] J. Slim,[13] H. Gatanaga,[14] P. Shalit,[15] S.-Y. Liu,[16] S.O. Klopfer,[17] F. Shihadeh,[16] N. Patel,[17] R.-C. Mercier,[16] M. Shaughnessy,[17] H. Dvory-Sobol,[16] D. SenGupta,[16] C. Llamoso,[17] M.S. Rhee,[16] and C. Orkin,[18] for the ISLEND-1 Study Team*

Switch to once-weekly, single-tablet islatravir–lenacapavir from daily standard of care for HIV-1 (ISLEND-2): a multicentre, randomised, open-label, active-controlled, phase 3 non-inferiority trial

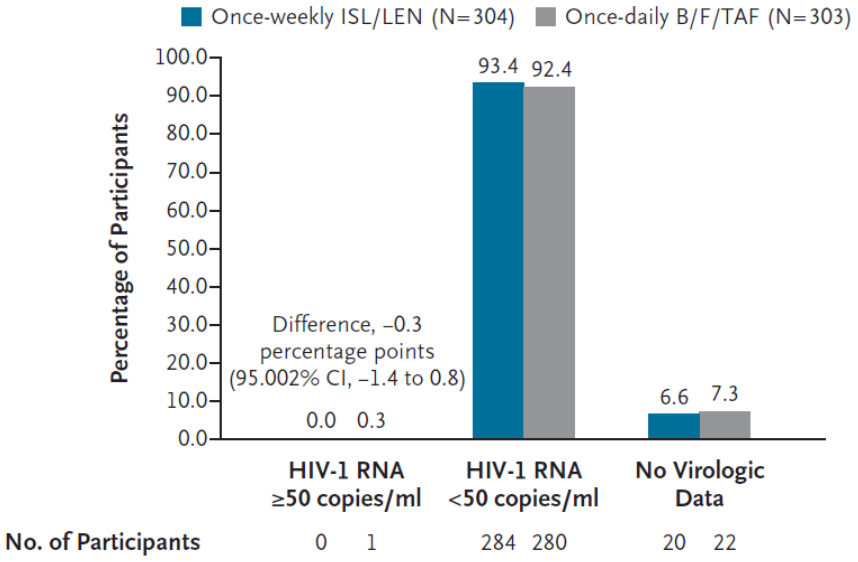
*Amy E Colson, Princy N Kumar, Peter J Ruane, Ploenchan Chetchotisakd, Winai Ratanasuwan, Afaaf Liberty, Ronald G Nahass, Alejandro Arenas-Pinto, Frank A Post, David A Baker, Pedro Cahn, Eveline Hofmann, Dai Watanabe, Po-Liang Lu, Anna H E Roukens, Miłosz Parczewski, Hongyuan Wang, Ke Chen, Fadi Shihadeh, Melissa Shaughnessy, Hadas Dvory-Sobol, Devi SenGupta, Cyril Llamoso, Martin Rhee, Onyema Ogbuagu, for the ISLEND-2 Study Team**

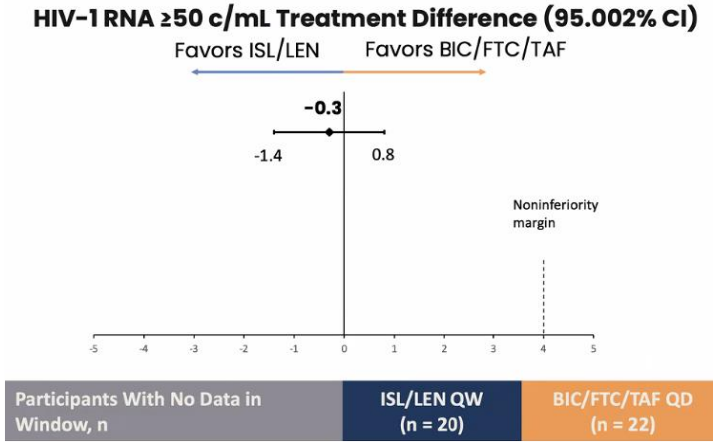




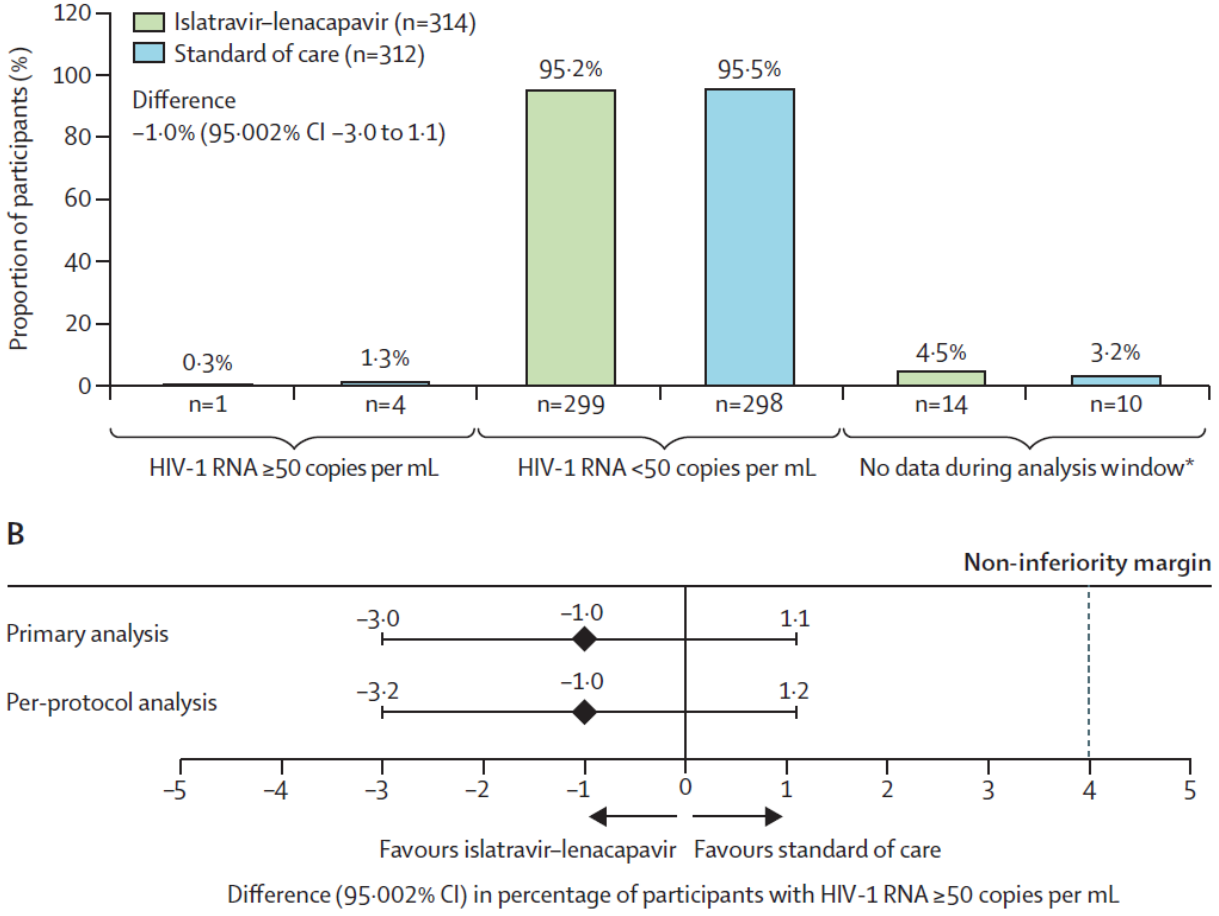
Rockstroh JK, et al. NEJM 2026; doi: 10.1056/NEJMoa2607973
Colson AE, et al. Lancet 2026; doi.org/10.1016/S0140-6736(26)01557-6

ISLEND-1, -2 Primary efficacy





Pill count for ISL/LEN showed mean adherence of 98.9%; 96% with ≥95% adherence



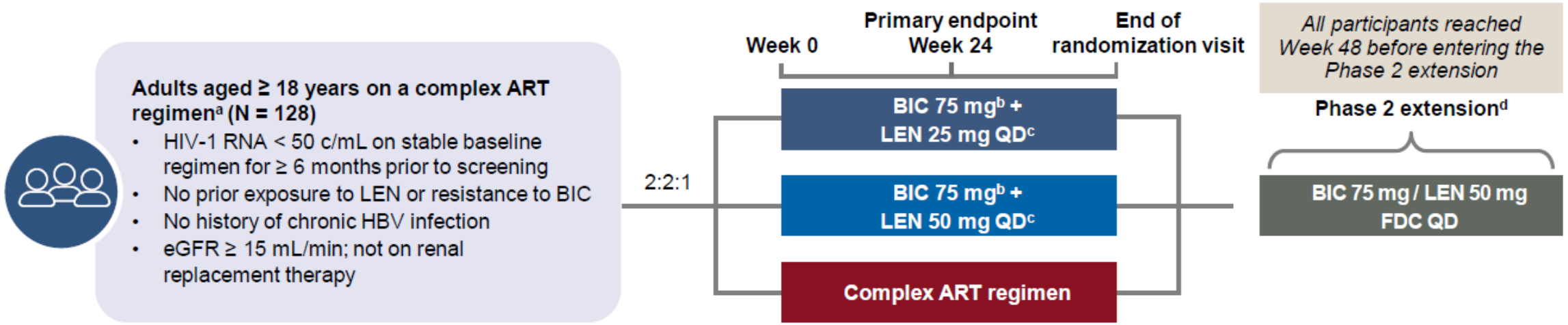
Pill count for ISL/LEN showed median adherence of 100%; 98% taking ≥90% of doses

Rockstroh JK, et al. NEJM 2026; doi: 10.1056/NEJMoa2607973
Colson AE, et al. Lancet 2026; doi.org/10.1016/S0140-6736(26)01557-6

ART: Switch in those with underlying resistance

ARTISTRY-1: LEN + BIC once daily

- ARTISTRY-1 is a Phase 2/3, randomized, open-label, multicenter study



Baseline resistance

NRTIs (82%)
NNRTIs (66%)
PI (47%)
INSTI (9%) (not to BIC)

Orkin C, et al. Lancet 2026; 407:1249-58

Switch to single-tablet bictegravir–lenacapavir from a complex HIV regimen (ARTISTRY-1): a randomised, open-label, phase 3 clinical trial

Chloe Orkin, Peter J Ruane, Malcolm Hedgcock, Cyril Gaultier, Marcelo H Losso, Benoit Trottier, Thomas Lutz, Mark O'Reilly, Mark Bloch, Jihad Slim, Moti Ramgopal, Simiso Sokhela, Karam Mounzer, Hung-Chin Tsai, Jorge Santana Bagur, Xu Zhang, Keith Aizen, Kwanza Price, Nicolas Margot, Jairo M Montezuma-Rusca, Peter Sklar, Martin Rhee, Pedro Cahn, on behalf of the ARTISTRY-1 Study Group

	Bictegravir–lenacapavir (n=371)	Complex regimen (n=186)	Difference for bictegravir–lenacapavir *vs* complex regimen (95·002% CI)	Difference for bictegravir–lenacapavir *vs* complex regimen (95% CI)
US Food and Drug Administration Snapshot algorithm (full analysis set)*				
HIV-1 RNA ≥50 copies per mL	3 (1%)	2 (1%)	−0·3% (−2·3 to 1·8)	..
HIV-1 RNA <50 copies per mL	356 (96%)	174 (94%)	2·4% (−1·8 to 6·6)	..
No virological data	12 (3%)	10 (5%)	..	..
Discontinued due to adverse event or death	7 (2%)†	1 (1%)‡	..	..
Discontinued study due to other reasons§ and last available HIV-1 RNA was <50 copies per mL	5 (1%)	8 (4%)	..	..
Had missing data during the analysis window but was still on study drug	0	1 (1%)	..	..
Missing=excluded analysis (full analysis set with non-missing HIV-1 RNA value at week-48 visit, while on treatment)*				
HIV-1 RNA <50 copies per mL	356/359 (99%)	174/176 (99%)	..	0·3% (−1·9 to 2·5)
HIV-1 RNA ≥50 copies per mL	3/359 (1%)	2/176 (1%)	..	..
50 to <200 copies per mL	2/359 (1%)	1/176 (1%)	..	..
200 to <1000 copies per mL	1/359 (<1%)	1/176 (1%)	..	..
Missing=failure analysis (full analysis set, while on treatment)*				
HIV-1 RNA <50 copies per mL	356/371 (96%)	174/186 (94%)	..	2·4% (−1·8 to 6·6)
HIV-1 RNA ≥50 copies per mL	3/371 (1%)	2/186 (1%)	..	..
50 to <200 copies per mL	2/371 (1%)	1/186 (1%)	..	..
200 to <1000 copies per mL	1/371 (<1%)	1/186 (1%)	..	..
Missing data	12/371 (3%)	10/186 (5%)	..	..

