IAS 2024: Conference Update

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Treatment Data

Real-world retrospective, observational study (Madrid, Spain)

3-Year Effectiveness Following Switch to B/F/TAF in PWH With and Without Previous NRTI RAMs

N=506

PWH who switched to B/F/TAF

- No NRTI RAMs (n=437)
- NRTI RAMs (n=69)

Outcome

HIV-1 RNA <50 c/mL at 96 and 144 weeks (ITT and PP populations)

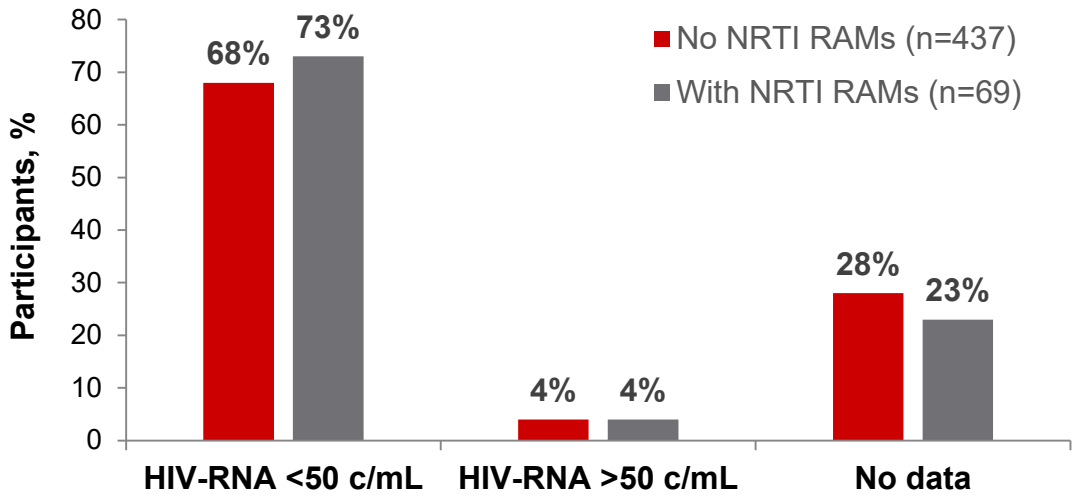
April 2019–February 2020

Overall, **13.6%** of participants had pre-existing **NRTI RAMs** and **86.6%** had HIV-1 RNA **<50 c/mL**

At baseline, among participants without versus with NRTI RAMs:

- Median age was **51.3 vs. 55.3 years**
- Median time since HIV diagnosis was **16.8 vs. 25.7 years**
- **13.6% vs. 11.6%** had HIV-1 RNA **>50 c/mL**

Virologic Outcomes at 144 Weeks



Overall VS (HIV-RNA <50 c/mL):

Week 96
ITT: 73%
PP: 95%

Week 144
ITT: 68%
PP: 94%

Switching to B/F/TAF maintained high rates of VS through 3 years, despite pre-existing NRTI RAMs

PP, per protocol; PWID, people who inject drugs; VS, virologic suppression

de Gea Grela A, et al. AIDS 2024, Poster THPEB100

BIC-PHI: Multicenter, single-arm trial (Europe & Latin America)

Rapid Initiation of B/F/TAF in People With Primary HIV Infection: Week 48 Results

N=64

People with PHI (<3 months postdiagnosis) treated with B/F/TAF

Outcomes

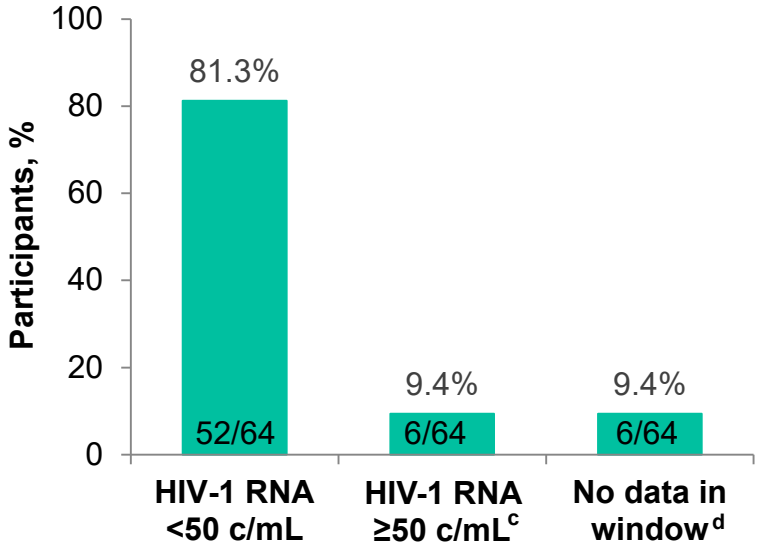
- Primary: HIV-1 RNA <50 c/mL at 48 Weeks (ITT; FDA Snapshot)
- Secondary: Safety and tolerability,[a] CESTA,[b] PSQI[b]

