Management of Persons Living with HIV: 2025

Eric S. Daar, M.D.
Chief, Division of HIV Medicine
Harbor-UCLA Medical Center
Professor of Medicine
David Geffen School of Medicine at UCLA

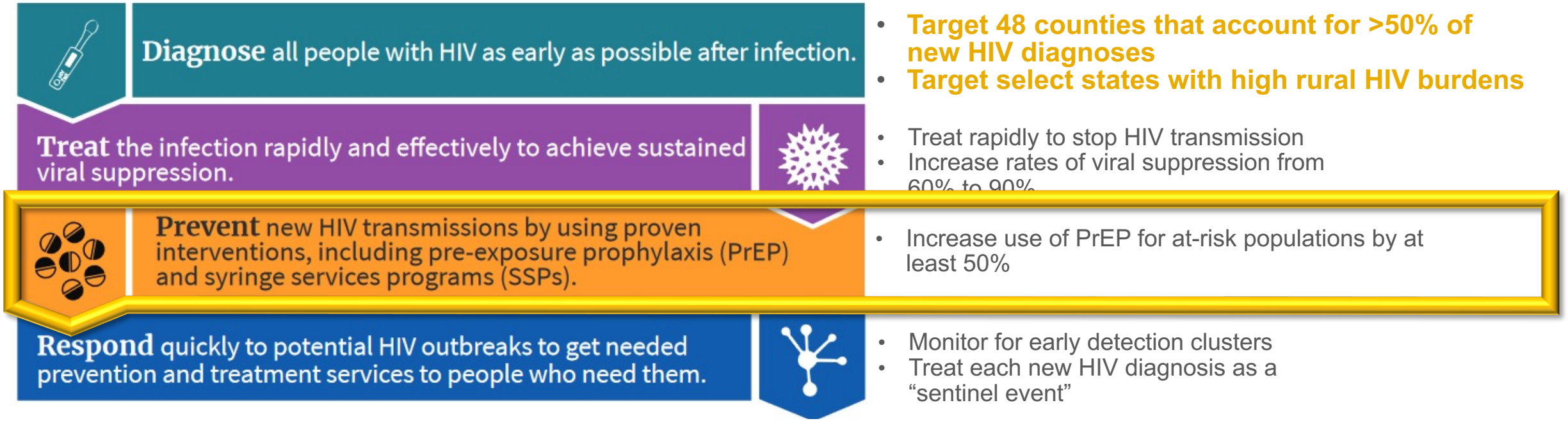
Disclosures

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

Outline

- 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

Key Steps to Ending the HIV Epidemic in the United States



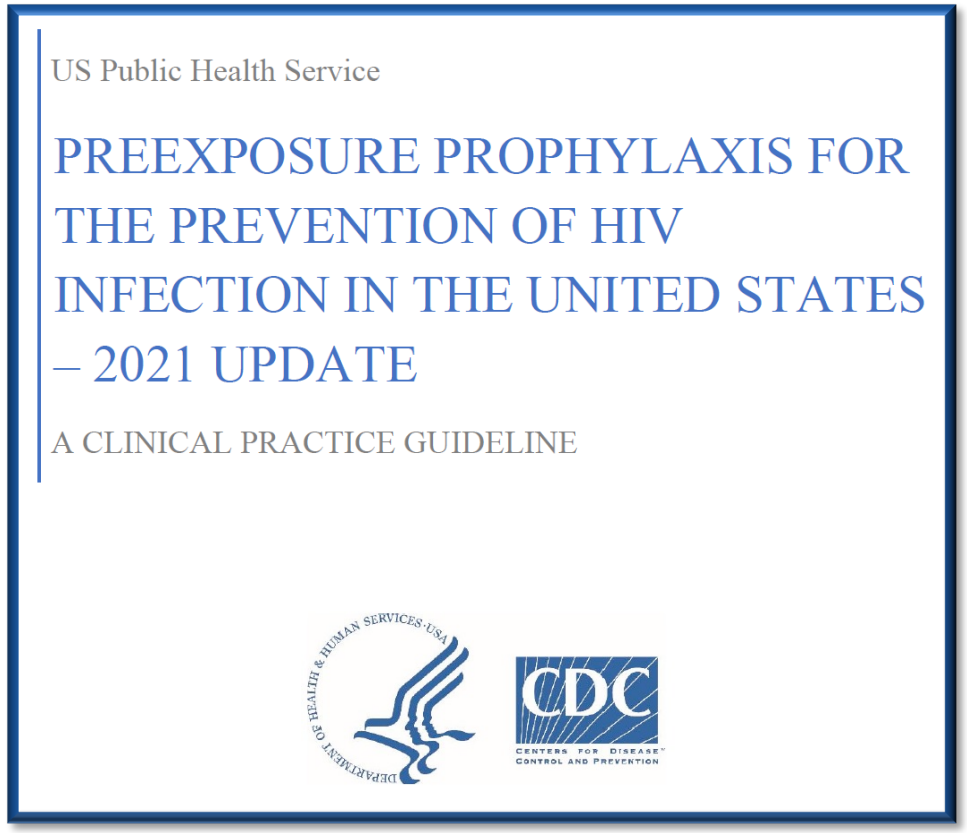
Ending the HIV Epidemic

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?



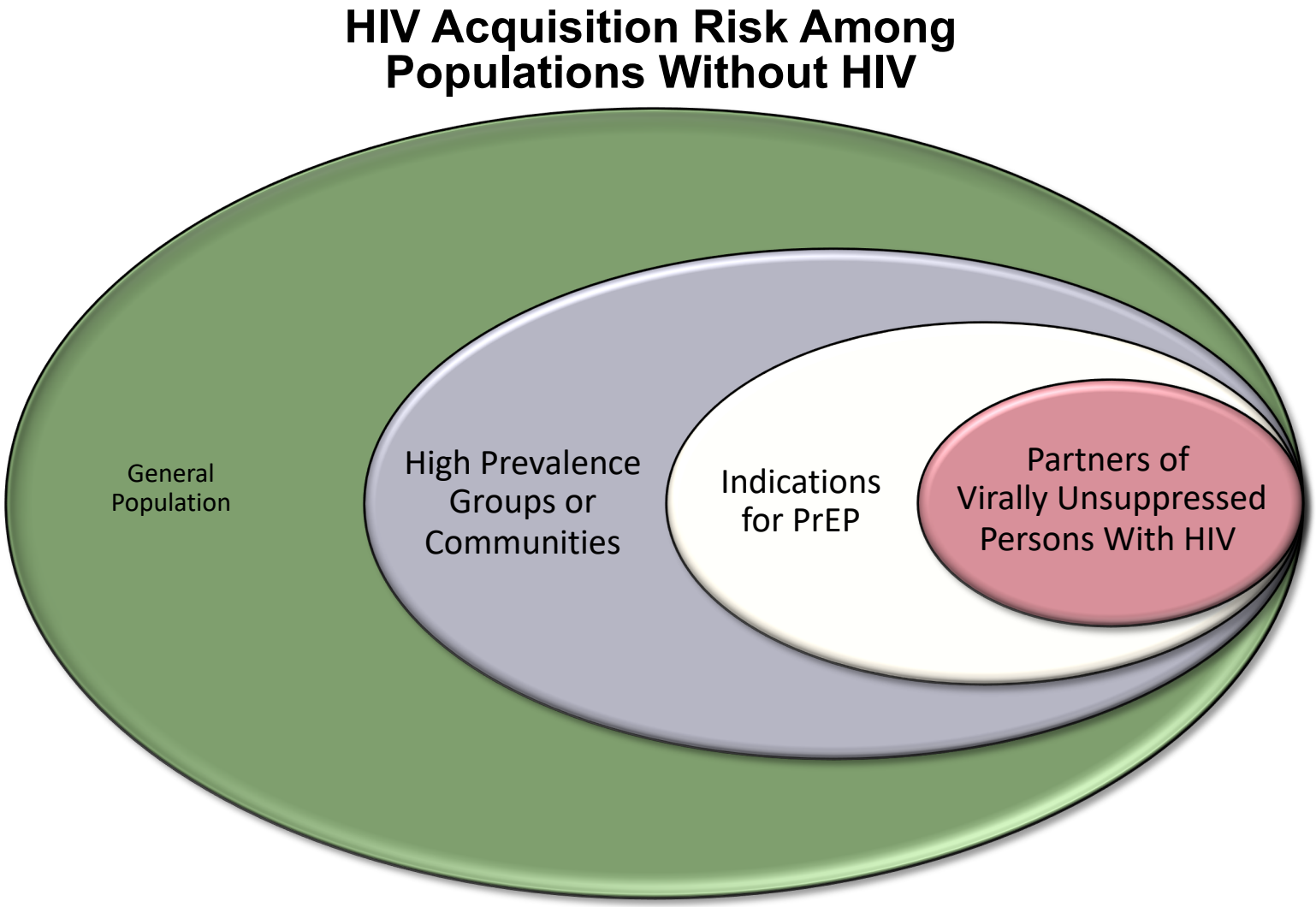
- Sexually active adults and adolescents who had anal or vaginal sex in the past 6 months **AND** any of the following
  - Sexually active partner with HIV (especially if partner has an unknown or detectable VL
  - Bacterial STI in past 6 months
  - History of inconsistent or no condom use with sexual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

Taking a Sexual History is a Necessary First Step

- Clinicians should not limit sexual history assessments to only selected patients
- All persons who desire PrEP should be offered PrEP



CDC. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf. Published December 2021.

PrEP Options

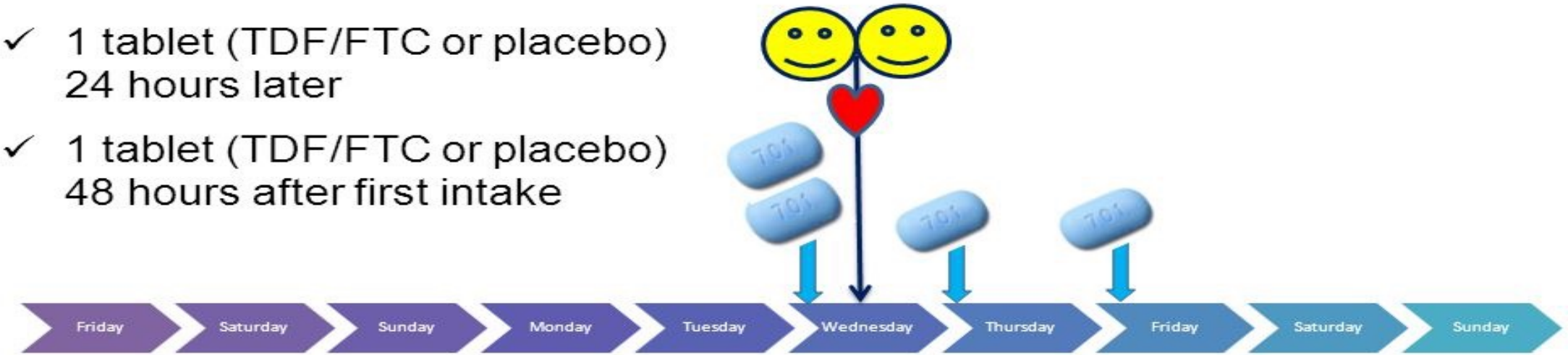
<table>
<tr><th></th><th colspan="2">Oral F/TDF</th><th>Oral F/TAF</th><th>Injectable CAB and LEN</th></tr>
<tr><th></th><th>Daily</th><th>On-Demand</th><th>Daily</th><th>Every 2 or 6 Months</th></tr>
<tr><td>MSM</td><td rowspan="4">FDA On-Label
Guideline Recommended
(DHHS, IAS-USA, WHO)</td><td>FDA Off-Label
Guideline Recommended
(IAS-USA, WHO)</td><td rowspan="2">FDA On-Label
Guideline Recommended
(DHHS, IAS-USA, WHO)</td><td rowspan="4">FDA On-Label*
Guideline Recommended
(DHHS, IAS-USA, WHO)</td></tr>
<tr><td>Transgender women
Heterosexual men</td><td rowspan="3">FDA Off-Label
Not Recommended</td></tr>
<tr><td>Heterosexual women</td><td rowspan="2">FDA Off-Label
Not Recommended</td></tr>
<tr><td>Transgender men</td></tr>
</table>

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.

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.
WHO. https://apps.who.int/iris/rest/bitstreams/1453332/retrieve. July 2022.

Ipergay : Event-Driven iPrEP

- ✓ 2 tablets (TDF/FTC or placebo) 2-24 hours before sex
- ✓ 1 tablet (TDF/FTC or placebo) 24 hours later
- ✓ 1 tablet (TDF/FTC or placebo) 48 hours after first intake



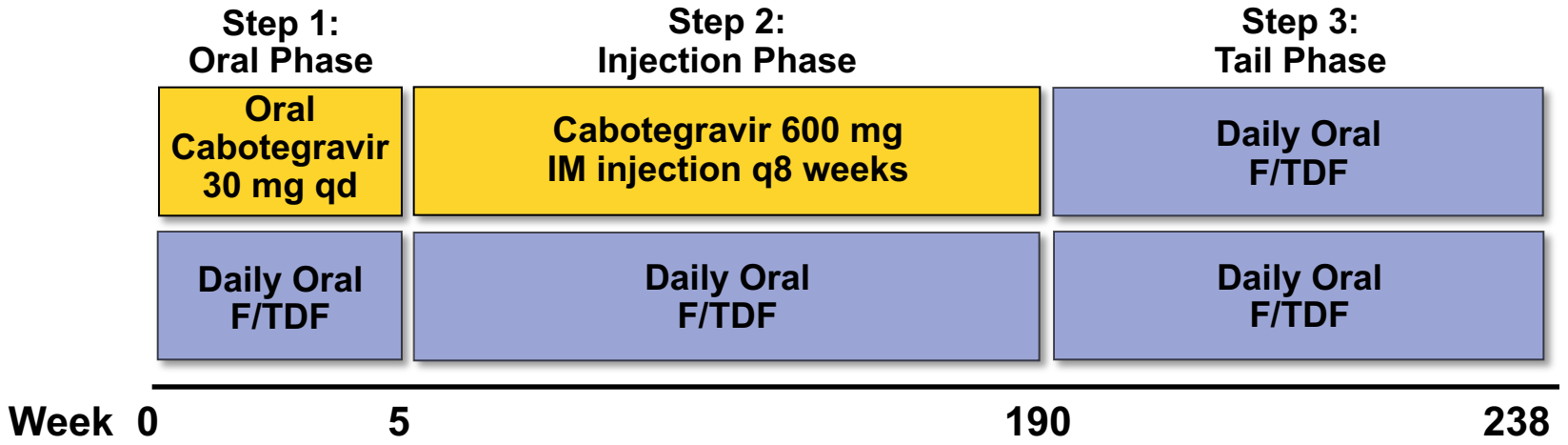
“2-1-1”

LA PrEP: HPTN 083 and HPTN 084

Phase 3 studies

Double-blind, double-dummy, active controlled
Persons at high-risk for HIV infection
In general good health
No IDU, HCV, HBV, seizure disorder, CVD, abnormal liver function

HPTN 083: MSM/transgender women
HPTN 084: cisgender women

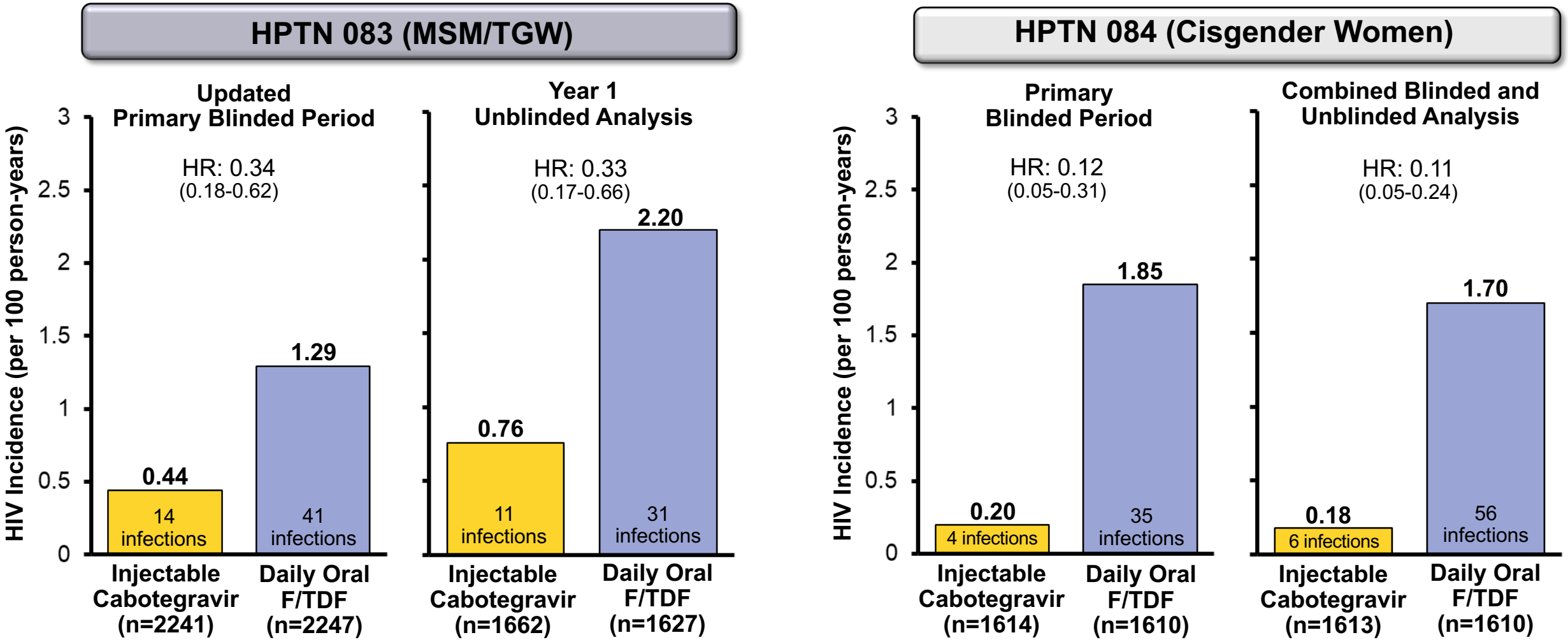


DSMB recommended early termination of blinded phase of both studies

Matching oral and IM placebos included in the oral and injection phase double-blind arms.
HPTN 083 was conducted in US, Brazil, Peru, Argentina, South Africa, Vietnam, and Thailand.
HPTN 084 was conducted in Botswana, Kenya, Malawi, South Africa, Swaziland, Uganda, and Zimbabwe.

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.

HPTN 083 and HPTN 084 Infection Rate

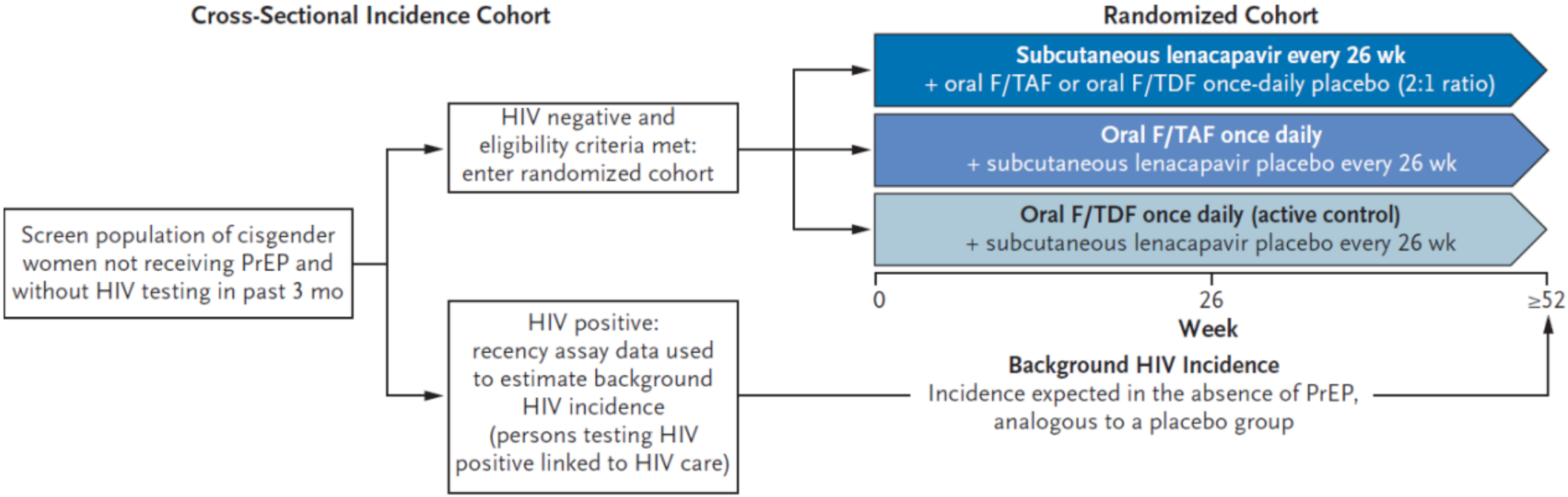


Landovitz RJ, et al. *N Engl J Med*. 2021;385:595-608.
Delany-Moretlwe S, et al. *Lancet*. 2022;399:1779-1789.
Delany-Moretlwe S, et al. *J Int AIDS Soc*. 2022;25(suppl 3):227-228. Abstract OALBX0107.

Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women

L.-G. Bekker, M. Das, Q. Abdool Karim, K. Ahmed, J. Batting, W. Brumskine, K. Gill, I. Harkoo, M. Jaggernath, G. Kigozi, N. Kiwanuka, P. Kotze, L. Lebina, C.E. Louw, M. Malahleha, M. Manentsa, L.E. Mansoor, D. Moodley, V. Naicker, L. Naidoo, M. Naidoo, G. Nair, N. Ndlovu, T. Palanee-Phillips, R. Panchia, S. Pillay, D. Potloane, P. Selepe, N. Singh, Y. Singh, E. Spooner, A.M. Ward, Z. Zwane, R. Ebrahimi, Y. Zhao, A. Kintu, C. Deaton, C.C. Carter, J.M. Baeten, and F. Matovu Kiweewa, for the PURPOSE 1 Study Team*

Trial Design



Bekker LG, et al. NEJM 2024;391:1179-92.

