More News from AIDS 2024 (Munich) on Antiretroviral Therapy, Cardiometabolic Health, and Anal Cancer Screening

Tristan J. Barber, MA, MD, FRCP

Consultant Physician, Ian Charleson Day Centre, Royal Free Hospital

Honorary Associate Professor, Institute for Global Health

University College London (United Kingdom)

This activity is jointly provided by Physicians' Research Network and the Medical Society of the State of New York.

ART

SSOAX0903LB

No Confirmed Virological Failures (CVF) for 144 Weeks When Switching 2-/3-/4-Drug ART to DTG/3TC in Heavily Treatment-Experienced PLWHA with Prior M184V/I and Multiple Virological Failures in the Prospective SOLAR-3D Study

G BLICK[1], E CERRETA-DIAL[1], G MANCINI[1], A COSENZA[1], L. FANG[2]

[1]Health Care Advocates International, Stratford CT USA

[2]Pharstat, Raleigh, NC USA

AIDS 2024

AIDS 2024, the 25th International AIDS Conference

HEALTH CARE ADVOCATES INTERNATIONAL

RATIONALE

- In the setting of M184V/I, 3TC can still exert a **modest antiviral effect (0.5 $\log_{10}$)** in PLWHIV with VF[1-6]. Therefore, not “monotherapy".
- HIV-1 containing M184V/I displays **reduced viral replication fitness/capacity**[6-8].
- If PCR<50 for years, **M184V/I may no longer persist/be archived** as minority variants in reservoirs, thus no longer clinically relevant regarding maintaining viral suppression[9-12].
- DTG/3TC may have clinically relevant **long-term safety advantages**, especially in economically developing nations that continue to utilize TDF-based regimens[13].
- There is a significant **cost advantage** to using 2-drug vs 3- or 4-drug ART that would positively impact both economically developed and developing nations[14-16].

[1]Campbell, et al. Clin Infect Dis. 2005;41:236-242. [2]Castagna, et al. AIDS. 2006;20:795. [3]Paton, et al. NEJM. 2014;371:234. [4]La Rosa, et al. Lancet HIV. 2016;3:e247. [5]Boyd, et al. Lancet. 2013;382:664. [6]Quercia R, et al. JAIDS. 2018;78(2):1-29. [7]Turner D, et al. Clin Diag Lab Immun. 2003;10(6):979-981. [8] Quan Y, et al. Antimicrob Agents Chemother. 2003;47(2):747-754. [9]Ciaffi, et al. Lancet HIV. 2017;4:e384. [10]Wirden, et al. J Antimicrob Chemother. 2011;66:709. [11]Delaugerre, et al. HIV Med. 2012;13:517. [12]Allavena, et al. J Virol Methods. 2018;251:106. [13]Cahn, et al. Lancet. 2019;393(10167):143-155. [14]Girouard, et al. Clin Infect Dis. 2016;62(6):784-791. [15]Priest, et al. Infect Dis Ther. 2023;12:2117-2133. [16]Fan, et al. Value in Health. 2022;25(12):S132-S133.

STUDY DESIGN

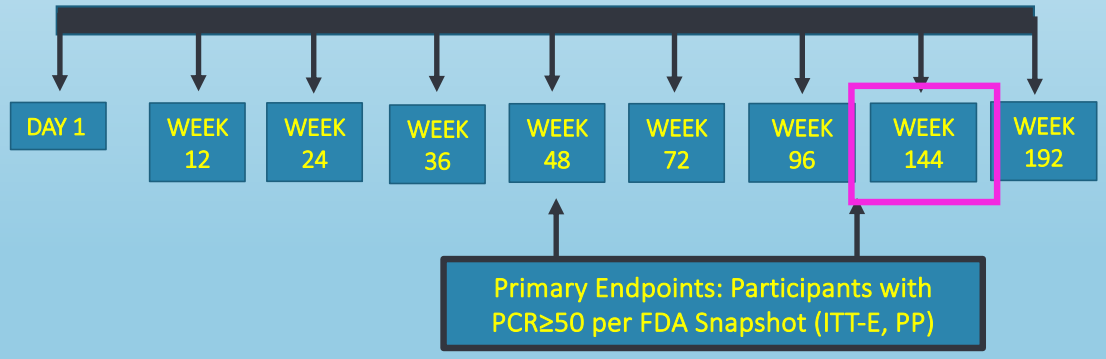
ELIGIBILITY CRITERIA:

- HIV+ Adults aged ≥18
- HIV-1 RNA <50c/mL for ≥6mos
- Any stable 2-/3-/4-drug ART for ≥6mos
- **Prior virologic failure** (≥2 prior ART with at least 1 of following: failure to attain PCR<50, confirmed rebound PCR>200, documented genotypic/ phenotypic resistance)
- **No exclusion for prior INSTI, any CD4, prior NRTI mutations, or M184V/I or K65R in BL Proviral DNA NGS (above a 10% threshold)**
- COVID Window +/- 1mo.

SOLAR-3D:
Prospective, open-label, comparative, 96-week study, [144-week extension] (n=100)

HISTORY OF PRIOR M184V/I (n=50)

NO HISTORY OF PRIOR M184V/I (n=50)



Individuals were consecutively consented and enrolled during regularly scheduled office appointments from 5/2/2019 through 6/16/2020

PRIMARY ENDPOINTS:

- Proportion of pts with PCR≥50 at Wks 48 & 96 (FDA Snapshot, ITT-E, Per Protocol)

SECONDARY ENDPOINTS:

- PCR<50 at Wks 48 & 96 (FDA Snapshot, ITT-E and Per Protocol)
- Discontinuations due to CVF (PCR≥50 followed by PCR>200)

Blick et al. IAS 2024, #SSOAX0903LB

BASELINE CHARACTERISTICS

Baseline Characteristic	All Patients (n = 100)	Historical M184V/I Resistance (n = 50)	No Historical M184V/I Resistance (n = 50)	*P* Value
Median Age, yrs (IQR)	58 (51-64)	61 (56-66)	55 (47-61)	<0.001
Cis-/Trans-Gender Female, n (%)	15 (15)	11 (22)	4 (8)	0.050
Median Time Since HIV Diagnosis, yrs (IQR)	25.3 (15.0-29.5)	28.4 (25.1-30.0)	15.5 (9.8-26.7)	<0.001
Median CD4 Nadir cell/mm3 (IQR)	190 (64-278)	160 (45-225)	225 (88-359)	0.006
History CD4<200, n (%)	53 (53)	33 (66)	20 (40)	0.009
Median ART Duration, yrs(IQR)	22.3 (14.3-25.7)	24.6 (22.0-28.1)	15.2 (8.8-22.6)	<0.001
Median Previous ART regimens, n(IQR)	7 (4-10)	9 (7-13)	4 (2-5)	<0.001
Median Duration of HIV-RNA suppression, yrs (IQR)	11.8 (8.2-14.6)	12.8 (10.2-14.4)	8.9 (4.4-14.7)	0.019

There were no significant differences observed for Age at time of HIV diagnosis, Race, HBV/HCV, highest PCR or History PCR>100,000c/mL

Median

Blick et al. IAS 2024, #SSOAX0903LB

BASELINE ART AND PROVIRAL MUTATIONS

AIDS 2024
AIDS 2024, the 25th International AIDS Conference

Baseline ART	All Patients (n=100)	Historical M184V/I (n=50)	No Historical M184V/I (n=50)
ART Regimen, n (%):			
• **2 NRTIs + INSTI:**	**58 (58)**	**30 (60)**	**28 (56)**
❖ TAF/FTC/BTG	4 (4)	3 (6)	1 (2)
❖ ABC/3TC/DTG	51 (51)	26 (52)	25 (50)
❖ TDF or TAF/FTC + DTG	3 (3)	1 (2)	2 (4)
• **2DR (NNRTI + INSTI):**			
❖ RPV/DTG	**21 (21)**	**12 (24)**	**9 (18)**
• **2 NRTIs + boosted INSTI:**			
❖ TAF/FTC/EVG/c	**6 (6)**	**0**	**6 (12)**
Historical GT vs Proviral DNA NGS			
M184V/I on Historical GT, n (%):	50 (50)	50 (100)	0
Proviral DNA by NGS, n (%):	70 (70)	41 (82)	29 (58)
• **M184V/I present**	15 (21)	**15 (37)**	0
• **M184V/I absent**	55 (79)	**26 (63)**	29 (100)
• K65R present	1 (1)	1 (2)	0
• K65R present with Q151M	1 (1)	0	1

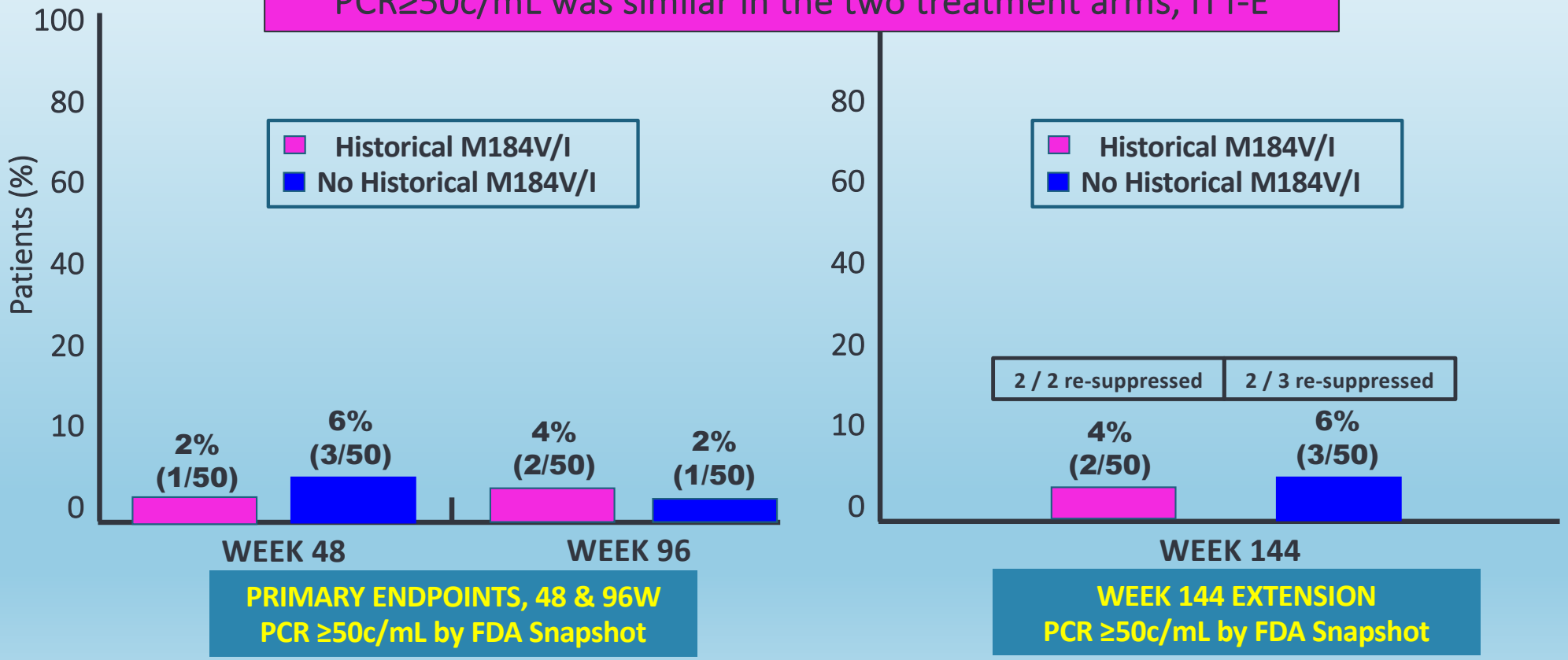
NGS = Next-Generation Sequence; Performed by Quest Diagnostics; Resistance-associated mutations present in 10% or more of viral species sequenced are reported

Blick et al. IAS 2024, #SSOAX0903LB

HEALTH CARE ADVOCATES INTERNATIONAL

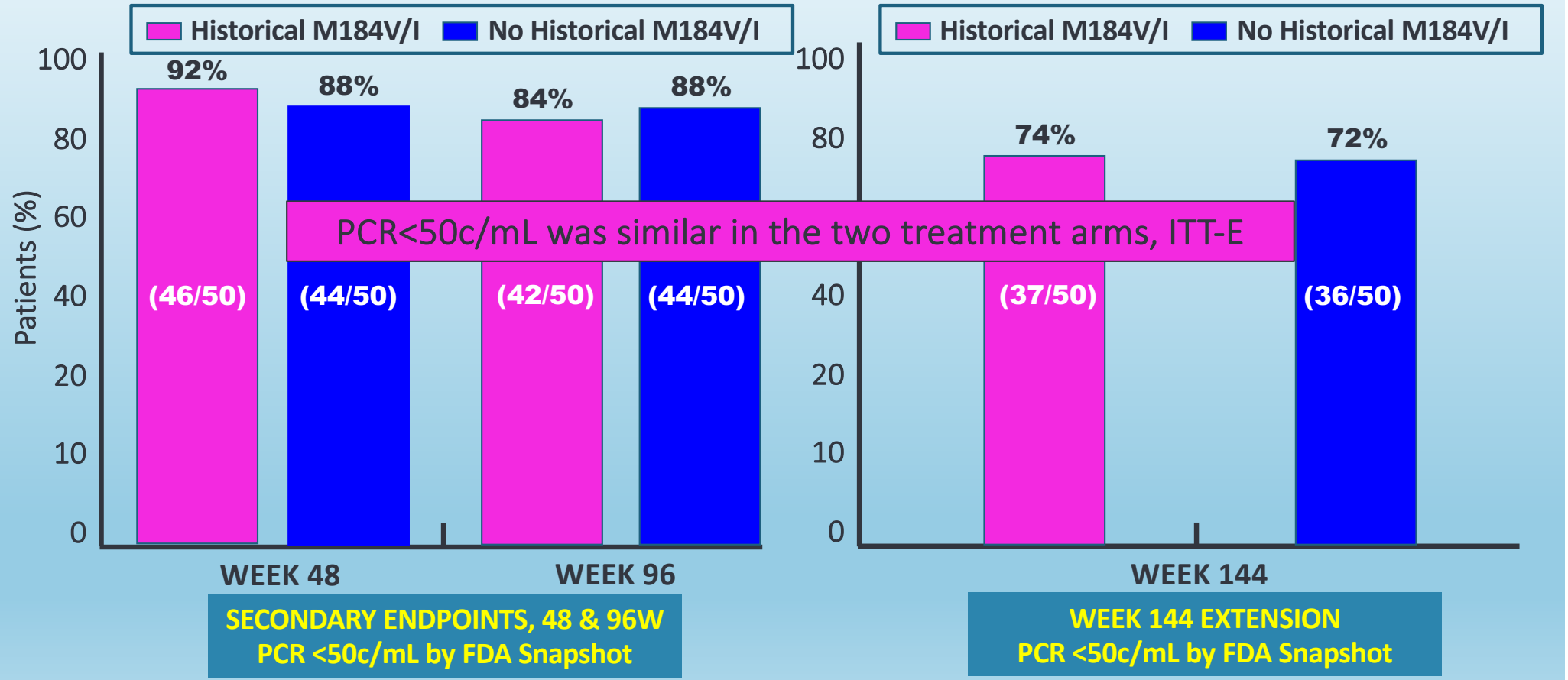
VIROLOGIC OUTCOMES:
Primary Endpoints, 48 & 96W, and Week 144, ITT-E