Not stated

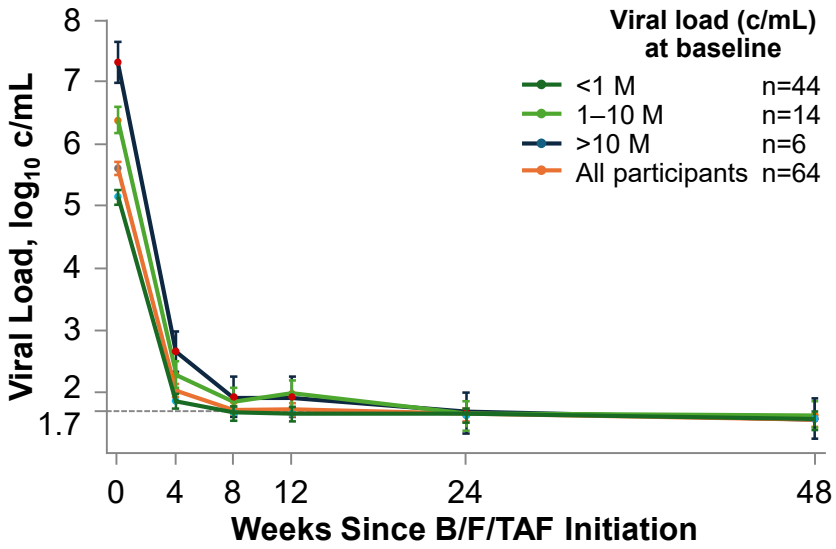
78% initiated B/F/TAF within **72 hours** of diagnosis

100% initiated B/F/TAF within **24 hours** of first specialist consultation

Virologic Outcome (FDA Snapshot)



VL Decay



72% had AEs, 3% were Grade 3/4

There were **0 AEs** leading to discontinuation and **0** SAEs related to B/F/TAF

89% were very satisfied according to **CESTA**

PSQI improved from baseline

Rapid initiation with B/F/TAF for the treatment of primary HIV infection resulted in rapid virologic decline, high suppression rate and was well tolerated through 48 weeks

[a]Total AEs and AE-related discontinuations; [b]Performed at 4 and 48 weeks; [c]VL: HIV-1 RNA 72, 130, 143 and 247 c/mL at Week 48; HIV-1 RNA 799 and 20,600 c/mL at early discontinuation; [d]4 had VL <50 c/mL at last visit, 2 had VL data available at baseline only. CESTA, Spanish Antiretroviral Treatment Satisfaction Questionnaire; PHI, primary HIV infection; PSQI, Pittsburgh Sleep Quality Index; VL, viral load

Ambrosioni J, et al. AIDS 2024, Poster WEPEB098

Open-label, single-arm study (Canada)

Switch to B/F/TAF Among PWH Who Use Drugs

N=45

PWH with TE who use drugs, with prior transient viremia

Switch to B/F/TAF (with enhanced adherence support)