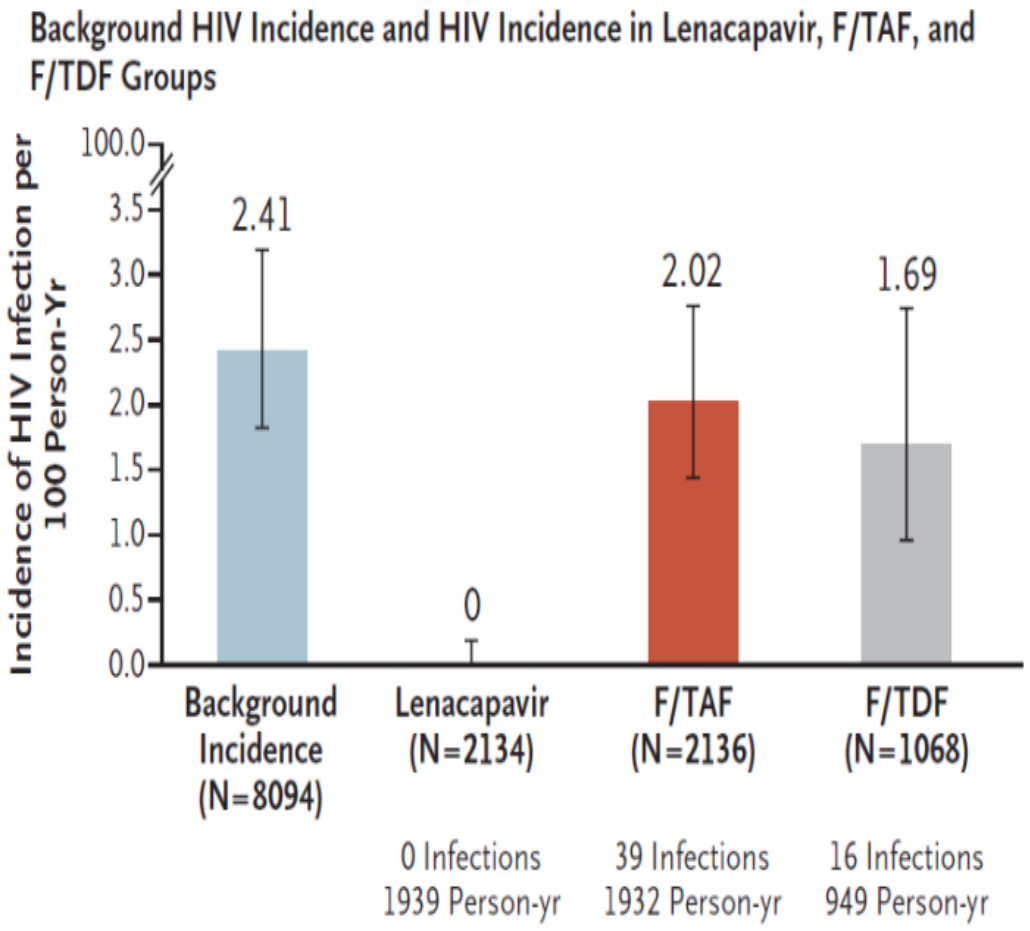


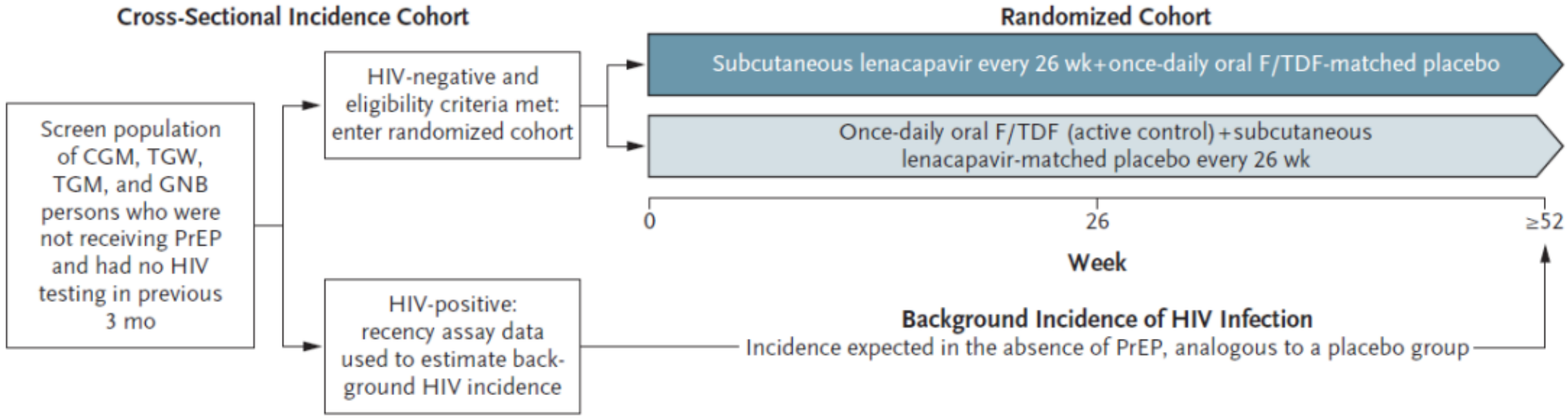
Table 2. Safety Findings.*

Variable	Lenacapavir (N=2138)	F/TAF (N=2137)	F/TDF (N=1070)
Adverse event — no. (%)†			
Any grade	1631 (76.3)	1665 (77.9)	830 (77.6)
Grade ≥2	1111 (52.0)	1078 (50.4)	533 (49.8)
Grade ≥3	88 (4.1)	95 (4.4)	50 (4.7)
Serious adverse event — no. (%)†	59 (2.8)	85 (4.0)	35 (3.3)
Adverse event leading to discontinuation of the trial regimen — no. (%)†‡	5 (0.2)	2 (<0.1)	0
Injection-site reactions¶			
No. of participants who received at least one injection	2138	2136	1070
Serious injection-site reaction — no. (%)	0	0	0
Injection-site reaction leading to premature discontinuation of the trial regimen — no. (%)	4 (0.2)	0	0
Grade — no. (%)			
Any	1470 (68.8)	755 (35.3)	363 (33.9)
1	1060 (49.6)	563 (26.4)	281 (26.3)
2	406 (19.0)	190 (8.9)	80 (7.5)
3	4 (0.2)	2 (<0.1)	2 (0.2)
4	0	0	0

Bekker LG, et al. NEJM 2024;391:1179-92.

Twice-Yearly Lenacapavir for HIV Prevention in Men and Gender-Diverse Persons

- International, double-blind, randomized phase III trial

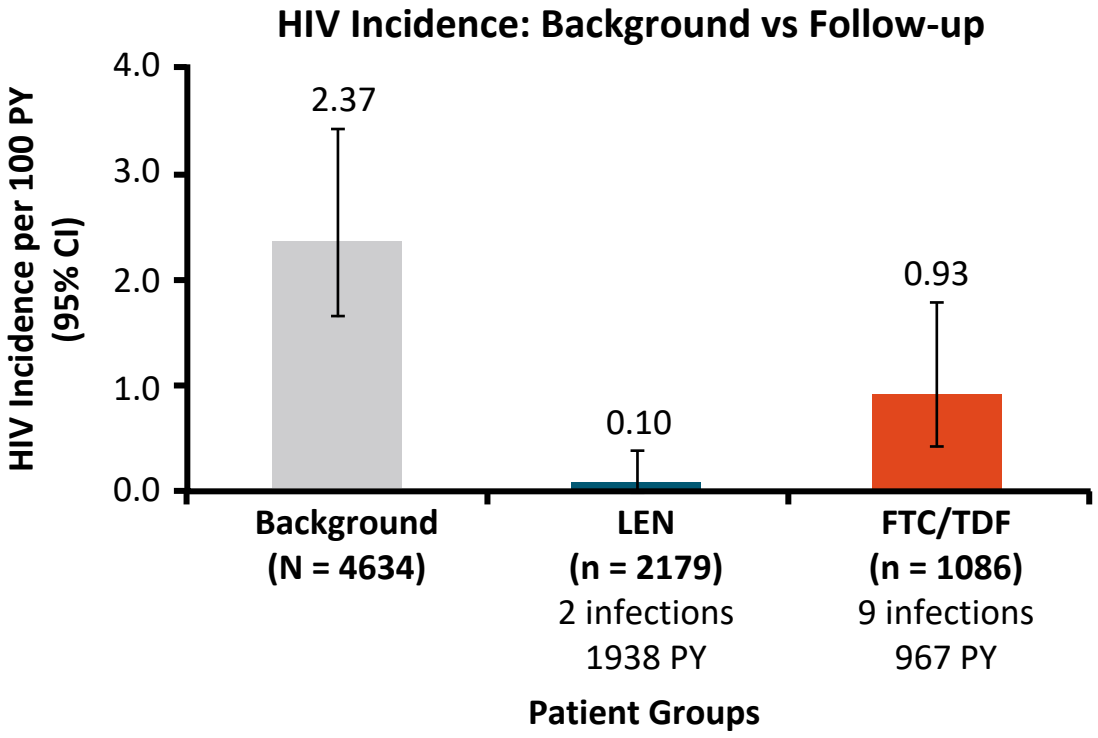


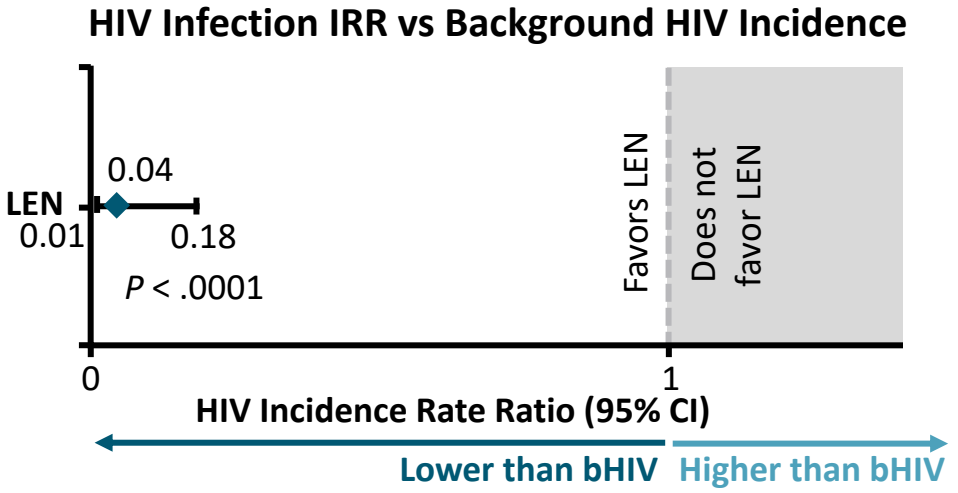
Coprimary endpoints: background HIV incidence per 100-PY at screening, HIV incidence

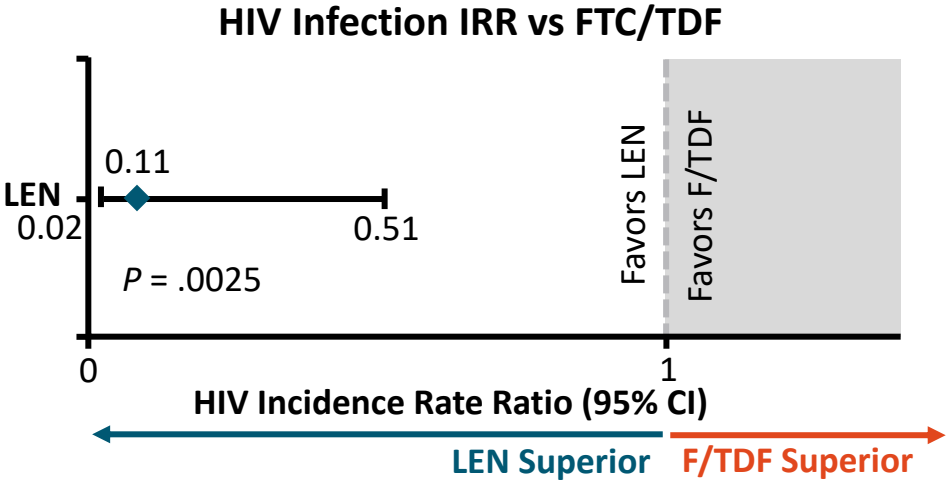
- **Key secondary endpoints**: HIV incidence while adherence to study therapy, safety
- **Interim analysis**: LEN vs background HIV incidence, LEN vs FTC/TDF during blinding

Kelley CF, et al. NEJM 2024: DOI: 10.1056/NEJM0a2411858

Purpose 2: Outcomes





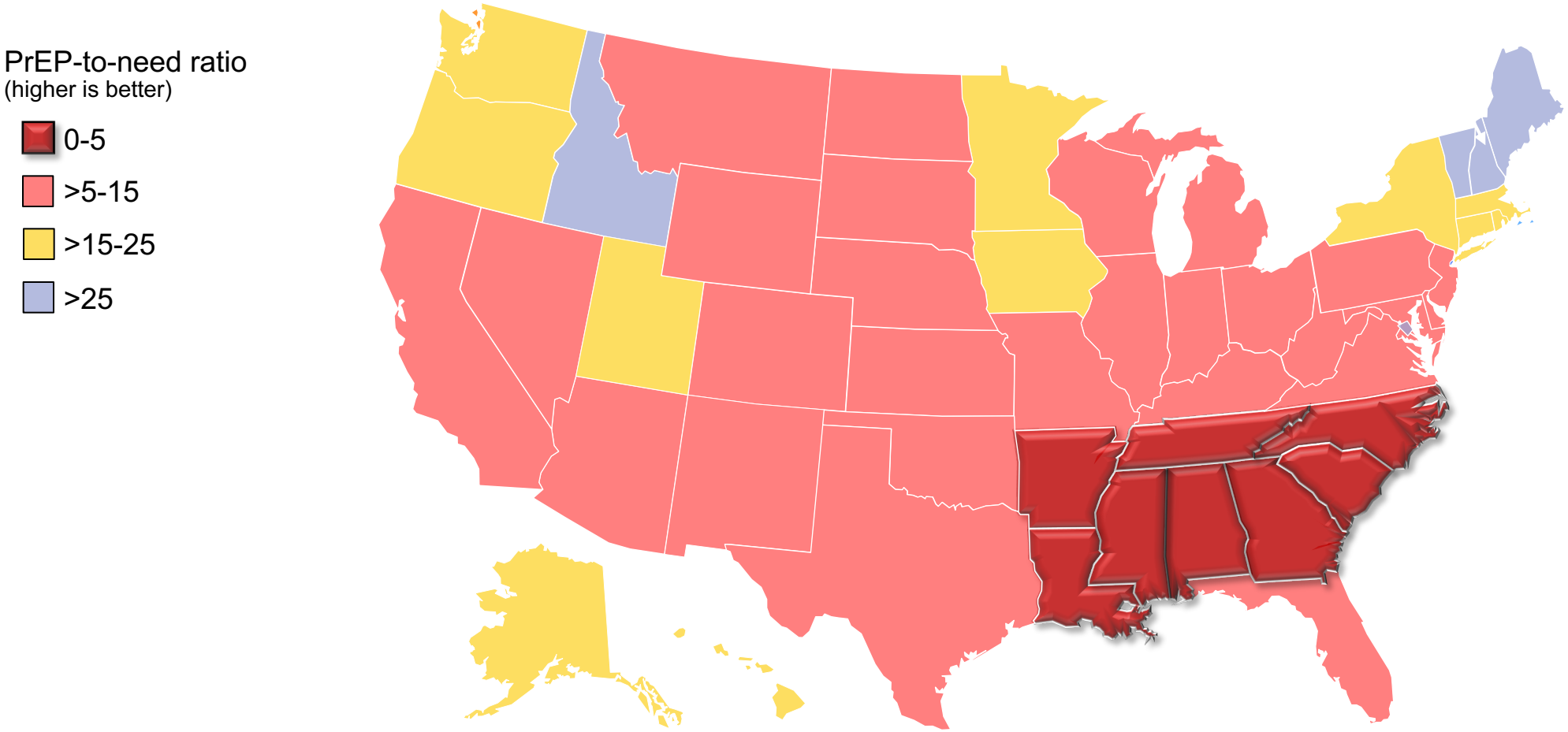


- Median follow-up: 39.4 wk
- In LEN arm, 2 HIV infections occurred
- LEN reduced HIV infections by 96% vs background incidence and by 89% vs daily oral FTC/TDF

29 D/C for ISR (26 LEN)

Kelley CF, et al. NEJM 2024:
DOI: 10.1056/NEJM0a2411858

PrEP-to-Need Ratio (2021)



PrEP-to-need ratio: the number of PrEP users to the number of people newly diagnosed with HIV.

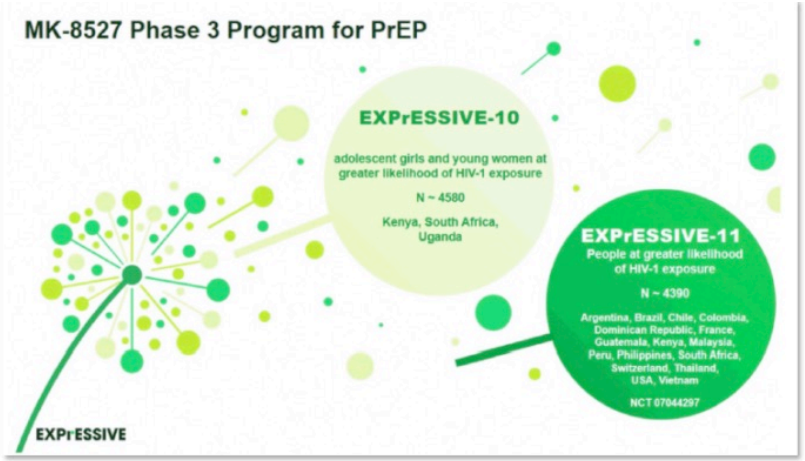
Adapted from AIDSVu. https://map.aidsvu.org/map.

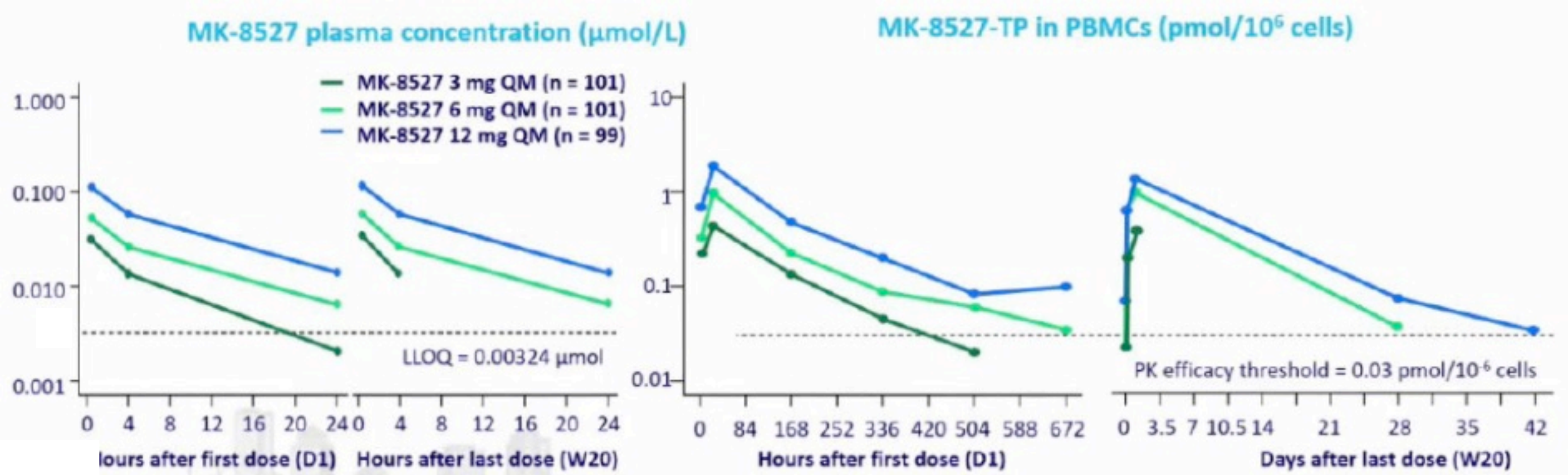
PrEP Uptake: Barriers and Potential Solutions

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.