PCR≥50c/mL was similar in the two treatment arms, ITT-E



Blick et al. IAS 2024, #SSOAX0903LB

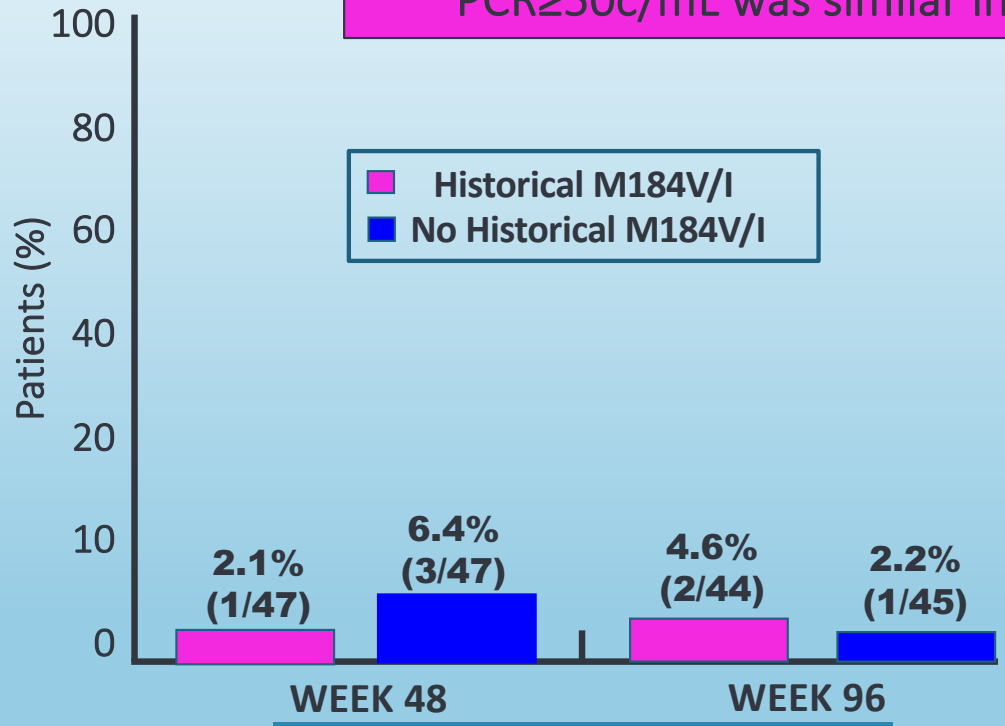
VIROLOGIC OUTCOMES:
Secondary Endpoints, 48 & 96W, and Week 144, ITT-E



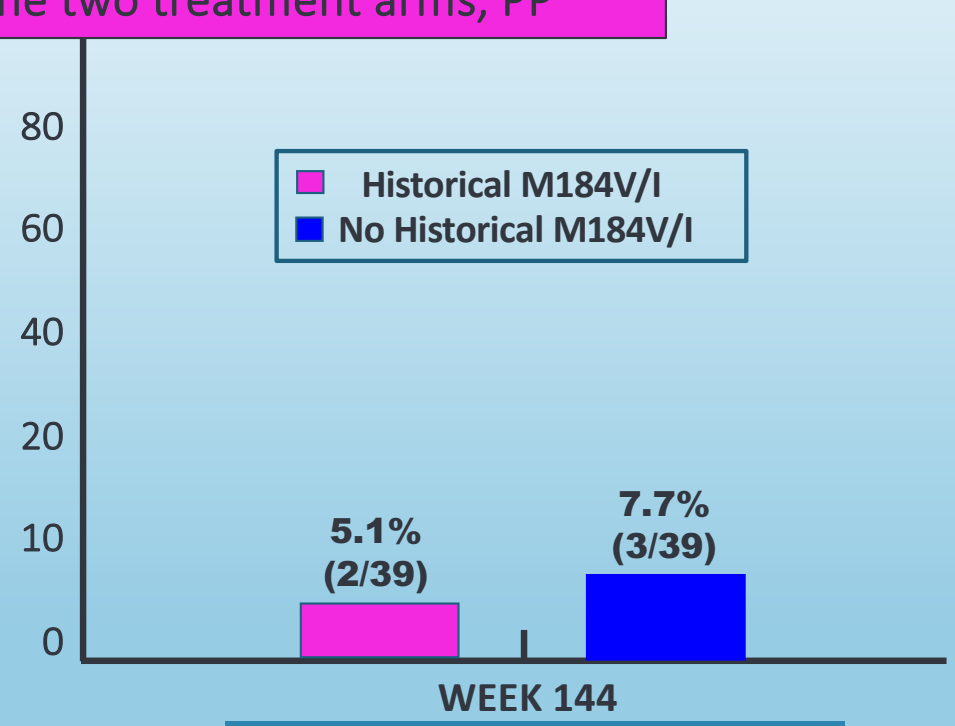
Blick et al. IAS 2024, #SSOAX0903LB

VIROLOGIC OUTCOMES:
Primary Endpoints, 48 & 96W, and Week 144, Per Protocol

PCR≥50c/mL was similar in the two treatment arms, PP



PRIMARY ENDPOINTS, 48 & 96W
PCR ≥50c/mL by FDA Snapshot



WEEK 144 EXTENSION
PCR ≥50c/mL by FDA Snapshot

Blick et al. IAS 2024, #SSOAX0903LB

VIROLOGIC FAILURES: Secondary Endpoint, Week 144

- There were no cases of Confirmed Virologic Failure (CVF)[§] in Historical M184VI treatment arm
- 1 CVF in No Historical M184V/I treatment arm through Week 144, due to non-adherence
- There were no cases of Treatment-Emergent Resistance across treatment arms through Week 144

[§]Confirmed Virologic Failure (CVF) is defined as a PCR≥50 followed by a second consecutive PCR>200

Blick et al. IAS 2024, #SSOAX0903LB

CONCLUSION

- SOLAR-3D is the largest prospective, comparative trial with longest follow-up to-date to demonstrate that neither prior/current M184V/I nor multiple prior VFs impact the efficacy and durability of switching virologically suppressed PLWHA to DTG/3TC through 144-weeks.

The D^{2}EFT study

- A prospective, multicenter, open-label international RCT
- Evaluation of 3 second-line regimens

Standard of care DRV/r + 2NRTI	Intervention Arm DTG + DRV/r	Intervention Arm DTG + TDF/XTC
• NRTI selection by genotyping or WHO algorithm • Drug class but not drug recycled • No coformulation possible	• No NRTI • No genotyping required • No drug class or drug recycled • Potential coformulation	• Recycled NRTI (TDF/XTC) • No genotyping required • Co-formulated

Stage 1 (Commenced in April 2017)

Stage 2 (Commenced in May 2018)

UNSW Kirby Institute

d^{2}eft

Key study eligibility

Inclusion

- > 18 years old
- Failed first-line NNRTI + 2NRTIs (at least two consecutive HIV RNA > 500 c/ml at least 7 days apart after a minimum 24-week exposure)

Exclusion

- Prior PI/INSTI exposure
- HBsAg positive
- Significant co-morbidity/active coinfection
- Pregnancy/breast feeding

Recruitment

- 826 participants from 14 countries (28 sites)
- 107 in stage 1and 721 in stage 2
- Exceptional retention and engagement of participants despite external challenges: 2 withdrawals and 4 LTFU

UNSW Kirby Institute

UNSW SYDNEY

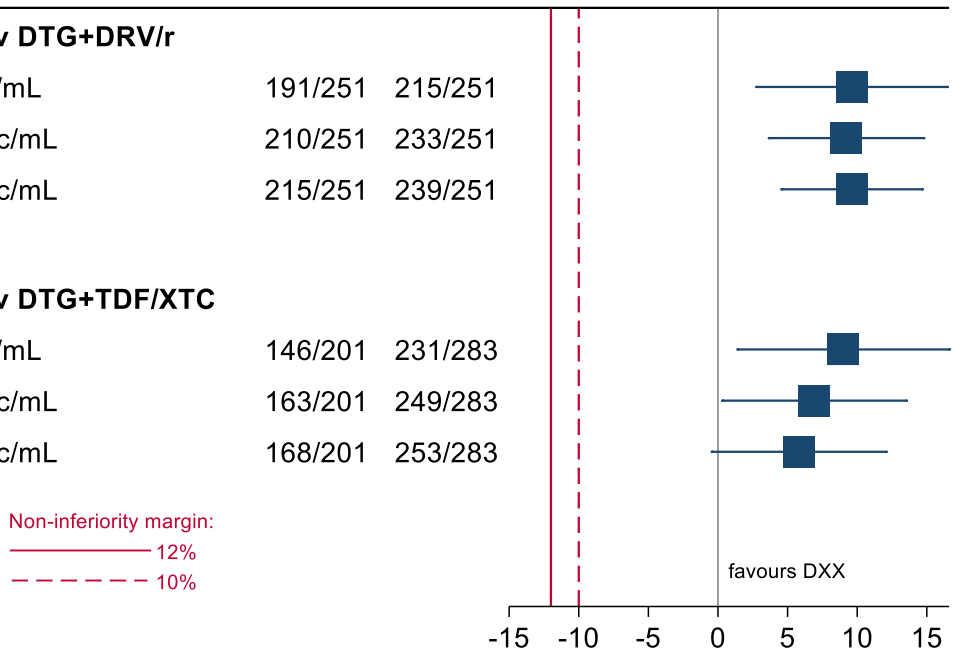
d²eft

Virological efficacy at week-96

Undetectable viral load at week 96

Available data

Comparison	SOC	DXX
SOC v DTG+DRV/r		
<50 c/mL	191/251	215/251
<200 c/mL	210/251	233/251
<400 c/mL	215/251	239/251
SOC v DTG+TDF/XTC		
<50 c/mL	146/201	231/283
<200 c/mL	163/201	249/283
<400 c/mL	168/201	253/283



Difference % [95% CI], p value

SOC vs DTG+DRV/r

<50 c/ml	9.6 [2.7, 16.4], P=0.01
<200 c/ml	9.2 [3.6, 14.7], P=0.002
<400 c/ml	9.6 [4.5, 14.6], P=0.004

SOC vs DTG+TDF/XTC

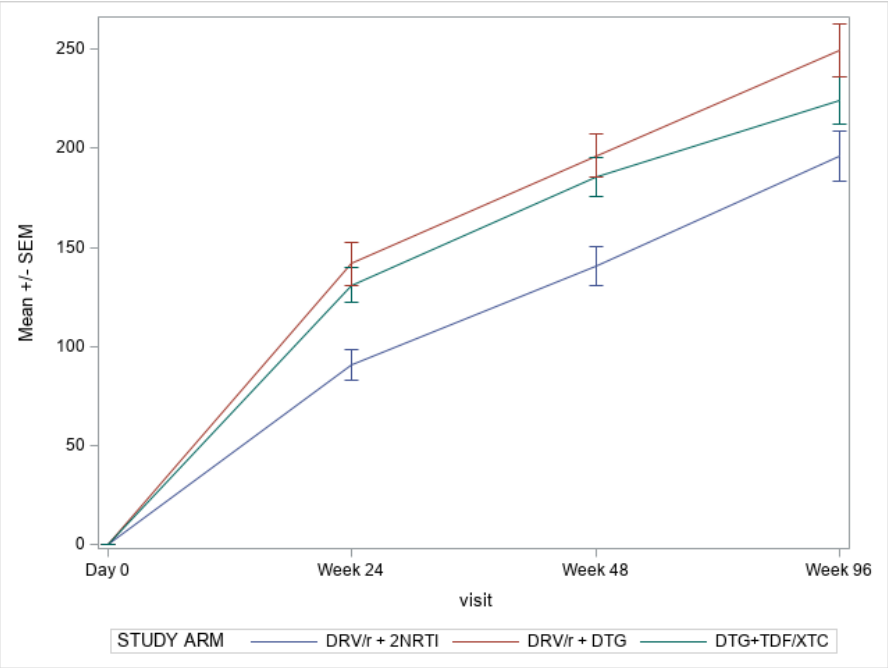
<50 c/ml	9.0 [1.4, 16.6], P=0.02
<200 c/ml	6.9 [0.3, 13.5], P=0.04
<400 c/ml	5.8 [-0.4, 12.1], P=0.07

UNSW Kirby Institute

UNSW SYDNEY

d2eft

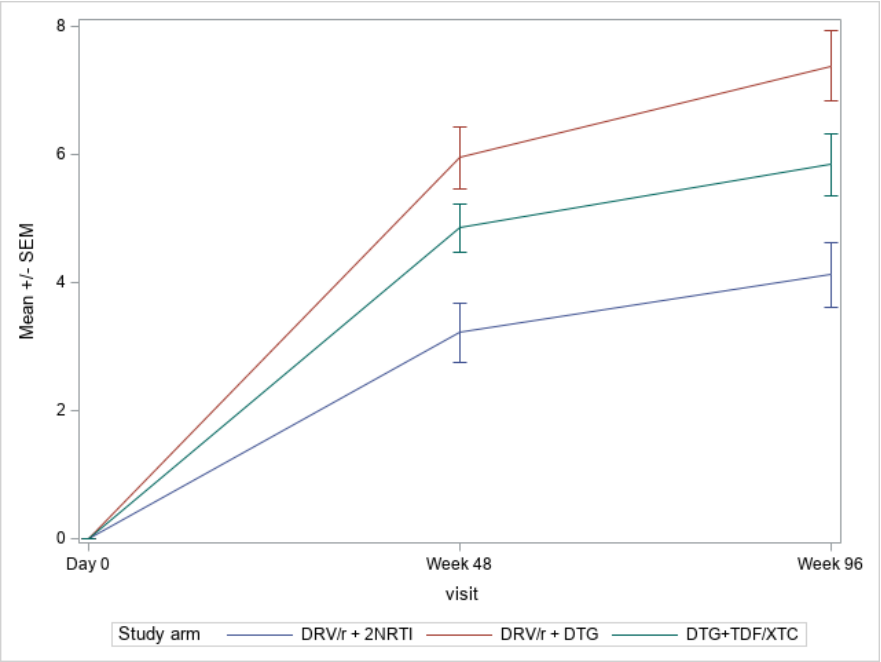
Mean CD4 change (cells/µL) at week-96



Mean CD4 change at week-96 (Stage 2 only)

Arm	Stage	Mean CD4 change at week-96 (cells/µL)	Mean Difference [95% CI]	P-value
DRV/r + 2NRTI	1+2	196 (194)	56 [26, 85]	P<0.001
DRV/r + DTG		250 (208)		
DRV/r + 2NRTI	2	189 (204)	42 [11, 72]	P=0.01
DTG+TDF+XTC		224 (195)		

Mean body weight change (kg) at week-96



Mean body weight change at week-96 (Stage 2 only)

Arm	Stage	Mean weight change at week-96 (kg)	Mean Difference [95% CI]	P-value
DRV/r + 2NRTI	1+2	3.9 (6.8)	3.4 [2.1, 4.7]	P<0.001
DRV/r + DTG		7.3 (7.9)		
DRV/r + 2NRTI	2	4.1 (7.2)	1.7 [0.3, 3.1]	P=0.01
DTG+TDF+XTC		5.8 (8.1)		

UNSW Kirby Institute

UNSW SYDNEY

d2eft

Conclusions

- DTG+DRV/r and DTG+TDF/XTC demonstrated superiority in terms of virological efficacy and immunological recovery compared to SOC following failure of NNRTI-based first-line therapy.
- The novel second-line strategy, DTG+DRV/r, exhibited excellent antiviral efficacy at week-96.
- Recycling TDF as DTG+TDF/XTC in the second-line regimen is as efficacious as WHO recommended algorithmic NRTI switch even if genotypic resistance testing is inaccessible.
- Both intervention arms demonstrated greater CD4 gains compared to SOC at week-96.
- Weight gain was significantly greater in both intervention arms.
- All arms are generally well tolerated with few treatment switches due to toxicity.