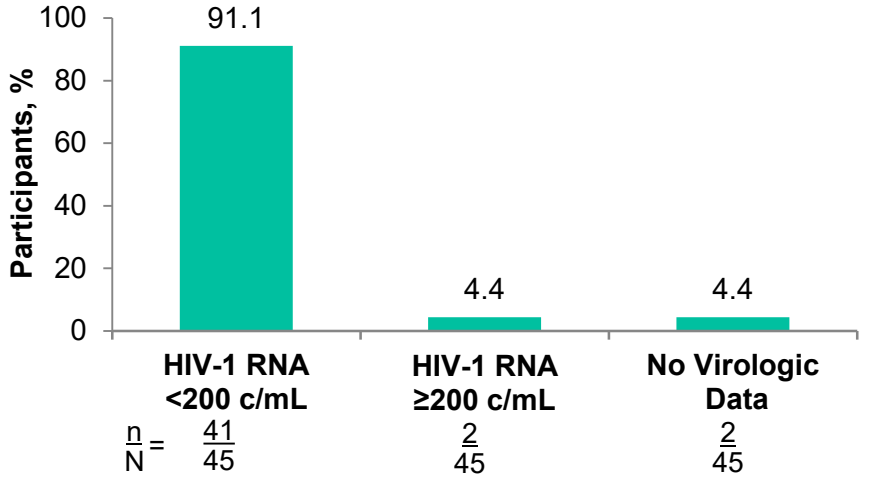
Outcomes

Proportion of participants with VS up to 42 months

Baseline characteristics

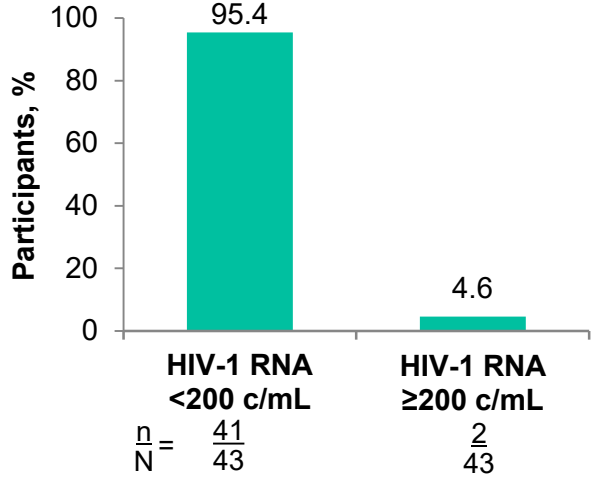
Median age 55 years
88.9% male
93.3% HIV-1 RNA <200 c/mL
91.1% used opiates
24.4% injected drugs
55.6% used opioid agonist therapy
17.8% with hepatitis C coinfection

Virologic Outcomes at Month 36



2 participants discontinued due to social/mental health problems (n=1) and moving out of area (n=1)

Virologic Outcomes at Month 42



2 participants had VL ≥200 c/mL at Month 42, which occurred following **treatment interruptions;** both were **resuppressed** on B/F/TAF

PWH who use drugs and who experienced prior transient viremia achieved long-term virologic suppression after switching to B/F/TAF with enhanced adherence support

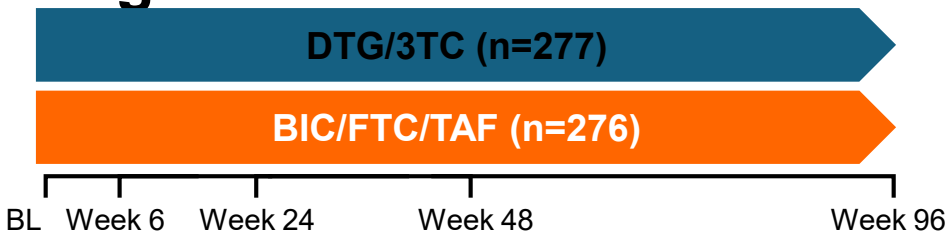
TE, treatment experience; VL, viral load; VS, virologic suppression

Conway B, et al. AIDS 2024, Poster THPEB126

Switching to DTG/3TC or BIC/FTC/TAF in Virologically Suppressed PWH: PASO-DOBLE Randomized Clinical Trial

Phase IV, Open-label, Multicentre, Randomized Clinical Trial (N=553)

Study Design



Inclusion criteria:

- 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

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

Baseline Characteristics

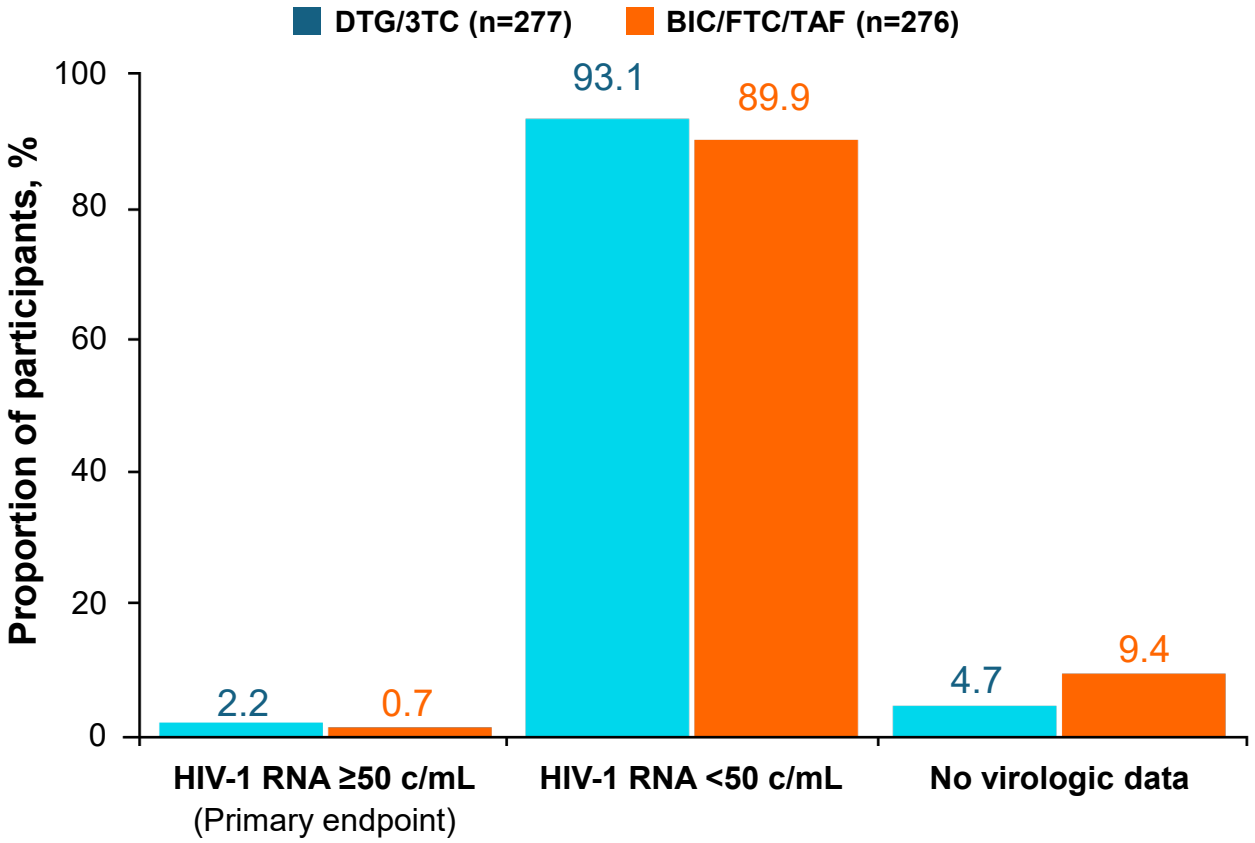
Parameter	DTG/3TC (n=277)	BIC/FTC/TAF (n=276)
Mean age, years	50	51
Female sex at birth, %	26.7%	26.4%
Caucasian, %	72.6%	72.8%
Latinx, %	23.8%	24.3%
Black	1.4%	1.8%
Other / unknown	2.2%	1.1%
Mean total time on ART, yrs	11.7	11.1
Mean time w HIV RNA <50 c/mL, mos	103.4	97.7
Mean duration of prior ART regimen, mos	66.2	62.8
Mean CD4 cells/mm^3	712	684
CD4 <350 cells/mm^3, %	9.4%	8.7%
Mean CD4 nadir cells/mm^3	293	302
BMI >25 kg/m^2, %	51.8%	48.6%