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

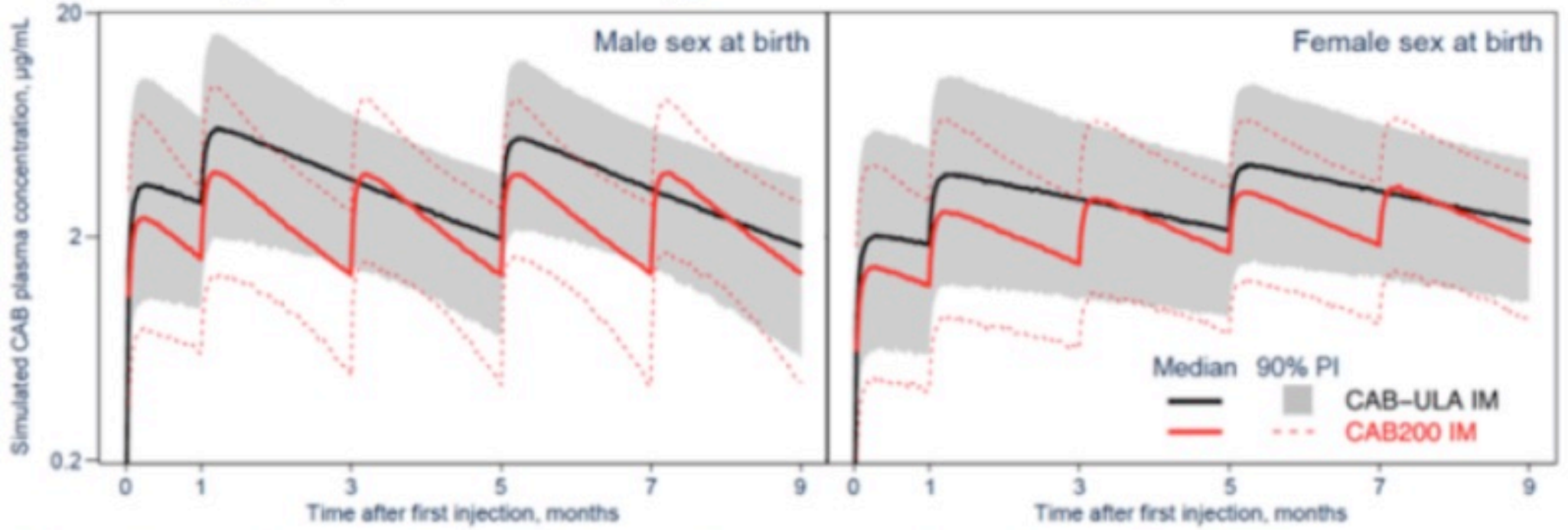




Mayer K, et al. IAS 2025; Abst. OA50106LB

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

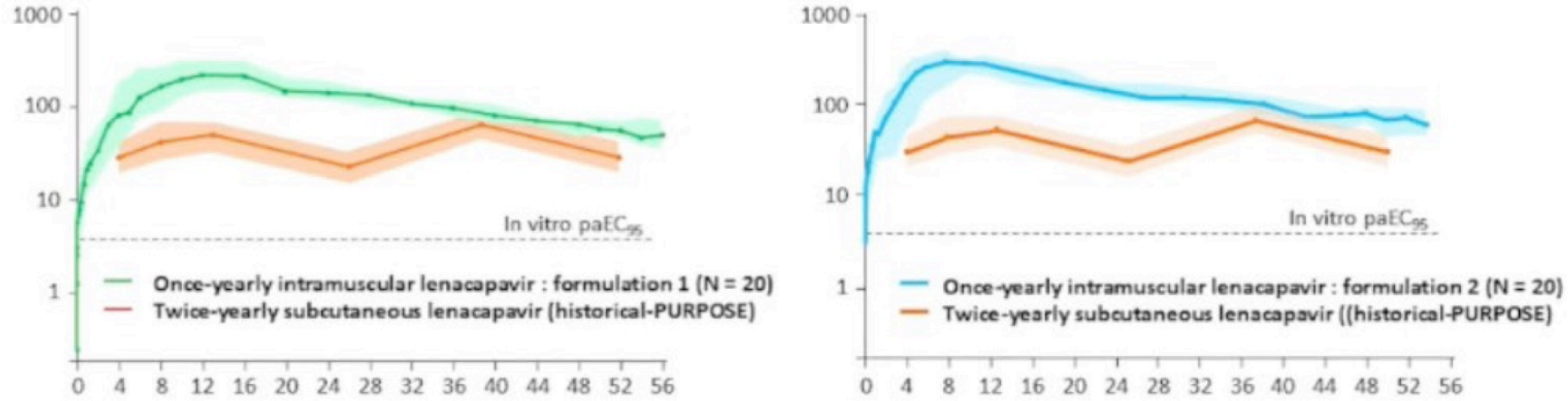


CAB, cabotegravir; IM, intramuscular; PI, prediction interval; PK, pharmacokinetics; Q4M, every 4 months; SC, subcutaneous; $t_{1/2}$, terminal half-life; ULA, ultra-long-acting. [a]1600-mg (3-mL) CAB-ULA per injection.

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)



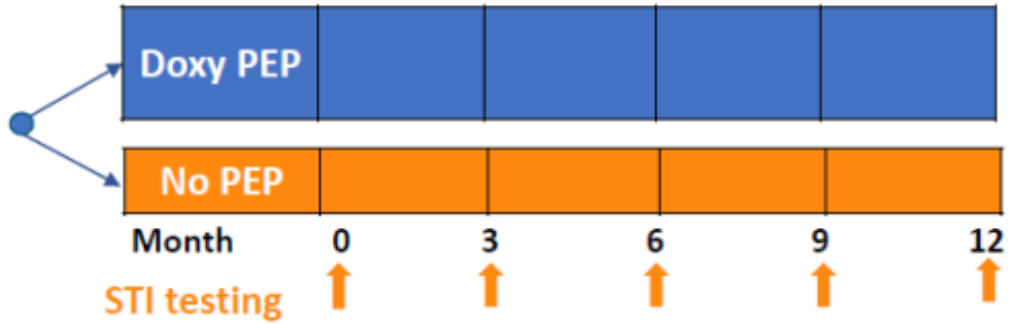
- Injection site pain :16 (80%) given formulation 1, 15 (75%) formuation
- ISR generally mild, resolved within 1 week and reduced by pretreatment with ice

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

DoxyPEP

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

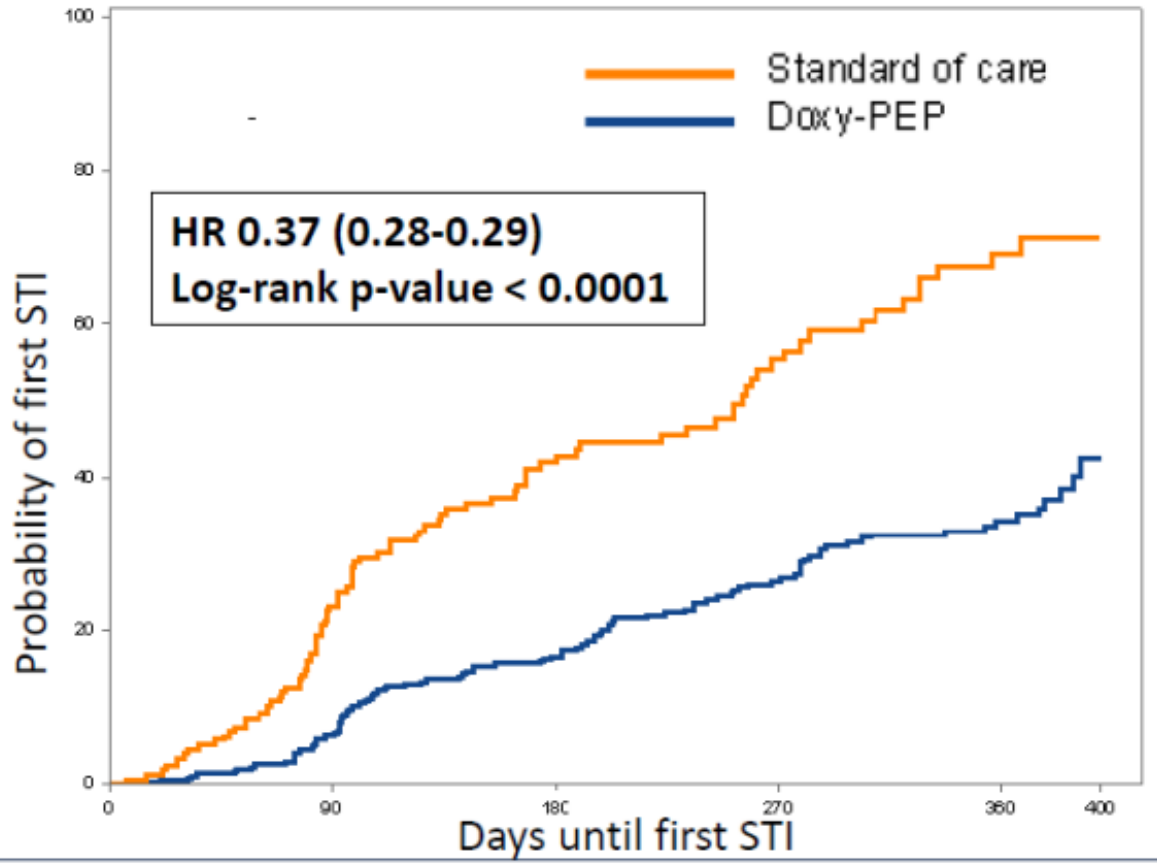
MSM & TW living with HIV *or* *2:1 randomization* without HIV on PrEP



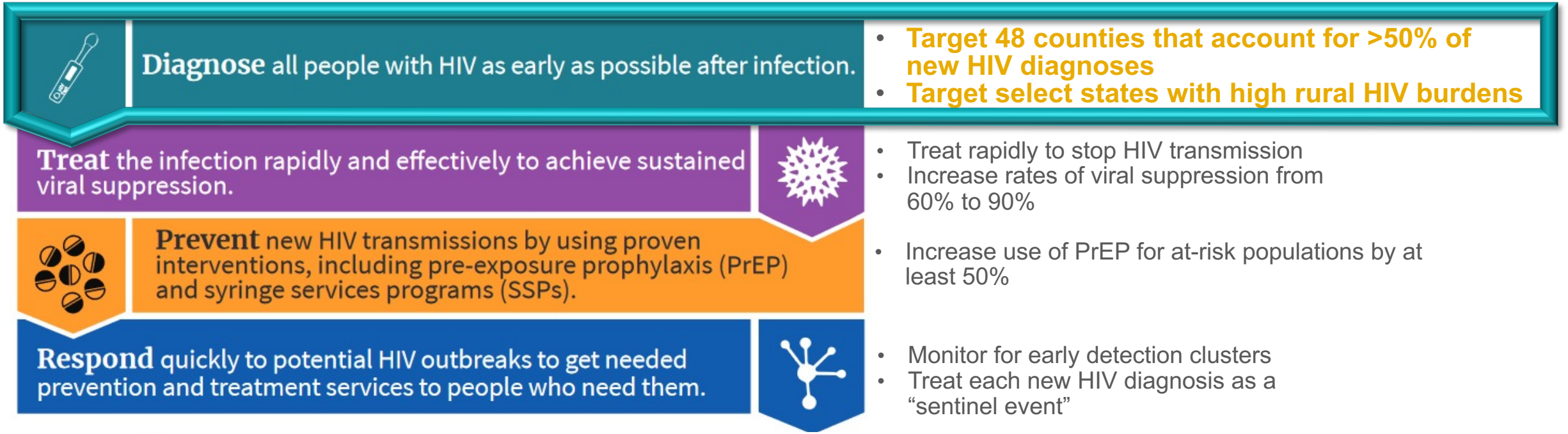
DoxyPEP Results

- 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

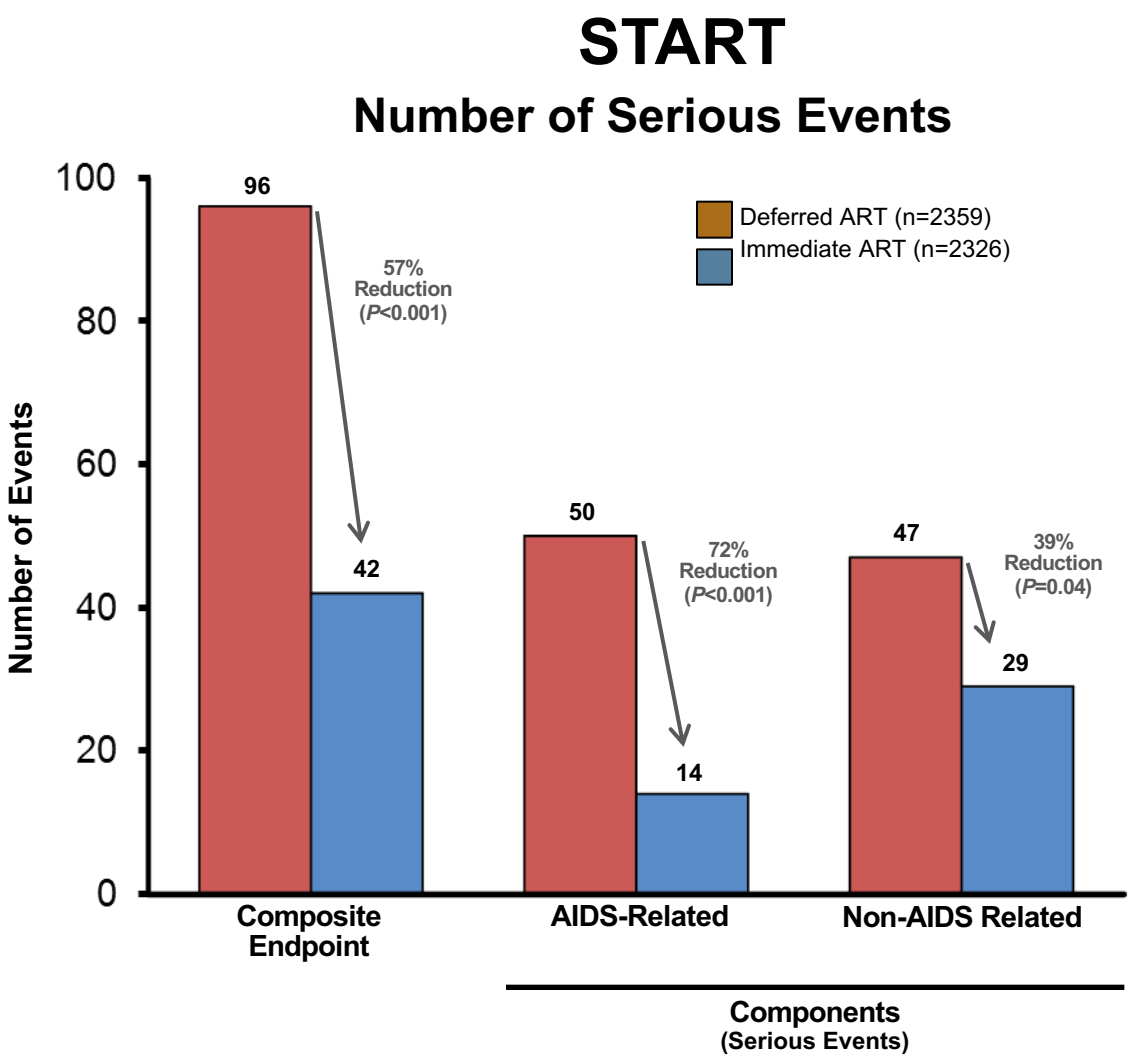
Overall Goal: Decrease the number of new HIV diagnoses to 9,588 by 2025 and 3,000 by 2030.

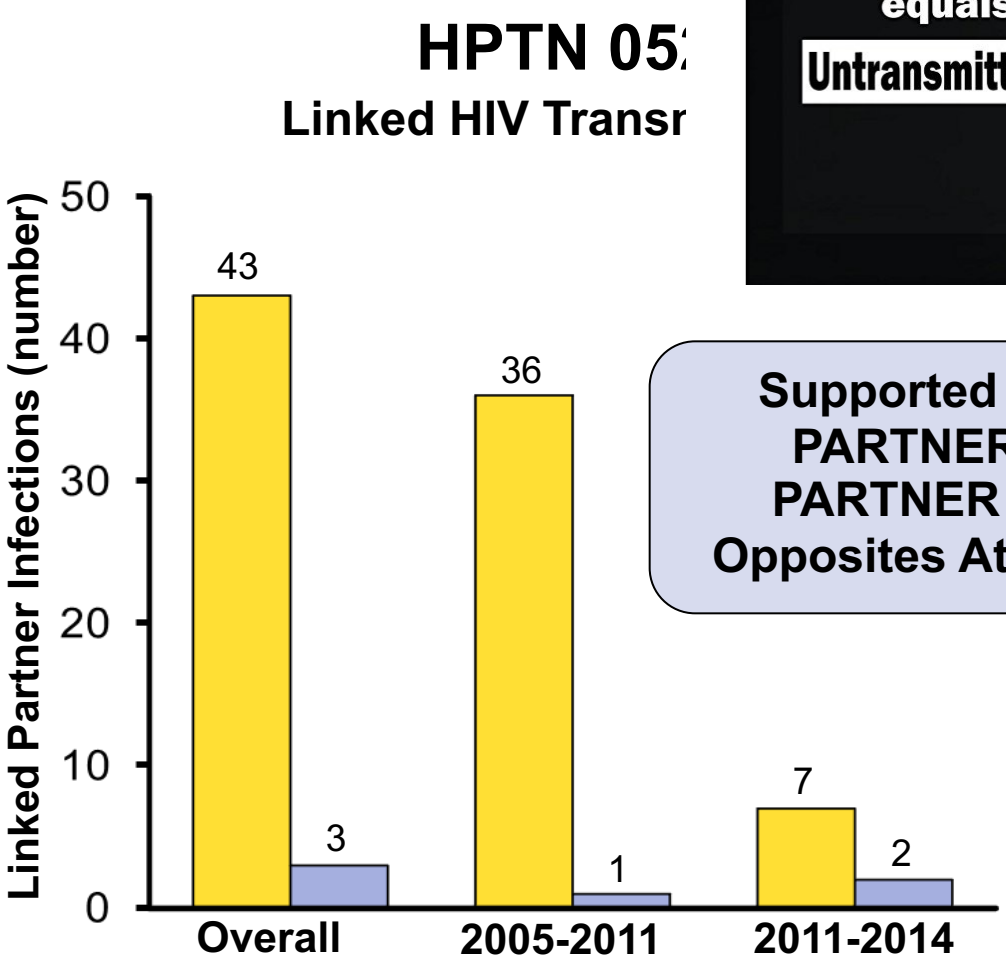
DHHS, 2021. *HIV National Strategic Plan for the United States: A Roadmap to End the Epidemic 2021-2025*. https://files.hiv.gov/s3fs-public/HIV-National-Strategic-Plan-2021-2025.pdf.

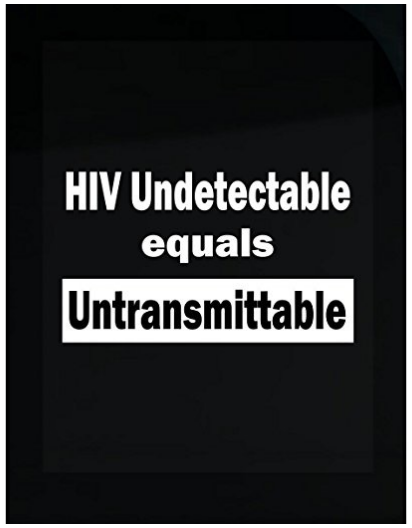
Harris NS, et al. *MMWR Morb Mortal Wkly Rep*. 2019;68:1117-1123.

ART: When to Start

When to Start





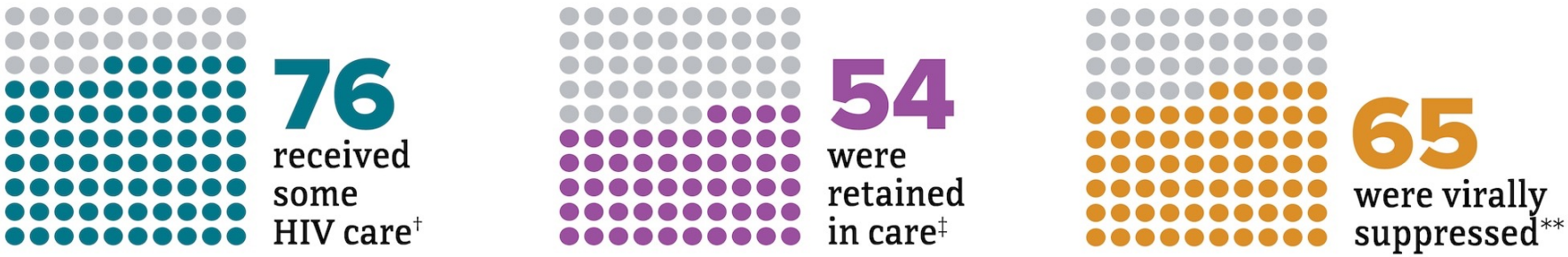


Supported by PARTNER, PARTNER 2, Opposites Attract

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

Challenges, including structural barriers such as housing instability, poverty, or transportation access, may prevent people from getting and staying in HIV care.

For every 100 people with diagnosed HIV in 2022:



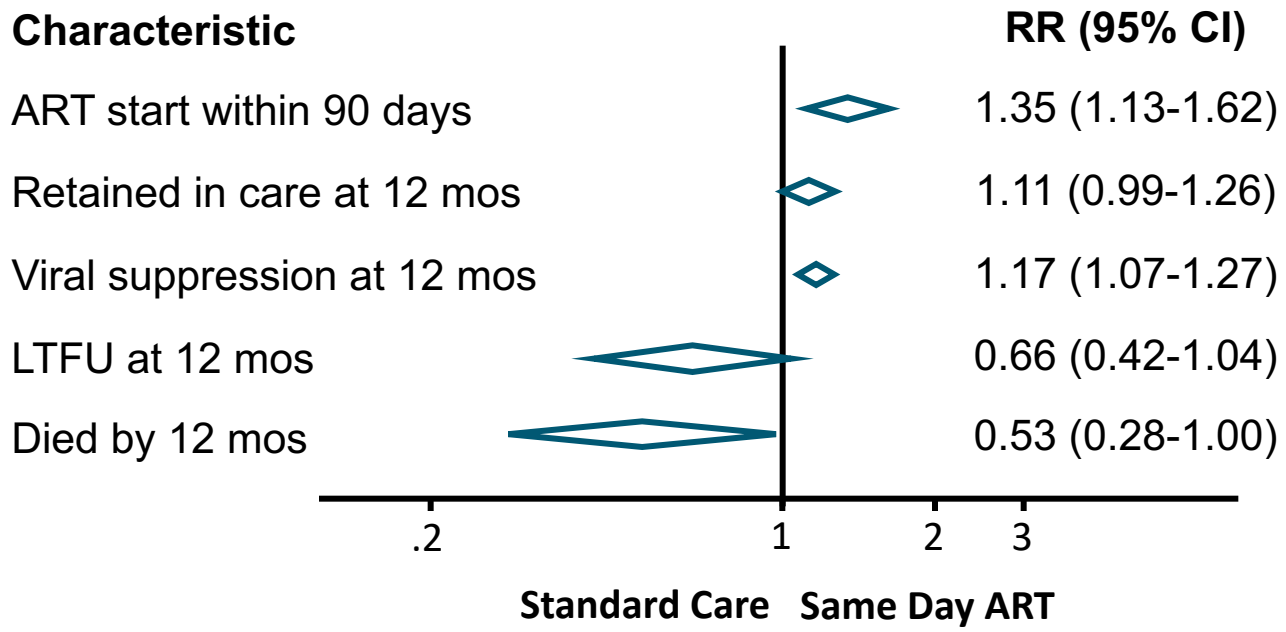
Ending the HIV Epidemic

Overall Goal: Increase the percentage of people with diagnosed HIV who are virally suppressed to at least 95% by 2025 and remain at 95% by 2030.

https://www.cdc.gov/hiv-data/nhss/national-hiv-prevention-and-care-outcomes.html

Improved Clinical Outcomes With Rapid ART Initiation

- Systematic review of ART initiation within 14 days of eligibility determination across 4 randomized clinical trials
  - Compared with standard care, same-day ART increased likelihood of ART initiation in first 90 days, patient retention, and viral suppression at 12 mos



Ford. AIDS. 2018;32:17.