UNSW Kirby Institute UNSW SYDNEY ARTCRS Chennai Antiviral Research and Treatment Clinical Research Site VHS IDMC INFECTIOUS DISEASES MEDICAL CENTRE d2eft

Dolutegravir with recycled Nucleoside Reverse Transcriptase Inhibitors maintains better viral suppression than Standard of Care Protease Inhibitor based Second line Antiretroviral therapy over 144 weeks: VISEND Trial

Dr Suilanji Sivile MD,MMed,MSc
Infectious Diseases Specialist
University Teaching Hospital
Zambia

AIDS 2024

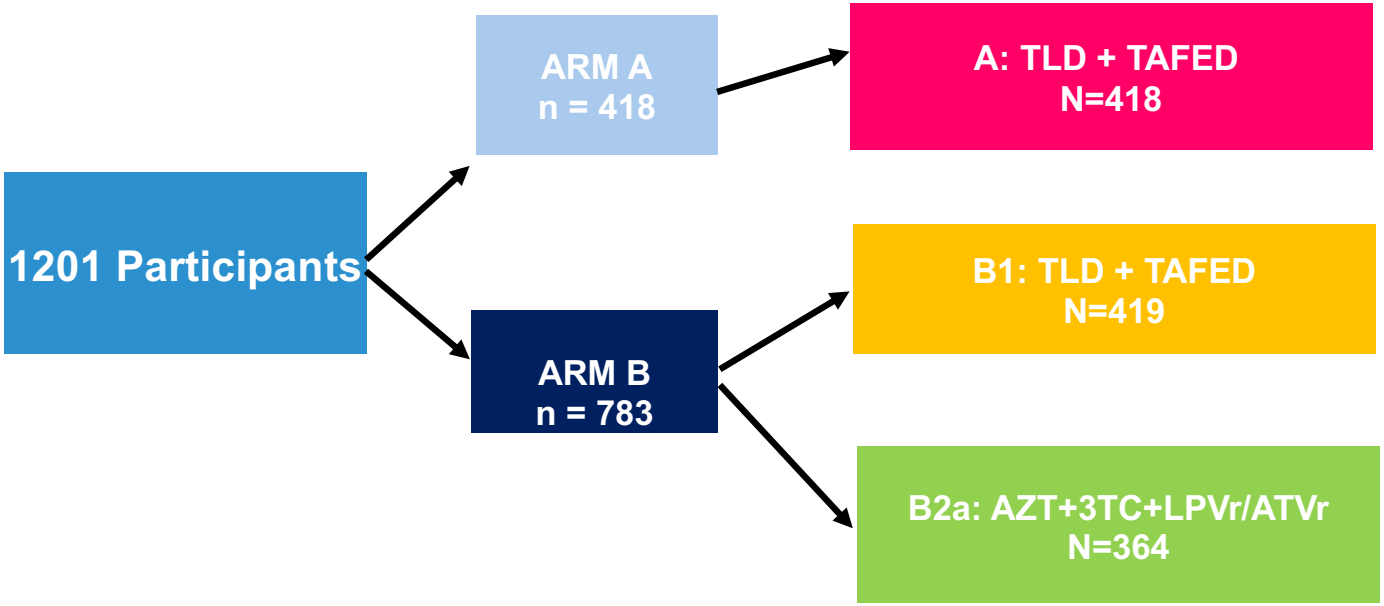
Background

- Dolutegravir (DTG) is recommended as part of first and second-line antiretroviral therapy (ART)
- Optimisation of nucleoside reverse transcriptase inhibitors (NRTIs) typically from tenofovir (TFV) analogues or Abacavir (ABC) to thymidine analogues (Zidovudine) is currently recommended by WHO when switching to second-line
- Use of HIVDR testing at first lines failure is unavailable in LMIC
- Despite emerging evidence on positive clinical outcomes among individuals failing NNRTI-based ART and switched to DTG-based regimens with maintained NRTI backbone, there is paucity in data on **longer-term** outcomes
- We hereby report the 144-week outcomes of the VISEND trial

Methodology: Trial Design

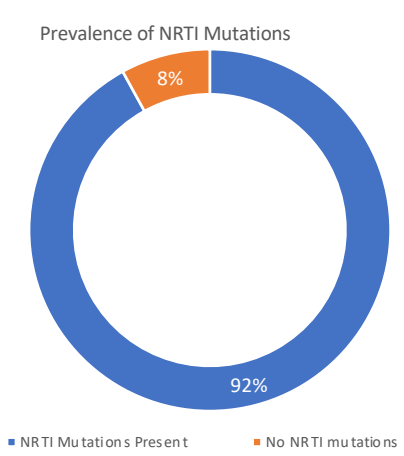
Inclusion criteria:

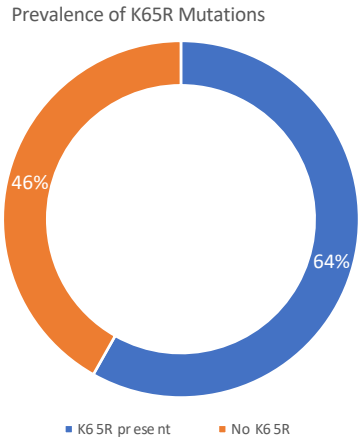
- HIV-1 positive adults (≥ 18 years) who are on TDF/XTC/EFV or NVP-based ART for at least 6 months



Open-label, 144-week study in Zambia
Study visits at Baseline, Week 4, 12, 24, 48, 72, 96 and 144

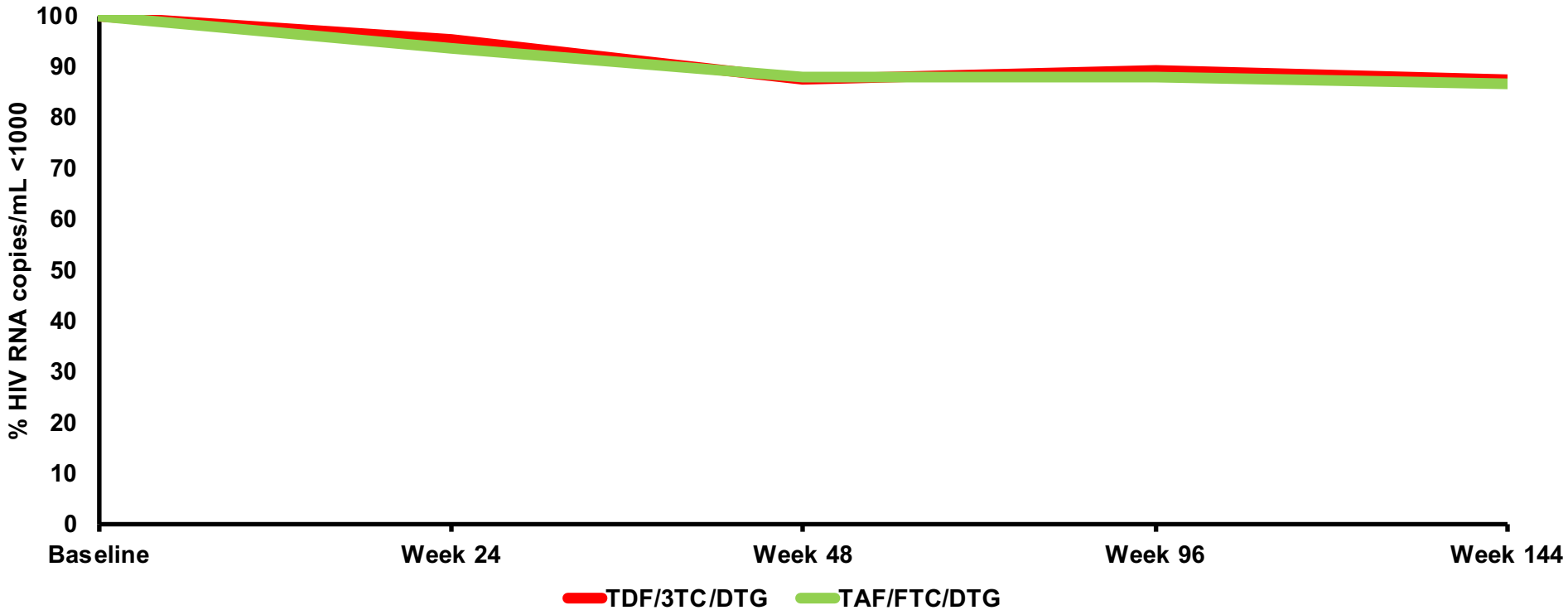
Baseline HIV Resistance



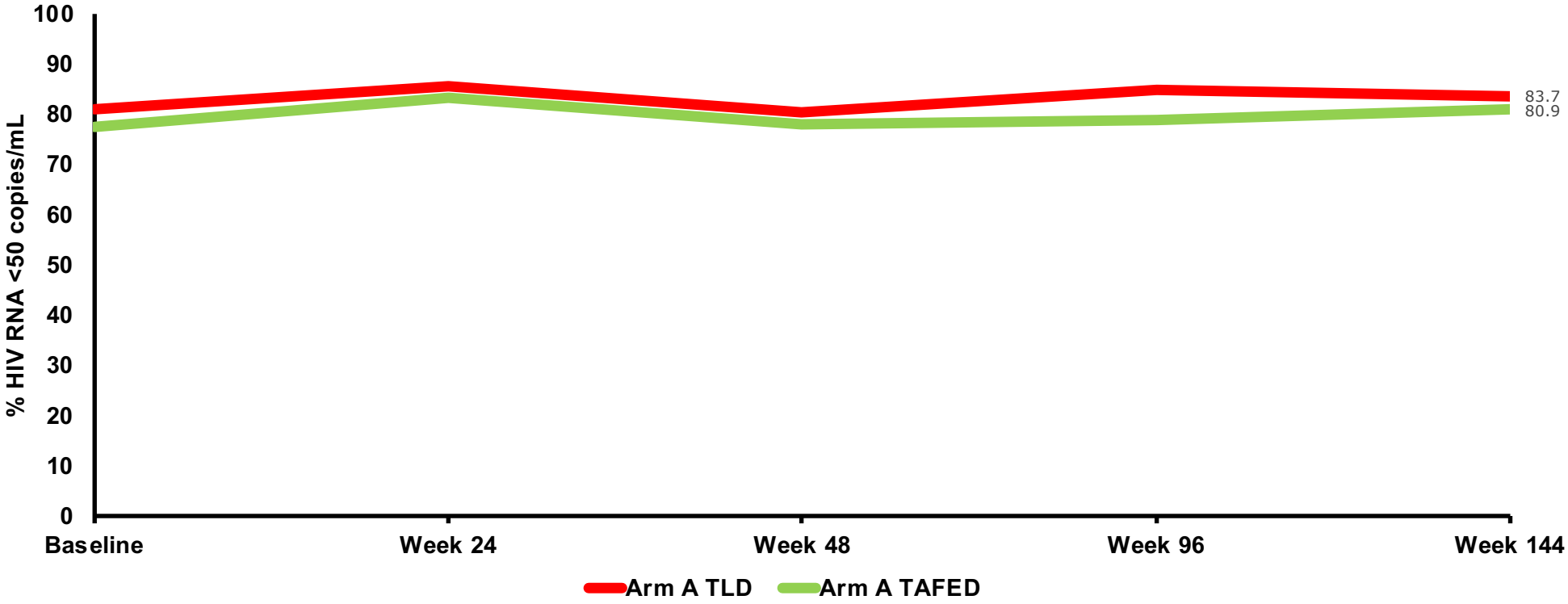


- Baseline NRTI resistant prevalence was 92%
  - 64% Tenofovir resistance
- In those randomised to TDF(TAF)/XTC/DTG
  - 56.5% had no predicted TFV activity
  - 75% had no predicted 3TC or FTC activity
- In those randomised to AZT/3TC/bPI
  - 46% had >= AZT associated mutations

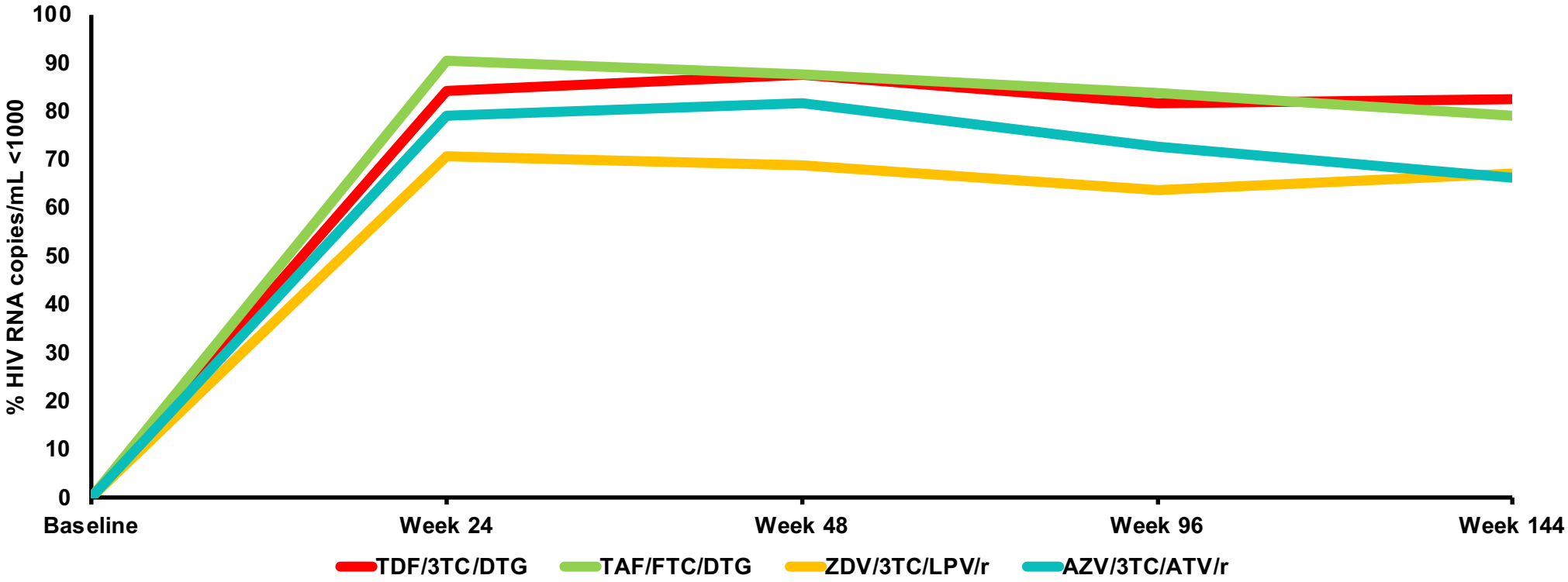
HIV-1 RNA < 1000 copies/mL over time (Arm A)



HIV-1 RNA <50 copies/mL over time (Arm A)

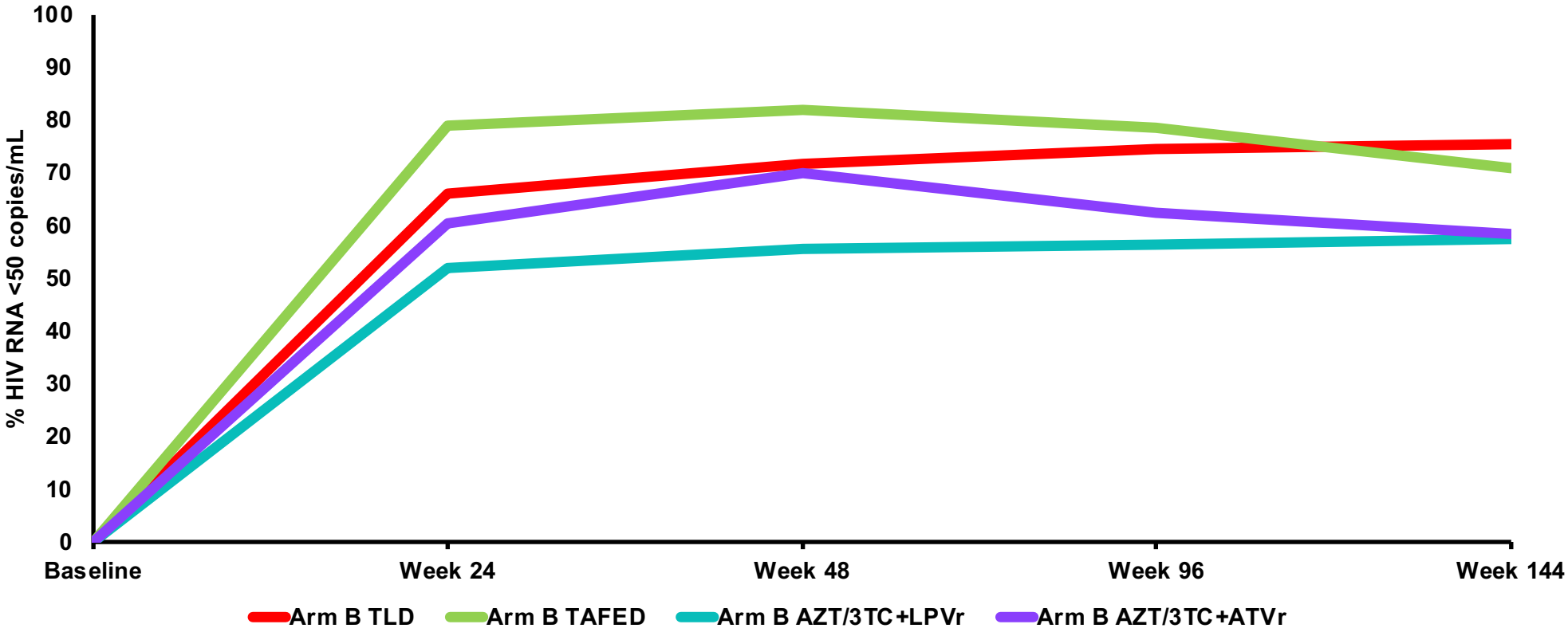


HIV-1 RNA <1000 copies/mL over time (Arm B)