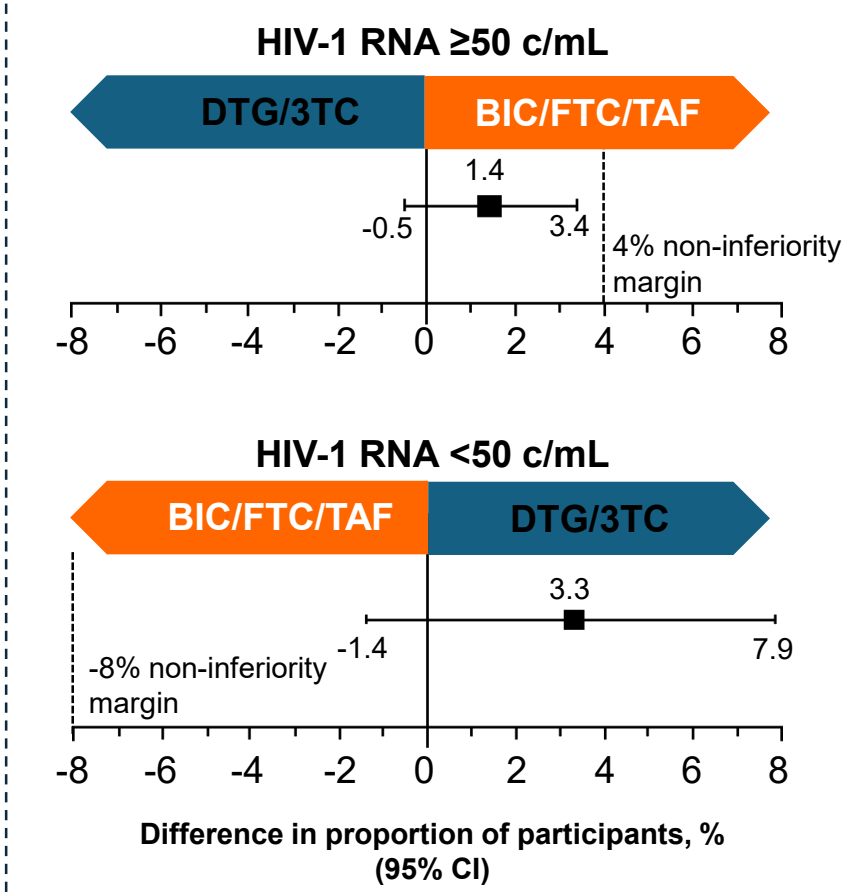
3TC, lamivudine; ART, antiretroviral therapy; BIC, bictegravir; BL, baseline; BMI, body mass index; cobi, cobicistat; DTG, dolutegravir; EFV, efavirenz; FTC, emtricitabine; TAF, tenofovir alafenamide; VF, virologic failure
Adapted from Martinez E, et al. AIDS 2024. Presentation #OAB3606LB.