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 HIV RNA <500,000 c/mL and CD4 >200 cells/uL, no HBV and resistance genotype available

Considerations that influence choice of ARVs

HBV infection

- Use potent, high barrier to resistance agent, i.e. TDF, TAF, Entecavir

Chronic kidney disease

- Avoid TDF if CrCl <60 mL/min or TAF if <30 mL/min

Cardiovascular risk factors

- Avoid ABC if possible

HLA-B5701 positive

- Avoid ABC

Drug-drug interactions

- Particularly relevant with ritonavir or cobicistat-containing regimens

ART: Switch in those with no underlying resistance

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

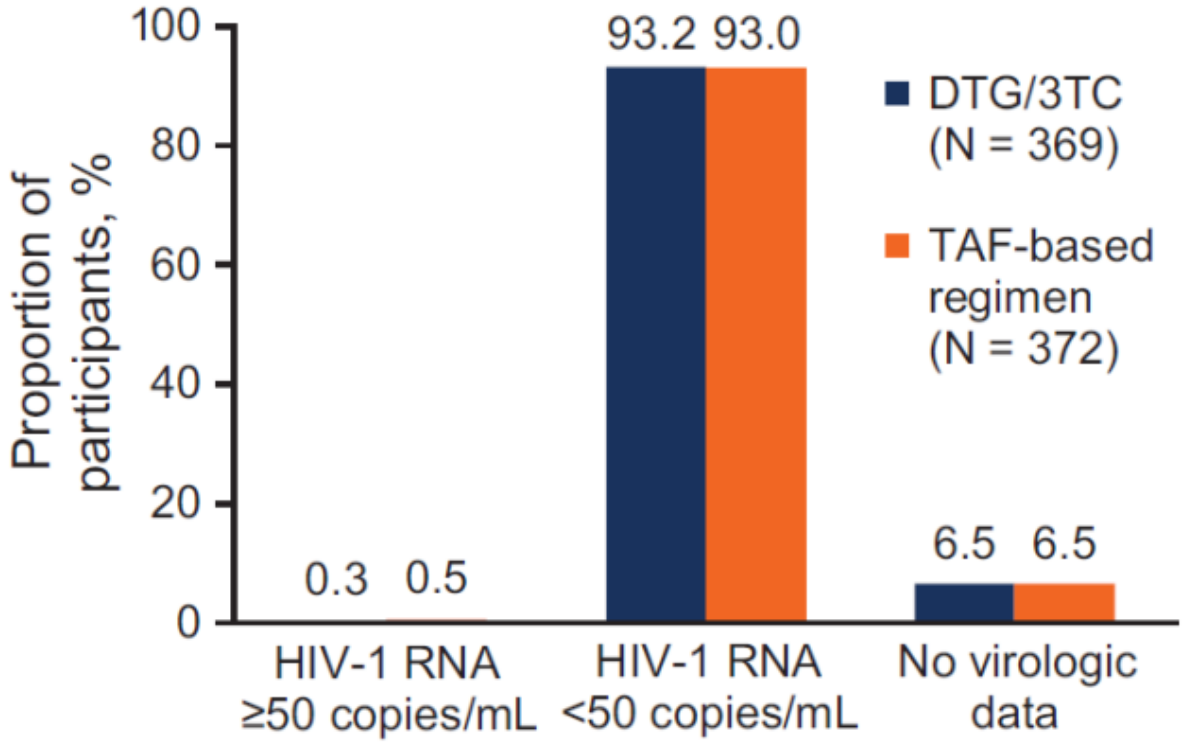
Comorbidity

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

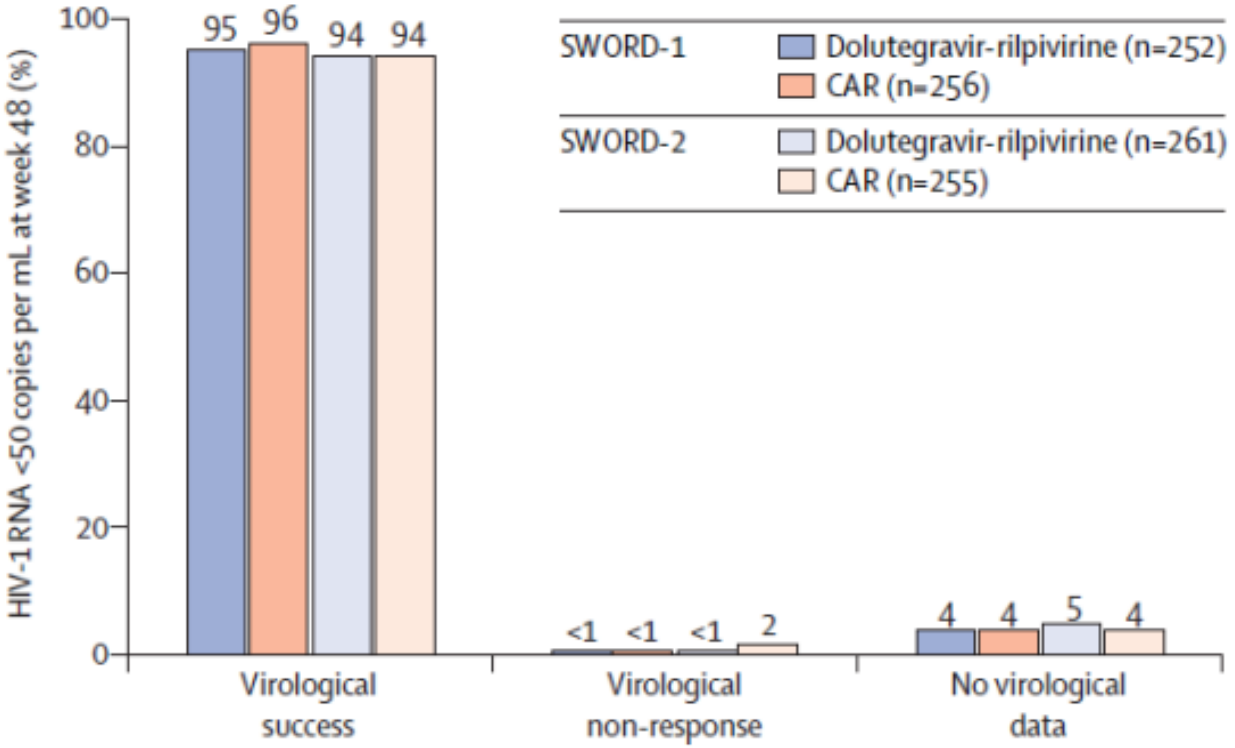
DHHS ART Guidelines, Https://clinicalinfo.hiv.gov/en/guidelines/ September 2024

TANGO and SWORD Studies
Novel 2-drug regimens

TANGO



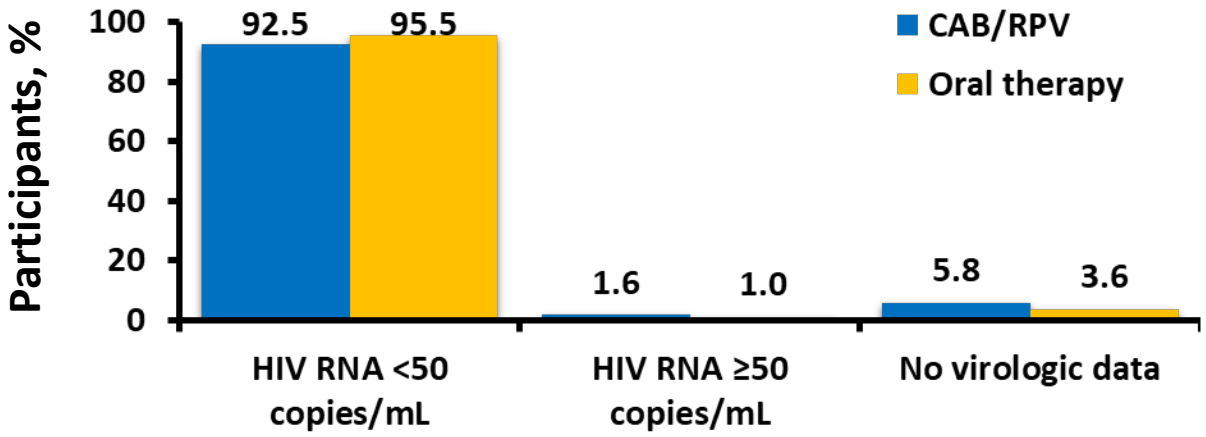
SWORD 1 and 2



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

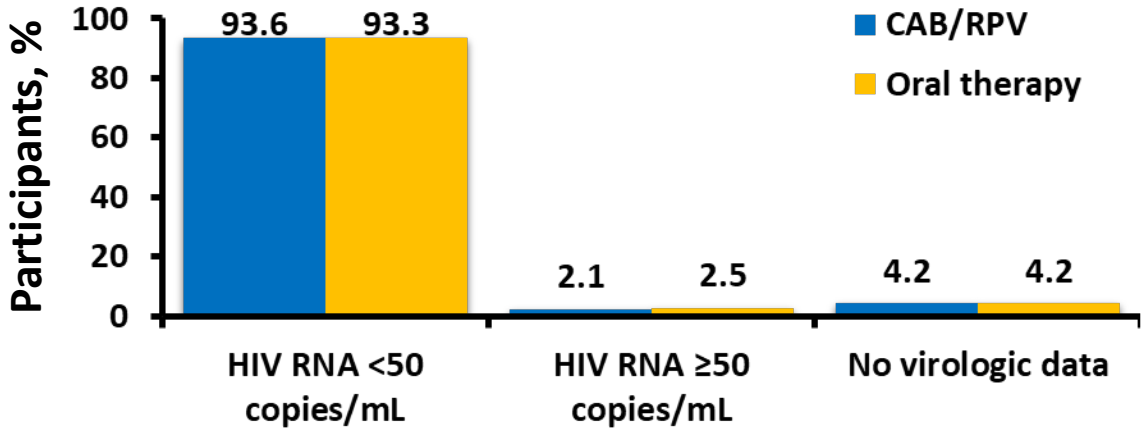
Long-Acting CAB/RPV vs Oral ART
ATLAS and FLAIR

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]



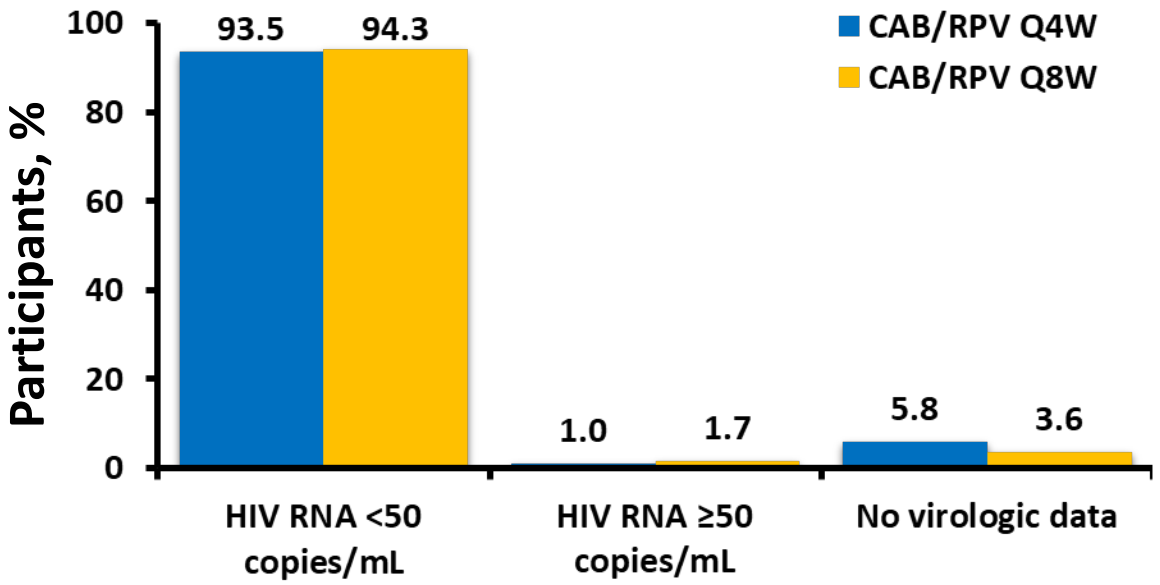
Injection site reactions were seen in 86% of CAB/RPV group and decreased to 20% at week 48

[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



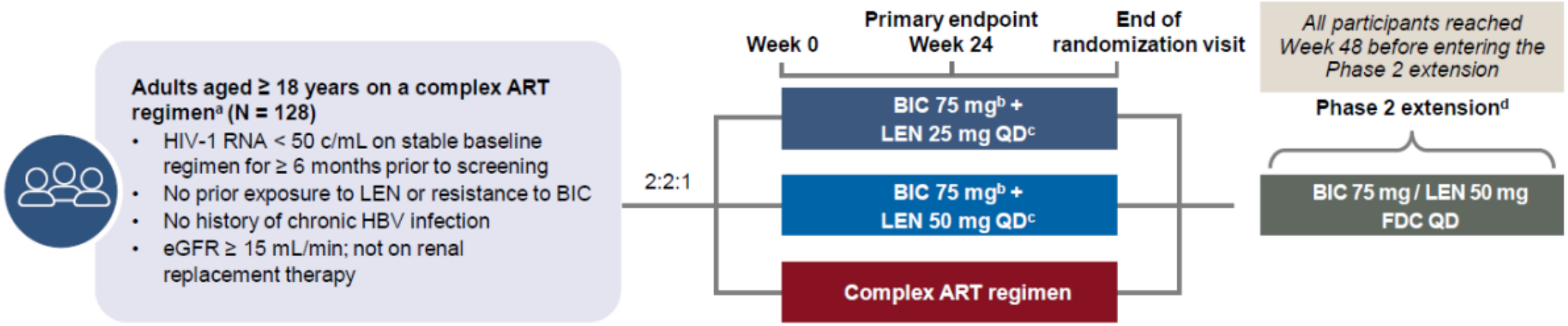
- Injection site reactions were rated as mild-to-moderate by 98% of participants experiencing them
  - Median duration of 3 days

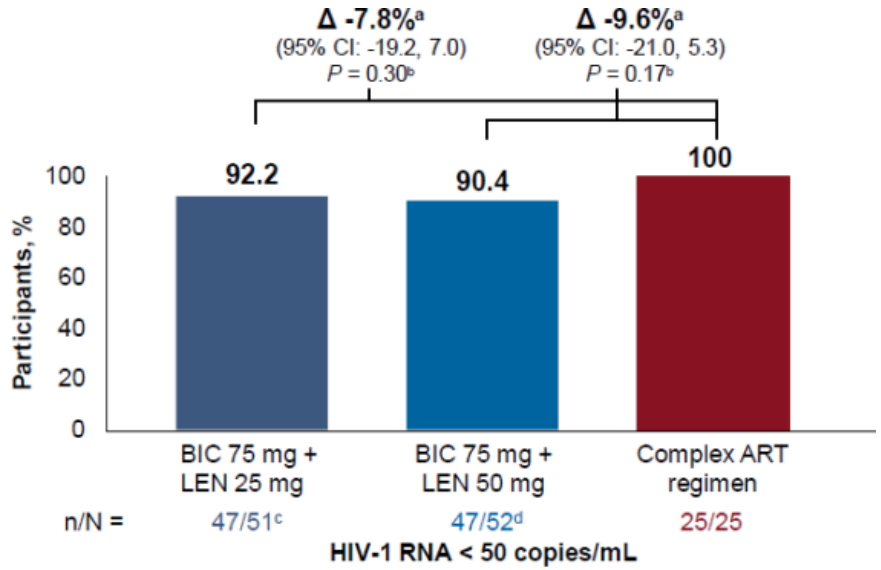
LA CAB/RPV only indicated for those virologically suppressed: Limited data in those with poor adherence or viremia

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

ARTISTRY-1: LEN + BIC once daily

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





November 13, 2025

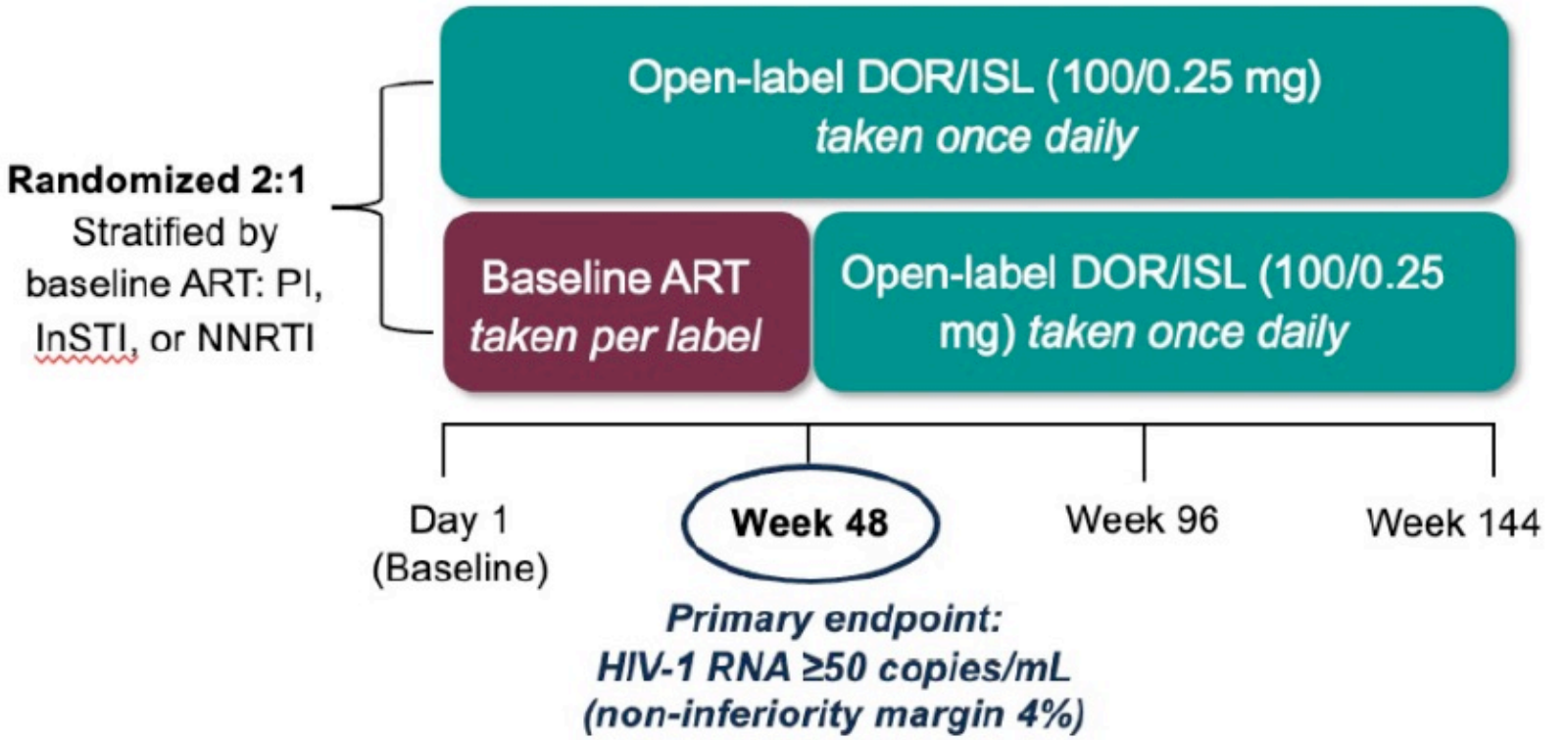
Gilead's Investigational Single-Tablet Regimen of Bictegravir and Lenacapavir for HIV-1 Treatment Meets Primary Endpoint in Phase 3 ARTISTRY-1 Trial

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

Population

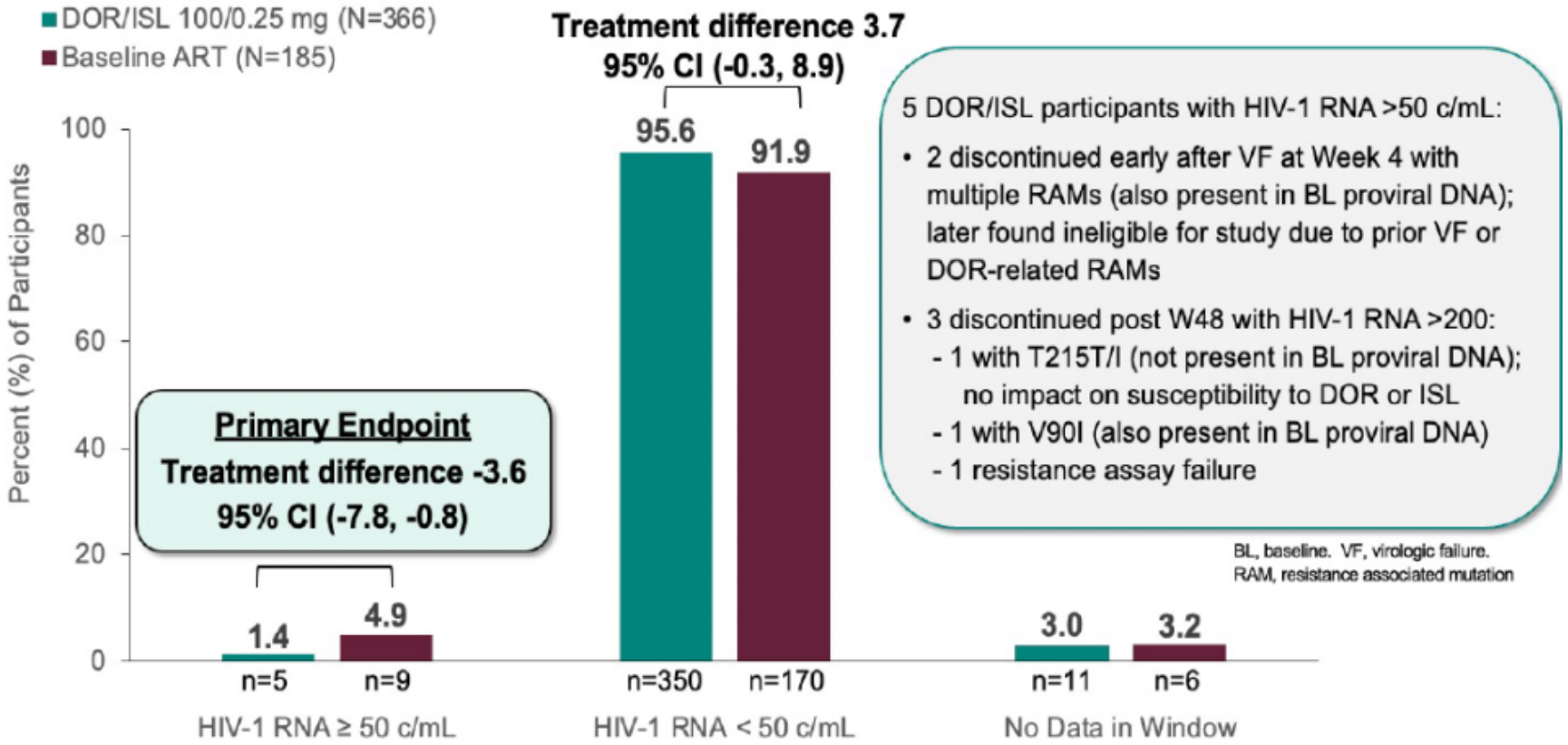
- Adults with HIV-1 RNA <50 copies/mL for ≥3 months on stable, oral 2- or 3-drug ART
- CD4 count ≥50 cells/mm^3 and total lymphocyte count ≥650 cells/mm^3
- No history of treatment failure on any regimen
- No known resistance to DOR*
- No active HBV infection