Orkin C, et al. Lancet 2026; 407:1249-58

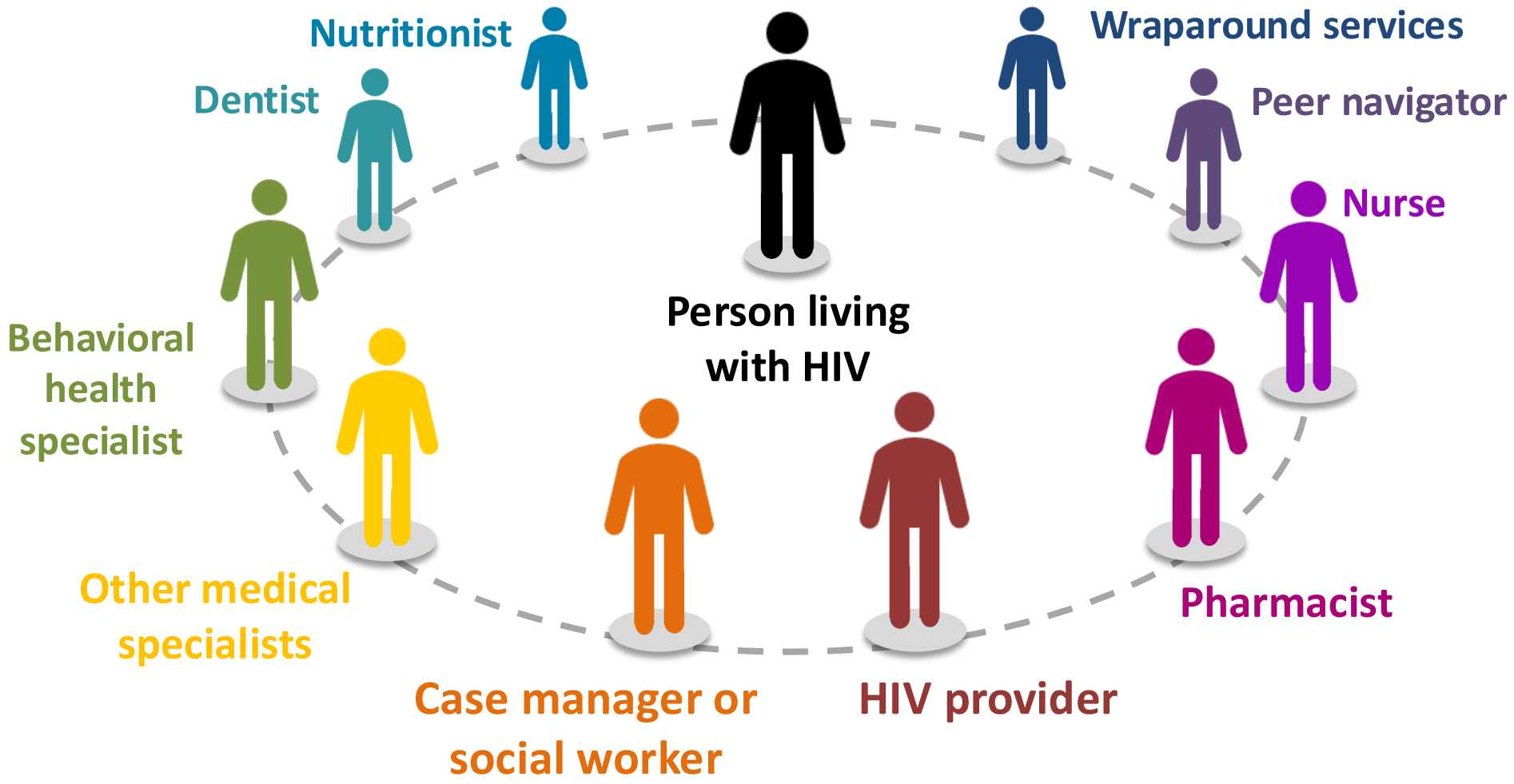
Managing virologic failure without underlying resistance (e.g., poor adherence)

Defining Virologic Response

- **Virologic suppression:** Confirmed HIV RNA level below the LLOD of available assays
- **Incomplete virologic response:** Two consecutive plasma HIV RNA levels ≥200 copies/mL after 24 weeks on an ARV regimen in a person who has not yet had documented virologic suppression on that regimen
- **Virologic blip:** After suppression, an isolated detectable HIV RNA level that is followed by a return to virologic suppression.
- **Low-level viremia:** Confirmed HIV RNA >LLOD but <200 copies/mL
- **Virologic failure:** The inability to achieve or maintain suppression of viral replication to HIV RNA level <200 copies/mL

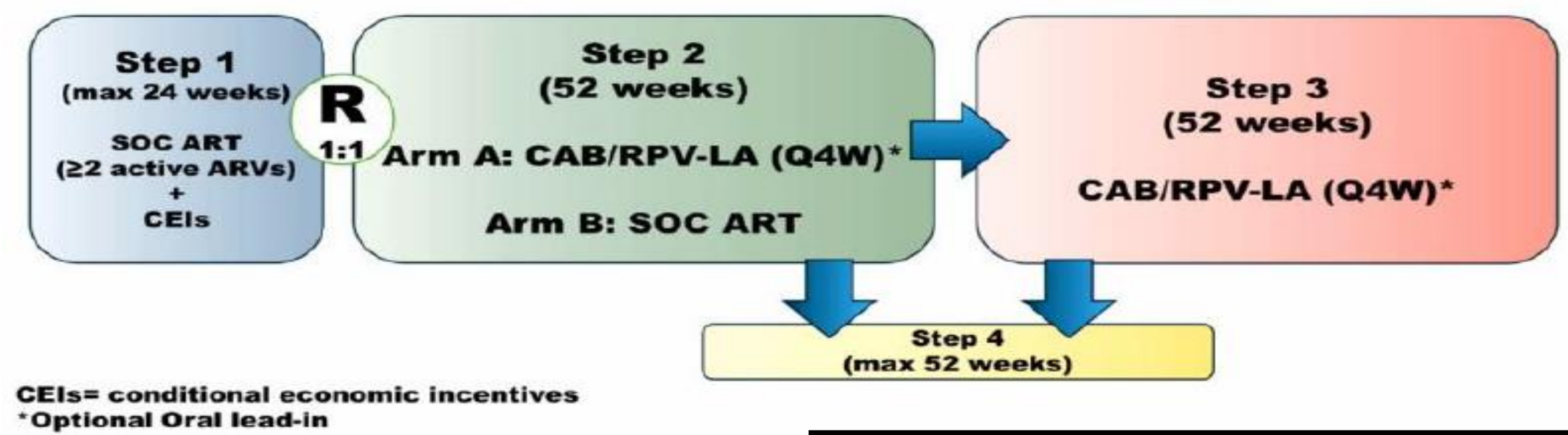
DHHS ART Guidelines. January 2025.

Comprehensive care needs for people living with HIV



LATITUDE (ACTG A5359): LA CAB/RPV q4wks in nonadherent patients

Phase 3, randomized, open-label trial in PLWH with barriers to adherence (poor viral response after oral ART ≥6 months or loss to clinical f/u with ART non-adherence for ≥ 6 months, no HBV, no ISTI or NNRTI Resistance



- **BL Step 1:** median 40 yrs, 30% female, 64% AA, BL>100,000 c/mL (14%); <200 c/mL (32%); median CD4 270 cells/uL
- **BL Step 2:** RNA >200 c/mL: LA CAB/RPV (17%); SoC (7%)

- **Primary outcome:** Regimen failure (confirmed VF or treatment discontinuation) in Step 2

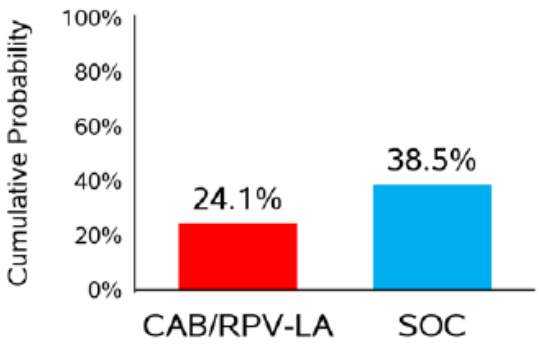
Rana AI, et al. CROI 2024, Abst. 212LB

LATITUDE (ACTG A5359): Outcomes

Primary Outcome

Regimen Failure

Difference	Nominal 98.75% CI
-14.5%	(-29.8%, 0.8%)



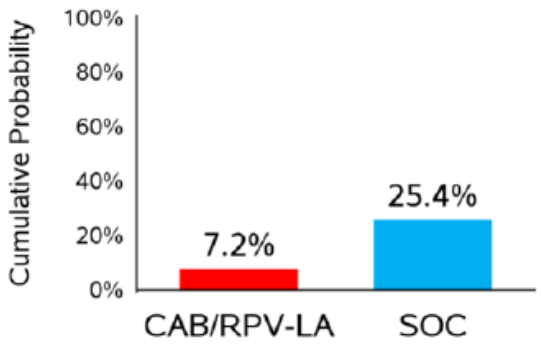
Number of participants

	CAB/RPV-LA	SOC
Regimen Failure	28	47
VF	5	28
TRT-DISC	23	19

Secondary Outcomes

Virologic Failure

Difference	Nominal 98.75% CI
-18.2%	**(-31.1%, -5.4%)**

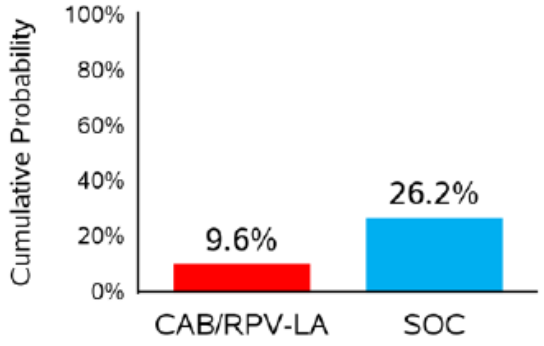


Number of participants

	CAB/RPV-LA	SOC
Virologic Failure	6	28

Treatment-related Failure

Difference	Nominal 98.75% CI
-16.6%	**(-29.9%, -3.3%)**

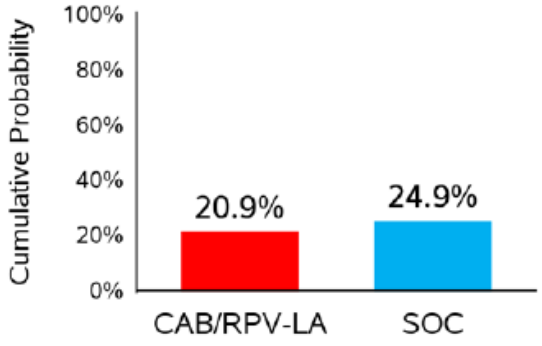


Number of participants

	CAB/RPV-LA	SOC
Treatment-related Failure	9	29
VF	6	28
TRT-DISC (AE)	3	1

Permanent Treatment Discontinuation

Difference	Nominal 98.75% CI
-4.1%	(-18.0%, 9.8%)



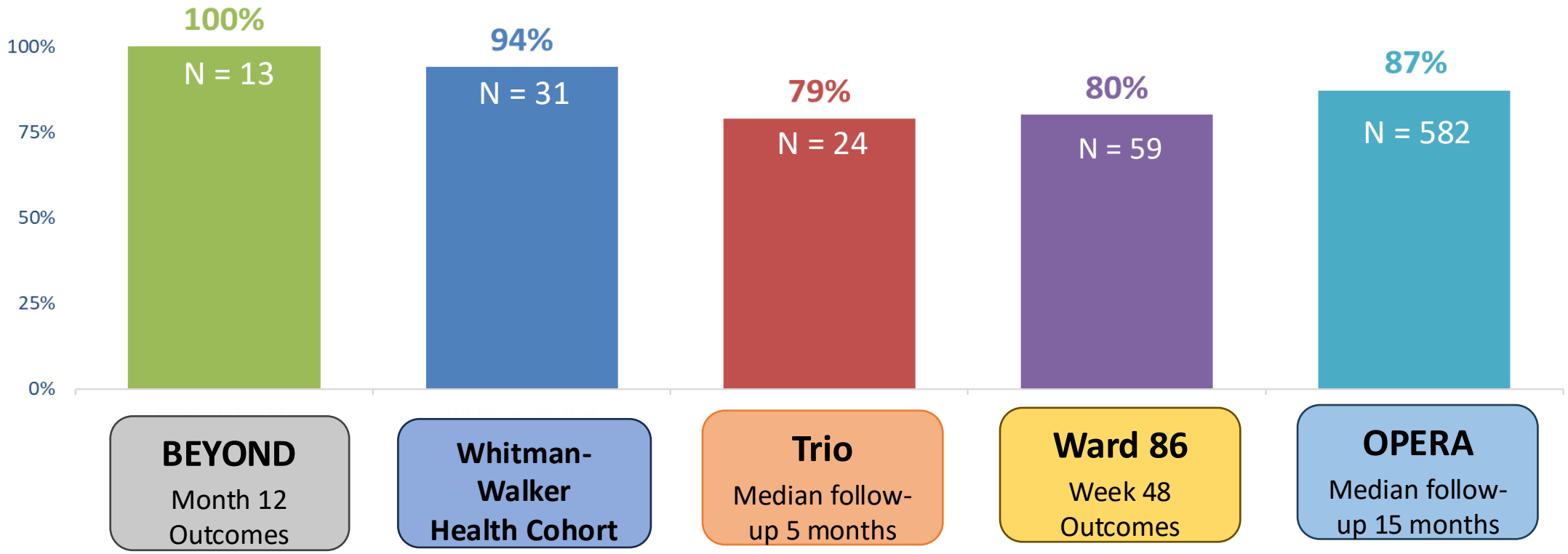
Number of participants

	CAB/RPV-LA	SOC
Permanent TRT-DISC	25	30

Rana AI, et al. CROI 2024, Abst. 212LB

LA CAB/RPV: Virologic Suppression in PWH with Detectable Viremia

Real-World People with HIV with Baseline VL ≥ 50 copies/mL (% suppressed)



IAS-USA and DHHS guidelines endorse this strategy for those with poor adherence with oral therapy and advanced HIV disease

Schneider S, et al. AIDS 2024. Poster THPEB099; Fessler D, et al. CROI 2024. Poster 1235; Elion RA, et al. IDWeek 2023. Poster 1592; Hickey MD, et al. *Clin Infect Dis.* 2024;ciae500 (online ahead of print); Hsu R, et al. CROI 2026. Poster 527. Gandhi R, et al. JAMA 2025; DHHS guidelines; https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv.