Switching to DTG/3TC or BIC/FTC/TAF in Virologically Suppressed PWH: PASO-DOBLE Randomized Clinical Trial

Phase IV, Open-label, Multicentre, Randomized Clinical Trial (N=553)

Virologic Efficacy: Snapshot outcomes at Week 48 (ITT-E population)

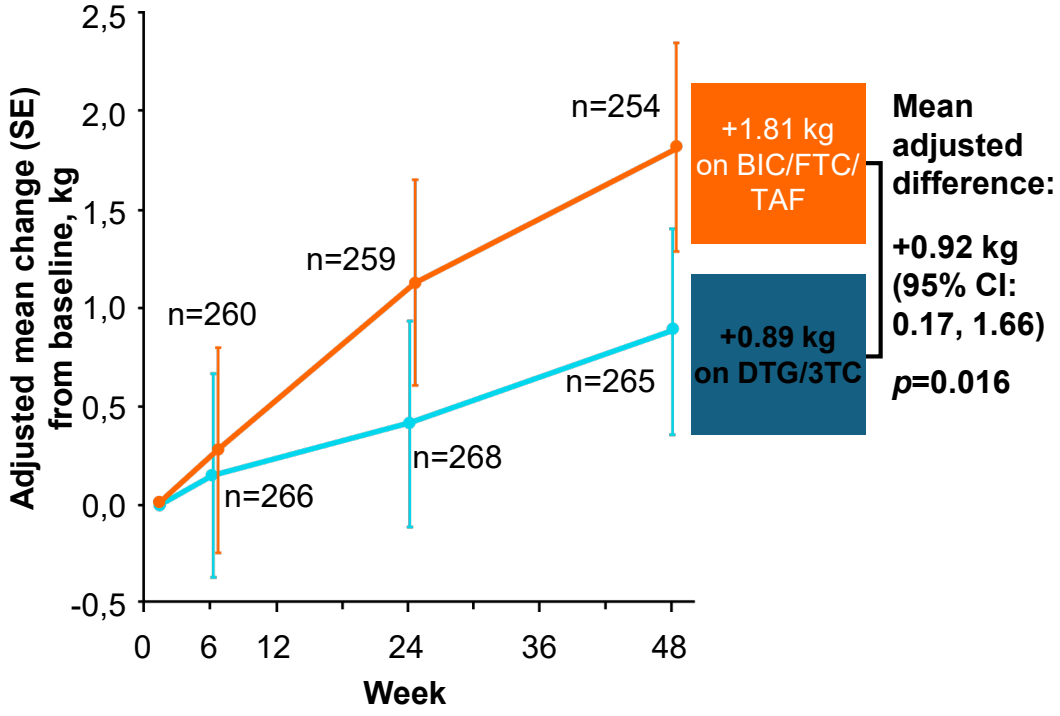




3TC, lamivudine; BIC, bictegravir; DTG, dolutegravir; FTC, emtricitabine; TAF, tenofovir alafenamide
Adapted from Martinez E, et al. AIDS 2024. Presentation #OAB3606LB.

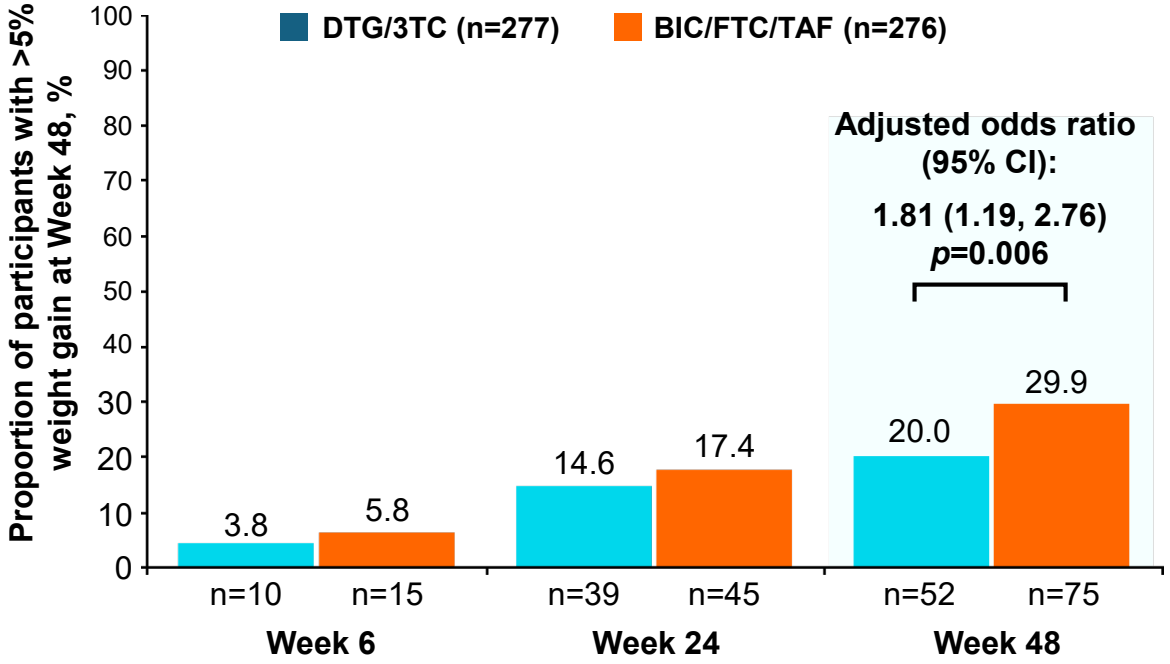
Switching to DTG/3TC or BIC/FTC/TAF in Virologically Suppressed PWH: PASO-DOBLE Randomized Clinical Trial