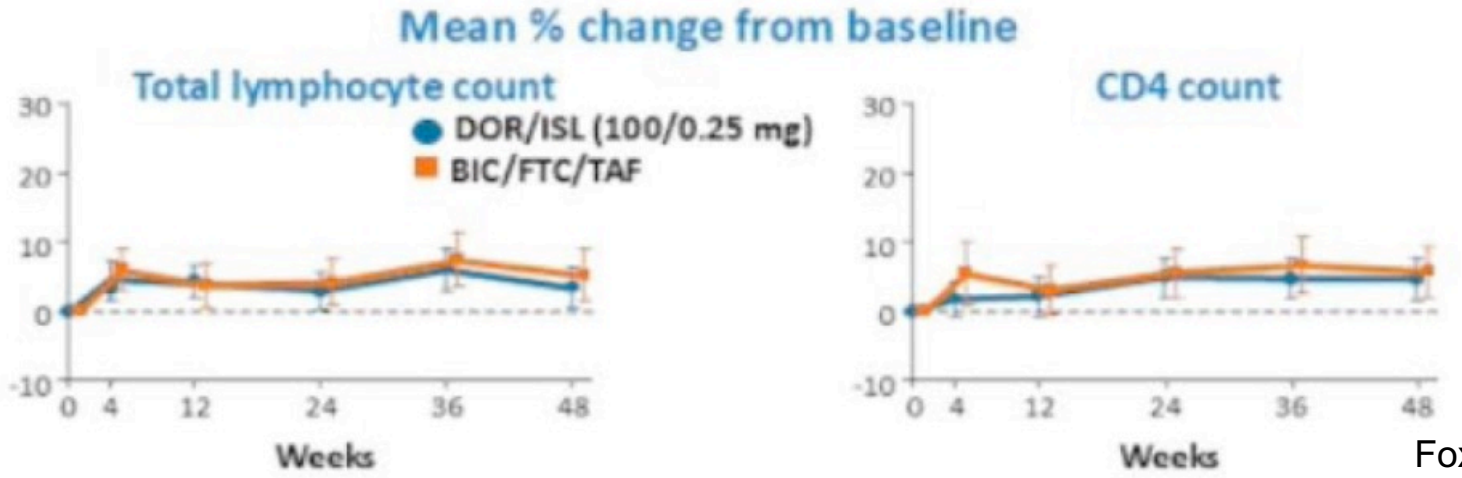
* V106A/M, V108I, Y188L, H221Y, P225H, F227C/L, M230I/L, L234I, P236L or Y318F



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)

Fox M, et al. CROI 2025, Abst 204B



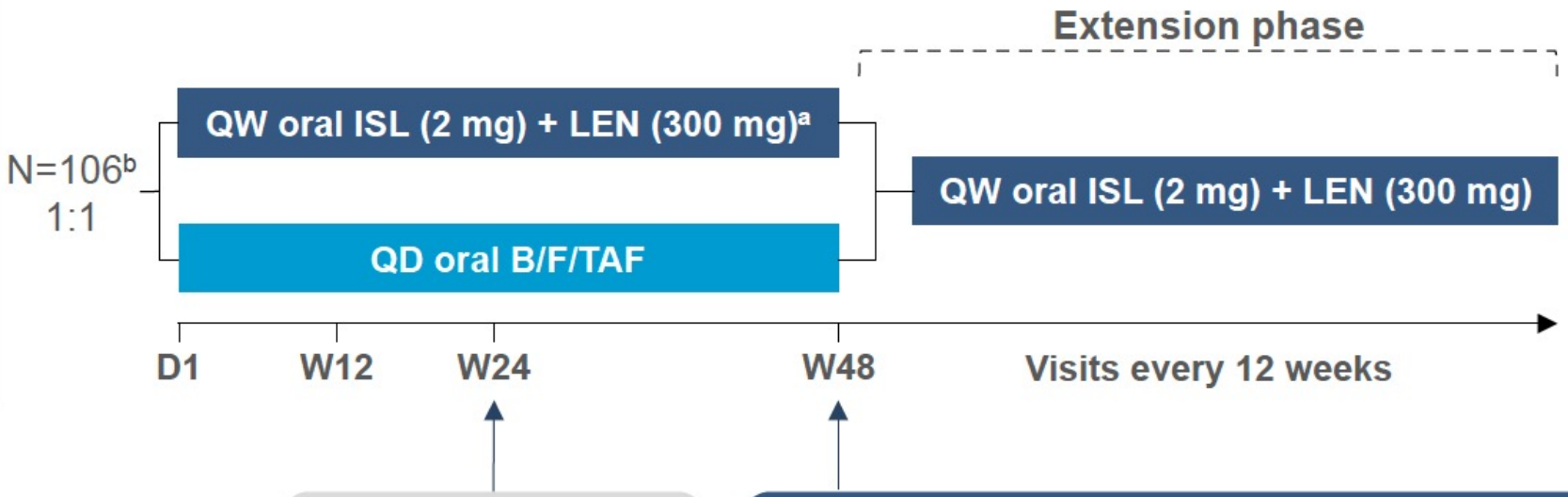


Fox M, et al. CROI 2025, Abst 204B

Once-weekly oral therapy on the horizon (Lenacapavir + Islatravir)

A Phase 2, Open-label, Active-controlled Study in Virologically Suppressed PWH

Eligibility criteria
- Aged ≥18 years
- On B/F/TAF for >6 months
- HIV-1 RNA <50 c/mL for >6 months
- No history of virologic failure
- CD4+ T-cell count ≥350 cells/µl
- Lymphocyte count ≥900 cells/µl
- No HBV infection

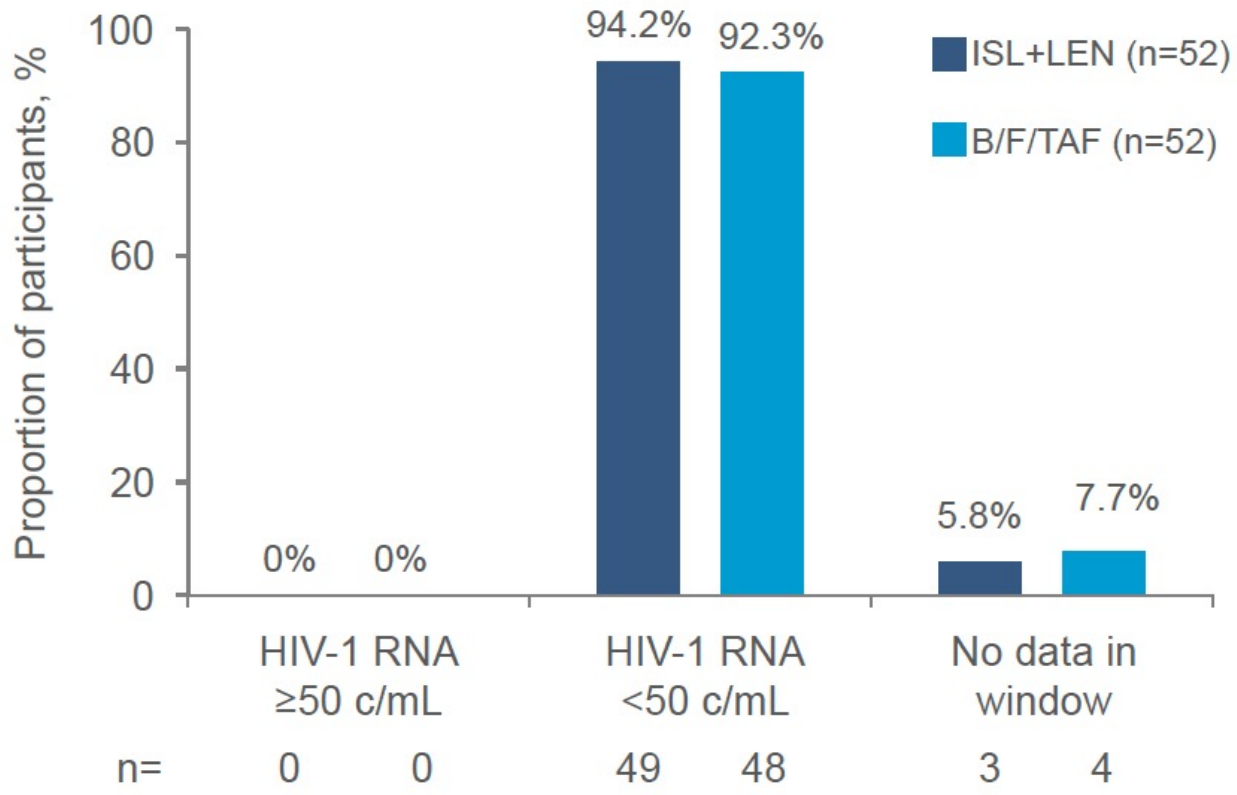


Primary endpoint:[1]
- Proportion with HIV-1 RNA ≥50 c/mL at Week 24 per FDA Snapshot algorithm

Secondary endpoints included in this presentation:
- Proportion with HIV-1 RNA ≥50 c/mL at Week 48
- Proportion with HIV-1 RNA <50 c/mL at Week 48
- Change from baseline in CD4+ T-cell count
- AEs leading to study drug discontinuation

[a]600 mg of LEN was given on D1 and D2 for pharmacologic loading. [b]Randomized, N=106; dosed, N=104.
AE, adverse events; **B/F/TAF**, bictegravir/emtricitabine/tenofovir alafenamide; **c/mL**, copies/mL; **D**, day; **FDA**, Food and Drug Administration; **HBV**, hepatitis B virus; **ISL**, islatravir; **LEN**, lenacapavir; **PWH**, people with HIV-1; **QD**, daily; **QW**, weekly; **W**, week.
1. Colson A, et al. CROI 2024; Abstract 208.

Virologic outcome at 48 weeks



Participants with no data in window:

ISL+LEN

- Two participants discontinued due to AEs not related to study drug
- One participant discontinued due to other reasons not related to study drug
- All participants had HIV-1 RNA <50 c/mL at study discontinuation

B/F/TAF

- Three participants discontinued due to other reasons not related to study drug and had HIV-1 RNA <50 c/mL at study discontinuation
- One participant had missing data during window, but remained on study drug

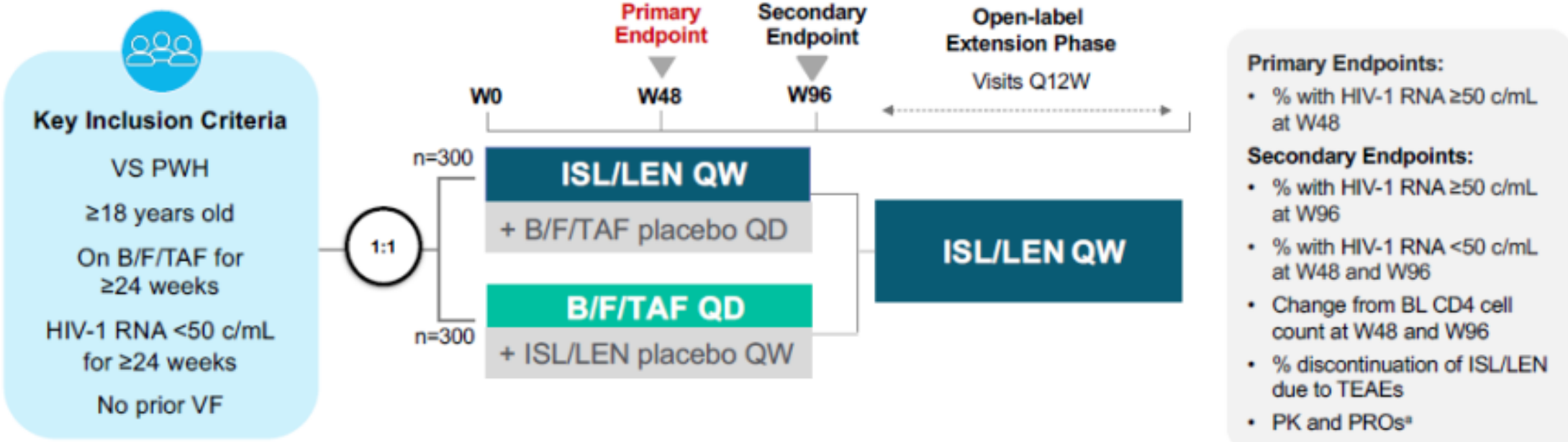
Participants in both treatment groups maintained high rates of virologic suppression

AE, adverse event; **B/F/TAF**, bictegravir/emtricitabine/tenofovir alafenamide; **c/mL**, copies/mL; **FDA**, Food and Drug Administration; **ISL**, islatravir; **LEN**, lenacapavir.

ISL/LEN Once-weekly vs. B/F/TAF

ISLEND-1

Phase 3, Randomized, Double-blind, Active-control, Multicenter Study to Evaluate Efficacy, Safety, and PK of ISL/LEN in VS PWH (N=600)[1,2]



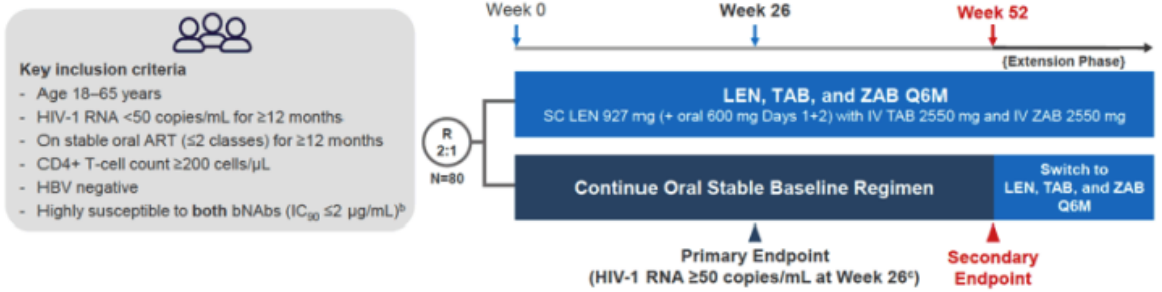
[a]PROs are an exploratory endpoint

BL, baseline; PK, pharmacokinetics; PRO, participant-reported outcome; QD, every day; QW, every week; Q12W, every 12 weeks; TEAEs, treatment-emergent adverse events; VF, virologic failure; VS, virologically suppressed; W, week

1. NCT06630286. https://clinicaltrials.gov/study/NCT06630286 (accessed October 08, 2024); 2. Data on file

LEN SC + 2 bNAbs IV (TAB + ZAB) in suppressed

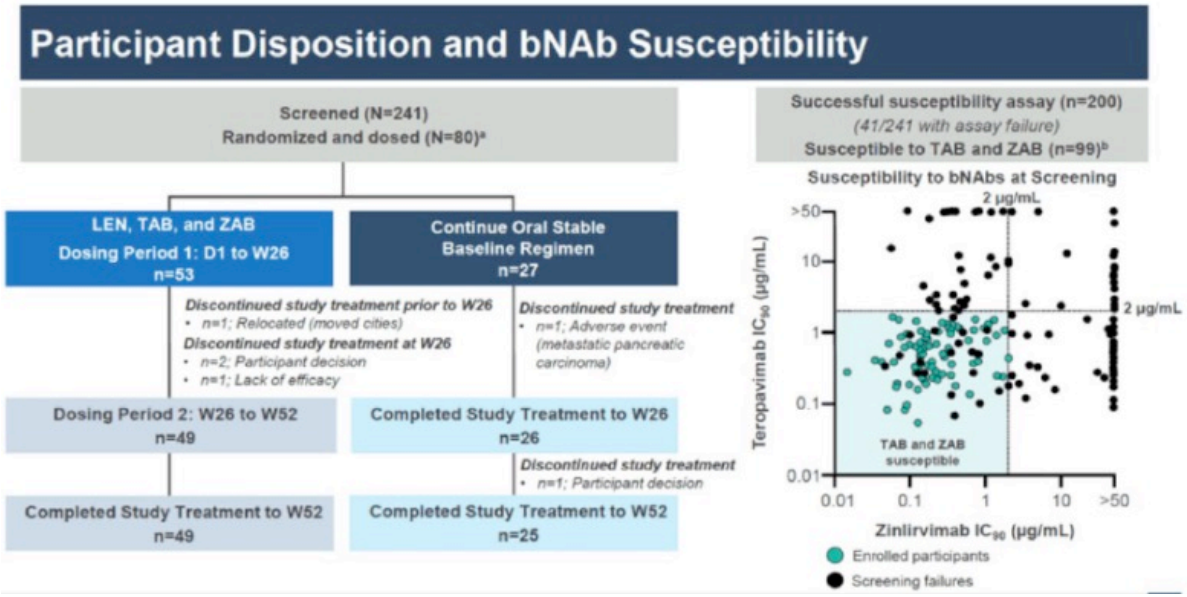
— Randomised, open-label, active-controlled, multicenter study[a]



Week 52 Secondary Outcomes:

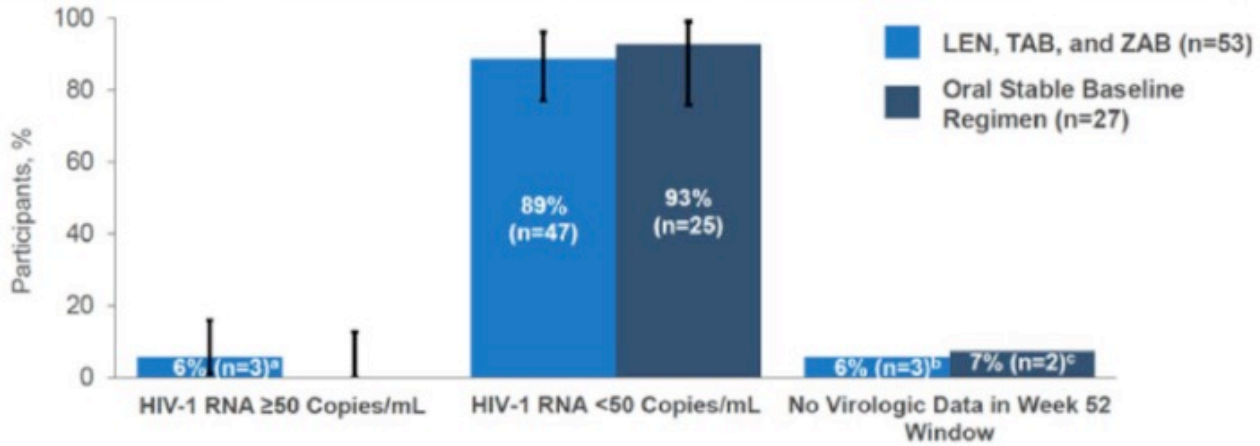
— HIV-1 RNA <50 copies/mL and ≥50 copies/mL per FDA Snapshot algorithm

— Change from baseline in CD4+ T-cell count; safety (adverse events); pharmacokinetics of LEN, TAB, and ZAB; anti-drug antibodies (ADAs)



Ogbuogu O, et al. CROI 2025, Abst 151

Week 52 Virologic Outcomes (FDA Snapshot Algorithm)



— Median (IQR) CD4+ T-cell count increased from baseline at Week 52:

- +32 (–43 to 119) cells/µl in the LEN, TAB, and ZAB group
- +38 (–30 to 146) cells/µl in the oral stable baseline regimen group

Safety Overview (Excluding ISRs related to SC LEN)

Participants, n (%)	LEN, TAB, and ZAB n=53	Oral Stable Baseline Regimen n=27
AEs	40 (76)[a]	21 (78)
Grade ≥3	4 (8)[b]	2 (7)
Treatment-related AEs	5 (9)[c]	0
Grade ≥3	0	0
Serious AEs	1 (2)[d]	1 (4)[e]
AEs leading to study drug discontinuation	0	1 (4)[e]
AEs in ≥5% of participants[f]		
Diarrhea	7 (13)	1 (4)
Upper respiratory tract infection	5 (9)	0

Managing virologic failure

Defining Virologic Response

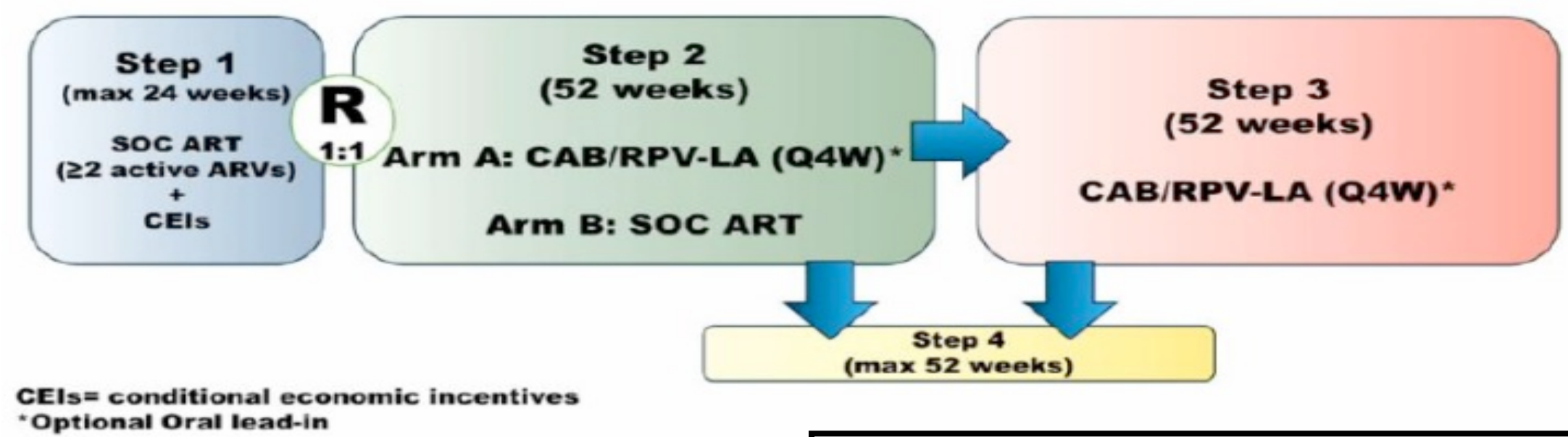
- **Virologic suppression:** Confirmed HIV RNA level below the LLOD of available assays.
- **Virologic failure:** The inability to achieve or maintain suppression of viral replication to HIV RNA level <200 copies/mL.
- **Incomplete virologic response:** Two consecutive plasma HIV RNA levels ≥200 copies/mL 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.