AIDS 2024

HIV RNA <50 copies/mL over time (Arm B)



Conclusion

- In the VISEND trial, HIV-positive adults with virologic failure to TDF/3TC/NNRTI, had favourable outcomes when switched to DTG with either TAF/FTC or TDF/3TC compared to those switched to SOC boosted-PI ART despite high baseline resistance to NRTIs at 144 week
- Resistance to DTG was not observed at week 144
- In view of high toxicity to thymidine analogues and logistics challenges recycling of NRTI backbone should be considered as an option in national and international guidelines

Paul E. Sax, MD

Division of Infectious Diseases, Brigham and Women's Hospital

Professor of Medicine, Harvard Medical School

Switching from a second-line ritonavir-boosted protease inhibitor-based regimen to bictegravir/emtricitabine/tenofovir alafenamide: Results of a randomized clinical trial

Dr. Samuel Pierre
GHESKIO Center, Haiti

Background

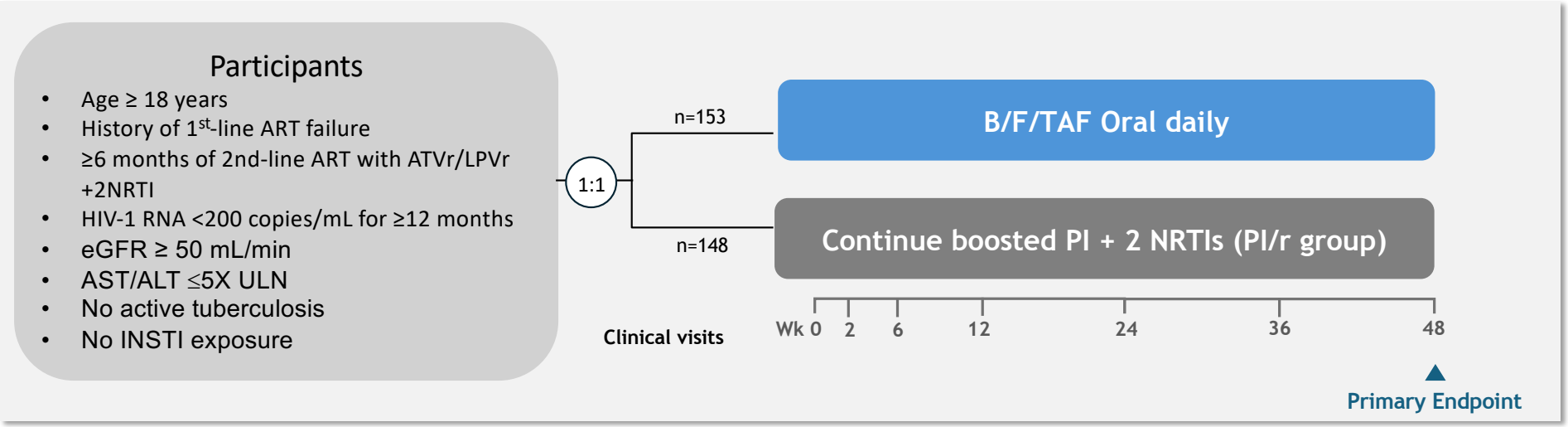
- Until recently, nearly all PWH on second-line treatment in LMICs received a boosted PI-based regimen
- Patients on second-line ART regimens in LMICs have high rates of NRTI resistance, but testing is rarely available
- In surveillance testing in Haiti, about 50% of PWH with failure on first-line EFV-based regimens have resistance to 3TC/FTC and 30% have resistance to tenofovir
- Single-tablet INSTI-based regimens (TLD, B/F/TAF) offer advantages over multi-tablet, PI-based regimens
    - Pill burden, drug interactions, tolerability and toxicity
- The 2SD study[1] found that switching to DTG was non-inferior to continuing the PI-based regimen
- No study has evaluated B/F/TAF in this setting

1 Ombajo LA, et al, NEJM 2023

Study Objective and Endpoints

- **Objective:** To evaluate the efficacy of continuing PI/r + 2 NRTIs vs. B/F/TAF in virally suppressed PWH on second-line PI/r treatment
- **Primary Endpoint:** Proportion with HIV-1 RNA ≥200 copies/mL at Week 48 as defined by US FDA-defined snapshot algorithm
- **Secondary Endpoints**:
  - Tolerability
  - Adverse events
  - Changes in weight and lipids
  - Adherence

Study Design



Primary Endpoint Analysis

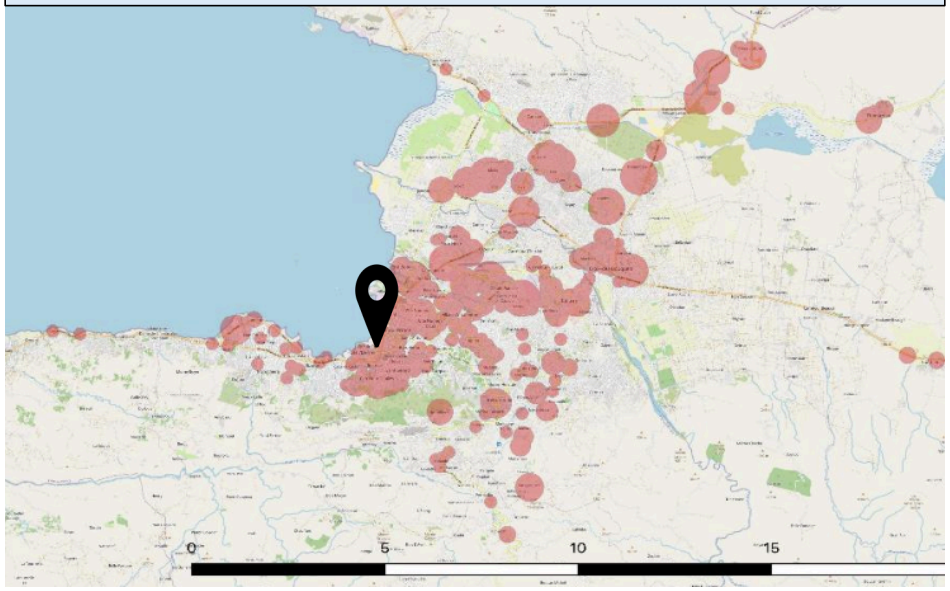
- Intention-to-treat
- FDA snapshot algorithm with 4% non-inferiority margin, 95% CI calculated by the exact method
- Non-inferiority established if the upper bound of the 2-sided 95% CI of the difference between treatment groups [B/F/TAF – boosted PI] in the percentage of participants with HIV-1 RNA ≥200 copies/mL is less than 4%.

ART antiretroviral therapy, NRTI nucleos(t)ide reverse transcriptase inhibitor, ATV/r ritonavir boosted atazanavir, LPV/r ritonavir boosted lopinavir, eGFR estimated glomerular filtration rate, INSTI integrase strand transfer inhibitor, PI protease inhibitor

Results: Situation update

- Enrollment Oct 2020 to Mar 2023
- Eligible clients lived in areas throughout Port-au-Prince
- For safety, participants who had to cross gang blockades were not enrolled
- Enrollment paused in Mar 2023 for patient safety due to gang violence
- DSMB recommended enrollment stop in Dec 2023 due to limited access to PI/r
- Boosted PI provided for the remaining study duration for the PI/r group

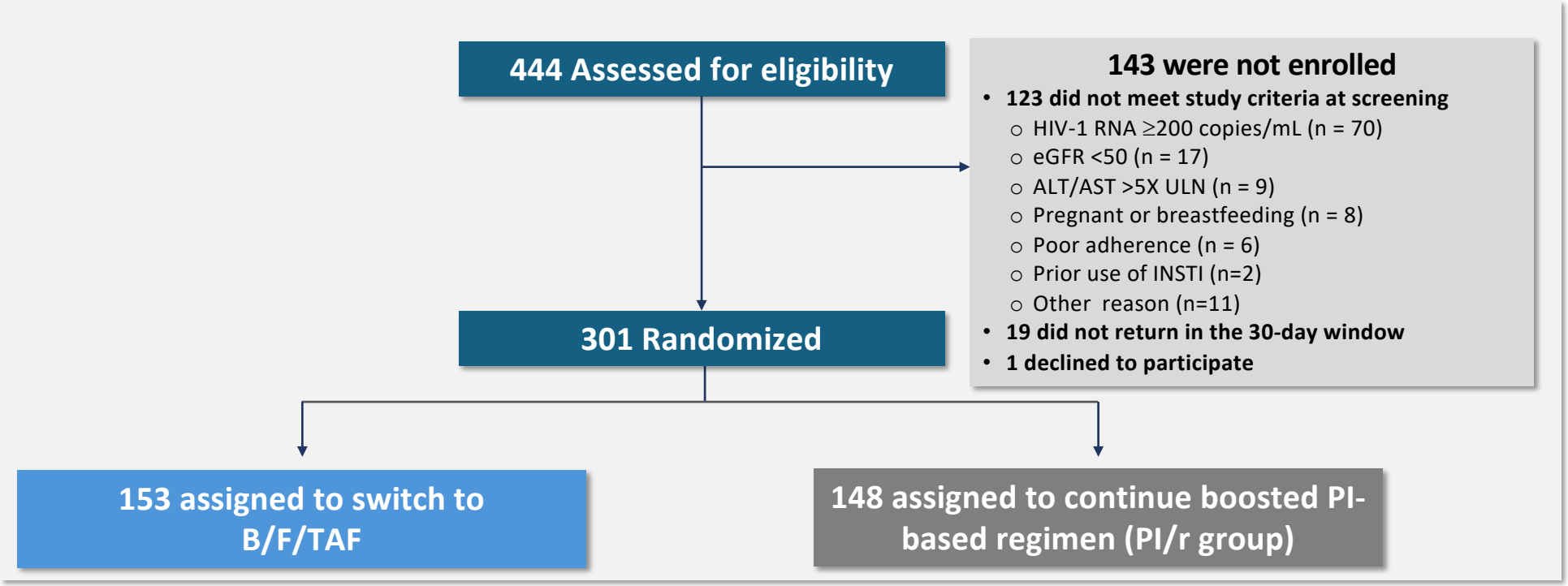
Gang Violence in Port-au-Prince, Haiti between July and September 2023



GHESKIO Centers

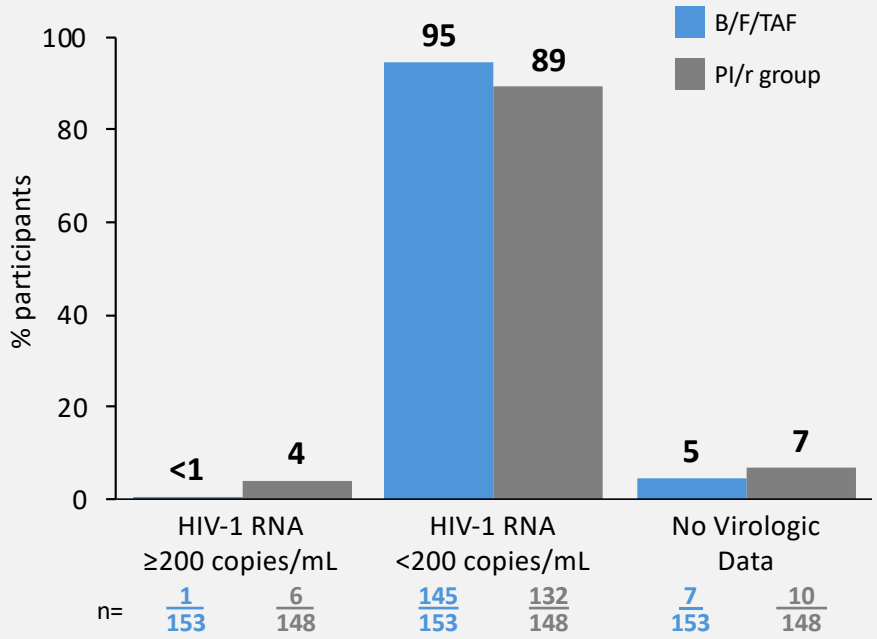
Map: United Nations Integrated Office in Haiti

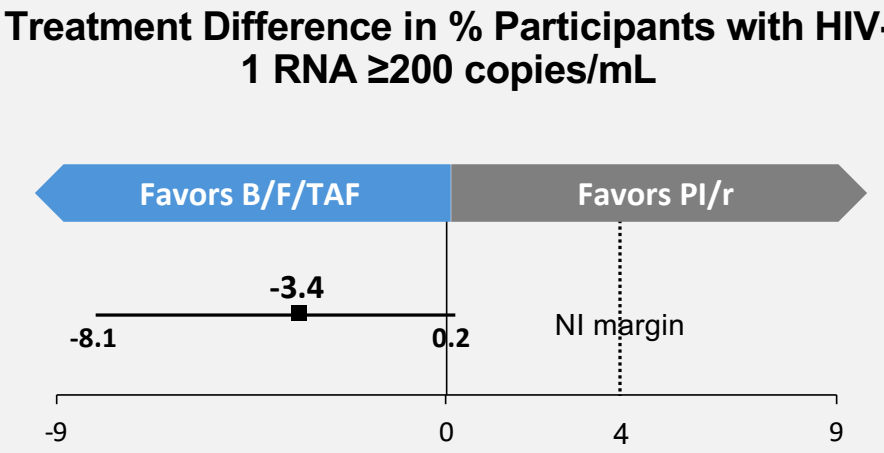
Screening and Randomization



- All participants who were randomized received at least one dose of the assigned study medication and are including in the primary analysis

Primary Efficacy Outcomes at Week 48 - Noninferiority





Switching to B/F/TAF was noninferior to staying on PI-based second-line regimen

- difference -3.4 (95% CI: -8.1 to 0.2)

CI, confidence interval; NI, noninferiority.

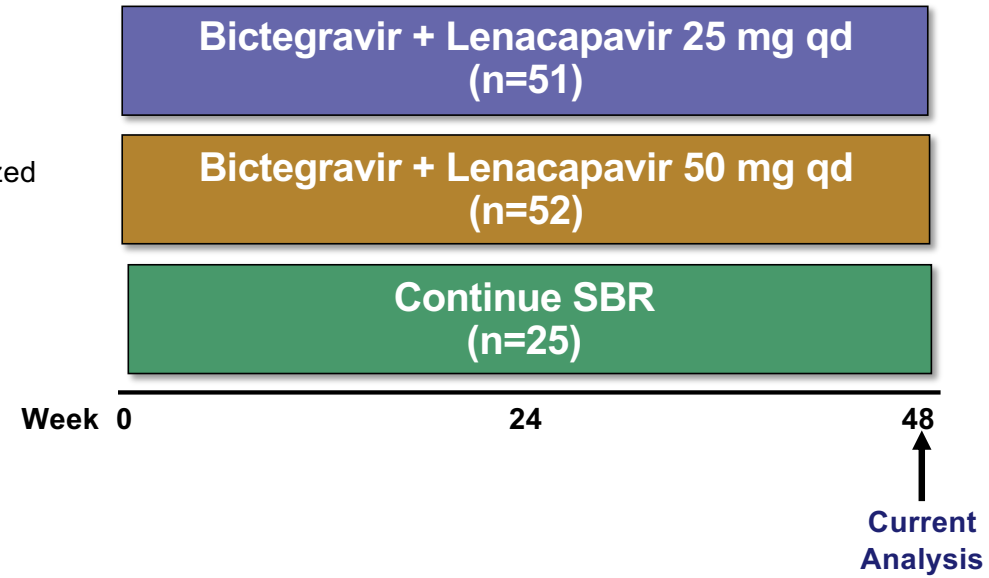
Conclusion

- Switching to B/F/TAF is non-inferior to continuing a boosted PI-based regimen, despite expected high rates of NRTI resistance
- Rates of viral suppression were high in both groups, despite severe civil unrest and the COVID-19 pandemic
- Evaluation of baseline NRTI resistance using proviral DNA sequencing ongoing

ARTISTRY-1 Study: Switch to Daily Bictegravir + Lenacapavir in PWH on Complex ART Regimens

Phase 2/3

Open-label
HIV RNA <50 copies/mL on SBR for ≥6 months
No prior lenacapavir exposure or bictegravir resistance
No HBV
eGFR: ≥15 mL/min



SBR: stable baseline regimen.
Primary outcome:
HIV RNA ≥50 copies/mL at week 24 (FDA snapshot).
Baseline characteristics:
Age (median): 60 years.
Male: 79%.
CD4: 610 cells/μL.
Prior AIDS: 28%.
Historical resistance mutations:
INSTI/NNRTI/NRTI/PI: 0%/52%/64%/36%.