Press Release

For media and investors only

Issued: 6 October, London UK

ViiV Healthcare's long-acting HIV treatment *Cabenuva* (cabotegravir + rilpivirine) meets primary endpoint of superior viral suppression vs. daily oral therapy in people with viremia

- ***CROWN is the first large, phase IIIb international trial to evaluate the investigational use of long-acting Cabenuva versus daily oral therapy in people with a history of antiretroviral treatment and unsuppressed HIV***
- ***Results build on LATITUDE study and robust body of evidence supporting investigational use of long-acting cabotegravir + rilpivirine treatment in delivering viral suppression across treatment-experienced populations, including people with viremia at initiation***
- ***Data to be shared with health authorities for regulatory review***

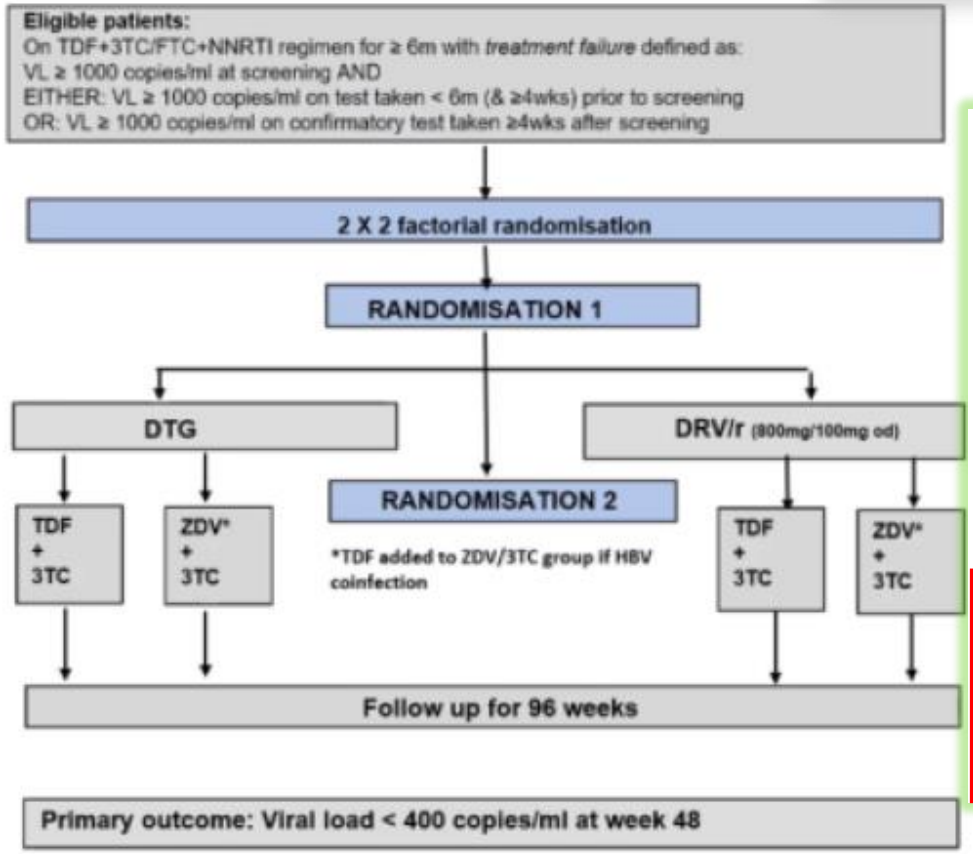
Managing virologic failure in patients with resistance

*National Clinician Consultation Service:
https://nccc.ucsf.edu/clinician-consultation/hiv-aids-management/

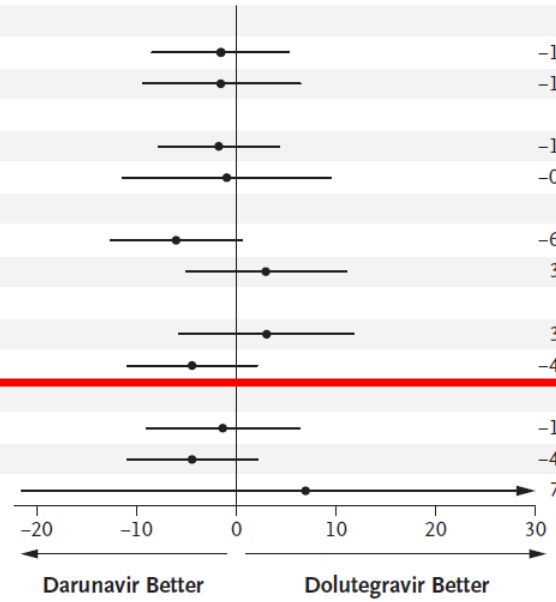
Dolutegravir or Darunavir in Combination with Zidovudine or Tenofovir to Treat HIV

Nicholas I. Paton, M.D., Joseph Musaazi, M.Sc., Cissy Kityo, Ph.D., Stephen Walimbwa, M.D., Anne Hoppe, Ph.D., Apolo Balyegisawa, M.D., Arvind Kaimal, M.D., Grace Mirembe, M.Med., Phionah Tukamushabe, R.N., Gilbert Ategeka, M.D., James Hakim, F.R.C.P., Henry Mugerwa, M.D., Abraham Siika, M.Med., Jesca Asienzo, B.P.L.M., Barbara Castelnuovo, Ph.D., Agnes Kiragga, Ph.D., and Andrew Kambugu, M.Med., for the NADIA Trial Team*

NADIA



Subgroup	Dolutegravir	Darunavir	Difference in Percentage Points (95% CI)
	no. of patients/total no. (%)		
NRTI randomization group			
Tenofovir	108/118 (91.5)	107/115 (93.0)	−1.5 (−8.4 to 5.3)
Zidovudine	104/117 (88.9)	103/114 (90.4)	−1.5 (−9.3 to 6.4)
Viral load at baseline			
<100,000 copies/ml	153/169 (90.5)	154/167 (92.2)	−1.7 (−7.7 to 4.3)
≥100,000 copies/ml	59/66 (89.4)	56/62 (90.3)	−0.9 (−11.4 to 9.5)
CD4+ cell count at baseline			
<200 cell/mm³	112/125 (89.6)	108/113 (95.6)	−6.0 (−12.5 to 0.6)
≥200 cell/mm³	100/110 (90.9)	102/116 (87.9)	3.0 (−5.0 to 11.0)
Sex			
Male	87/95 (91.6)	77/87 (88.5)	3.1 (−5.7 to 11.8)
Female	125/140 (89.3)	133/142 (93.8)	−4.4 (−10.9 to 2.1)
No. of predicted active NRTIs			
0	85/92 (92.4)	75/80 (93.8)	−1.3 (−8.9 to 6.2)
1	107/118 (90.7)	116/122 (95.1)	−4.4 (−10.9 to 2.1)
≥2	13/18 (72.2)	15/23 (65.2)	7.0 (−21.4 to 35.4)



INSTI resistance in 9 (2.3%) PI resistance in 0

Paton NI, et al. N Engl J Med 2021;385: N330-41.

Managing confirmed virologic failure (Consider expert consultation*)

- If a fully active second generation INSTI or boosted PI available:
  - DTG + tenofovir + emtricitabine
  - BIC/TAF/FTC
  - Boosted DRV + tenofovir + emtricitabine
  - Boosted DRV + second generation INSTI ± NRTIs
- Neither 2nd generation INSTI or boosted PI available (use 2-3 active agents ± partially active):
  - Lenacapavir
  - Maraviroc (if R5 only)
  - Fostemsavir
  - Ibalizumab
  - Other?

- Unboosted PIs not recommended since 2008
- 2nd gen INSTI largely replaced 1st gen in 2014

*National Clinician Consultation Service: https://nccc.ucsf.edu/clinician-consultation/hiv-aids-management/

Populations Likely to be Out of Care and Virally Unsuppressed in the U.S.?

- Associated demographic factors
  - Younger age
  - Black/African American
  - Cisgender women
  - Transgender & gender diverse
- Key Barriers: The big 3
  - Unstable housing
  - Substance use disorders
  - Mental health disorders

Underlying Factors

Poverty
Racism
Early life trauma
Stigma
Social isolation
Incarceration
Food insecurity
Domestic violence
Health beliefs
Migration…..

Sources: Bulsara, AIDS and Behavior, 2016; Aidala, AJPH 2016; Mautner, Population Health Management 2013, Dickson-Gomez, AIDS and Behavior 2016; Levison, AIDS Patient Care and STDs, 2016; O'Donnell, AIDS Care, 2017; Ports KA, J Urban Health, 2017; Ross J, Curr Opin Infect Dis

HIV Care Re-Engagement Interventions



AIDS and Behavior (2022) 26:132–146
https://doi.org/10.1007/s10461-021-03365-y

SUBSTANTIVE REVIEW

Re-Engagement into HIV Care: A Systematic Review

Natalia Blanco[1] · Marie-Claude C. Lavoie[1] · Emily Koech[2] · David J. Riedel[1] · Caroline Ngeno[3] · Sylvia Adebajo[4] · Emilie Ludeman[5] · Kristen A. Stafford[1]

(125 U.S. studies, published through 2020)

Using data to identify, trace & contact out-of-care PWH

Health workers provide added support

Multicomponent interventions (most with counseling, reminders)

"Irrespective of the interventions, mixed results were found for re-engagement into care or ART re-initiation. **None of the studies led to an improvement in viral suppression."**

Blanco N, AIDS and Behav 2022; Higa D, AIDS 2022

ARV Pipeline (partial list)

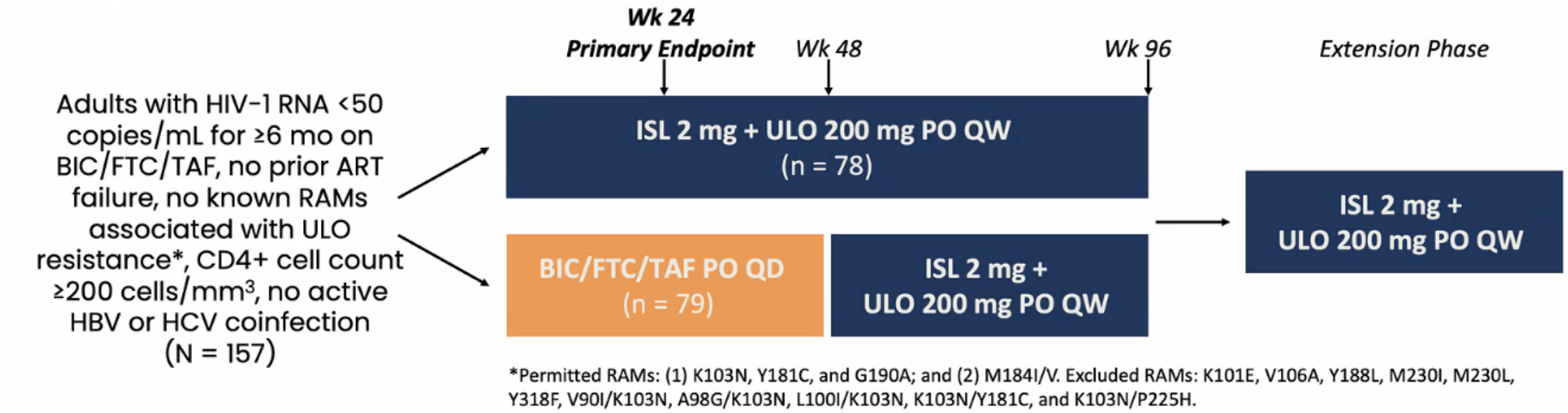
Class	Phase 1	Phase 2	Phase 3	Approved
NRTTI			**alimatravir (AMI)** (q1 mo po) **islatravir (ISL)/LEN*** (qwk po)	**ISL/DOR** (qd po)
NNRTI	**bavtavirine** (GS-5894; q1 mo po)	**ulonivirine (ULO)** (qwk)	**RPV-ULA** (q4 mos IM)	
INSTI	**VH-310** (q6 mo CAB pro-drug)	**GS-3242** (q6 mo IM) **lepetegravir** (GS-1720; qwk po) **VH-184**	**CAB-ULA** (q4 mos IM) **LEN** (yearly IM)	**CAB+RPV** (q2 mo IM) **CAB+LEN*** (q2+q6 mo IM/SC) **BIC/LEN*** (qd po)
Capsid	**GS-3107** (q1 mo po LEN pro-drug) **VH-359**	**VH-499** (q6 mo IM)		
Entry		**TMB-365**		
BNAb	**VH-079** (bispecific)	**lotivibart (LVB)+CAB** (q4+q2 mo IV/IM) **TMB-380** (VRC07-523LS; q 2mo)	**LEN+TAB+ZAB** (q6 mo IV/IM)	