DHHS ART Guidelines. January 2025.

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

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

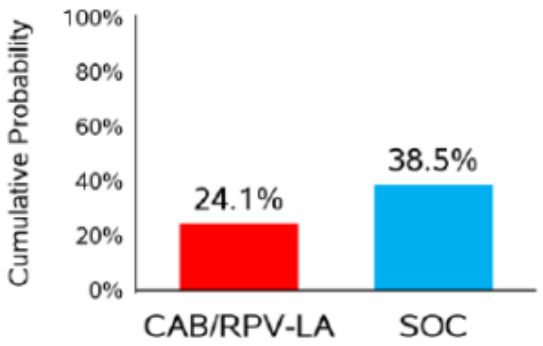
Rana AI, et al. CROI 2024, Abst. 212LB

LATITUDE (ACTG A5359): Outcomes

Primary Outcome

Regimen Failure

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



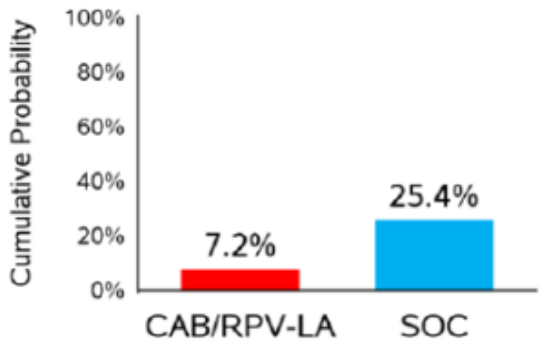
Number of participants

	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%)**

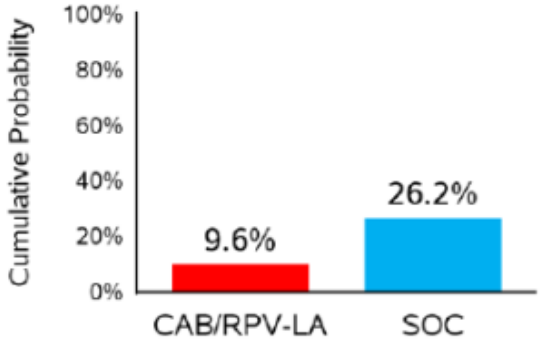


Number of participants

	CAB/RPV-LA	SOC
Virologic Failure	6	28

Treatment-related Failure

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

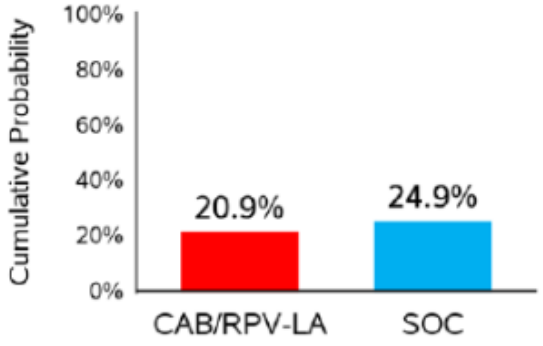


Number of participants

	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%)



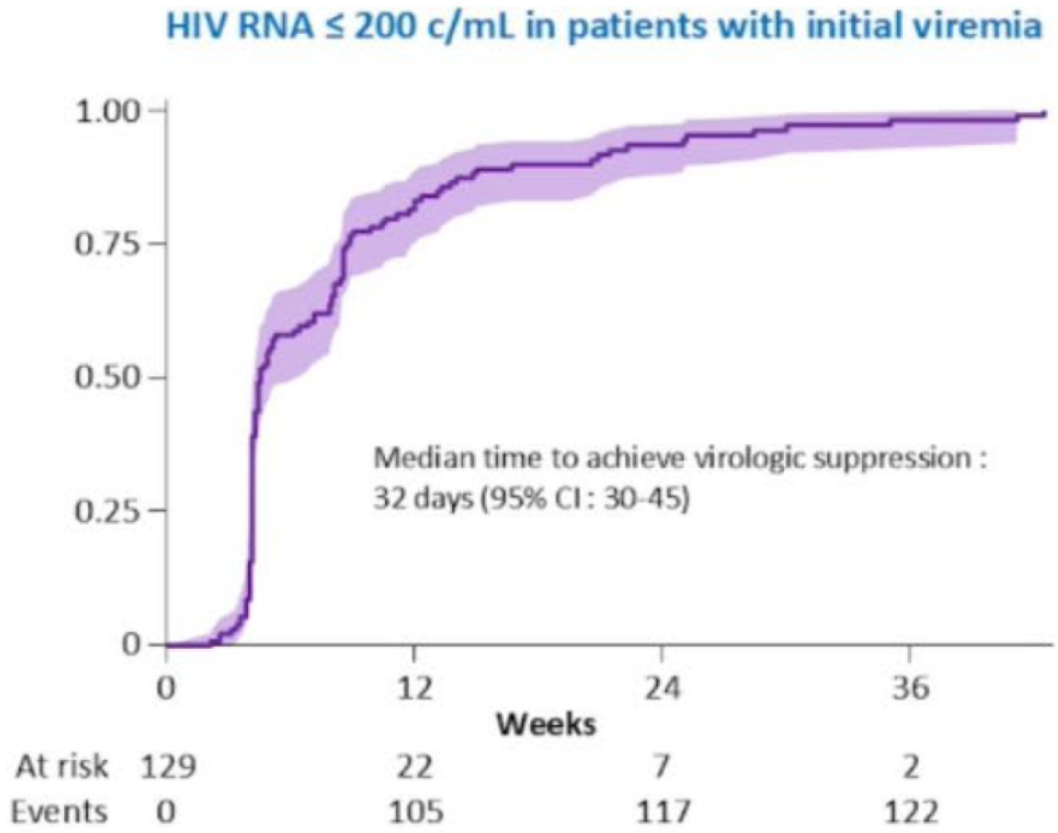
Number of participants

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

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

LA CAB/RPV in VulnerableViremic Patients without Resistance

- Ward 86 HIV Clinic
- Retrospective study of 370 PWH with high rates housing instability, substance use and low CD4 count (241 suppressed;129 viremic)
- LA CAB/RPV Jan 2021-2024
- Virologic suppression (RNA <200 c/mL) at week 48
  - 99.4% suppressed at BL
  - 97.9% viremic at BL



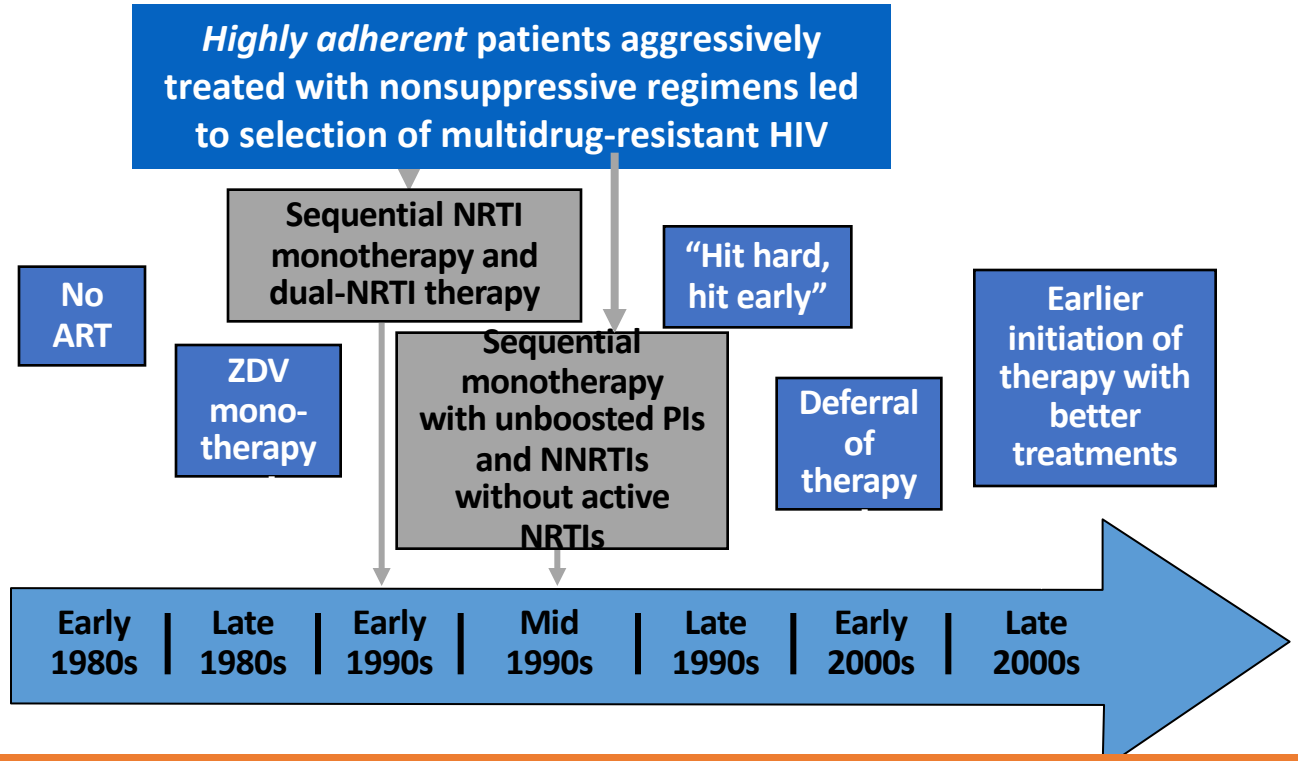
Gistand NL, et al. CROI 2025, Abst 689

Managing virologic failure in patients with resistance

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

Data informing the management of those with underlying resistance

Virologic failure(s), often with NRTIs, NNRTIs and unboosted PIs



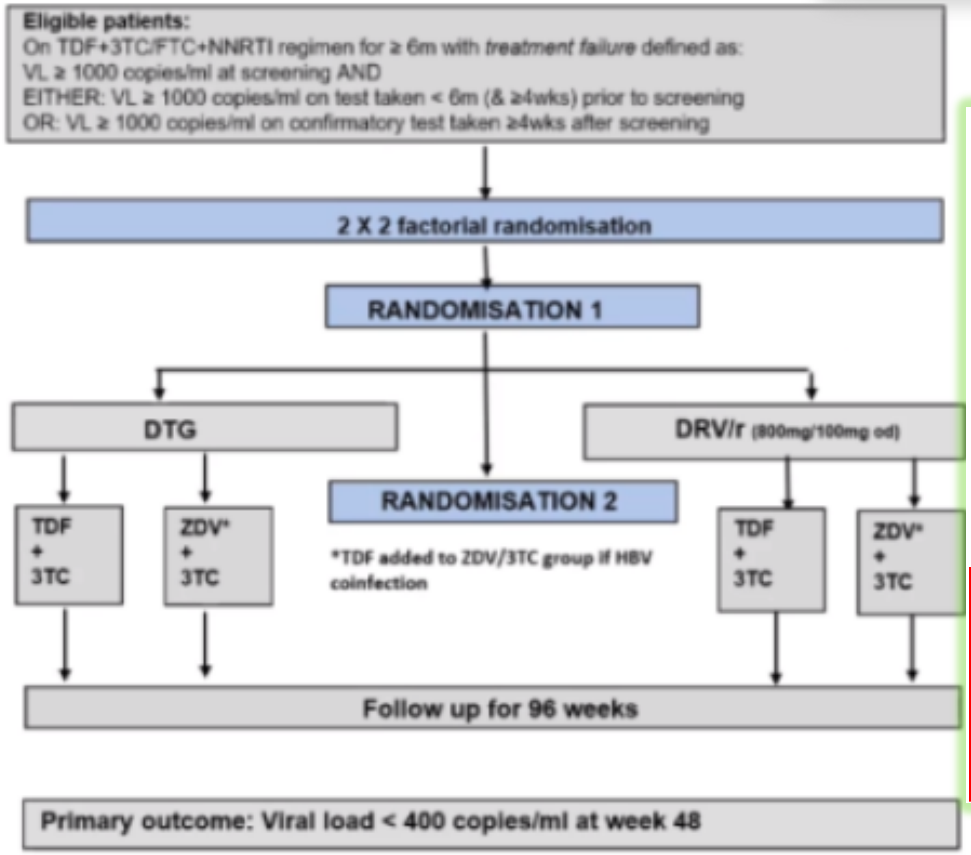
Virologic failure on NRTIs and NNRTIs

hiv.gov/hiv-basics/overview/history/hiv-and-aids-timeline.

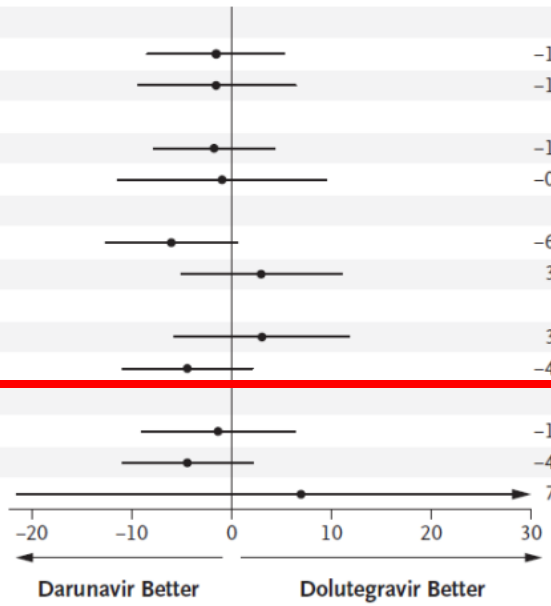
Dolutegravir or Darunavir in Combination with Zidovudine or Tenofovir to Treat HIV

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



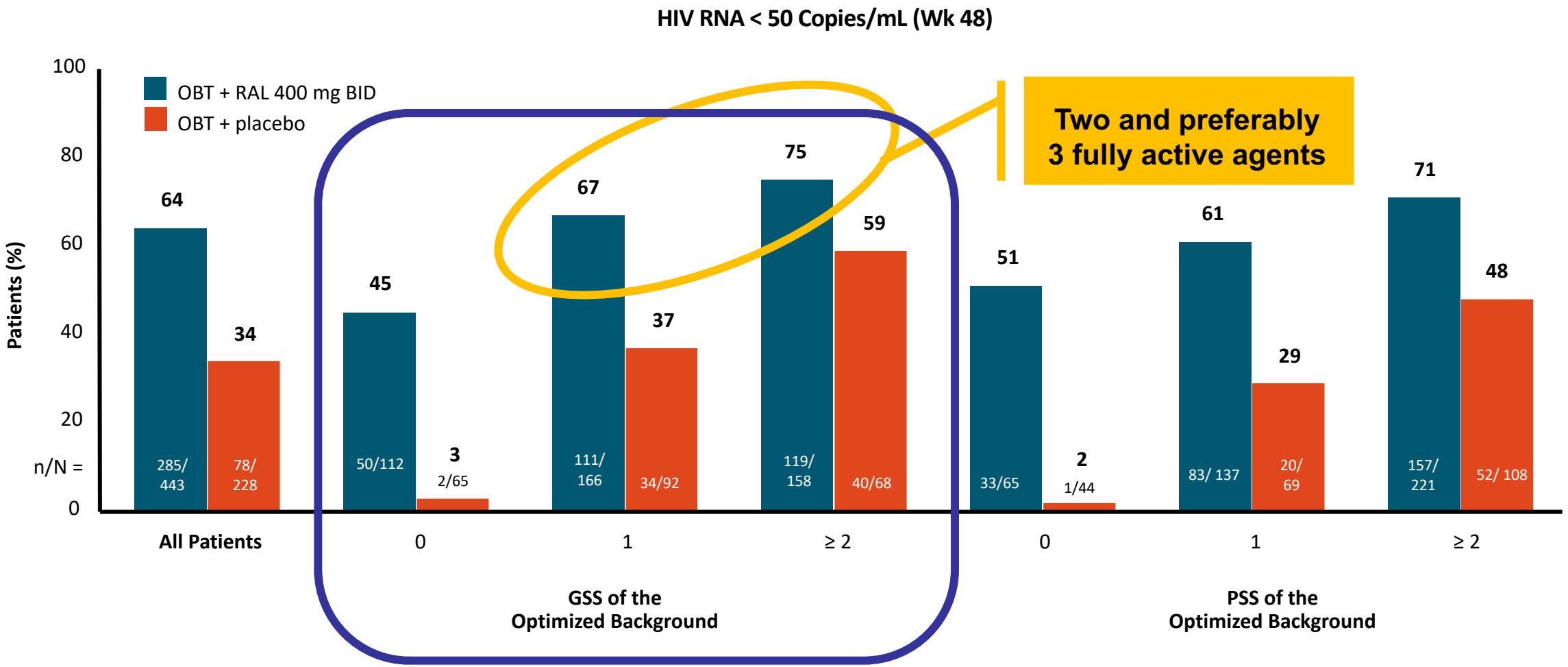
Subgroup	Dolutegravir	Darunavir	Difference in Percentage Points (95% CI)
	no. of patients/total no. (%)		
NRTI randomization group			
Tenofovir	108/118 (91.5)	107/115 (93.0)	−1.5 (−8.4 to 5.3)
Zidovudine	104/117 (88.9)	103/114 (90.4)	−1.5 (−9.3 to 6.4)
Viral load at baseline			
<100,000 copies/ml	153/169 (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 Virologic Failure: BENCHMRK, when there are no fully active high barrier drug



Cooper. NEJM. 2008;359:355.

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

Check for updates

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)

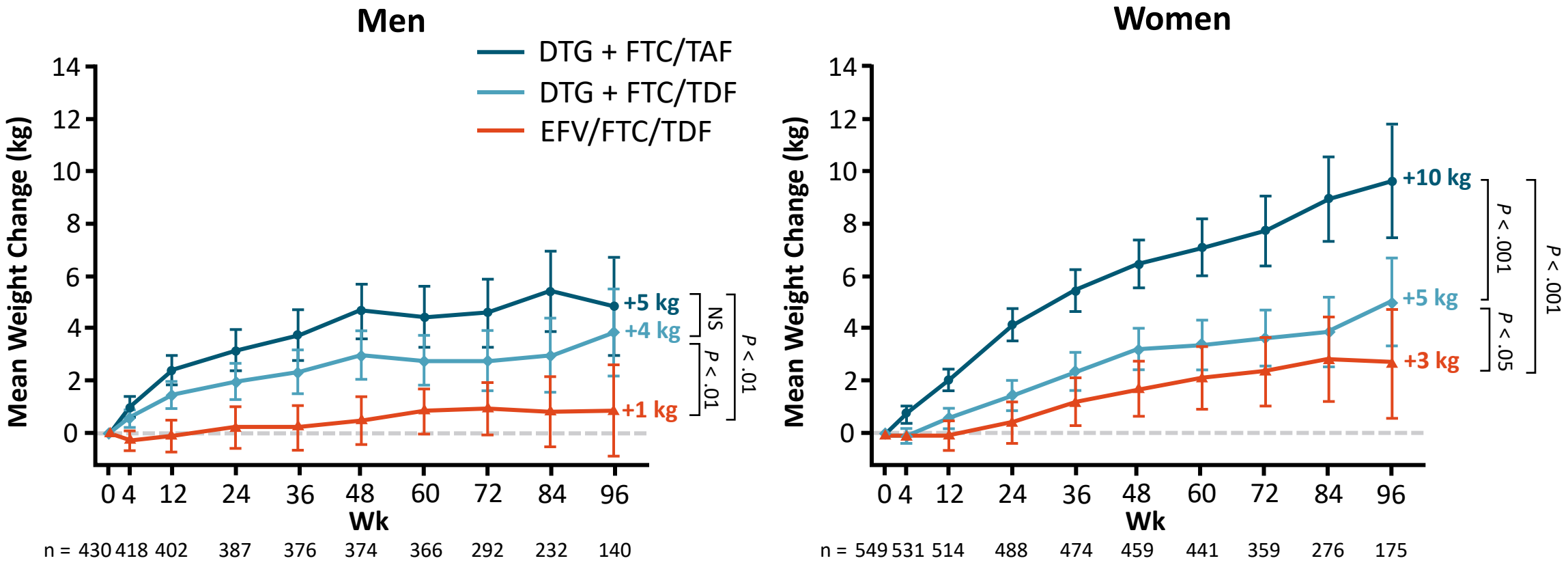
"Irrespective of the interventions, mixed results were found for re-engagement into care or ART re-initiation. **None of the studies led to an improvement in viral suppression."**