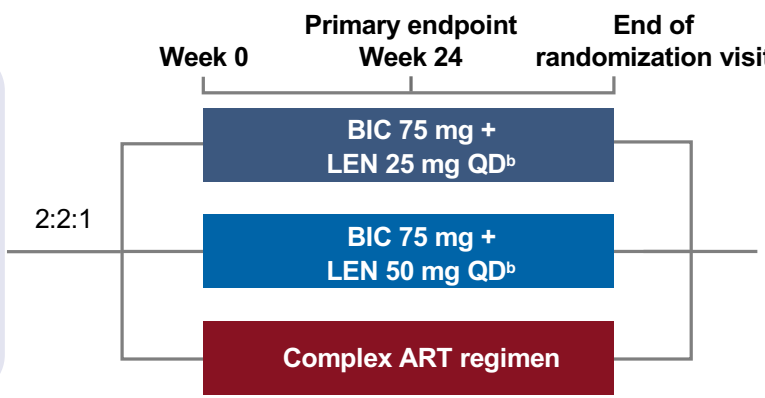
Mounzer K, et al. IAS 2024. Abstract OAB2602.

Study Design of Phase 2 of ARTISTRY-1 (NCT05502341)

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

Adults aged ≥ 18 years on a complex ART regimen[a] (N = 128)

- HIV-1 RNA < 50 c/mL on stable baseline regimen for ≥ 6 months prior to screening
- No prior exposure to LEN or resistance to BIC
- No history of chronic HBV infection
- eGFR ≥ 15 mL/min; not on renal replacement therapy



All participants reached Week 48 before entering the Phase 2 extension

Phase 2 extension[c]

BIC 75 mg / LEN 50 mg FDC QD

A **complex antiretroviral regimen** was defined as:

- A regimen containing a boosted PI or NNRTI plus ≥ 1 other third agent from a class other than NRTI, or
- A regimen of ≥ 2 pills/day, or a regimen requiring dosing more than QD, or
- A regimen containing parenteral agent(s) (excluding a complete long-acting injectable regimen) as well as oral agents

Endpoints at Week 48

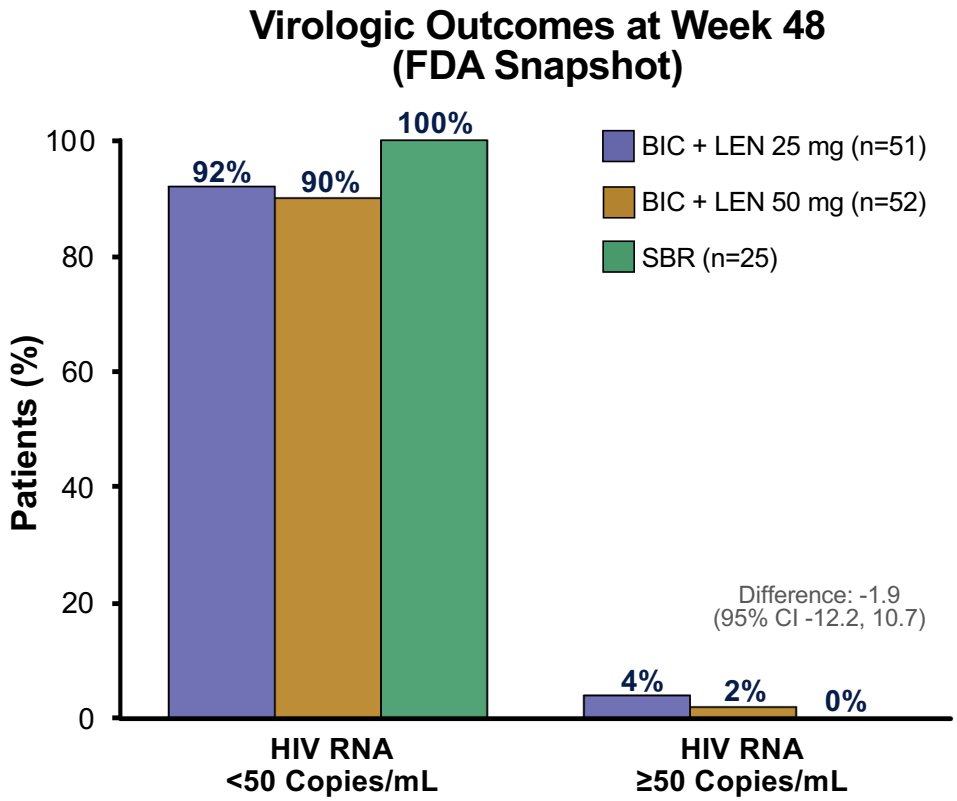
- Proportions of participants with HIV-1 RNA < 50 c/mL, determined using US FDA Snapshot analysis
- Change from baseline in CD4 cell count
- Proportion of participants with AEs

[a]Due to viral resistance, intolerance, or contraindication to existing STRs. [b]All participants receiving BIC + LEN received an oral loading dose of LEN 600 mg on Days 1 and 2 of treatment. [c]Participants who switch from a complex antiretroviral regimen in the extension phase will receive the oral loading doses of LEN.

AE, adverse event; **ART**, antiretroviral therapy; **BIC**, bictegravir; **c**, copies; **CD**, cluster of differentiation; **eGFR**, estimated glomerular filtration rate; **FDA**, Food and Drug Administration; **FDC**, fixed-dose combination; **HBV**, hepatitis B virus; **LEN**, lenacapavir; **NNRTI**, non-nucleoside reverse transcriptase inhibitor; **NRTI**, nucleos(t)ide reverse transcriptase inhibitor; **PI**, protease inhibitor; **QD**, once daily; **STR**, single-tablet regimen.

ARTISTRY-1 Study: Outcomes at Week 48

- Virologic outcomes comparable among groups
  - Switching to bictegravir + lenacapavir was effective in maintaining viral suppression
- CD4 cell gains were comparable among groups
- All regimens were well tolerated
  - Similar safety profiles regardless of lenacapavir dose
- Data support the continued evaluation of bictegravir and lenacapavir to optimize ART in virologically suppressed PWH who are receiving complex regimens



Mounzer K, et al. IAS 2024. Abstract OAB2602.

Cardiometabolic Health

AIDS 2024

PASO-DOBLE study: Design

Phase IV, open-label, multicentre, randomised clinical trial[1]

30 sites across Spain

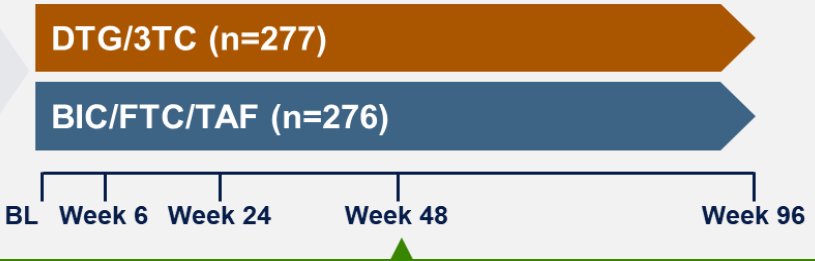
Collaborative study between **Fundación SEIMC-GeSIDA** and ViiV Healthcare

Screening

- HIV-1 RNA <50 c/mL for ≥24 weeks
- Current ART containing >1 pill/day, cobi booster, EFV or TDF
- No prior VF or known/suspected resistance
- No prior DTG or BIC
- No chronic hepatitis B

Randomised 1:1

Stratified by BL TAF use and sex at birth



Primary endpoint: Participants with plasma HIV-1 RNA ≥50 c/mL (FDA Snapshot; non-inferiority margin 4%)
Key secondary endpoint: Weight change (study was powered to assess differences)

Other secondary endpoints include efficacy, safety, tolerability, immune recovery, metabolic parameters, kidney function, blood pressure, body and bone composition, PROs, and genotypic resistance analysis in case of virological failure

Four sub-studies: Omics | Senescence | Fat biopsies | Liver steatosis

1. PASO DOBLE. Available at: https://clinicaltrials.gov/ct2/show/NCT04884139.

AIDS 2024

PASO-DOBLE study: Baseline characteristics

	DTG/3TC (n=277)	BIC/FTC/TAF (n=276)
Age, years	50 (41-57)	51 (39-58)
Female sex at birth	74 (26.7%)	73 (26.4%)
Ethnicity		
Caucasian	201 (72.6%)	201 (72.8%)
Latinx	66 (23.8%)	67 (24.3%)
Black	4 (1.4%)	5 (1.8%)
Other/unknown	6 (2.2%)	3 (1.1%)
Total time on ART, years	11.7 (7.2-19.3)	11.1 (7.0-19.2)
Time with HIV RNA <50 cp/mL, months	103.4 (43.0-170.2)	97.7 (41.5-163.3)
Duration of prior ART regimen, months	66.2 (43.5-97.0)	62.8 (41.1-88.7)
CD4 cells/mm^3	712 (516-918)	684 (473-859)
CD4 <350 cells/mm^3	26 (9.4%)	24 (8.7%)
CD4 nadir cells/mm^3	293 (144-472)	302 (159-476)
BMI, kg/m^2	25.1 (22.3-28.49)	24.8 (22.2-28.2)
Overweight/obese (BMI >25 kg/m^2)	143 (51.8%)	134 (48.6%)

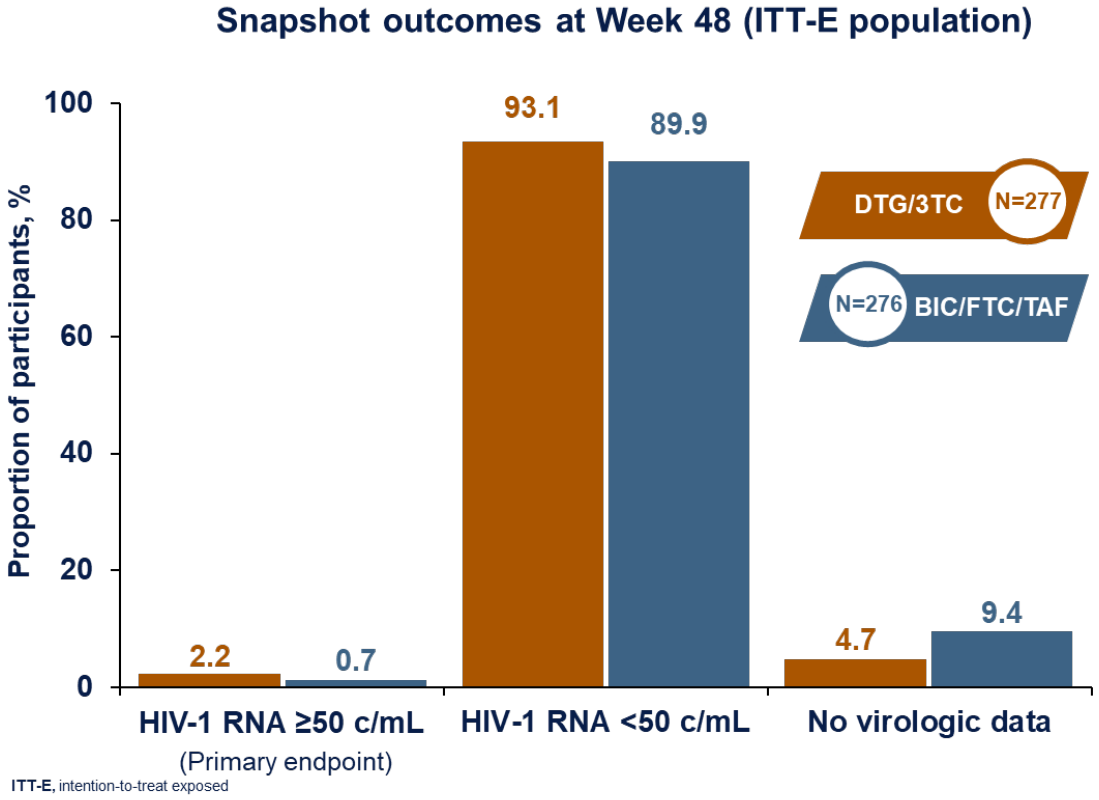
PASO-DOBLE study: Pre-switch ART

	DTG/3TC (n=277)	BIC/FTC/TAF (n=276)
NRTI 1 in previous ART regimen		
TAF	77 (27.8%)	78 (28.3%)
ABC	59 (21.3%)	52 (18.8%)
TDF	92 (33.2%)	103 (37.3%)
No NRTI 1	49 (17.7%)	43 (15.6%)
NRTI 2 in previous ART regimen		
3TC	70 (25.3%)	64 (23.2%)
FTC	182 (65.7%)	190 (68.8%)
No NRTI 2	25 (9.0%)	22 (8.0%)
Core drug in previous ART regimen		
NNRTI only	138 (49.8%)	141 (51.1%)
INSTI only	44 (15.9%)	49 (17.8%)
PI only	93 (33.6%)	82 (29.7%)
>1 core drugs	2 (0.7%)	4 (1.4%)

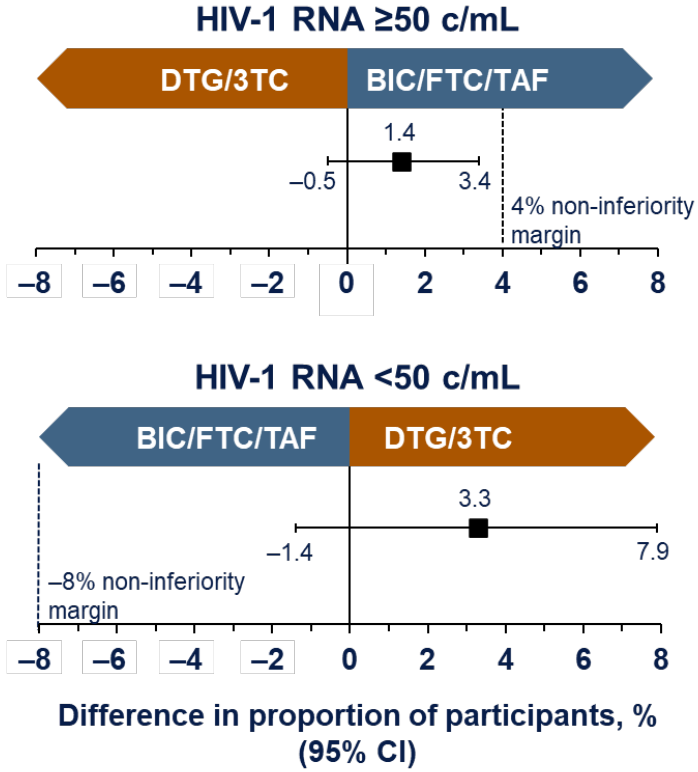
PASO-DOBLE study: Pre-switch ART

	DTG/3TC (n=277)	BIC/FTC/TAF (n=276)
NRTI 1 in previous ART regimen		
TAF	77 (27.8%)	78 (28.3%)
ABC	59 (21.3%)	52 (18.8%)
TDF	92 (33.2%)	103 (37.3%)
No NRTI 1	49 (17.7%)	43 (15.6%)
NRTI 2 in previous ART regimen		
3TC	70 (25.3%)	64 (23.2%)
FTC	182 (65.7%)	190 (68.8%)
No NRTI 2	25 (9.0%)	22 (8.0%)
Core drug in previous ART regimen		
NNRTI only	138 (49.8%)	141 (51.1%)
INSTI only	44 (15.9%)	49 (17.8%)
PI only	93 (33.6%)	82 (29.7%)
>1 core drugs	2 (0.7%)	4 (1.4%)