Mean Weight Change, Baseline to Week 48



Proportion with ≥5% Weight Gain

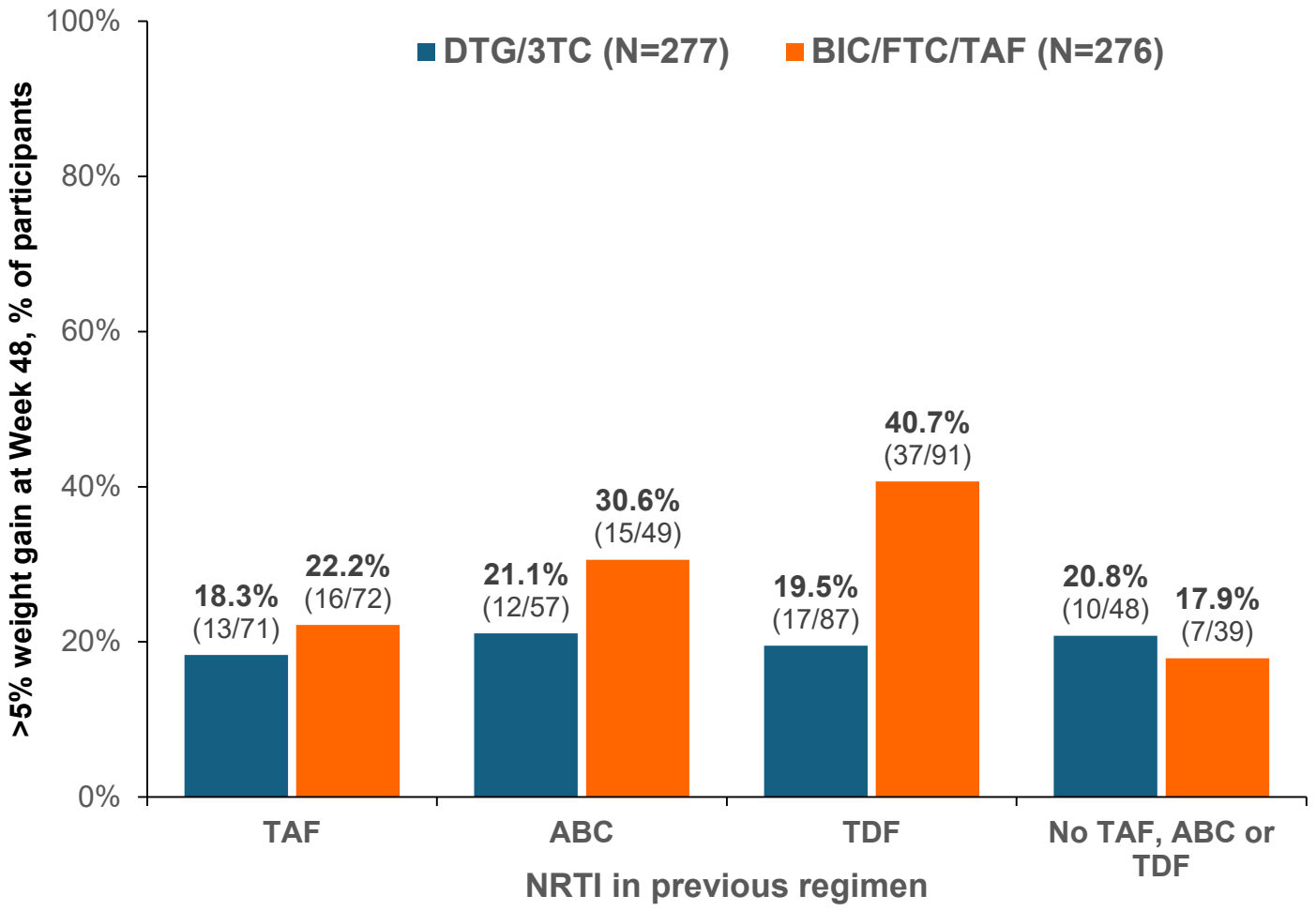
Weight change of ≥5% is considered clinically meaningful.