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

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

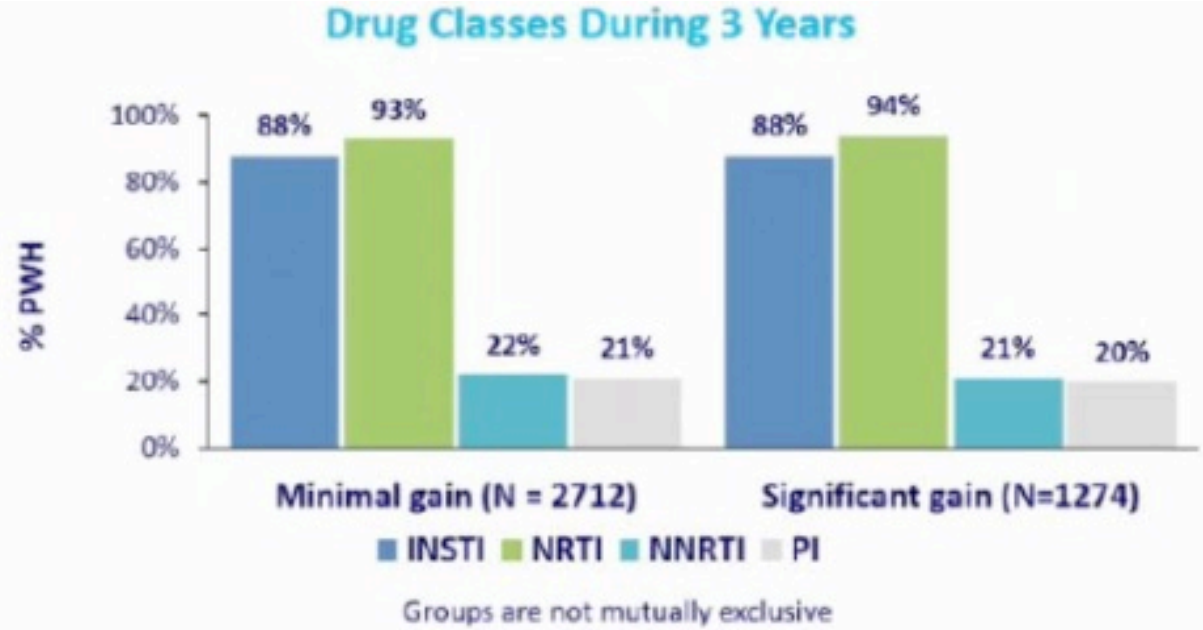


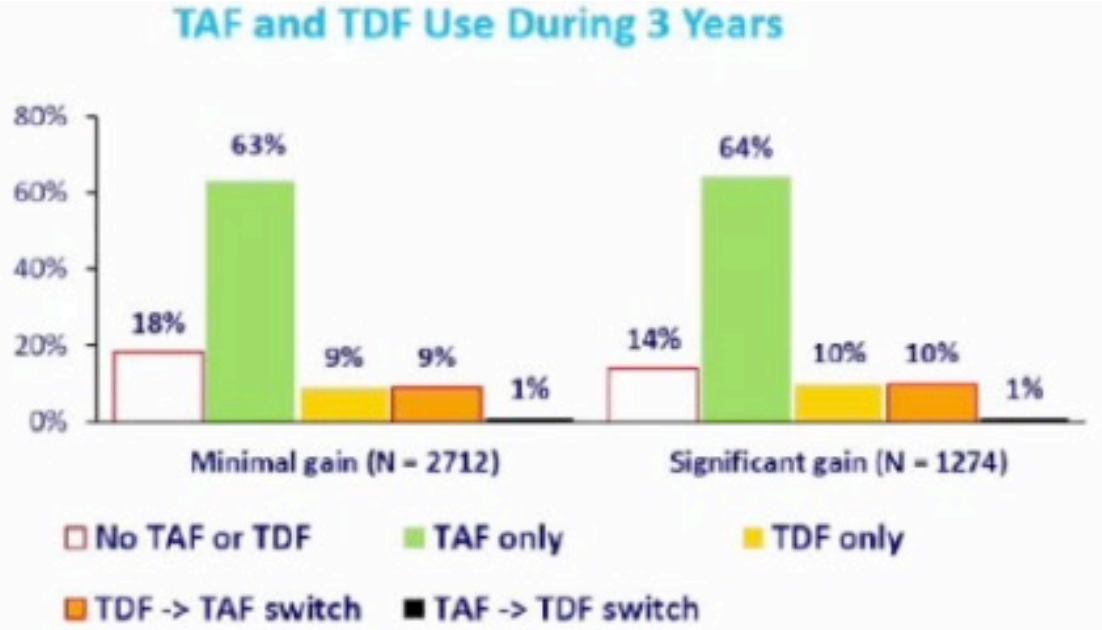
Hill. IAS 2019. Abstr MOAX0102LB. Reproduced with permission.

*Wilcoxon rank-sum comparison at Wk 96.

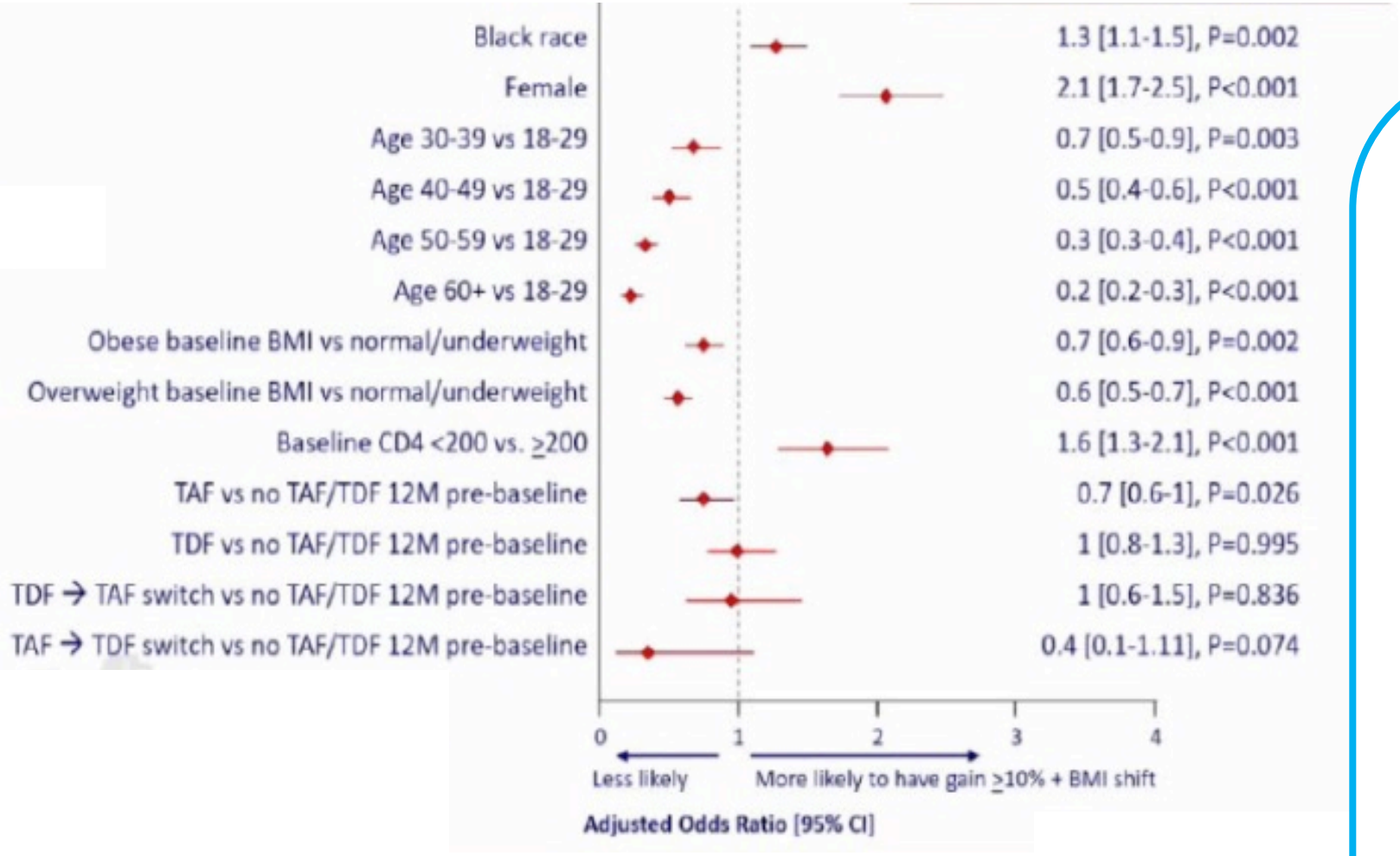
Predictors of weight gain over 3 years

- 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

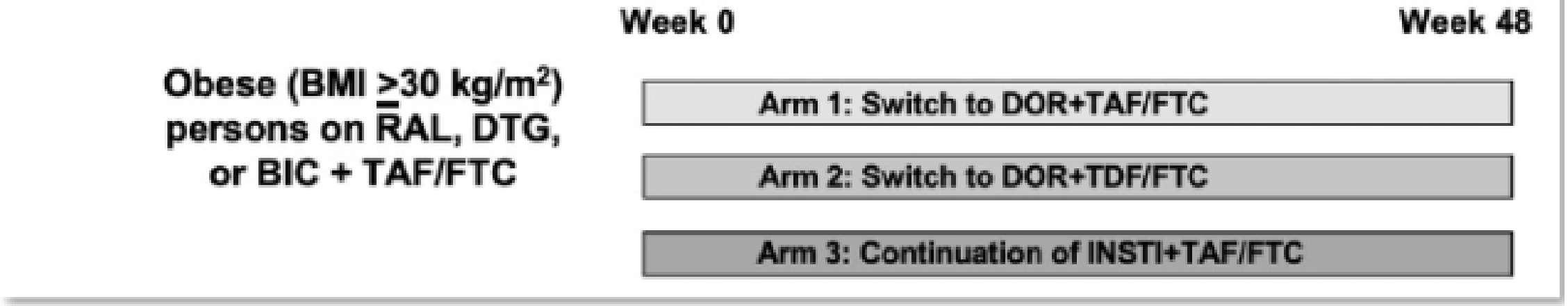
Weight gain observed in PWH is reflective of the general population and community characteristics rather than direct effect of ART

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-based regimen (The DO-IT Trial)

- A 48-week, 3 parallel group, open-label, multicenter, superiority, randomized, controlled trial in adult PWH with obesity on an INSTI (bictegravir [BIC], dolutegravir [DTG], or raltegravir [RAL]) and TAF/FTC for at least 48 weeks with sustained viral suppression.
- Statistical power for a 5% between-arm treatment effect on body weight (either DOR arm vs. INSTI) after 1 year was 80% with 150 participants.



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

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

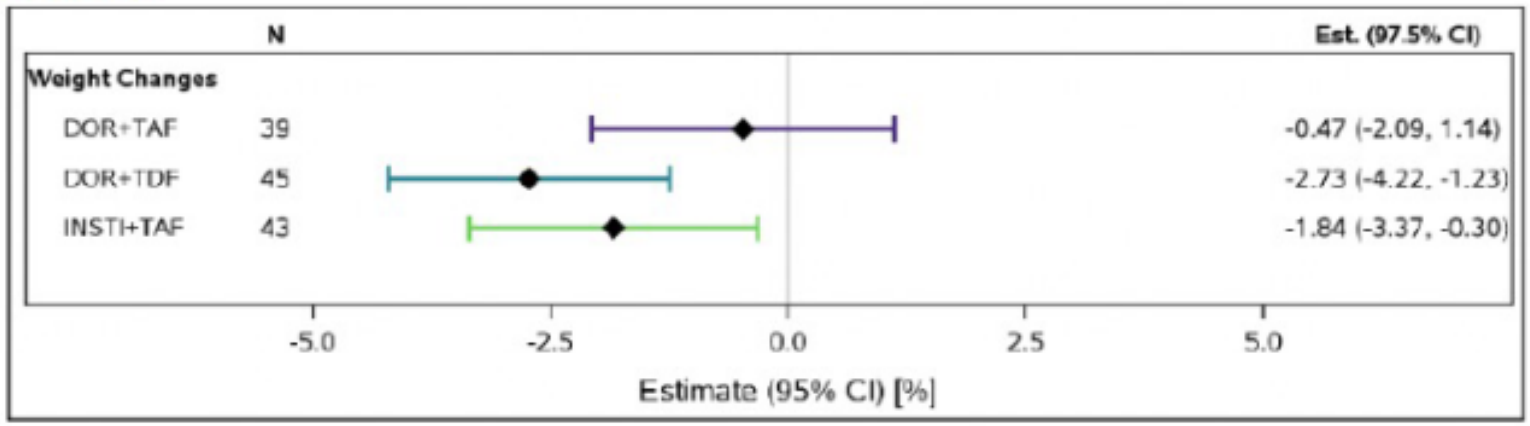
- July 2021-Nov 2023, 145 from 25 sites in US randomized 1:1:1
- 49% female, 53% black and 18% Hispanic
- Median age 49 yrs, BMI 34.9 kg/m^2, CD4 688 cells/uL
- Median time on current ART= 3.4 yrs, 86%on BIC, 13% DTG
- 65% had >10% wt gain in first 1-3 yrs of INSTI-based regimen

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

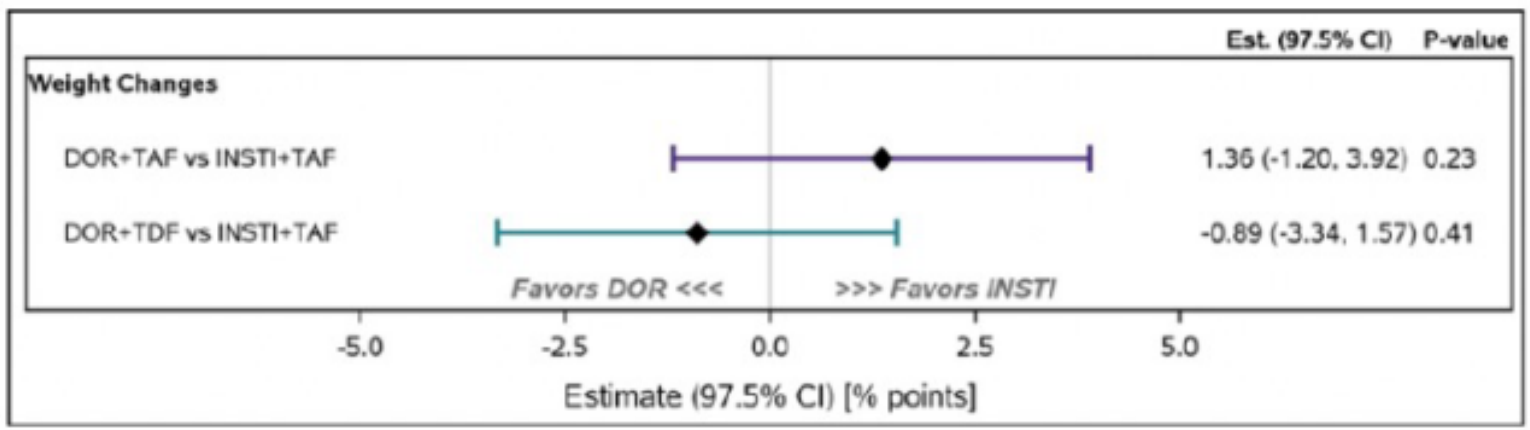
IAS 2025

Primary Outcome: Weight Change at 48 Weeks

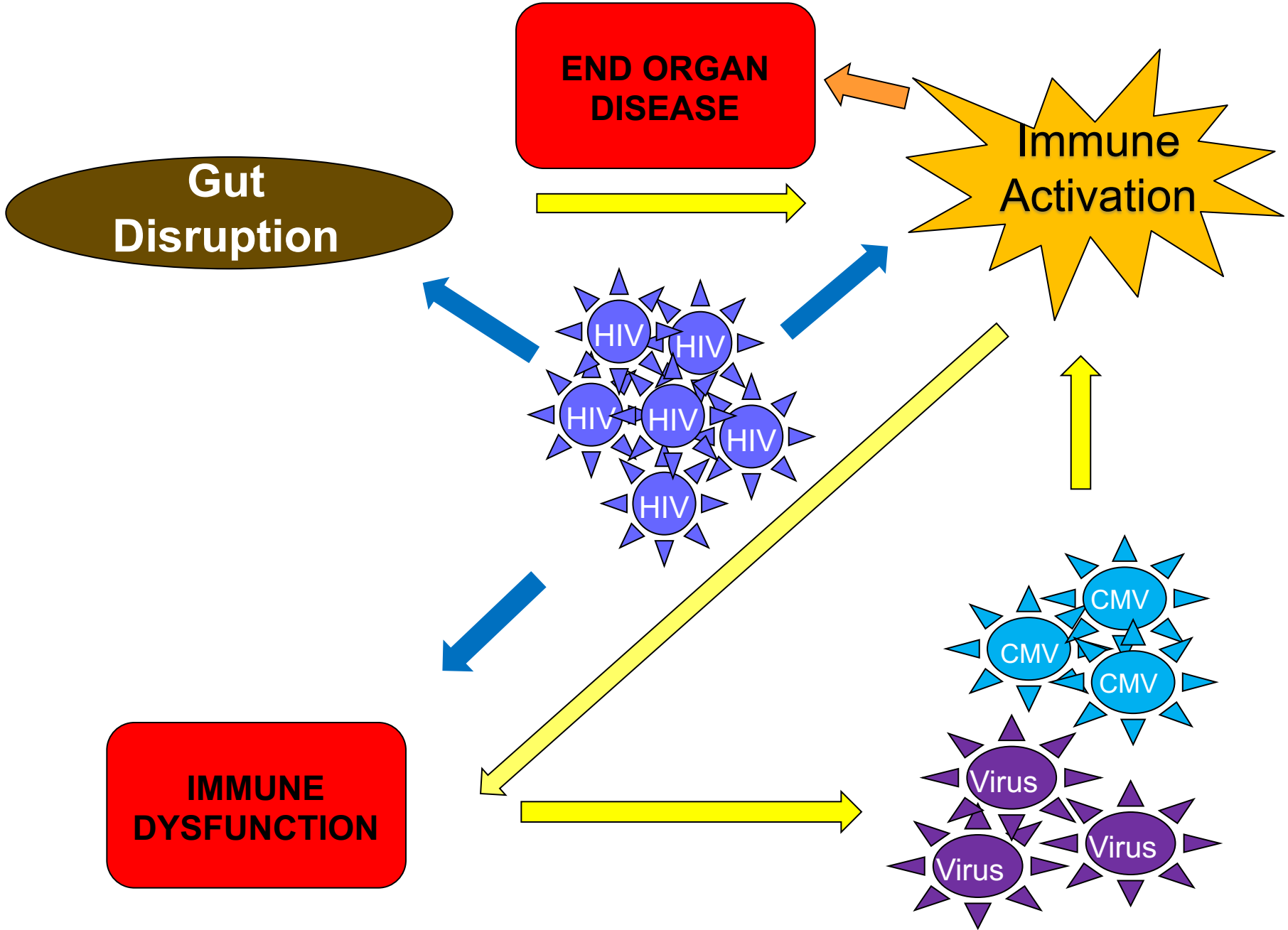
Within Arm:



Pairwise Treatment Arm Comparisons:

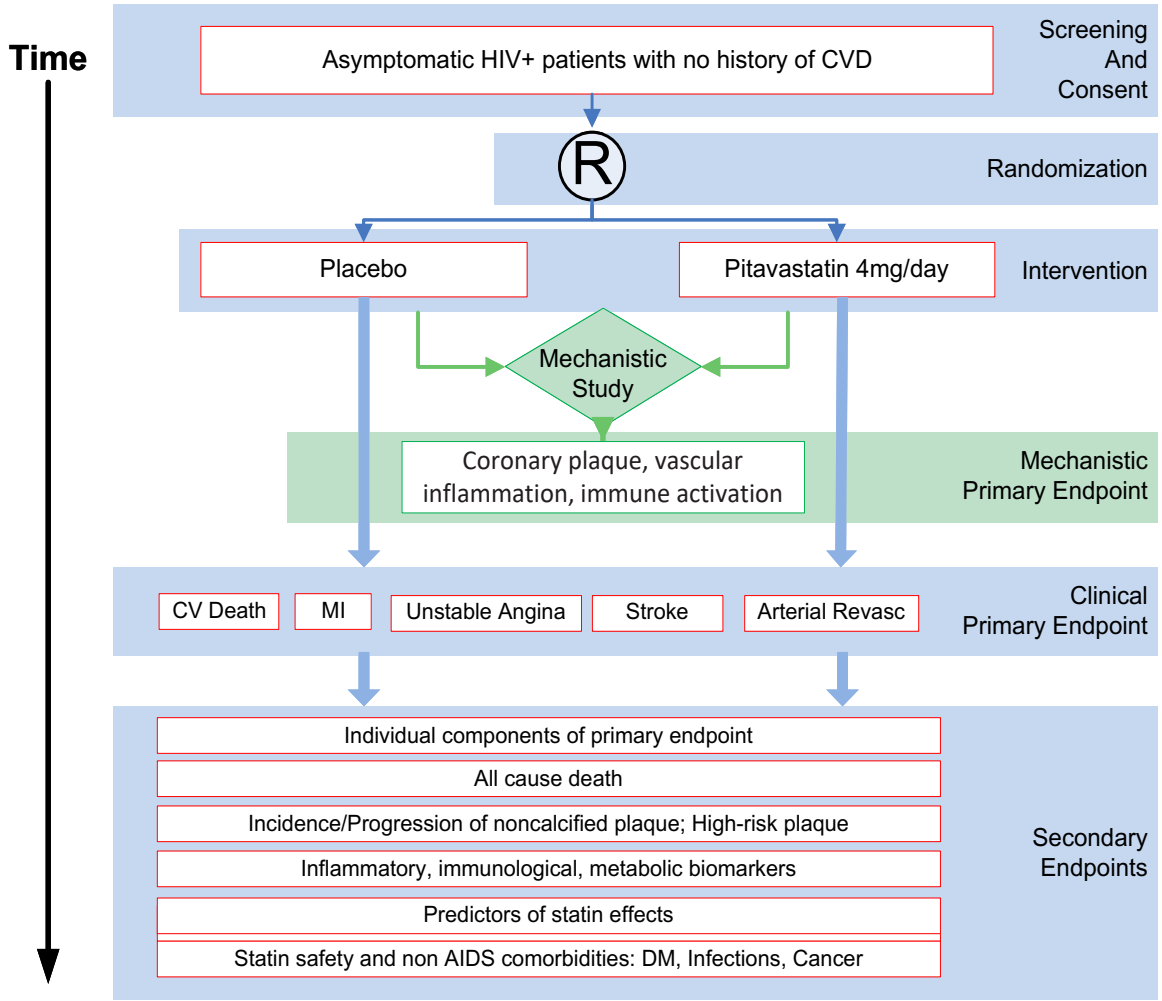


Chronic inflammation persists on antiretrovirals



REPRIEVE

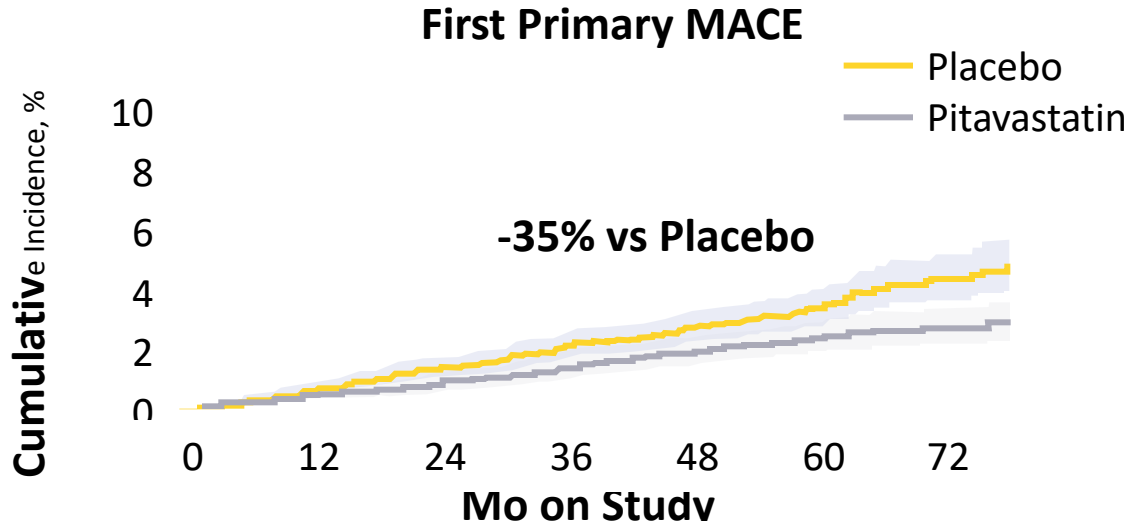
Randomized Trial to Prevent Vascular Events in HIV