* Individual drugs approved, regimen remains investigional

Gulick R. HIV Glasgow 2026,Plenary

Switch to weekly Islatravir (ISL) 2 mg plus MK-8507 (Ulonivirine [ULO]) 200 mg vs continued BIC/TAF/FTC

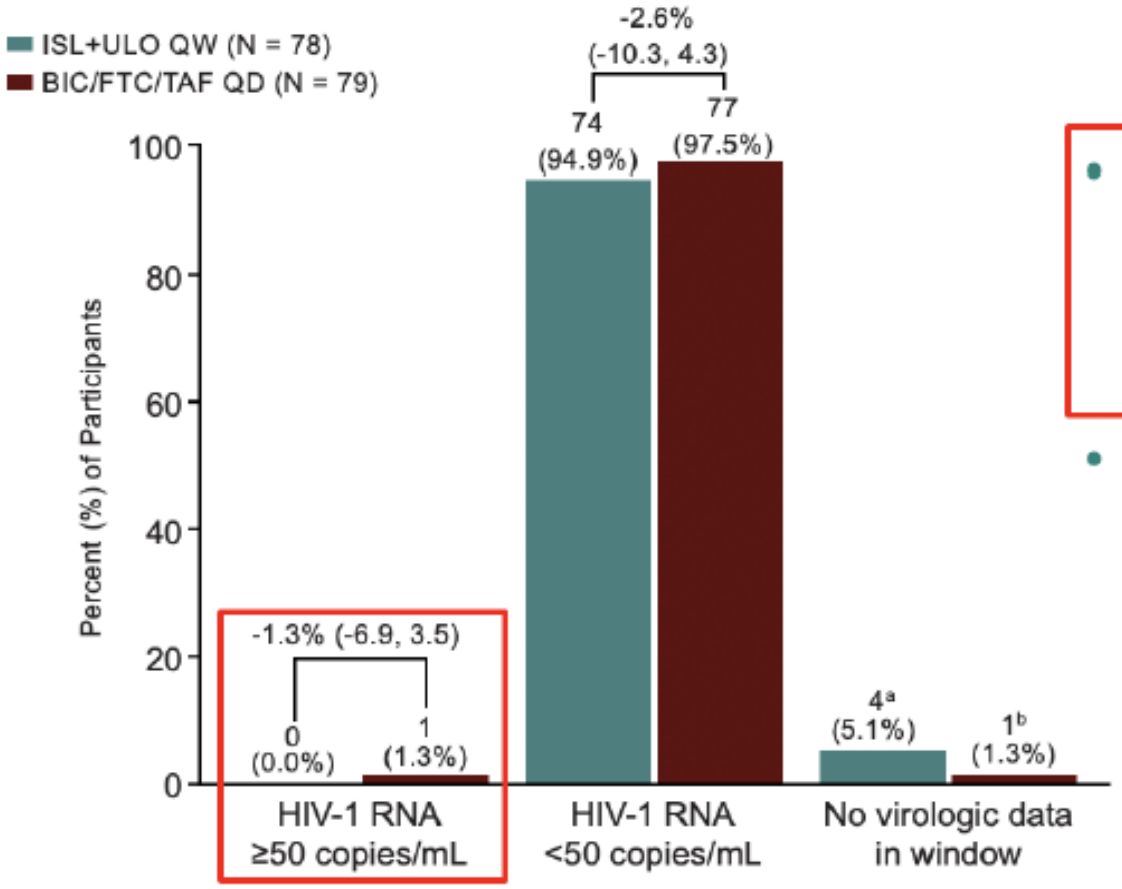
- ULO is investigational NNRTI with activity against NNRTI-resistant variants
- Multicenter, open-label phase 2b, RCT of ISL plus ULO: Primary endpoint HIV RNA ≥50 copies/mL at wk 24; AEs, overall and leading to discontinuation



Luetkemeyer A, et al. AIDS 2026, Abst OAB1405LB

Switch to weekly oral ISL plus ULO: Efficacy

Virologic outcomes (FDA snapshot approach)

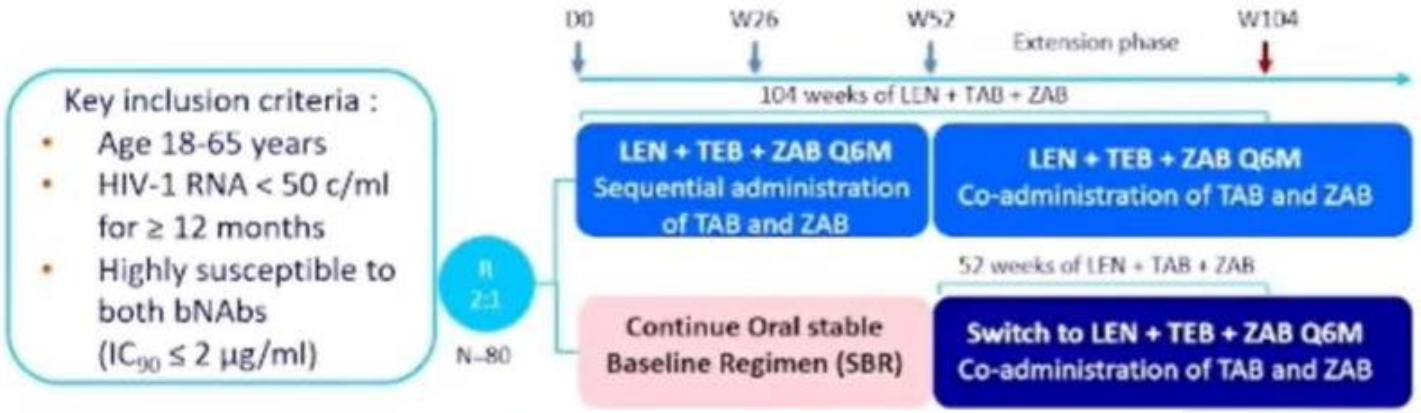


- **Primary endpoint**: at Week 24, **0.0% (0/78) of the participants who switched to ISL+ULO had HIV-1 RNA ≥50 copies/mL** vs 1.3% (1/79) of those continuing BIC/FTC/TAF (difference: -1.3%; 95% CI: -6.9, 3.5)
- No participants had HIV-1 RNA ≥200 copies/mL, and thus none met criteria for post-baseline resistance analysis

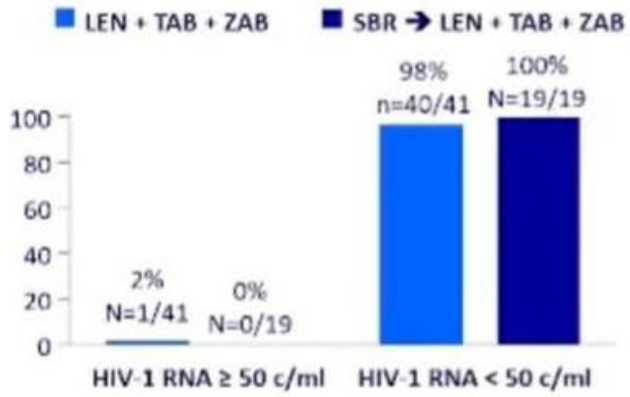
Luetkemeyer A, et al. AIDS 2026, Abst OAB1405LB

Twice yearly LEN + Teropavimab (TAB) plust Zinlirvimab (ZAB)

Twice yearly LEN + Teropavimab (TAB) + Zinlirvimab (ZAB)



Virologic outcomes at W104 (M=E)



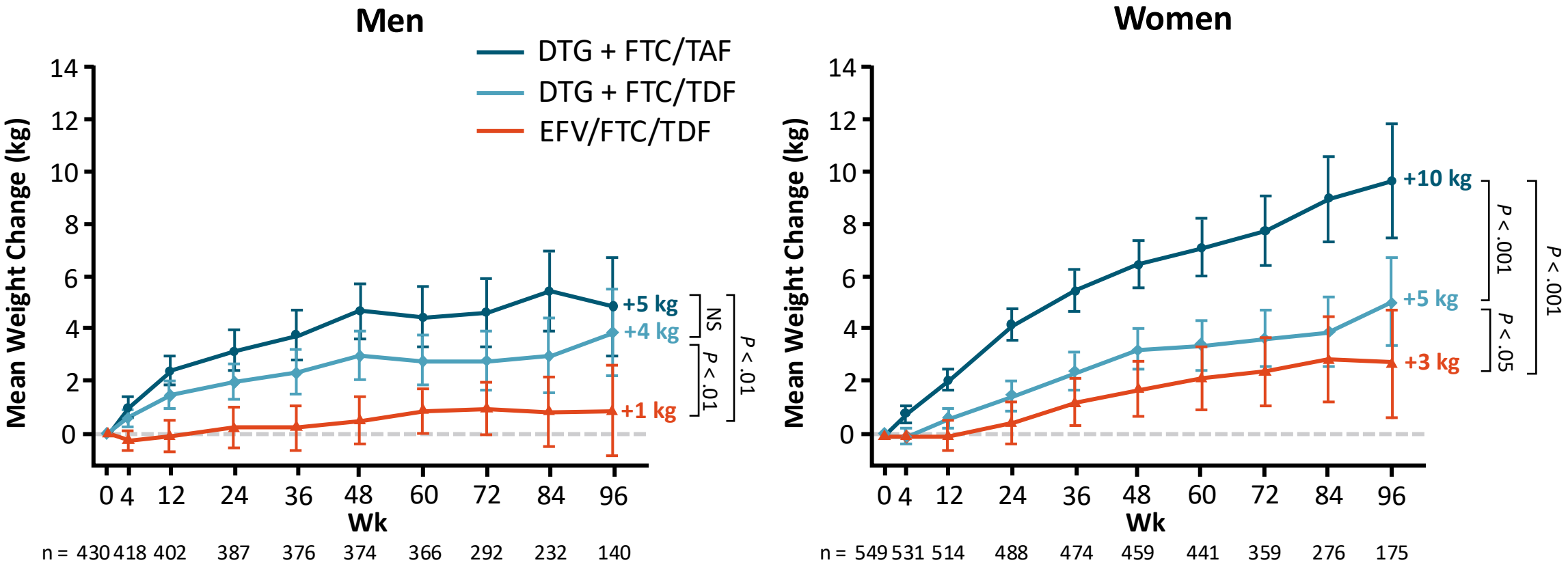
1 participant in the deferred LEN+TAB+ZAB group had confirmed virologic rebound at W90, discontinued study treatment prior to W104 : exluded from M=E analysis

McMahon JH, AIDS 2026; Abs OAB 1403

Managing comorbid conditions in PLWH

ADVANCE: Mean Change in Weight After ART

- Significantly greater weight increase* with DTG vs EFV, with TAF vs TDF; plateauing in weight gain after Wk 48 observed in men but not in women