Adjusted by baseline value, sex, presence of TAF in previous ART, age, and ethnicity
3TC, lamivudine; BIC, bictegravir; DTG, dolutegravir; FTC, emtricitabine; TAF, tenofovir alafenamide
Adapted from Martinez E, et al. AIDS 2024. Presentation #OAB3606LB.

PASO-DOBLE Randomized Clinical Trial: Proportion With >5% Weight Gain at Week 48 by Baseline NRTI

- Change in weight with BIC/FTC/TAF may depend on the NRTI used in the previous regimen
  - **DTG/3TC** arm: proportion with >5% weight gain was similar regardless of BL NRTI
  - **BIC/FTC/TAF** arm: proportion with >5% weight gain was highest after switch from TDF or ABC

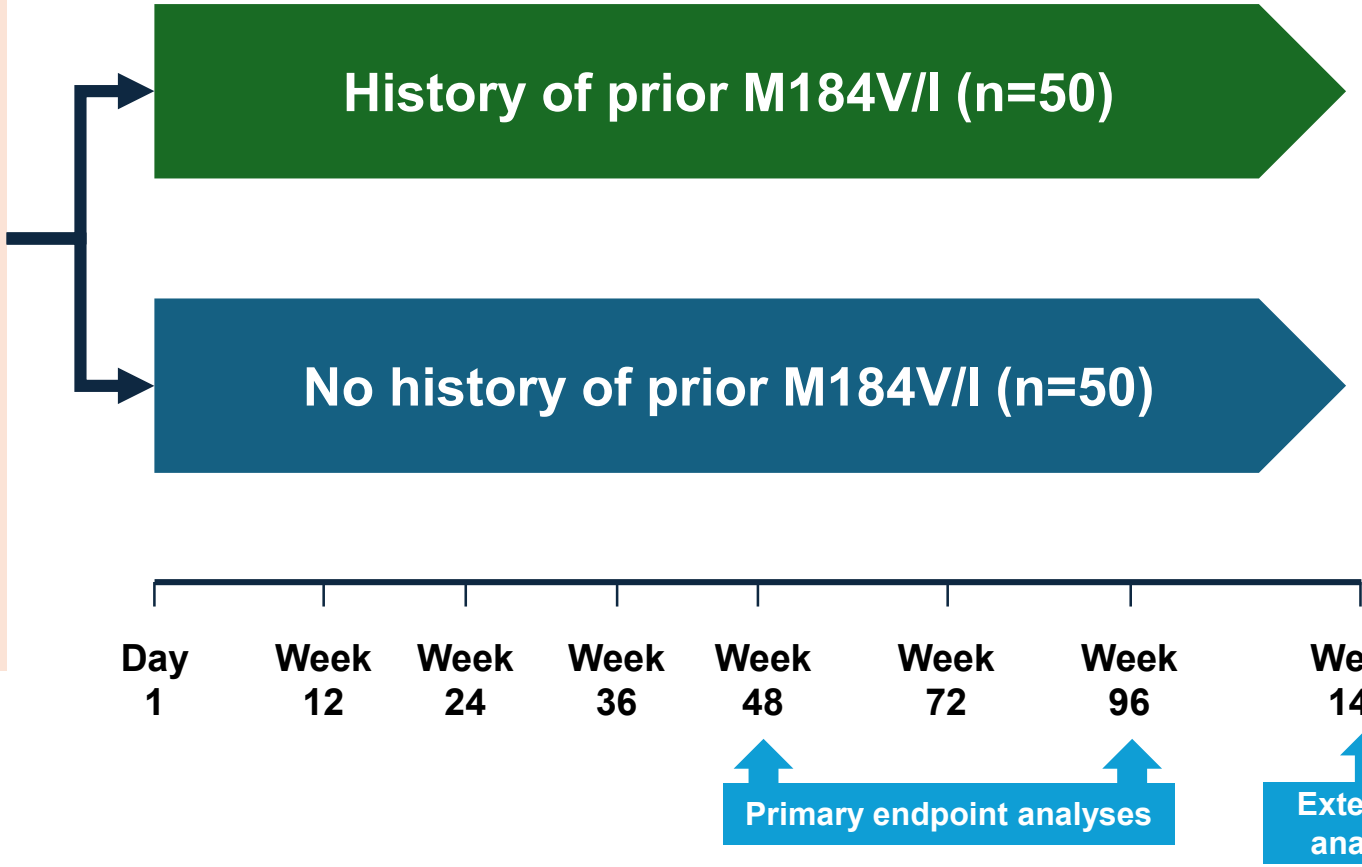


Adjusted by baseline value, sex, presence of TAF in previous ART, age, and ethnicity
3TC, lamivudine; ABC, abacavir; BIC, bictegravir; BL, baseline; DTG, dolutegravir; ; FTC, emtricitabine; TAF, tenofovir alafenamide
Adapted from Martinez E, et al. AIDS 2024. Presentation #OAB3606LB.