PASO-DOBLE study: Virologic efficacy

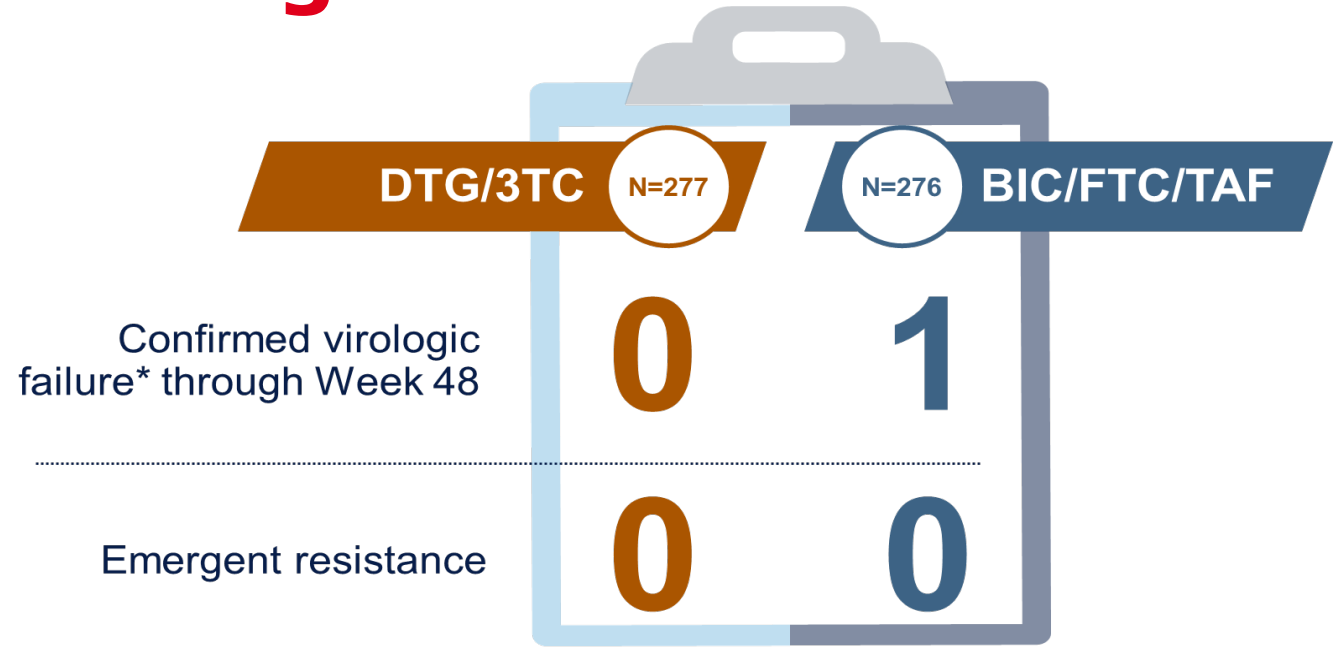


ITT-E, intention-to-treat exposed



AIDS 2024

PASO-DOBLE study: Virological failure and emergent resistance



*Confirmed virologic failure was defined as HIV-1 RNA ≥50 cp/mL followed by a second consecutive HIV-1 RNA assessment ≥200 cp/mL

PASO-DOBLE study: Adverse events

Participants with AEs, n (%)	DTG/3TC n=277	BIC/FTC/TAF n=276	p-value
Any AE *	207 (74.7)	216 (78.3)	0.327
Grade 3–4 AEs	3 (1.1)	10 (3.6)	0.049
Serious AE	12 (4.3)	13 (4.7)	0.831
Drug-related AEs	19 (6.9)	27 (9.8)	0.213
AEs leading to withdrawal #	1 (0.4)	2 (0.7)	0.561

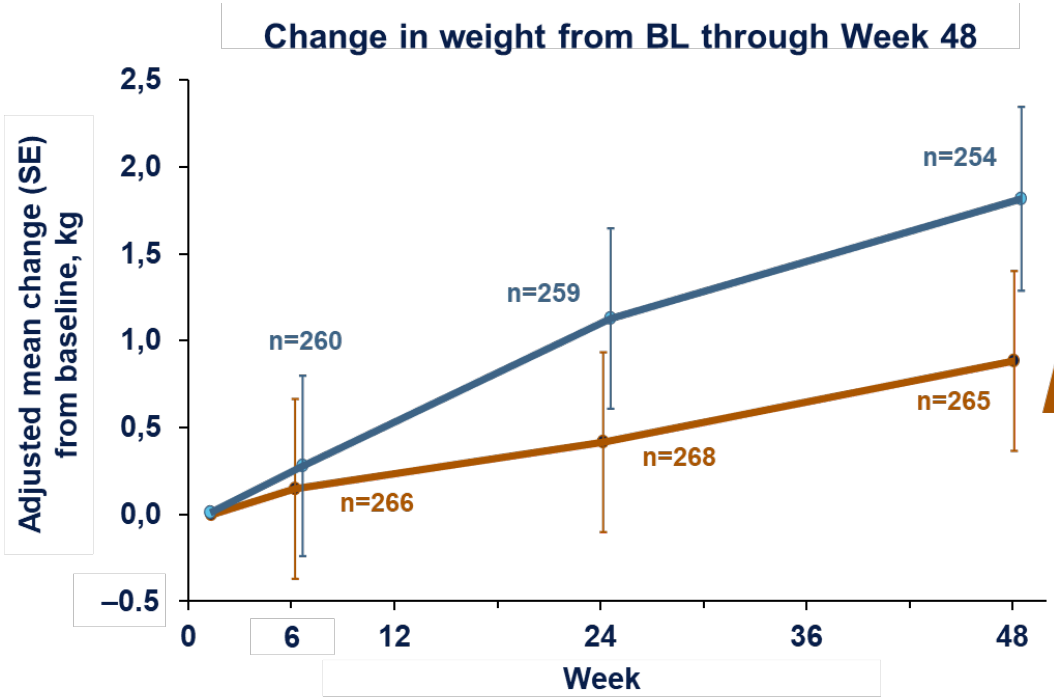
DTG/3TC: General discomfort and arthromyalgia (n=1)
BIC/FTC/TAF: Insomnia (n=1), sleep disturbances (n=1)

No drug-related AEs or AEs leading to death were reported in either arm.

* Most common AEs (>10% in either arm) per system organ class for DTG/3TC and BIC/FTC/TAF arms were:

- infections (36.8% and 45.3%)
- musculoskeletal (19.5% and 18.5%)
- gastrointestinal (17.3% an 10.5%),
- metabolism (13.7% and 9.4%), and
- psychiatric (9.7% and 13.4%)

PASO-DOBLE study: Weight change



+1.81 kg on BIC/FTC/TAF

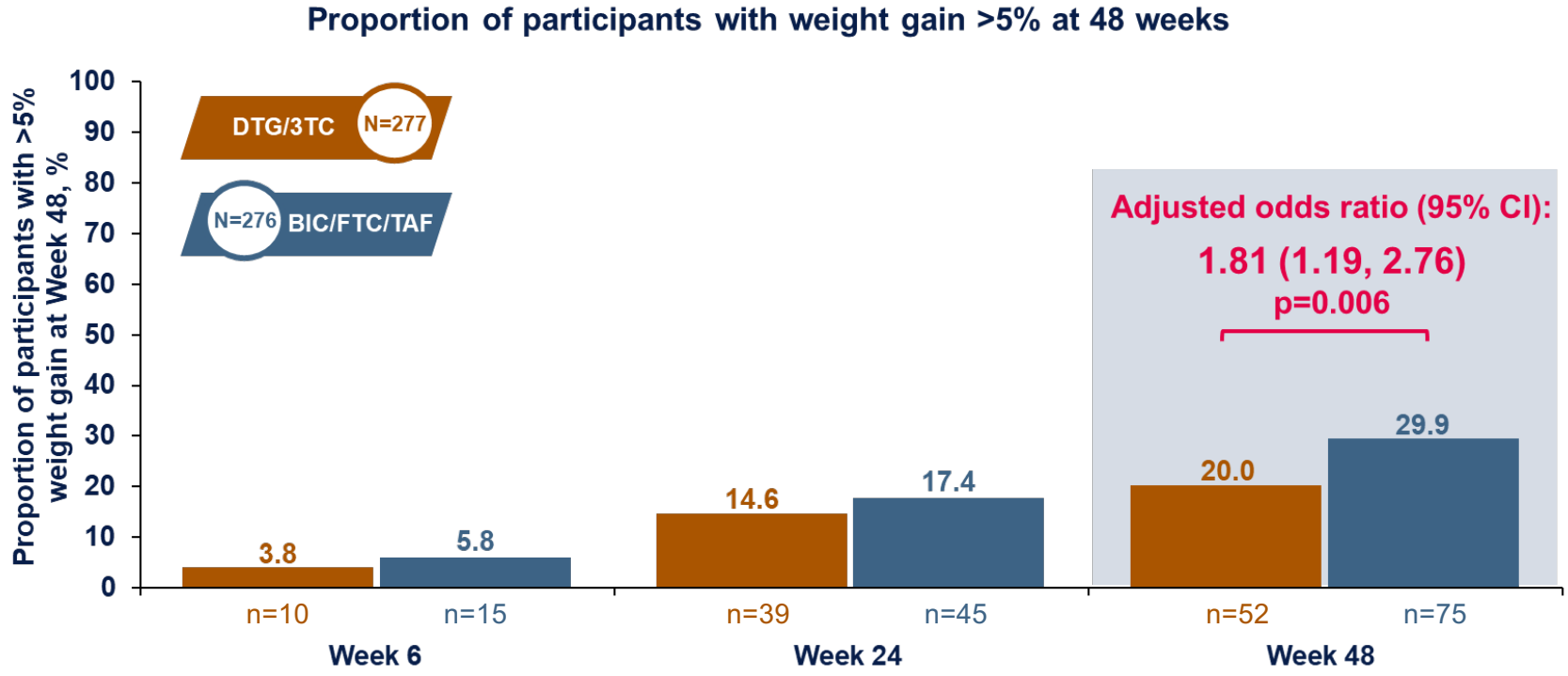
+0.89 kg on DTG/3TC

Mean adjusted difference: +0.92 kg (95% CI: 0.17, 1.66)

P=0.016

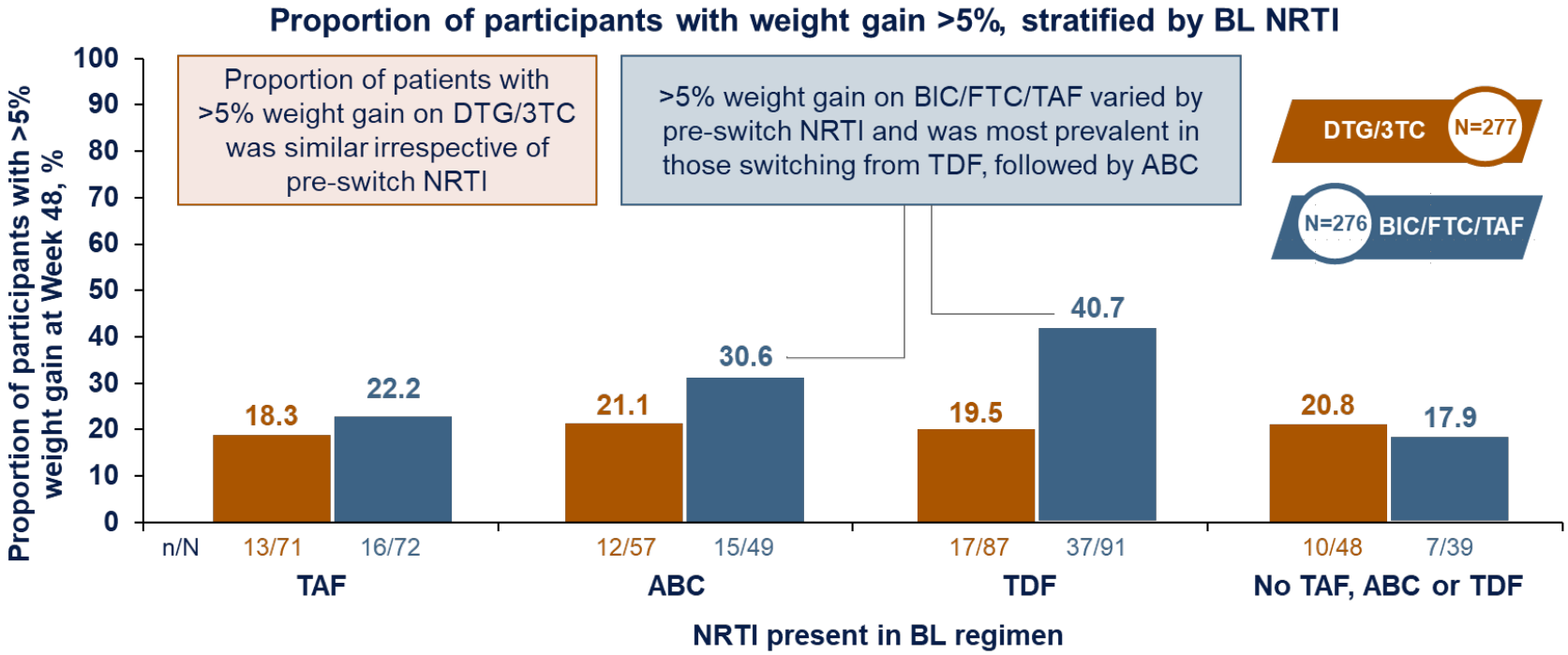
Adjusted by baseline value, sex, presence of TAF in previous ART, age and ethnicity.
The only association that was statistically significant in the model was treatment group

PASO-DOBLE study: Weight gain >5%

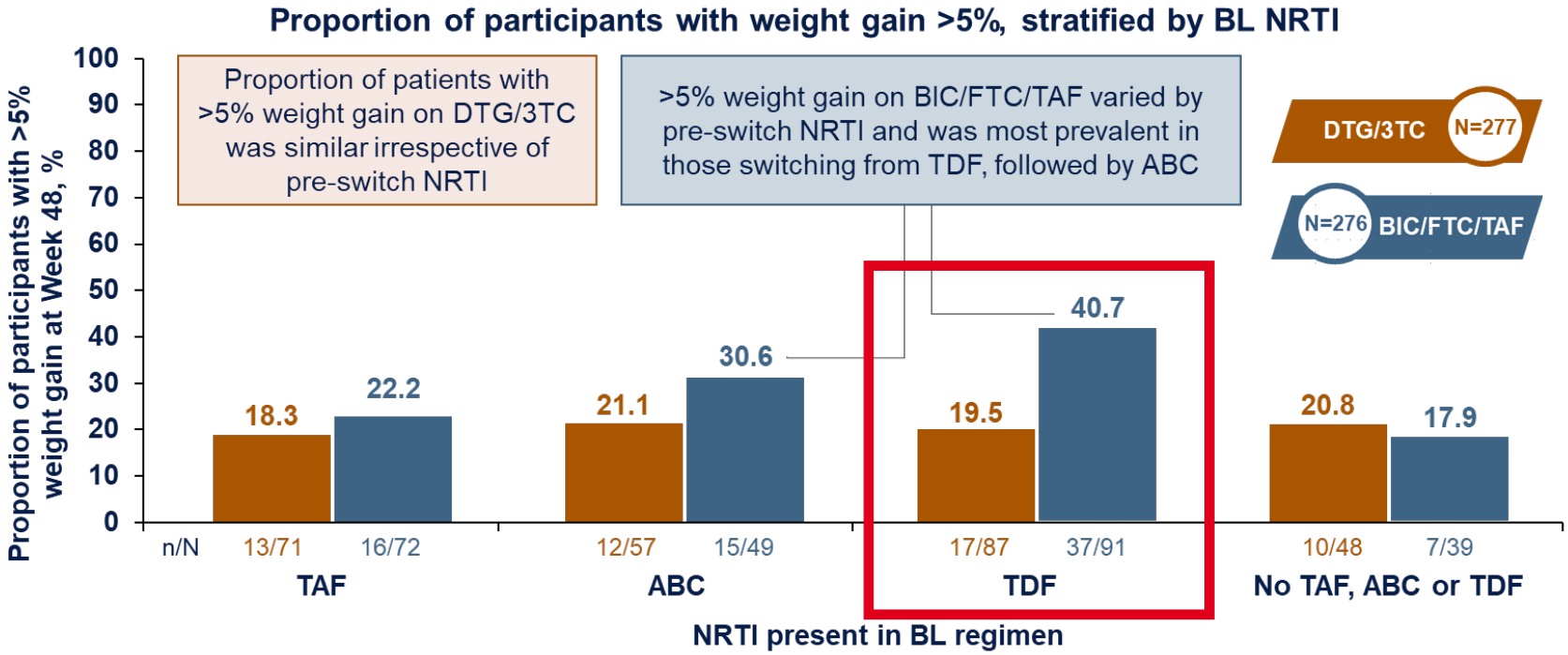


Adjusted by baseline value, sex, presence of TAF in previous ART, age and ethnicity

PASO-DOBLE study: Weight gain >5% by pre-switch NRTI 1



PASO-DOBLE study: Weight gain >5% by pre-switch NRTI 1



Conclusions

In virologically suppressed persons with HIV with ART regimens who are eligible and may benefit,

1. Switching to DTG/3TC demonstrated non-inferior efficacy than switching to BIC/FTC/TAF at 48 weeks.
2. DTG/3TC and BIC/FTC/TAF showed similarly high barrier to resistance.
3. DTG/3TC and BIC/FTC/TAF were both well tolerated, with exceptional discontinuations due to adverse effects.
4. Switching to BIC/FTC/TAF led to more weight gain than switching to DTG/3TC at 48 weeks.
5. Weight gain with BIC/FTC/TAF, but not with DTG/3TC, depended on the NRTI 1 in the ART regimen discontinued.