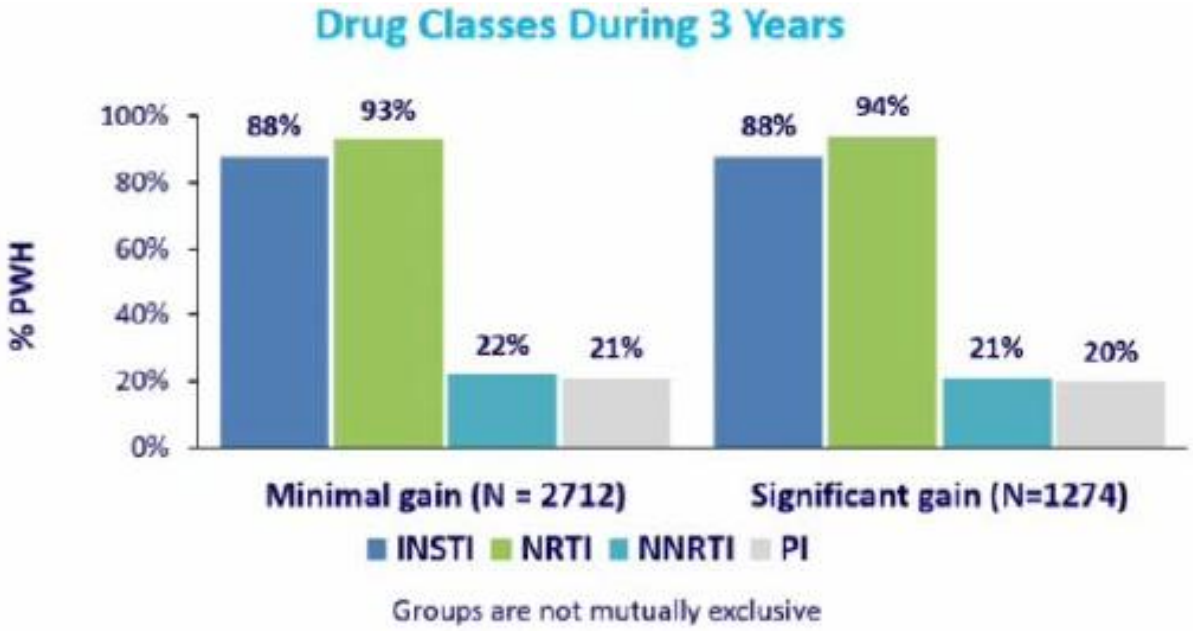


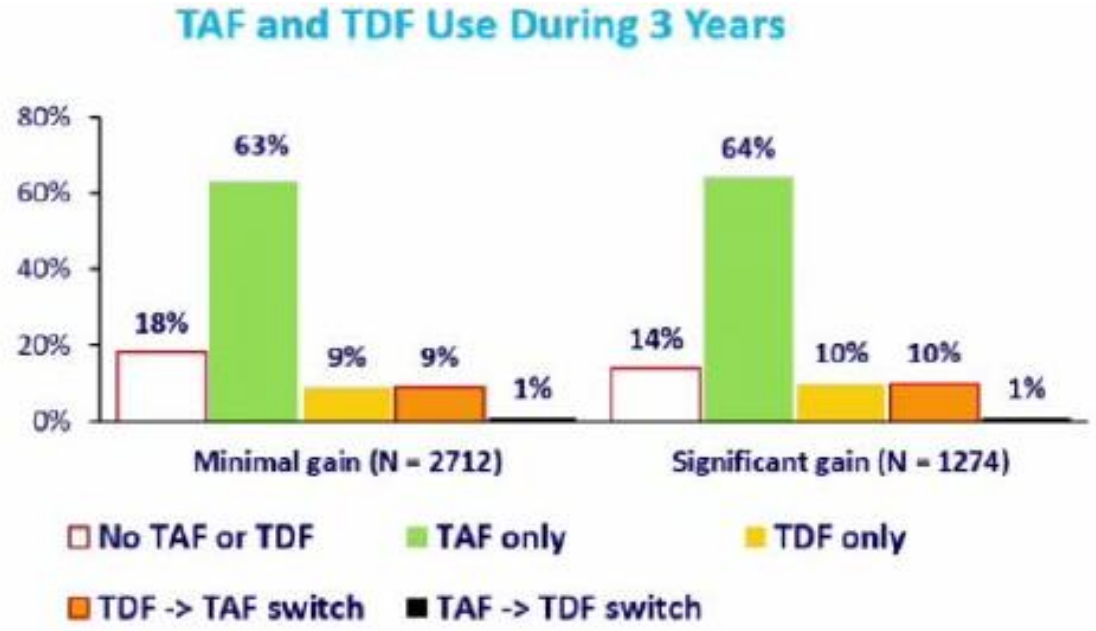
Hill. IAS 2019. Abstr MOAX0102LB. Reproduced with permission.

*Wilcoxon rank-sum comparison at Wk 96.

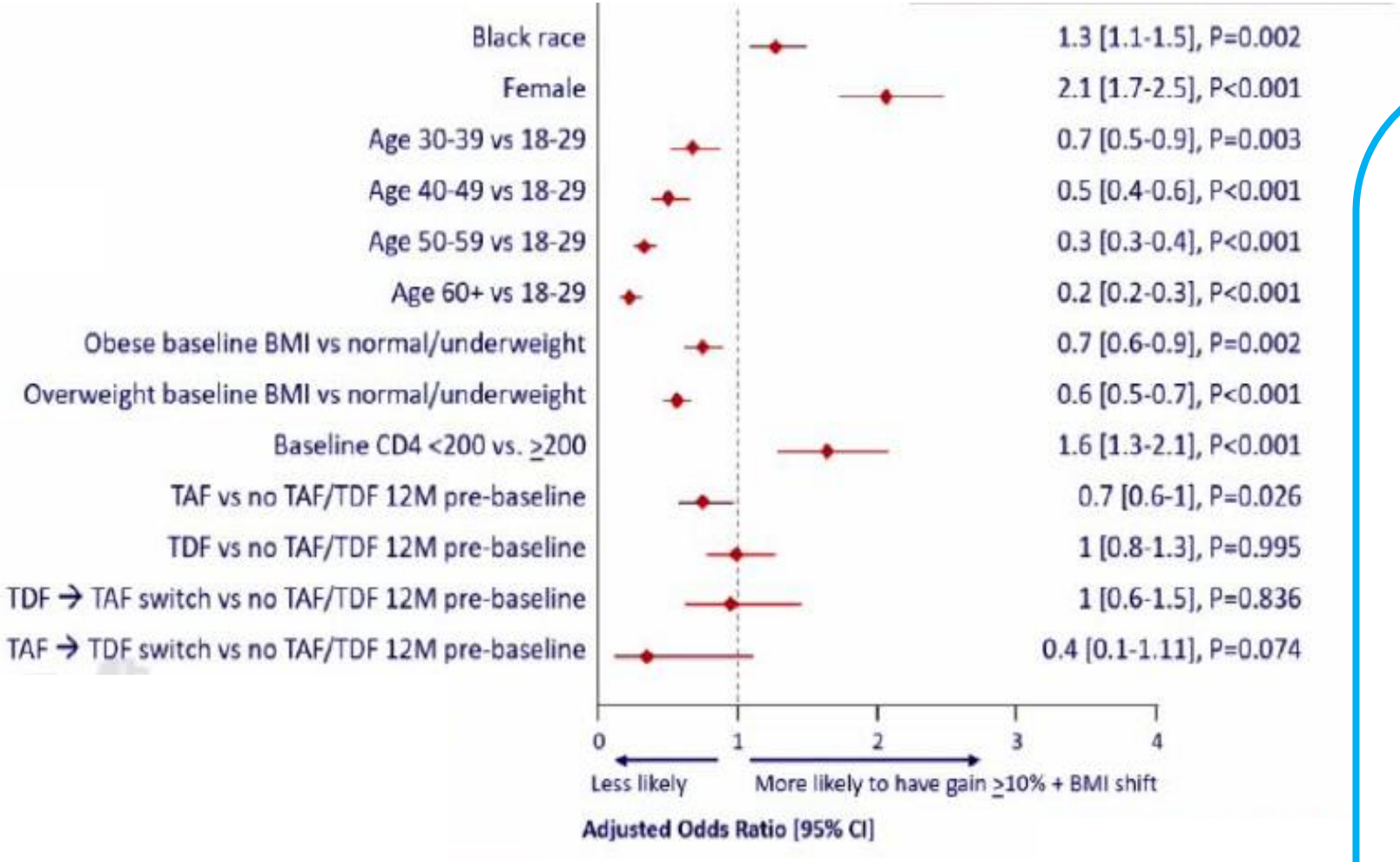
Predictors of weight gain over 3 years

- Retrospective case-control study, TRIO HIV Research data base (12 clinics in US)
- 2015-2023: adults virologically suppressed during 3 years
- Case: >10% weight gain (n=1274)
- Control: 0 - <5% weight gain (n=2712)





Elion RA, et al. IAS 2025, Abst. OAB0204



Conclusion

Weight gain observed in PWH is reflective of the general population and community characteristics rather than direct effect of ART

Significant weight gain (>10%) associated with

- Black race
- Female gender
- Younger baseline age
- Normal baseline BMI
- Lower baseline CD4 count
- No ART factors
- TAF exposure vs. no TAF or TDF exposure 12 months pre-baseline was associated with lower odds of significant weight gain during 3 yrs

A5391: Randomized 3-arm controlled trial for people with obesity on INSTI + TAF (The DO-IT Trial)

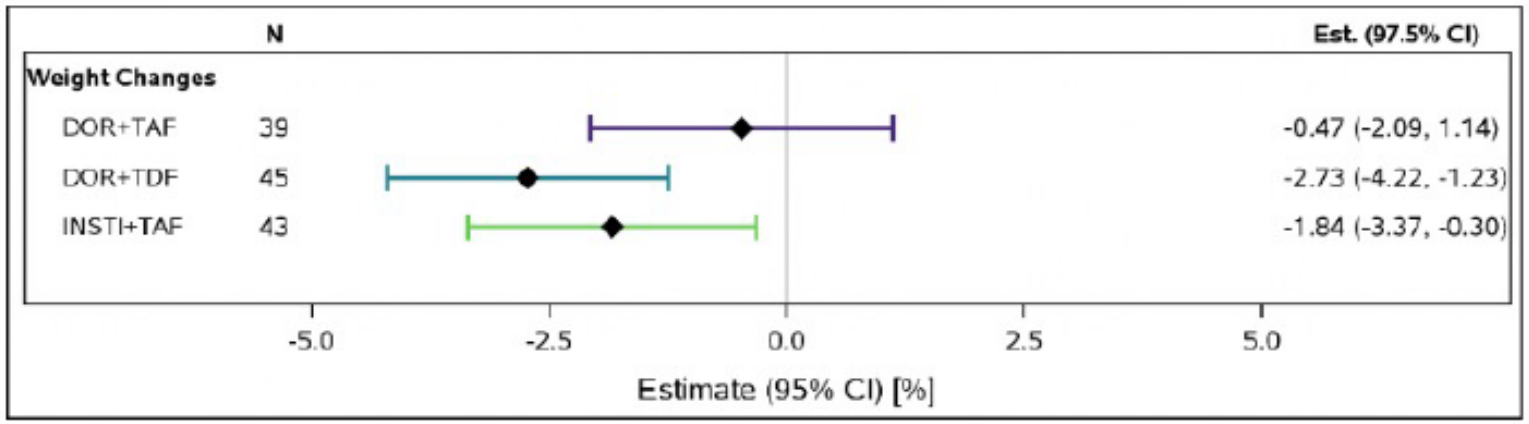
- July 2021-Nov 2023, 145 from 25 sites in US randomized 1:1:1
- 49% female, 53% black and 18% Hispanic
- Median age 49 yrs, BMI 34.9 kg/m^2, CD4 688 cells/uL
- Median time on current ART= 3.4 yrs, 86%on BIC, 13% DTG
- 65% had >10% wt gain in first 1-3 yrs of INSTI-based regimen