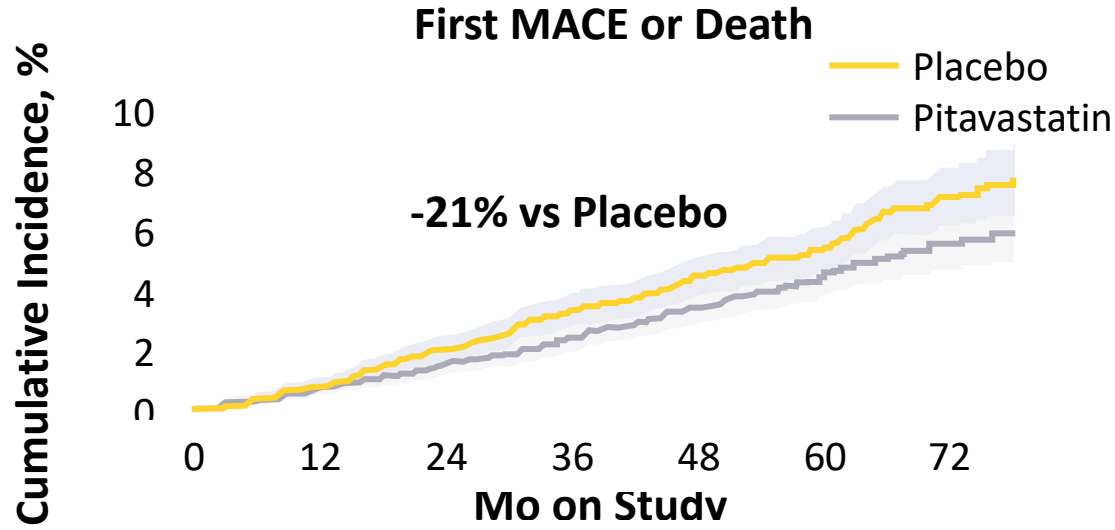
Grinspoon. NEJM. 2023

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%
Patients at Risk, n	0%	0.7%	1.4%	2.1%	2.7%	3.4%	4.4%
Pitavastatin	3888	3647	3475	3364	2997	1947	1052
Placebo	3881	3693	3506	3356	2997	2182	959

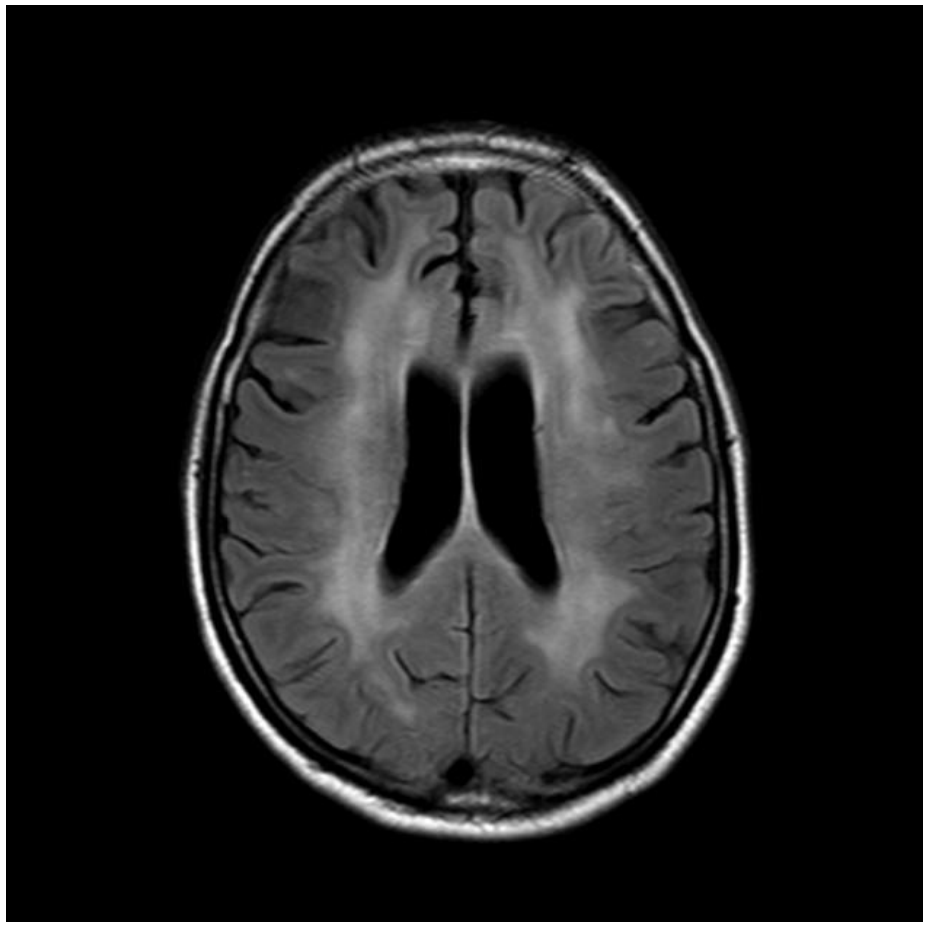


Cumulative incidence of event							
	0%	0.8%	1.6%	2.4%	3.4%	4.5%	5.5%
Patients at Risk, n	0%	0.8%	2.0%	3.3%	4.4%	5.3%	7.1%
Pitavastatin	3888	3647	3475	3364	2998	1948	1027
Placebo	3881	3693	3506	3356	2997	1975	919

Grinspoon. NEJM. 2023

HIV encephalopathy: Cognitive Impairment

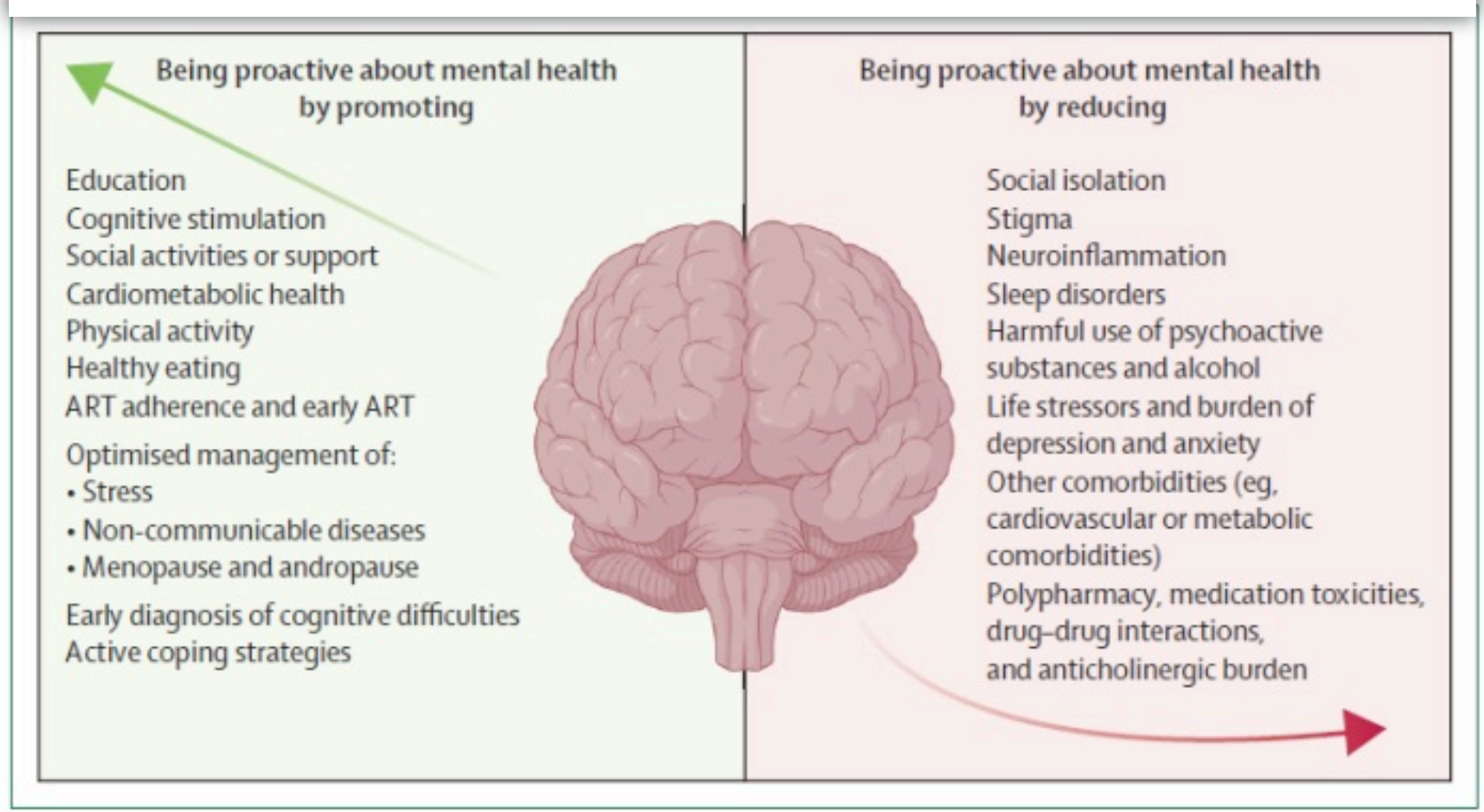
- Highly prevalent
  - ALLRT
    - 39% mild impairment
    - 21% developed impairment after baseline
  - CHARTER
    - 40% neurocognitive impairment
- Pathogenetic mechanisms
  - HIV in the CNS
  - Ongoing immune activation
- IDSA management guidelines recommend screen for and work-up cognitive deficits*



*Horberg M et al. CID 2024

Fostering healthy cognitive ageing in people living with HIV

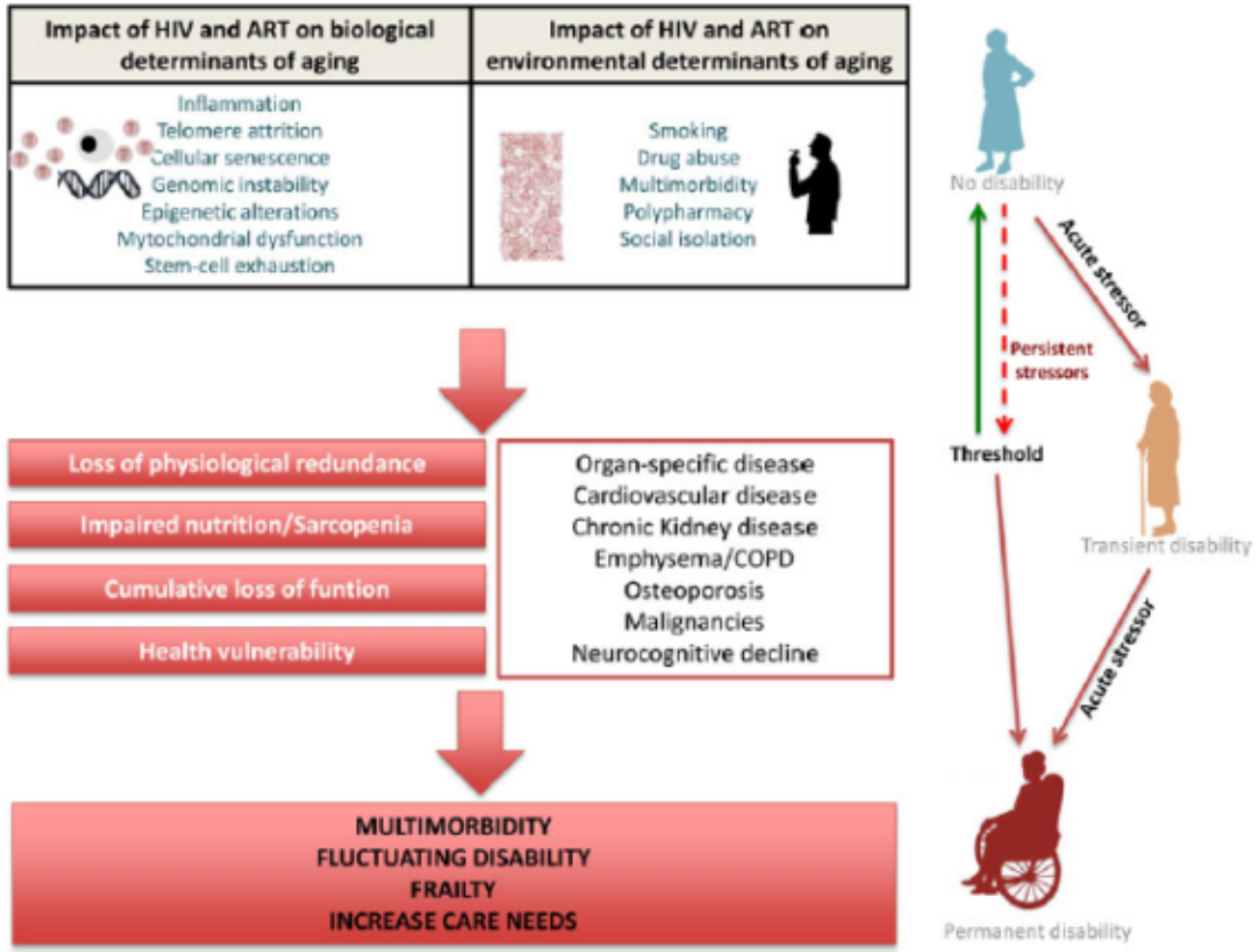
Lucette A Cysique, Jules Levin, Chris Howard, Jeff Taylor, John Rule, Jane Costello, Jane Bruning, Priscilla Njeri, Amy B Mullens, Edwina Wright, Hetta Gouse, Kirstie Daken, Mattia Trunfio, Htein Linn Aung, Reuben N Robbins, Christopher M Ferraris, Jose A Muñoz-Moreno, Steven P Woods, David J Moore, 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]

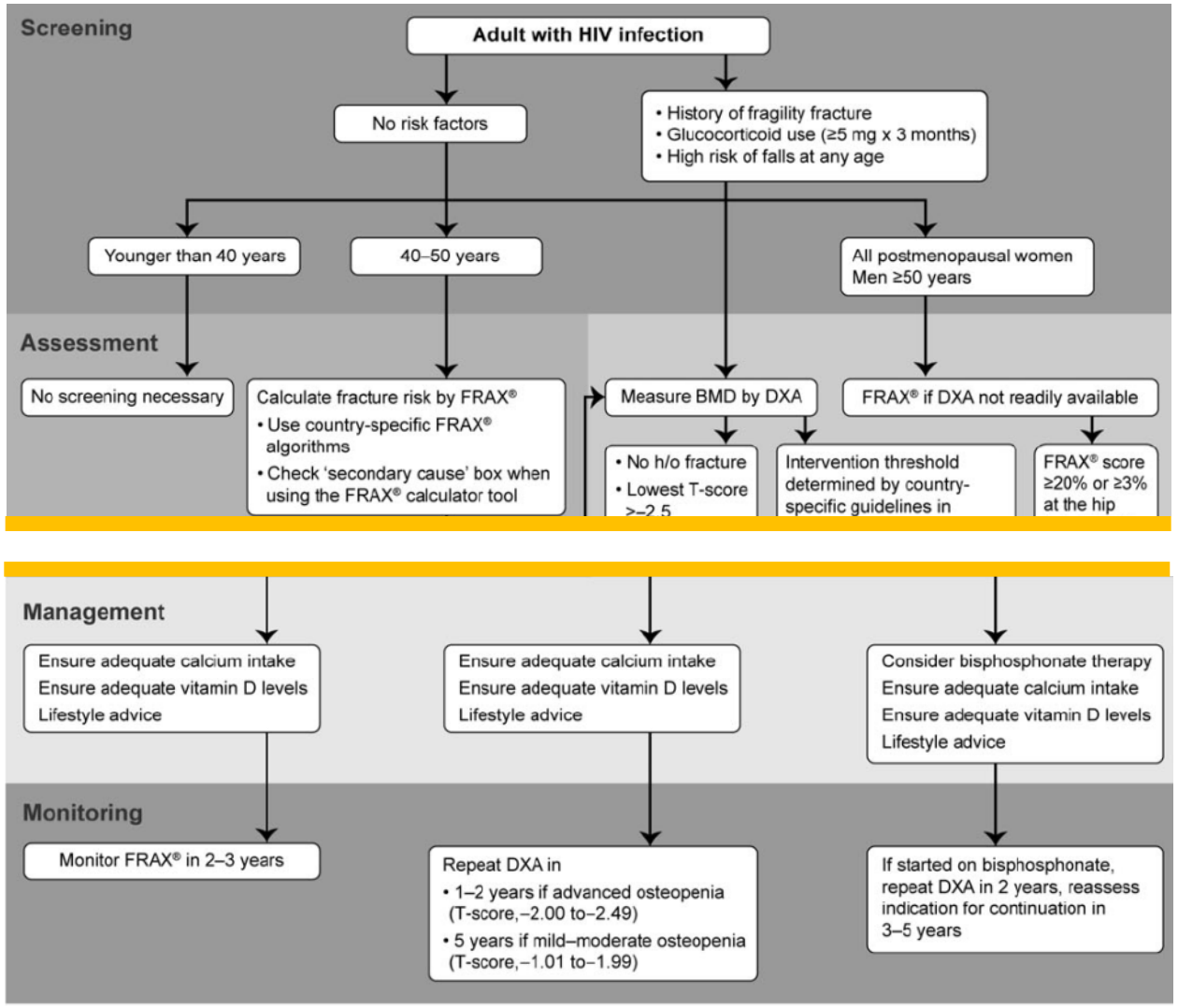


IDSA Primary Care Guidelines 2024[2]

- 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

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

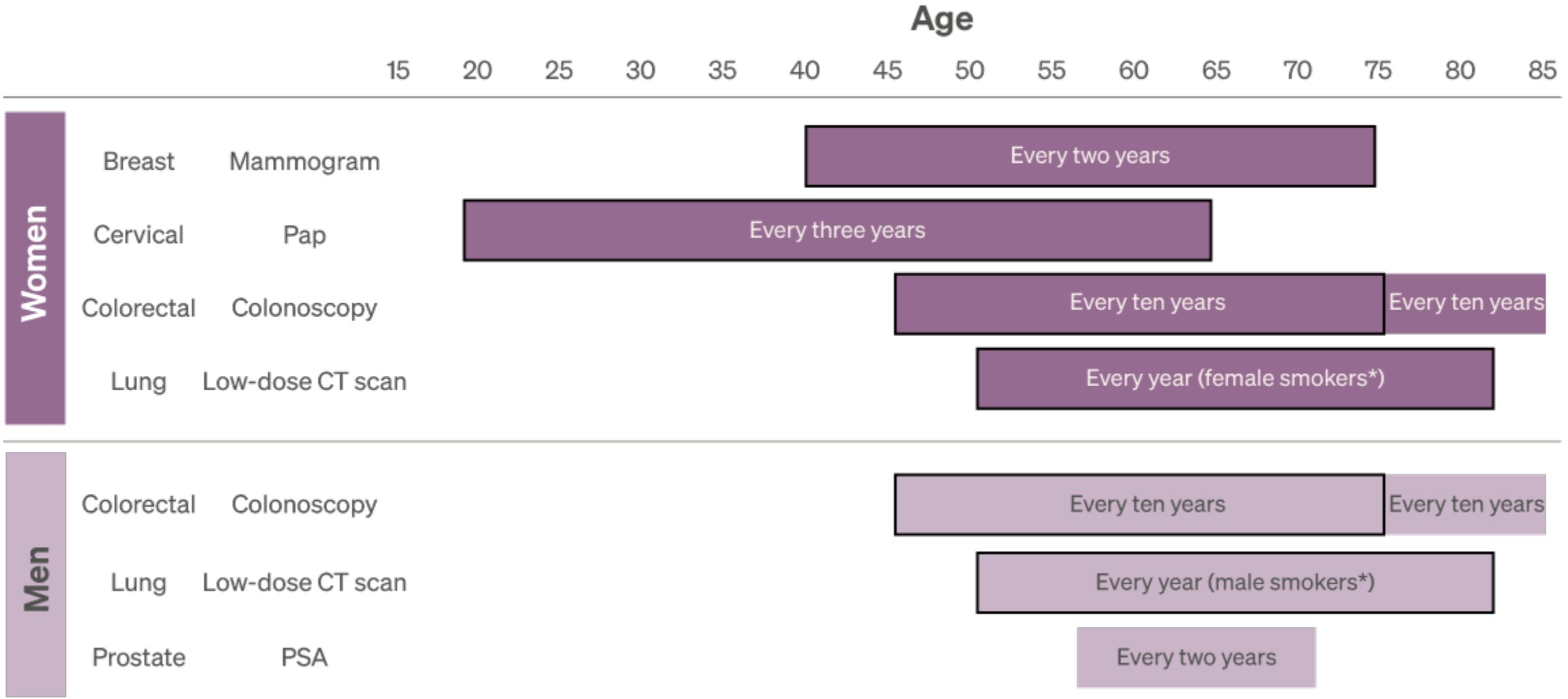
Zoster Infection & Vaccination as Determinants of Vascular and Cognitive Outcomes in PLWH

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!!