Elvstam O (Lund University, Sweden), Ryom L, Neesgaard B, Tau L, Günthard H, Zangerle R, Vehreschild JJ, Wit F, Sönnerborg A, Abutidze A, Pethoumenos K, Jaschinski N, Hosein S, Bogner J, Grabmeister-Pfistershammer K, Garges H, Rooney J, Young L, Law M, Kirk O, for the RESPOND Study Group

Co-morbidities: The heart of the matter

Detailed modelling of viremia exposure does not independently predict cardiovascular diseases in people with HIV

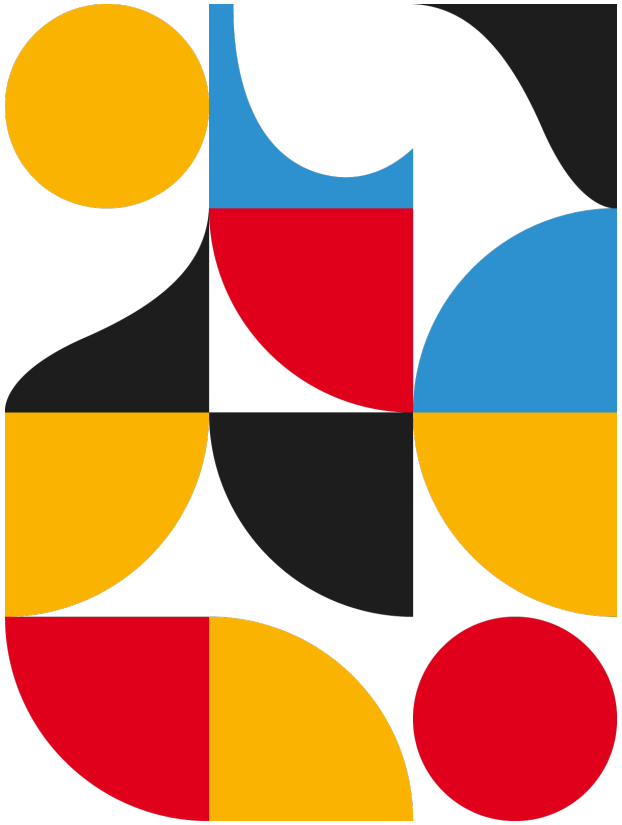
AIDS 2024

22 – 26 July · Munich, Germany and virtual aids2024.org

RESPOND International Cohort Consortium of Infectious Diseases

AIDS 2024

Summary



What is your main question?

Does consideration of HIV viremia improve prediction of cardiovascular diseases (CVD) among people with HIV?

What did you find?

Neither current, pre-antiretroviral therapy (ART), peak during ART, nor cumulative viremia had statistically significant associations with CVD when adjusting for other risk factors.

None of the viremia measures improved predictive capacity.

Why is it important?

Viremia has been associated with incident CVD in previous observational studies. Our study, which could adjust for a wide range of relevant CVD factors, indicates that HIV viremia is not an independent CVD risk factor.

RESPOND International Cohort Consortium of Infectious Diseases

Methods

Study design

RESPOND consortium – 19 cohorts across Europe and Australia

>18 years

Data from 2012–2021

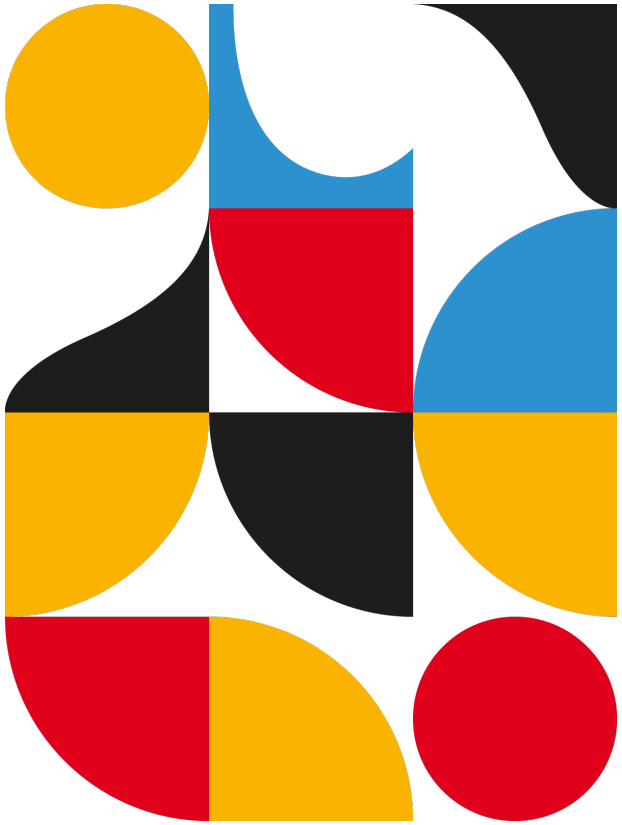
Outcome: CVD (myocardial infarction, stroke, invasive cardiovascular procedures)

Variables in the D:A:D CVD risk score: age, gender, smoking, family history, diabetes, cumulative PI and NRTI, recent abacavir, CD4 count, blood pressure, cholesterol, high-density lipoprotein (HDL)

Viremia classification	
1. Most recent viral load (VL)	
2. Pre-ART VL	
3. Peak viremia category during ART	
	Suppression ≤200 c/mL
	Low-level viremia 201–999 c/mL
	Non-supression ≥1000 c/mL
Cumulative viremia (viremia-copy-years)	
	4. Including all available VLs
	5. During ART (>12 months after start of ART)
	6. Recent (sliding 3-year window)

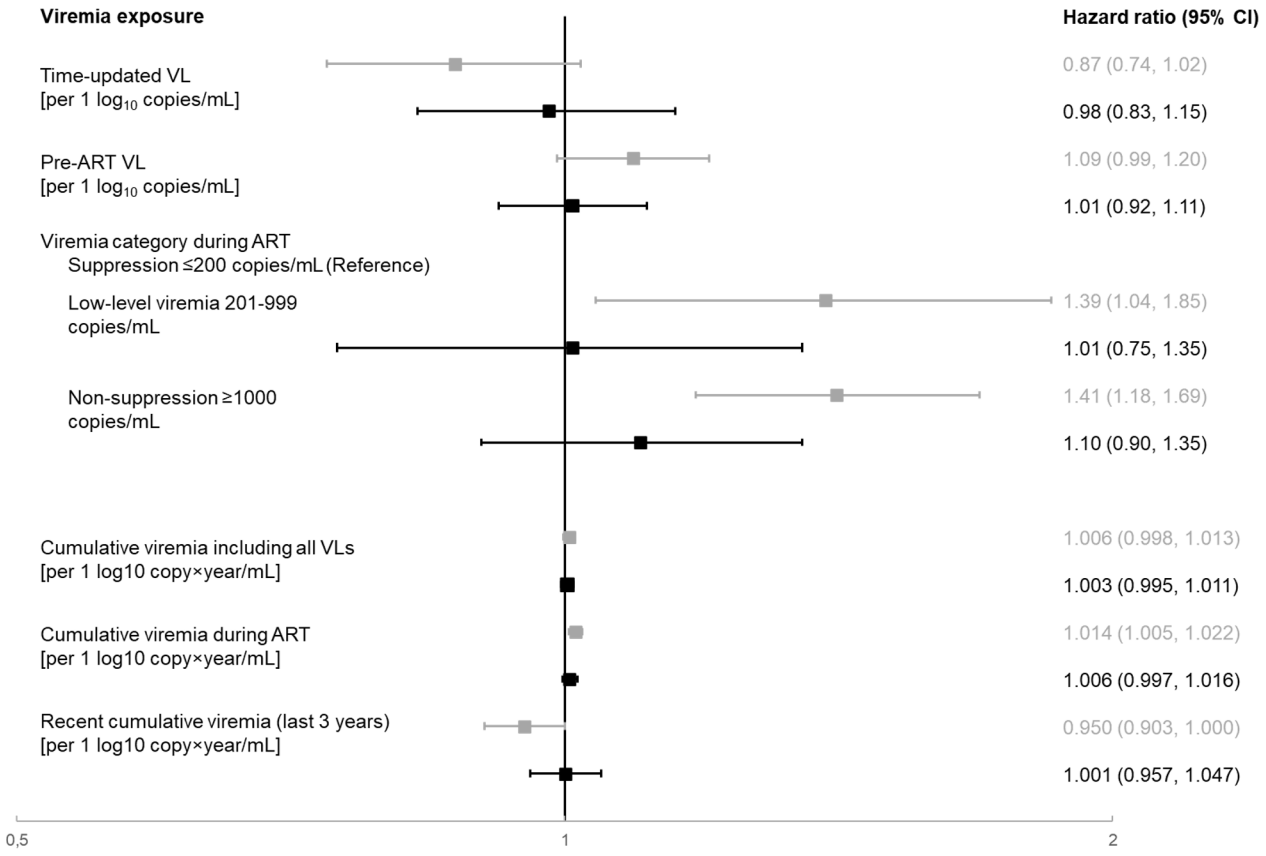
AIDS 2024

Study population



Characteristics of study participants (n=17,479)	
Sex/gender	
Male	13,265 (76%)
Female	4,232 (24%)
Age [median (IQR) years]	45 (37,52)
Ethnicity	
White	13,297 (76%)
Black	1,489 (9%)
Other	894 (5%)
Unknown or missing	1,817 (10%)

Associations between viremia variables and CVD



- 109,381 person-years; 547 events of CVD
- Variables related to viremia exposure during ART had statistically significant associations in univariable analyses.
- No viremia variable had statistically significant association when adjusting for established risk factors.

No statistically significant association when adjusting for CVD risk factors

AIDS 2024

	Model 1 Unadjusted	**Model 2** Adjusted for age, gender, CD4 count	**Model 4 (Adjusted for all D:A:D variables)** Further adjusted for smoking, blood pressure, cholesterol, HDL, family history, abacavir, PI, NRTI	**Model 5** Extended model further adjusted for CKD, BMI, risk group, ethnicity, INSTI
Time-updated VL[a]	0.87 (0.74, 1.02)	0.98 (0.83, 1.16)	0.98 (0.83, 1.15)	0.98 (0.83, 1.16)
Pre-ART VL[a]	1.09 (0.99, 1.20)	1.01 (0.93, 1.11)	1.01 (0.92, 1.11)	1.01 (0.92, 1.10)
Viremia category during ART				
Low-level viremia 201-999 copies/mL	**1.39 (1.04, 1.85)**	1.08 (0.81, 1.43)	1.01 (0.75, 1.35)	1.01 (0.75, 1.35)
Non-suppression ≥1000 copies/mL	**1.41 (1.18, 1.69)**	1.18 (0.98, 1.41)	1.10 (0.90, 1.35)	1.10 (0.90, 1.35)
Cumulative viremia including all VLs[b]	1.006 (0.998, 1.013)	1.006 (0.998, 1.013)	1.003 (0.995, 1.011)	1.003 (0.995, 1.011)
Cumulative viremia during ART[b]	**1.014 (1.005, 1.022)**	**1.010 (1.001, 1.019)**	1.006 (0.997, 1.016)	1.006 (0.997, 1.016)
Recent cumulative viremia[b]	0.950 (0.903, 1.000)	1.005 (0.962, 1.051)	1.001 (0.957, 1.047)	1.000 (0.956, 1.047)

Data are hazard ratio (95% CI). [a]per 1 $\log_{10}$ copies/mL. [b]per 1 $\log_{10}$ copy×year/mL.

Viremia does not improve CVD prediction

	Calibration (mean predicted 5-year risk)	Discriminiation (Harrell's C)
Kaplan-Meier estimate of 5-year CVD risk (95% CI)	2.44% (2.20%, 2.71%)	
D:A:D model	2.34%	0.75
D:A:D model + time-updated VL	2.34%	0.75
D:A:D model + pre-ART VL	2.20%	0.75
D:A:D model + peak viremia category	2.35%	0.75
D:A:D model + cumulative, all VLs	2.34%	0.75
D:A:D model + cumulative, during ART	2.35%	0.75
D:A:D model + cumulative, recent	2.32%	0.75

Limitations and strengths

Limitations

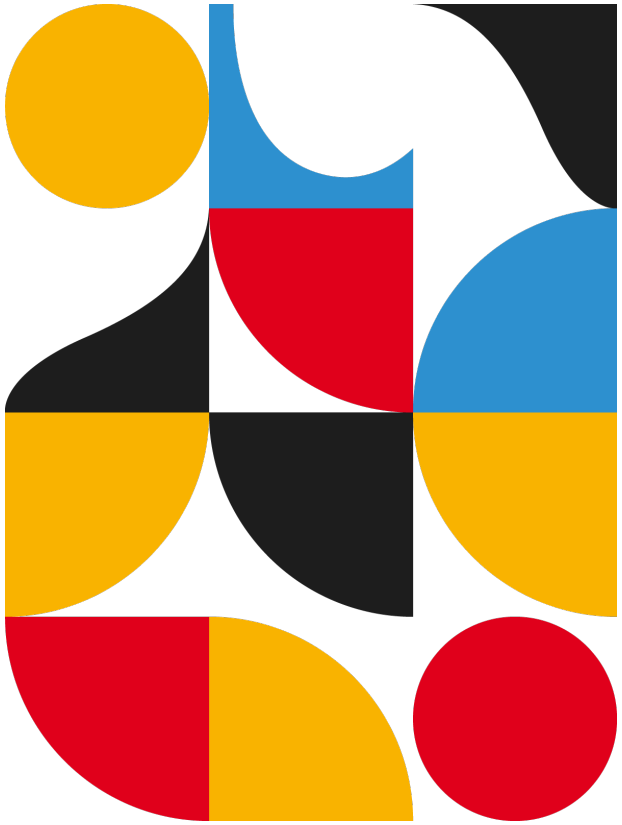
- Limited median follow-up (5-year risk)
- HIV viremia before diagnosis is unknown
- Generalizability
  (high CD4 counts, high degree of viral suppression, relatively few non-white people with HIV, Europe/Australia)
- Excluded 51% of the cohort (and excluded individuals had higher CVD risk)
  - Main reason (35%), cohort with low reporting of CVD events or risk factors
- Lack data on e.g. recreational drug use

Strengths

- Large cohort
- Rigorously validated endpoints
- Rich data on CVD risk factors

AIDS 2024

Conclusions



Exposure to HIV viremia was not associated with higher CVD risk.