Koethe J, et al. IAS 2025, Abst. OAB0206LB

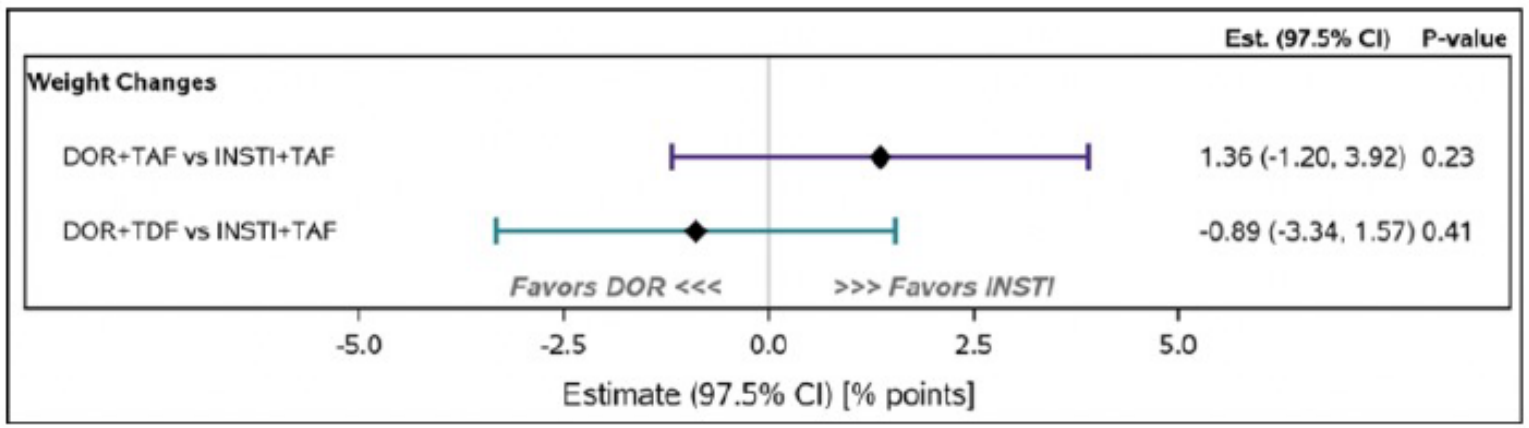
IAS 2025

Primary Outcome: Weight Change at 48 Weeks

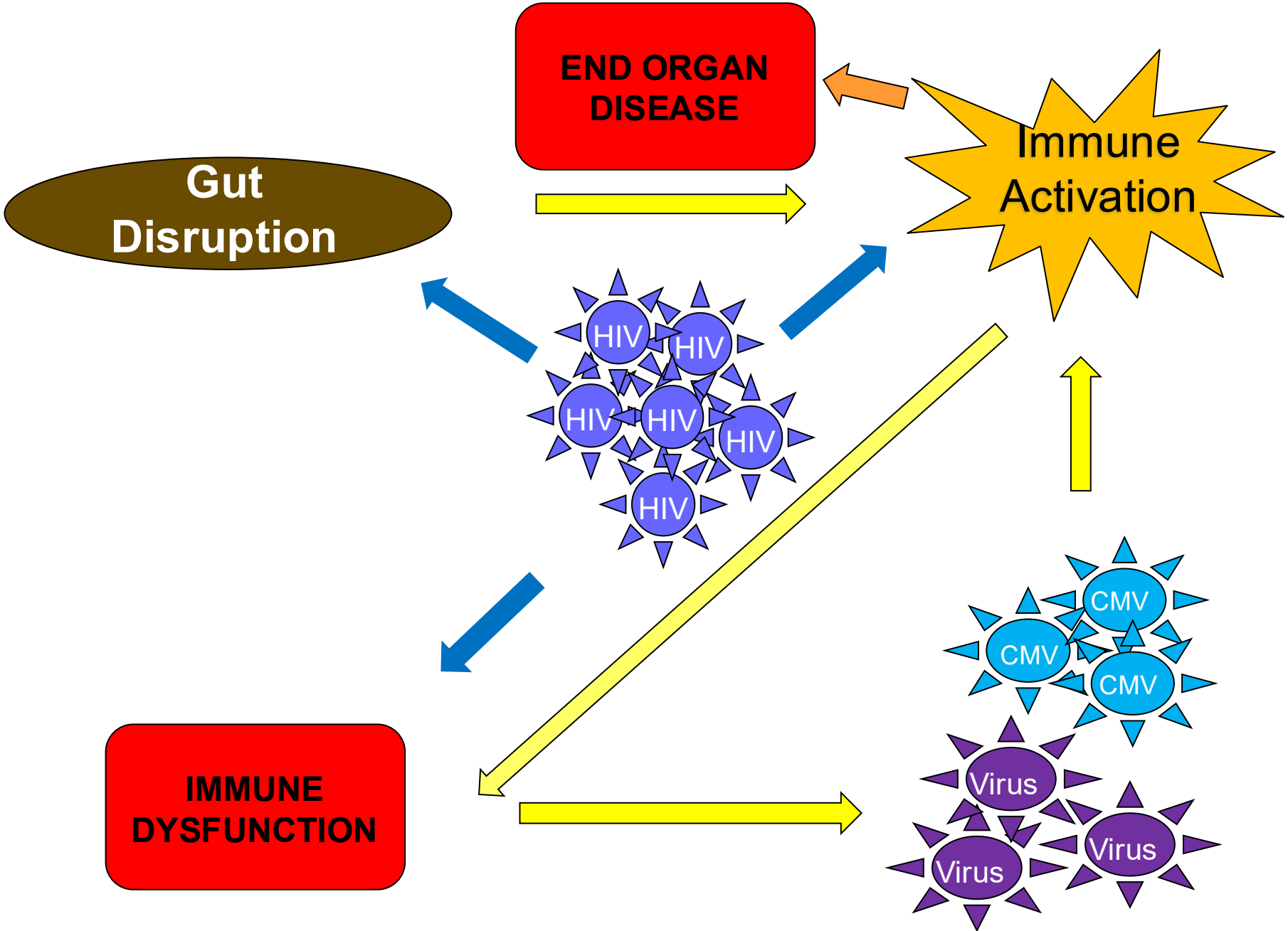
Within Arm:



Pairwise Treatment Arm Comparisons:

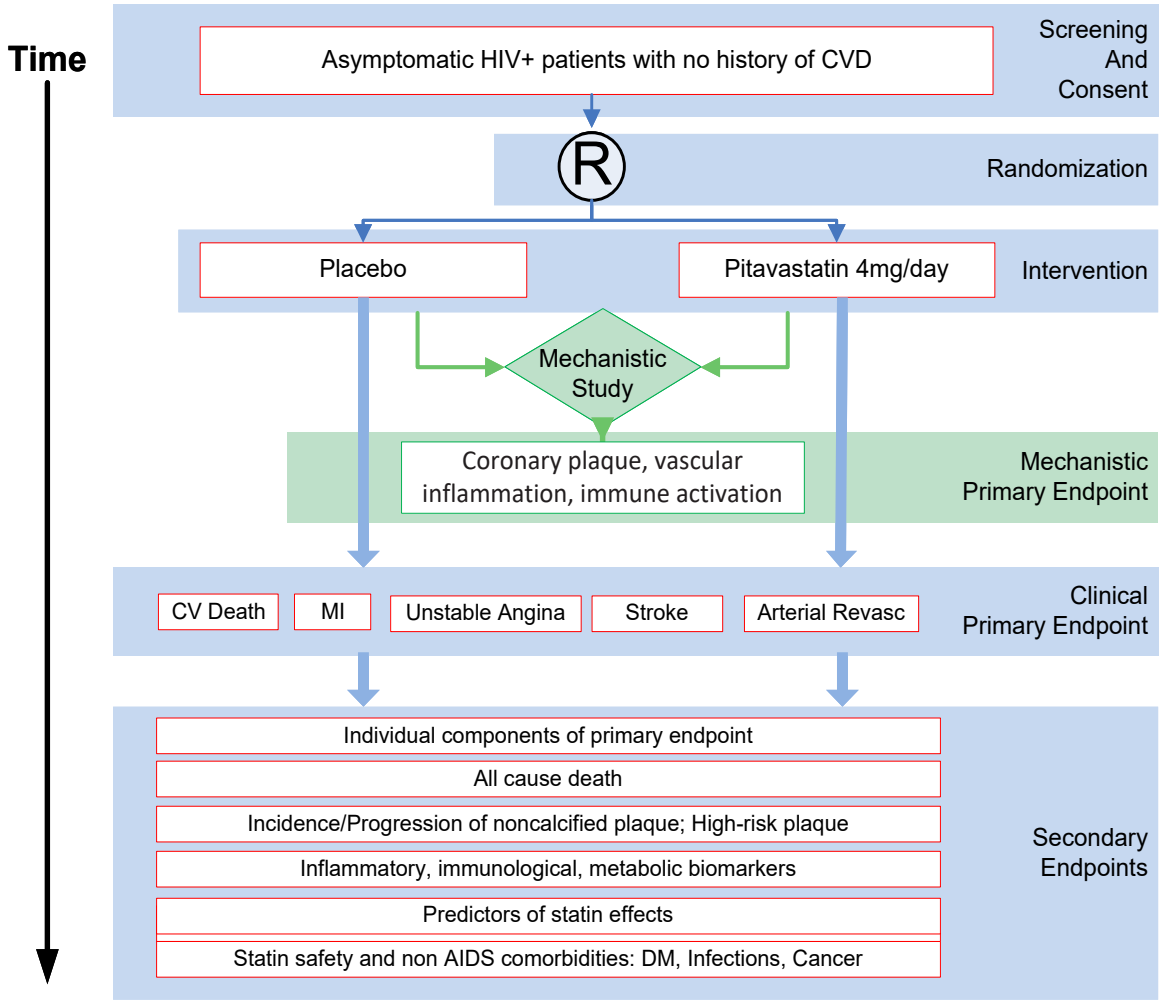


Chronic inflammation persists on antiretrovirals



REPRIEVE

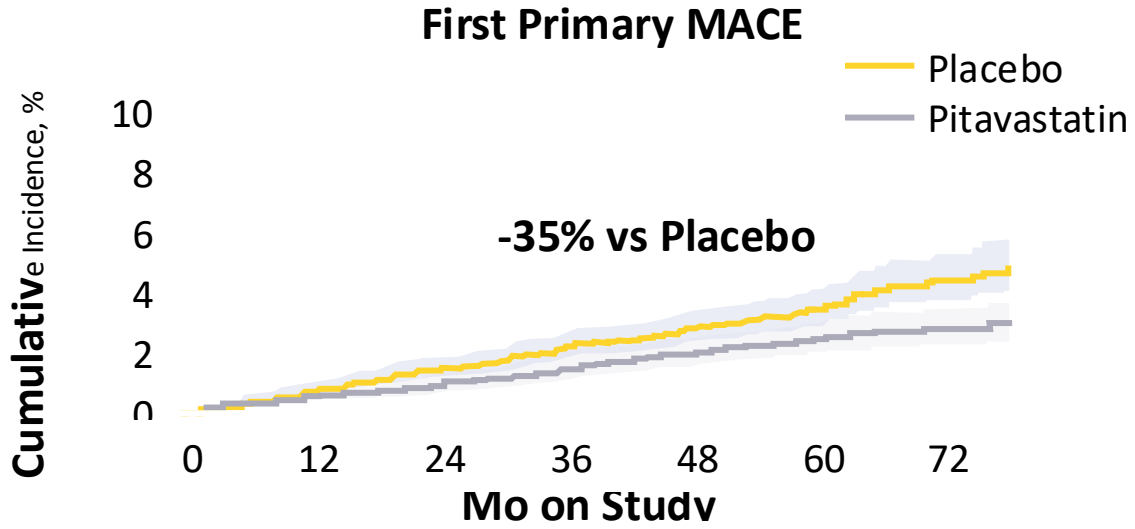
Randomized Trial to Prevent Vascular Events in HIV



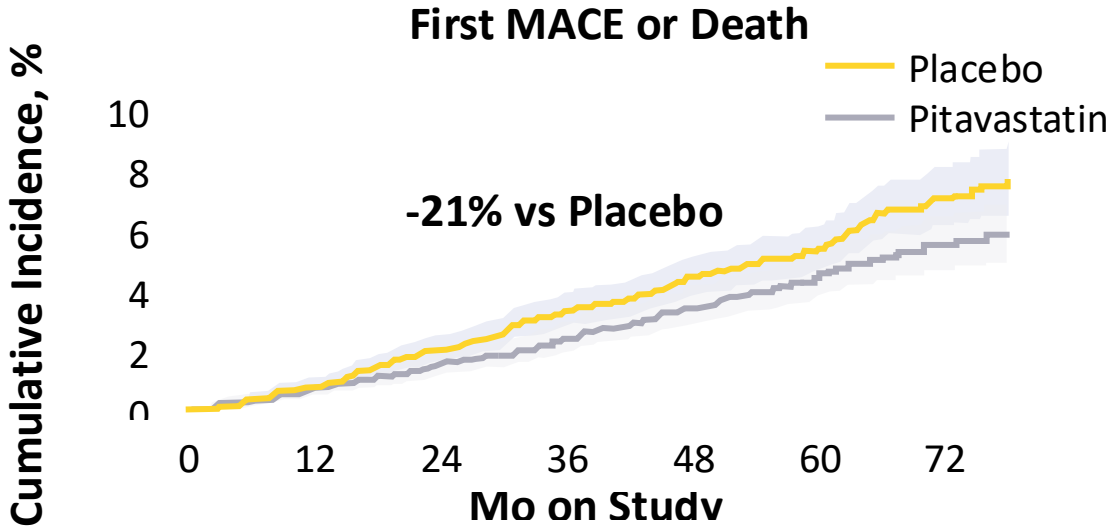
Grinspoon. NEJM. 2023

REPRIEVE: Time to First Major Cardiovascular Event

- Baseline characteristics well balanced between treatment arms; median ASCVD risk score 4.5% (IQR: 2.1 to 7.0) and median LDL cholesterol 108 mg/dL (IQR 87 to 128)
- Pitavastatin prolonged time to first MACE vs placebo



	Cumulative incidence of event						
	0%	0.6%	1.0%	1.4%	1.9%	2.4%	2.7%
	0%	0.7%	1.4%	2.1%	2.7%	3.4%	4.4%
Patients at Risk, n							
Pitavastatin	3888	3647	3475	3364	2997	1947	1052
Placebo	3881	3693	3506	3356	2997	2182	959

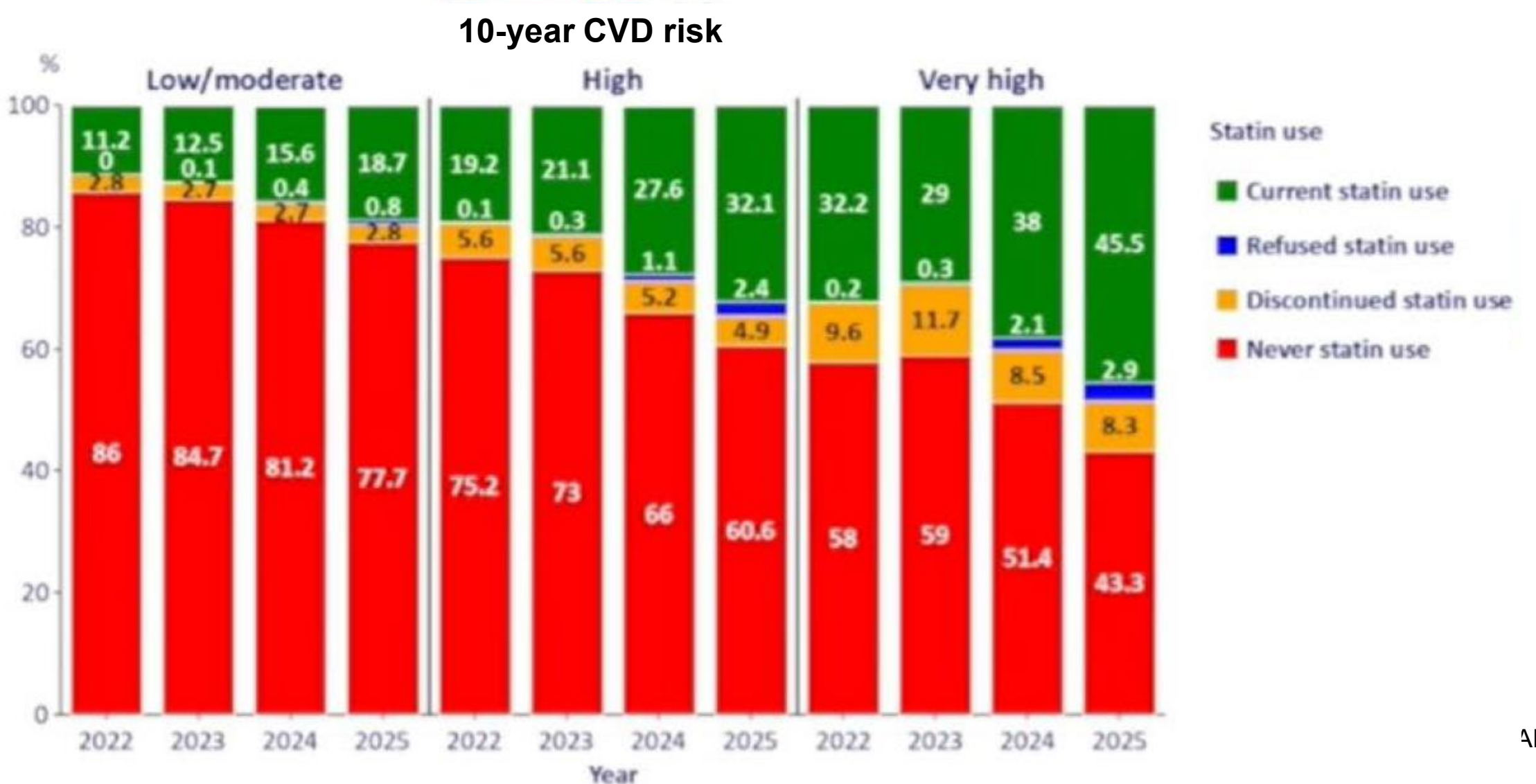


	Cumulative incidence of event						
	0%	0.8%	1.6%	2.4%	3.4%	4.5%	5.5%
	0%	0.8%	2.0%	3.3%	4.4%	5.3%	7.1%
Patients at Risk, n							
Pitavastatin	3888	3647	3475	3364	2998	1948	1027
Placebo	3881	3693	3506	3356	2997	1975	919

Grinspoon. NEJM. 2023

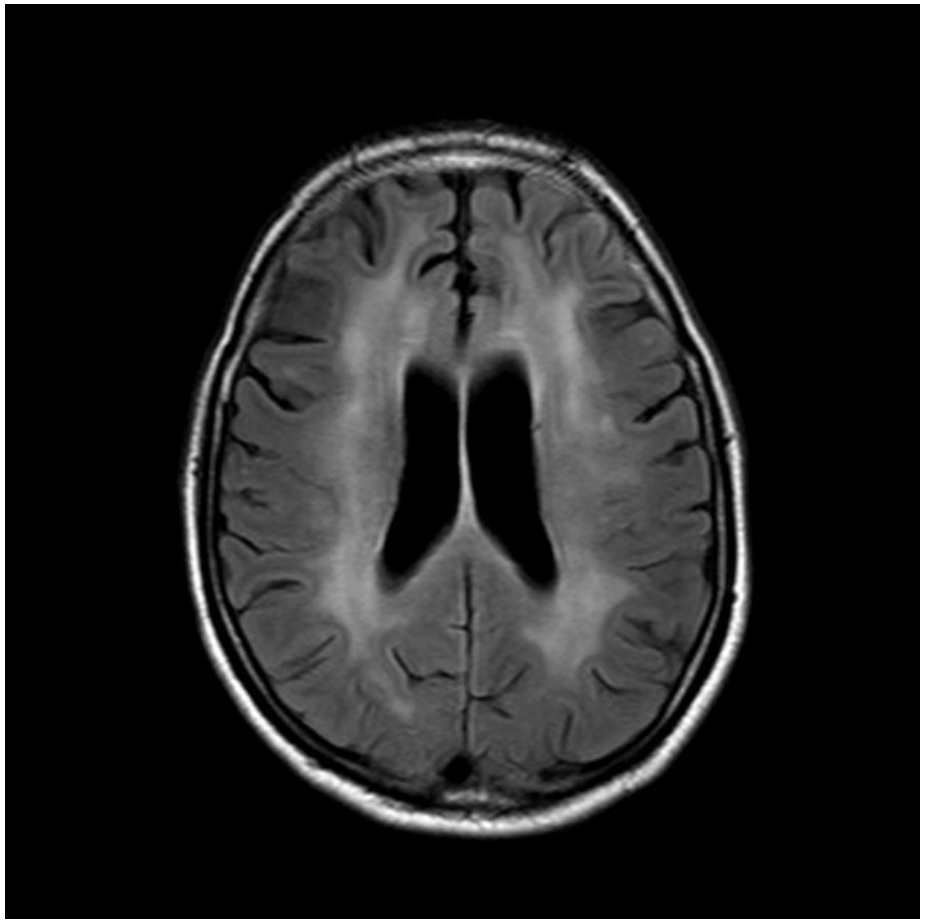
Statin for primary CVD prevention (Netherlands)

ATHENA Netherlands cohort, PLWH 40-75 yrs without CVD event or DM (N=15,243)



HIV encephalopathy: Cognitive Impairment

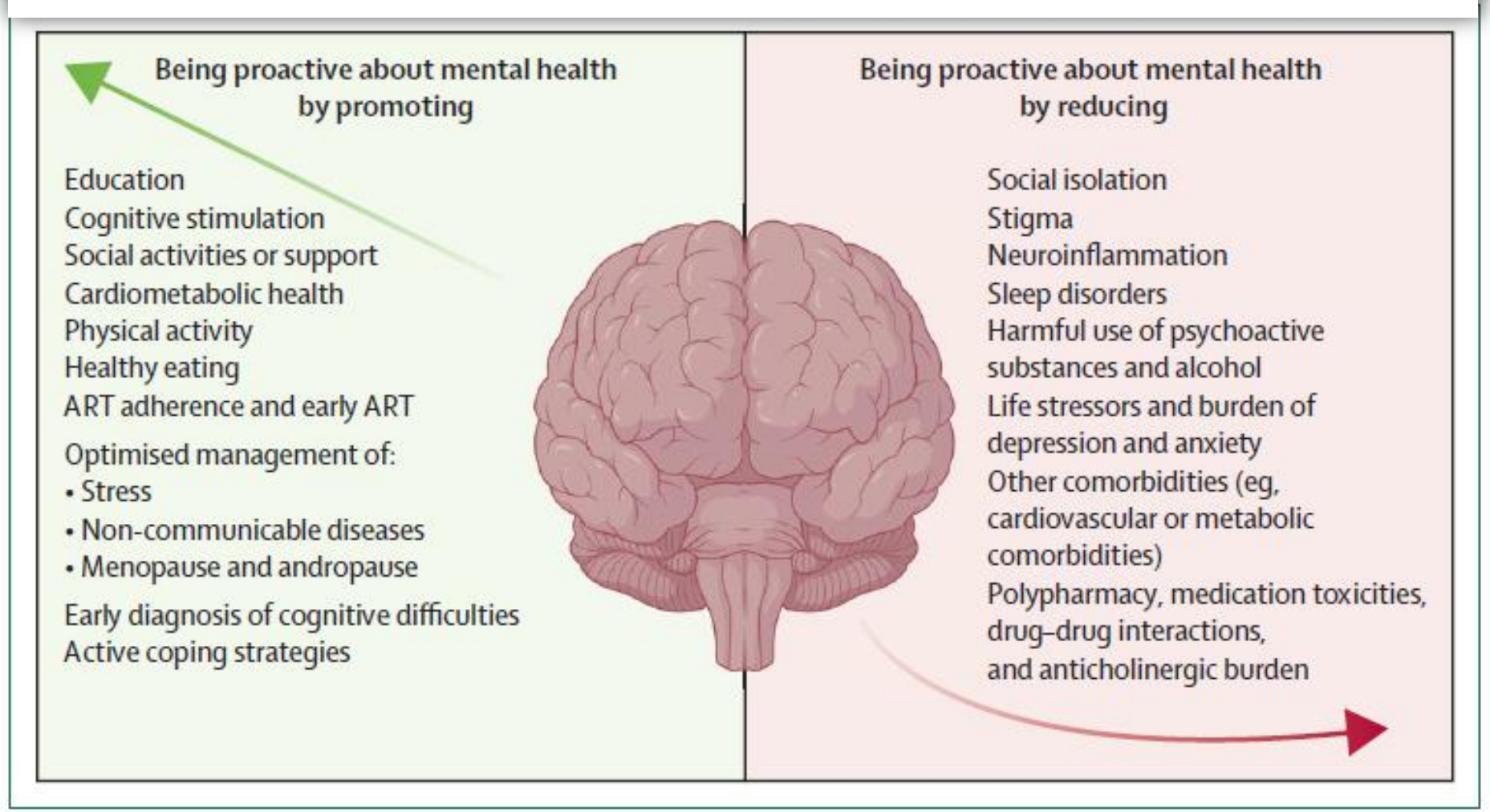
- Highly prevalent
  - ALLRT
    - 39% mild impairment
    - 21% developed impairment after baseline
  - CHARTER
    - 40% neurocognitive impairment
- Pathogenetic mechanisms
  - HIV in the CNS
  - Ongoing immune activation
- IDSA management guidelines recommend screen for and work-up cognitive deficits*



*Horberg M et al. CID 2024

Fostering healthy cognitive ageing in people living with HIV

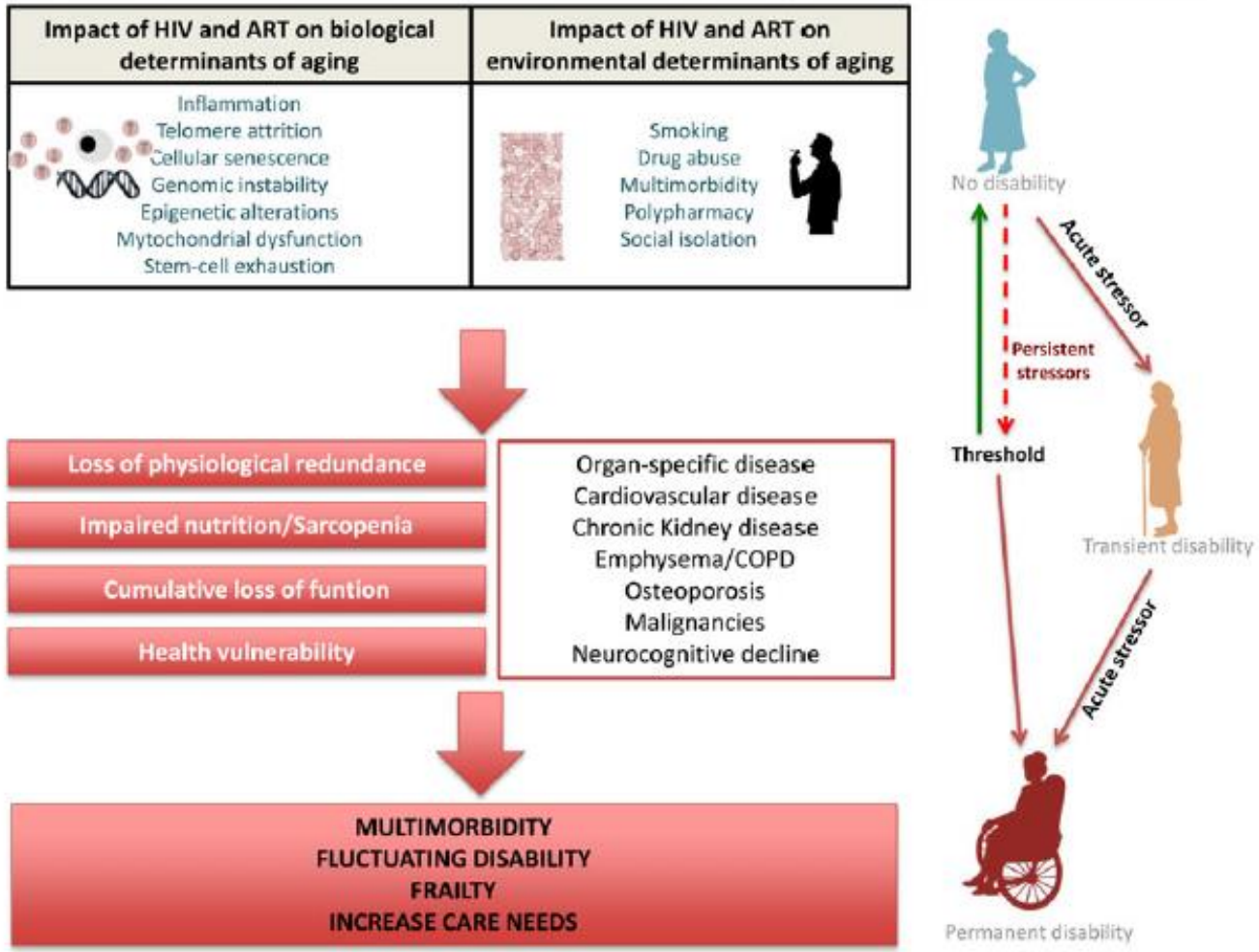
Lucette A Cysique, Jules Levin, Chris Howard, Jeff Taylor, John Rule, Jane Costello, Jane Bruning, Priscilla Njeri, Amy B Mullens, Edwina Wright, Hetta Gouse, Kirstie Daken, Mattia Trunfio, Htein Linn Aung, Reuben N Robbins, Christopher M Ferraris, Jose A Muñoz-Moreno, Steven P Woods, David J Moore, Christopher Power, Pui Li Wong, Kejal Hasmukharay, Primrose Nyamayaro, Jaime Vera, Reena Rajasuriar, Robert K Heaton, Karl Goodkin, Scott Letendre, Ronald J Ellis, Bruce J Brew, Sean B Rourke*, on behalf of the NeuroHIV and Aging Advocacy Group†*



Cysique L, et al. .Lancet HIV 2024, doi.org/10.1016/S2352-3018(24)00248-0

Human Immunodeficiency Virus as a Chronic Disease: Evaluation and Management of Nonacquired Immune Deficiency Syndrome-Defining Conditions