Consideration of viremia history did not improve CVD prediction.

Viral suppression undoubtedly remains an important goal – though not associated with CVD.

Underscores complex pathogenesis of CVD among people with HIV.

Abstract OAB3406LB

REPRIEVE

Randomized Trial to Prevent Vascular Events in HIV

AIDS 2024

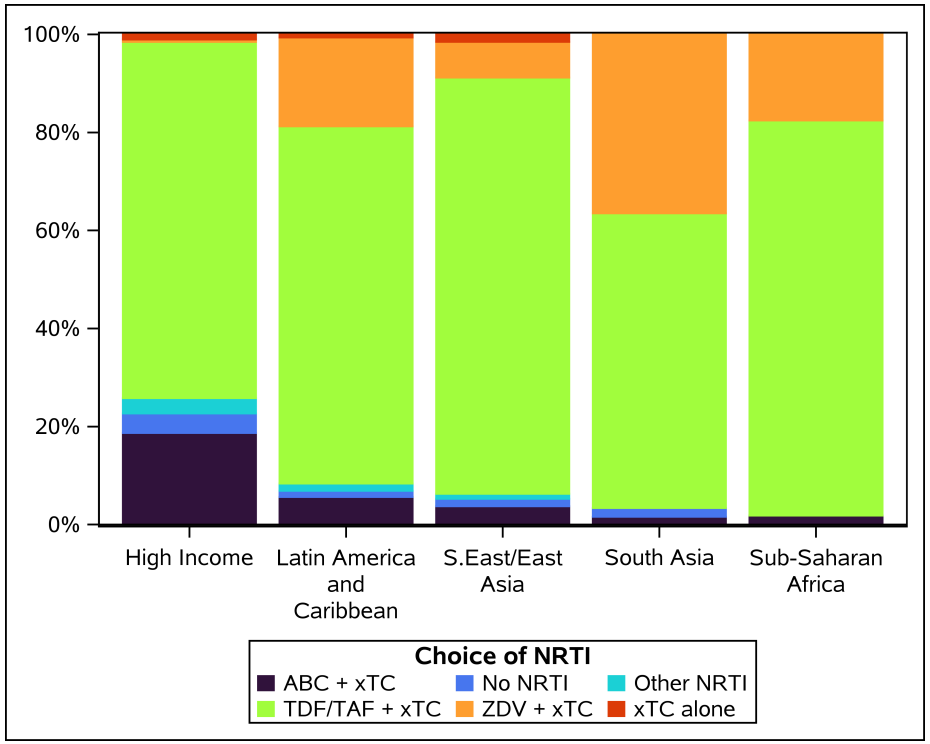
Abacavir is associated with Elevated Risk of Cardiovascular Events in the REPRIEVE Trial

Carl J. Fichtenbaum, Carlos D. Malvestutto, Maya G. Watanabe, Emma Davies Smith, Heather J. Ribaudo, Sara McCallum, Kathleen V. Fitch, Judith S. Currier, Marissa Diggs, Judith A. Aberg, Michael T. Lu, Javier Valencia, Cristina Gómez-Ayerbe, Indira Brar, Jose Valdez Madruga, Gerald S. Bloomfield, Pamela S. Douglas, Steven K. Grinspoon, Markella V. Zanni, for REPRIEVE Investigators.

Abacavir use in REPRIEVE Trial

AIDS 2024

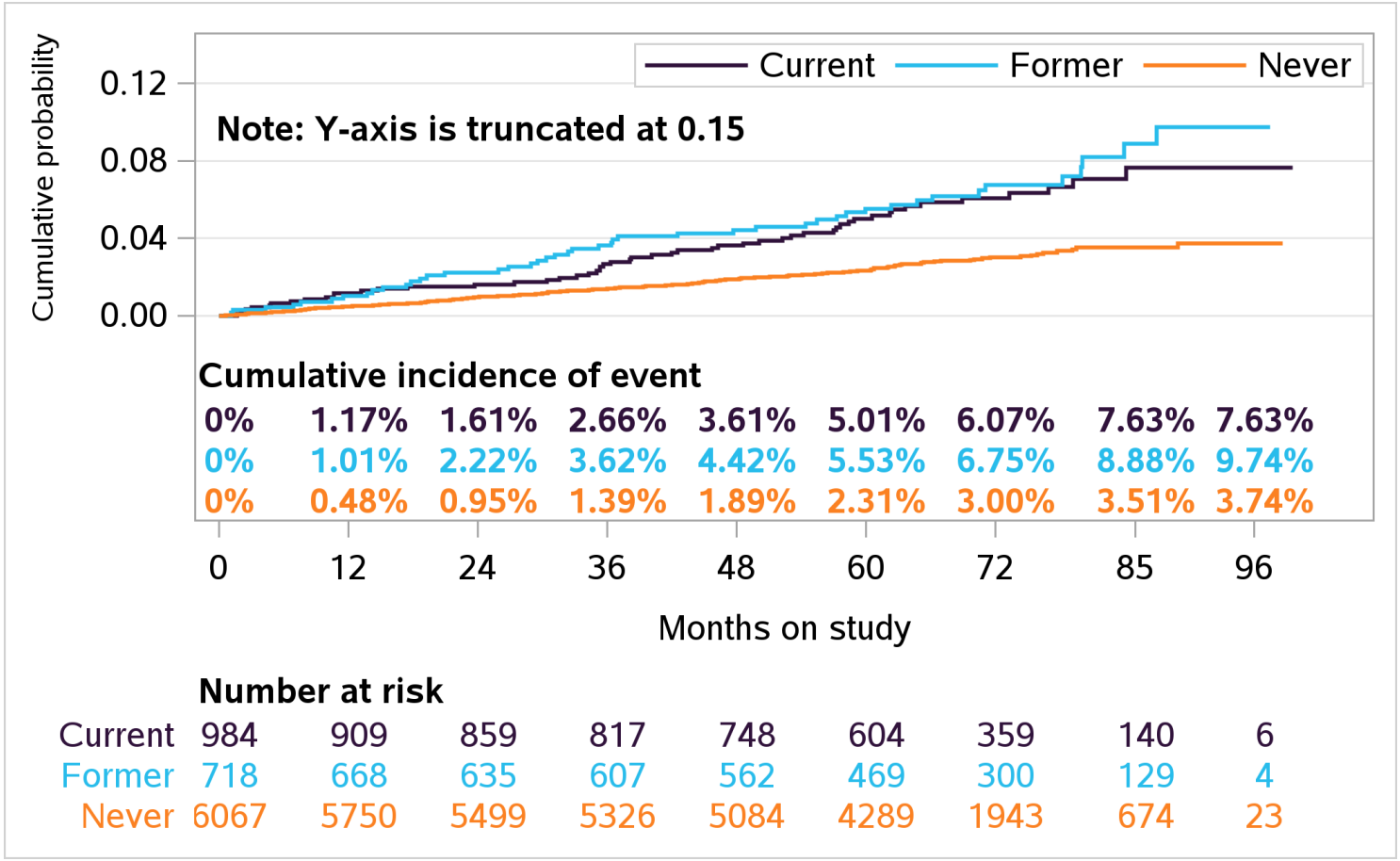
Global distribution of NRTI Use at Study Entry



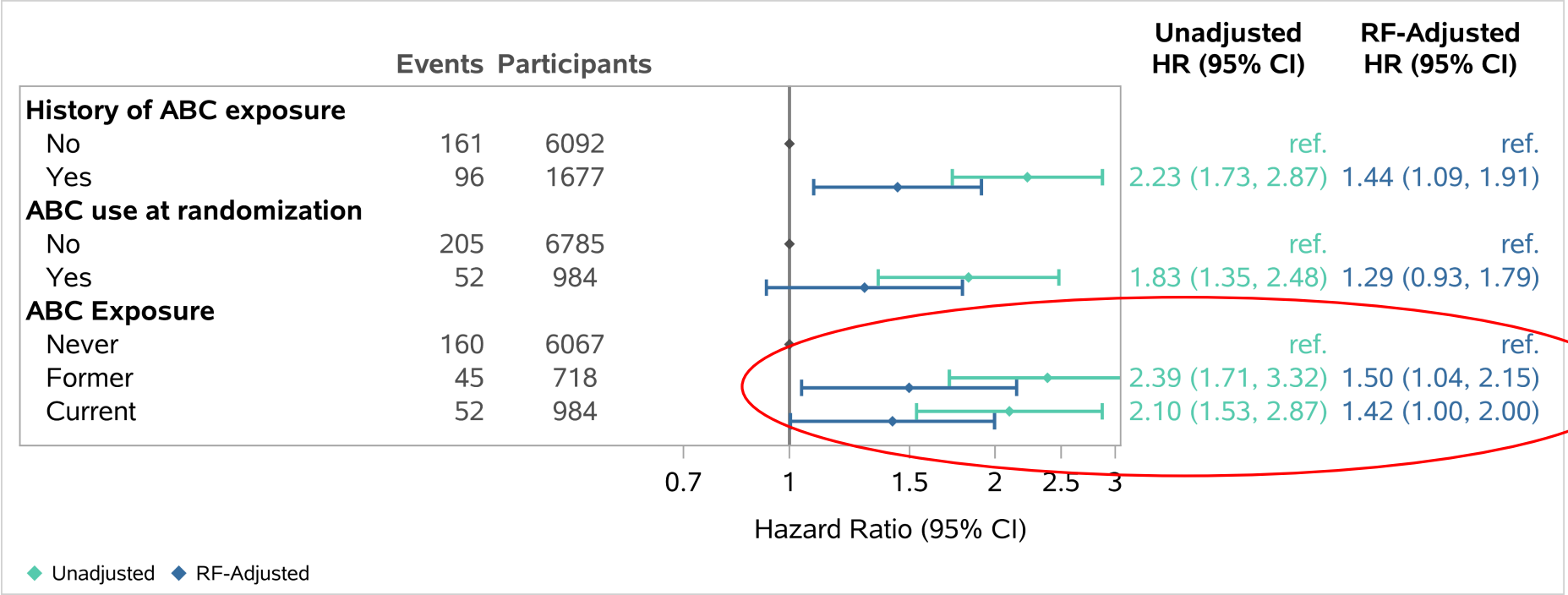
- 22% of participants had a history of ABC exposure
- 9% had former exposure to ABC
  - Median duration of prior use = 3.0 years (1.10, 6.90)
- 13% of participants were on ABC at randomization
  - Median duration = 1.47 years (0.604, 3.17)
- 78% of participants never had any ABC exposure

xTC=3TC or FTC

Cumulative Incidence of MACE with Abacavir



Abacavir exposure and MACE



All models are stratified by randomized study treatment group.

Adjusted model components included: age, natal sex, race, global burden of disease region, family history of CVD, smoking, hypertension, BMI, substance use, nadir CD4, HIV viral load, entry baseline ART regimen class, creatinine clearance, fasting glucose and lipids.

RF= Risk factor

Summary and Conclusions

AIDS 2024

- Current and former use of abacavir was associated with a higher incidence of subsequent major adverse cardiovascular events in the REPRIEVE trial (~42%-50% higher risk).
  - Global study population enrolled without prior known cardiovascular disease.
  - Low-to-moderate risk population (ASCVD median score – 4.5%)
  - Independently adjudicated cardiovascular endpoints.
- Current and former use of Tenofovir, Protease Inhibitors and Thymidine analogs were not associated with subsequent MACE.
- Future REPRIEVE analyses planned:
  - Time updated analyses of ART use evaluated for their impact on MACE.

Anal Cancer Screening

Yuxin Liu[1], Ashish Deshmukh[2], Keith Sigel[1], Michael Gaisa[1]

1.Icahn School of Medicine at Mount Sinai

New York, NY (USA)

2. College of Medicine, Medical University of South Carolina

Charleston, SC (USA)

The effectiveness of different anal cancer screening strategies for people living with HIV/AIDS

AIDS 2024

22 – 26 July · Munich, Germany and virtual aids2024.org

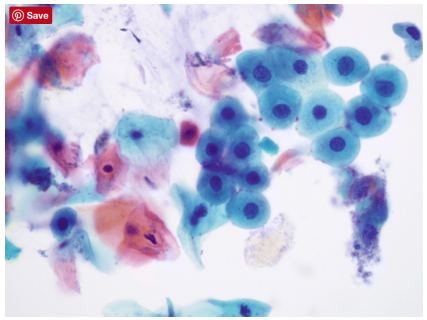
Background

- People living with HIV/AIDS have the highest risk of HPV-associated anal cancer.
- The IANS anal cancer screening guidelines, published in 2024, outline **five screening strategies** in high-resource settings:

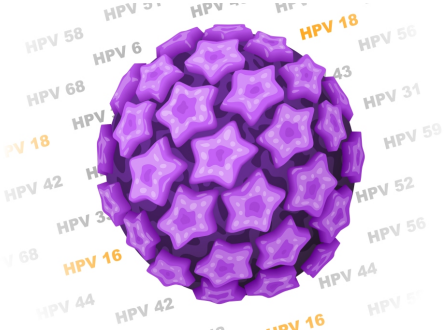
1. **Cytology alone**
2. **Cytology with hrHPV testing triage of >ASCUS**
3. **hrHPV testing alone**
4. **hrHPV testing with cytology triage of hrHPV positive**
5. **Cytology and hrHPV co-testing**

Aim

- To compare the effectiveness of these strategies in detecting anal cancer/precancer using data from a large cohort of people living with HIV/AIDS undergoing primary screening.



Anal cytology



hrHPV testing

AIDS 2024

Methods

- 1,620 people living with HIV/AIDS who underwent anal cytology, hrHPV testing, and high-resolution anoscopy (HRA)-guided biopsy between 2012 – 2019 were included.

median age 45 years (range: 34-54)

90% men who have sex with men living with HIV/AIDS

Anal HSIL rate 42%

- Using biopsy-proven anal HSIL as an endpoint, we calculated sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and the number of HRA referrals triggered by each screening strategy.

The performance of each screening strategy

	Screening strategy	Results triggering HRA referral	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	# HRAs
1	**Cytology alone**	ASCUS or worse	88 (85-90)	30 (27-33)	48 (45-51)	77 (72-81)	1,252 (77%)
2	**Cytology with hrHPV triage**	ASCUS/hrHPV+ LSIL/hrHPV+ ASC-H/HSIL	85 (82-88)	47 (44-50)	54 (51-57)	81 (78-84)	1,080 (67%)
3	**hrHPV alone**	hrHPV+	96 (95-97)	27 (25-30)	49 (47-52)	92 (88-95)	1,341 (83%)
4	**hrHPV with cytology triage**	hrHPV+/ASCUS or worse All HPV16+	85 (82-88)	48 (44-51)	54 (51-57)	81 (78-84)	1,073 (66%)
5	**Cytology and hrHPV cotesting**	NILM/hrHPV+ ASCUS/hrHPV+ LSIL/hrHPV+ ASC-H/HSIL All HPV16+	89 (86-91)	40 (37-44)	52 (49-55)	83 (80-87)	1,167 (72%)

Results

- 1. All strategies showed comparable performance metrics.
- 2. hrHPV testing alone had the highest sensitivity (96%) and NPV (92%), but triggered the most diagnostic procedures (HRA).
- 3. hrHPV with cytology triage showed the highest specificity (48%).
- 4. hrHPV with cytology triage, or vice versa, yielded the highest PPV (54%) and triggered the least number of HRAs.

Conclusions

1. **All screening strategies outlined in the new guidelines demonstrate comparable effectiveness in detecting anal cancer/precancer among people living with HIV/AIDS.**
2. **The combined approach of cytology and hrHPV testing, whether utilized as cotesting or triage, proves more effective than cytology or hrHPV testing alone.**
3. **The incorporation of hrHPV testing substantially increases specificity and results in a reduced number of HRA referrals, a critical consideration given the limited HRA capacity, even in high-resource settings.**

Summary

- Second generation integrase inhibitors are mostly pretty good
- LEN/BIC looks promising
- CV risk and weight gain are still not fully understood
- Despite the ANCHOR Study, more needs to be thought about for practical implementation of screening
  - And an alternative treatment trial would be good…

Thank you!

t.barber@nhs.net

@tristanjbarber

Thank you!

t.barber@nhs.net

@tristanjbarber


Thank You for Your Attendance!
Please visit us at:
www.prn.org