Sergio Serrano-Villar,[1] Félix Gutiérrez,[2] Celia Miralles,[3] Juan Berenguer,[4] Antonio Rivero,[5] Esteban Martínez,[6] and Santiago Moreno[1]



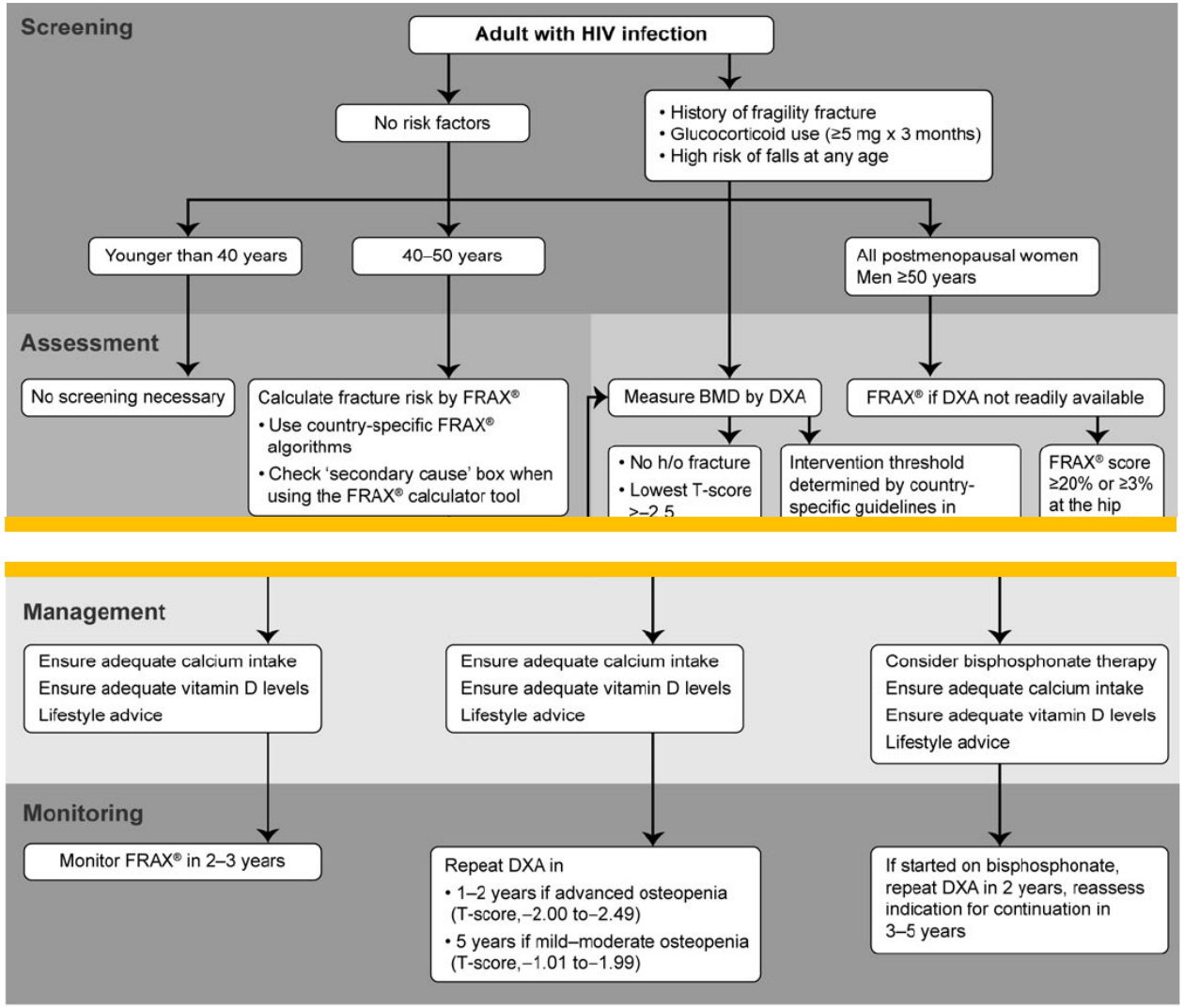
IDSA Primary Care Guidelines 2024[2]

- Annual screening for frailty should be considered in PLWH over 50 years of age
  - Frailty Phenotype or Frailty Index
  - The most effective interventions to prevent and treat frailty are increasing physical activity and structured exercise
  - Nutritional optimization is efficacious and increases the efficacy of an exercise intervention
  - Diagnosing and treating depression is also important

1. Serrano-Villar et al. OFID 2016, doi: 10.1093/ofid/ofw097; 2. Horberg M et al. CID 2024

Bone Health in People Living with HIV



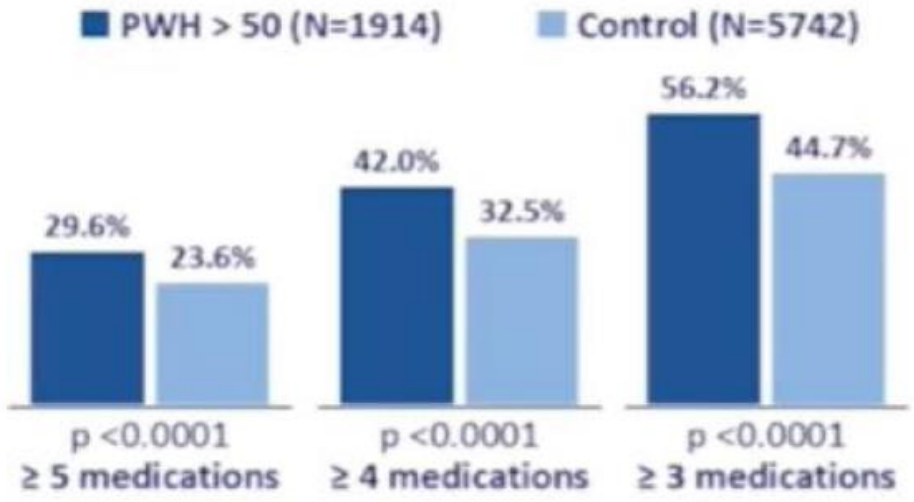


Ahmed M, et al. Microorganisms 2023; 11:789; Brown TT, et al. CID 2015; 60:1242-51

Polypharmacy and potential drug interactions in PLWH over 50 years

- Case-control study (2024)
- Representative 2% of PWH from French national health data system (N=1914 PLWH >50 yrs
- Controls matched on year of birth, sex, socio-economic status (n=5742)

Exposure to polypharmacy by group and number of non-ART medications



Ailovena C, et al Glasgow 2026, Abst PO73

Recommended Adult Immunization Schedule
for ages 19 years or older

UNITED STATES 2025

Vaccine	19–26 years	27–49 years	50–64 years	≥65 years
COVID–19	1 or more doses of 2024–2025 vaccine (See Notes)			2 or more doses of 2024-2025 vaccine (See Notes)
Influenza inactivated (IIV3, ccIIV3) **Influenza recombinant** (RIV3)	1 dose annually			1 dose annually (HD–IIV3, RIV3, or aIIV3 preferred)
Influenza inactivated (aIIV3; HD–IIV3) **Influenza recombinant** (RIV3)	Solid organ transplant (See Notes)			
Influenza live, attenuated (LAIV3)	1 dose annually			
Respiratory syncytial virus (RSV)	Seasonal administration during pregnancy (See Notes)		60 through 74 years (See Notes)	≥75 years
Tetanus, diphtheria, pertussis (Tdap or Td)	1 dose Tdap each pregnancy; 1 dose Td/Tdap for wound management (See Notes)			
	1 dose Tdap, then Td or Tdap booster every 10 years			
Measles, mumps, rubella (MMR)	1 or 2 doses depending on indication (if born in 1957 or later)			For health care personnel (See Notes)
Varicella (VAR)	2 doses (if born in 1980 or later)		2 doses	
Zoster recombinant (RZV)	2 doses for immunocompromising conditions (See Notes)		2 doses	
Human papillomavirus (HPV)	2 or 3 doses depending on age at initial vaccination or condition	27 through 45 years		
Pneumococcal (PCV15, PCV20, PCV21, PPSV23)			See Notes	
				See Notes
Hepatitis A (HepA)	2, 3, or 4 doses depending on vaccine			
Hepatitis B (HepB)	2, 3, or 4 doses depending on vaccine or condition			
Meningococcal A, C, W, Y (MenACWY)	1 or 2 doses depending on indication (See Notes for booster recommendations)			
Meningococcal B (MenB)	19 through 23 years	2 or 3 doses depending on vaccine and indication (See Notes for booster recommendations)		
***Haemophilus influenzae* type b** (Hib)	1 or 3 doses depending on indication			
Mpox	2 doses			
Inactivated poliovirus (IPV)	Complete 3-dose series if incompletely vaccinated. Self–report of previous doses acceptable (See Notes)			

Recommended vaccination for adults who meet age requirement, lack documentation of vaccination, or lack evidence of immunity

Recommended vaccination for adults with an additional risk factor or another indication

Recommended vaccination based on shared clinical decision–making

No Guidance/ Not Applicable

SCHOOL OF MEDICINE
CASE WESTERN RESERVE UNIVERSITY

University Hospitals
The Science of Health. *The Art of Compassion*

Zoster Vaccination in People Living with HIV Is Associated with Reduced Mortality and Cardiovascular Risk: A Real-World Matched Cohort Study

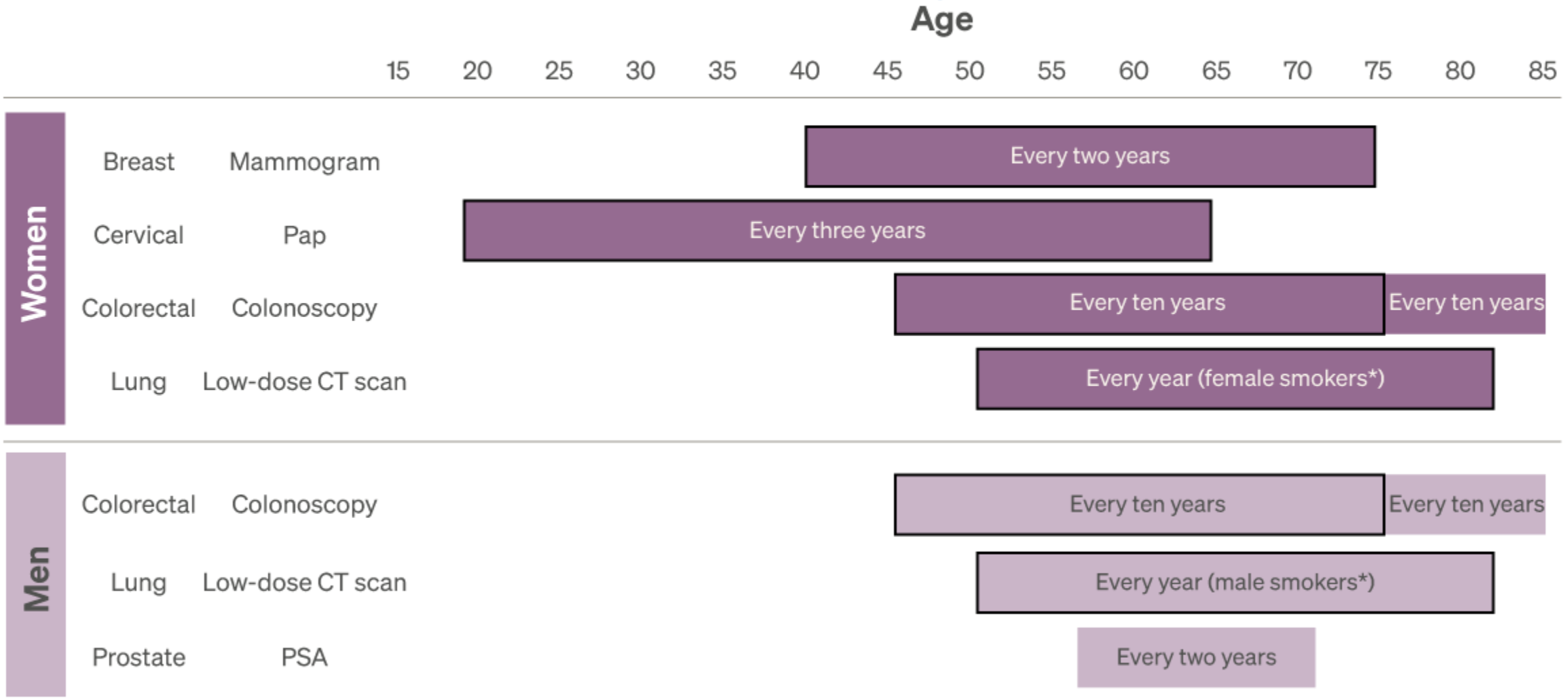
Zoster Infection & Vaccination as Determinants of Vascular and Cognitive Outcomes in PLWH

Ali Dehghani DO[1] & George Yendewa MD, MPH[2]

[1]Department of Medicine, Case Western Reserve University School of Medicine, Cleveland, OH, United States.

[2]Division of Infectious Diseases and HIV Medicine, University Hospitals Cleveland Medical Center, Cleveland, OH, United States

United States Preventative Services Task Force Cancer Screening Guidelines



All borders = Screening recommended by USPSTF, age range specified
No side borders = Screening recommendd by USPSTF, no age range specified
No borders = Screening classified as optional by USPSTF

*Smokers are defined according to USPSTF criteria as individuals with a 20 pack year smoking history who currently smoke or have quit within the past 15 years

Thank You!!