No Confirmed Virological Failures After Switch to DTG/3TC in PWH with Prior M184V/I and Virological Failures

144-week Results from the Prospective, Open-label SOLAR-3D Study, N=100

Eligibility criteria:
- ≥18 years
- HIV-1 RNA <50 c/mL for ≥6 months
- Any stable 2-, 3- or 4-drug ART for ≥6 months
- **Prior virologic failure***
- **No exclusion for prior INSTI use, any CD4, prior NRTI mutations or M184V/I or K65R in baseline proviral DNA NGS (above a 10% threshold)**



Primary endpoint:
- % of patients with PCR ≥50 at weeks 48 & 96 (FDA snapshot, ITT-E, per protocol)

Secondary endpoints:
- PCR <50 at weeks 48 & 96
- Discontinuations due to CVF (PCR≥50 followed by PCR>200)

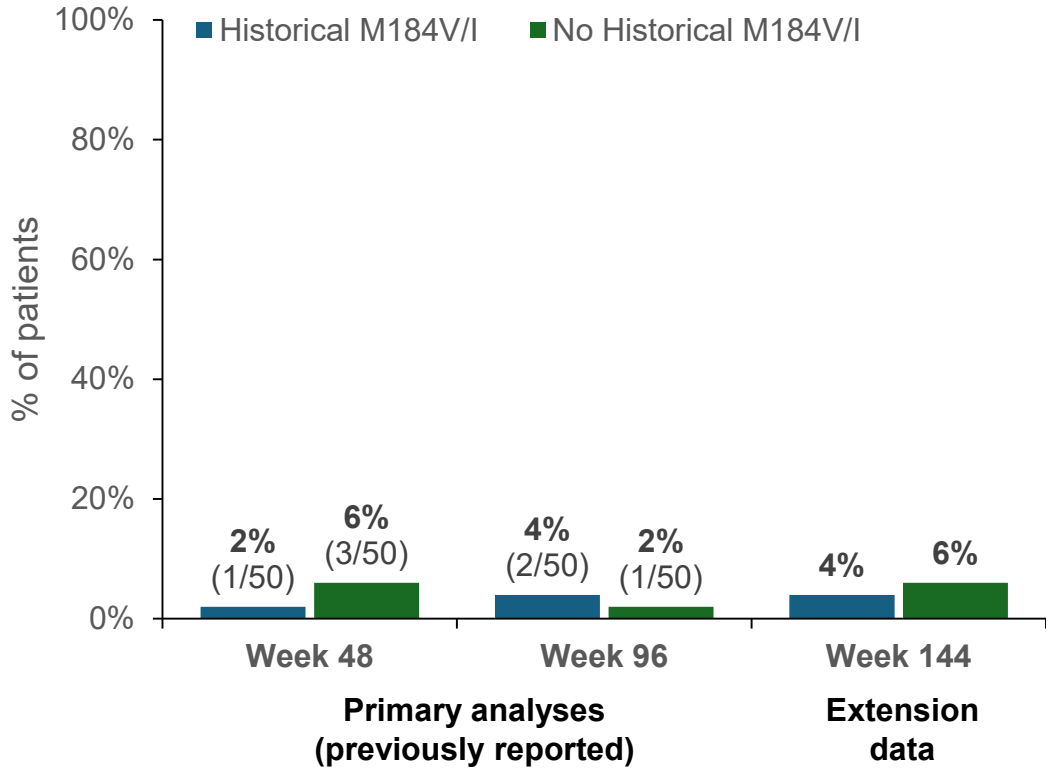
***≥2 prior ART with ≥ 1 of the following: failure to attain PCF<50, confirmed rebound PCR >200, documented genotypic phenotypic resistance)**
3TC, lamivudine; ART, antiretroviral therapy; CVF, confirmed virologic failure; DTG, dolutegravir; INSTI, integrase strand inhibitor; ITT, intention to treat; NRTI, nucleoside reverse transcriptase inhibitor; PCR, polymerase chain reaction; PWH, people with HIV
Adapted from Blick G, et al. AIDS 2024. Presentation #SS0403LB.

SOLAR-3D: Baseline Mutations and Primary Virologic Outcomes

Historical GT *vs*. Proviral DNA NGS

n (%)	All Patients (n = 100)	Historical M184V/I (n = 50)	No Historical M184v/I Resistance (n = 50)
M184V/I on Historical GT	50 (50)	50 (100)	0
Proviral DNA by NGS	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

HIV-1 RNA ≥ 50c/mL by FDA Snapshot



Investigators' key conclusion: **Neither prior/current M184V/I nor multiple prior VFs impact the efficacy and durability of switching virologically suppressed PWH to DTG/3TC through 144 weeks**

3TC, lamivudine; DTG, dolutegravir; NGS, next generation sequencing; PWH, people with HIV; VF, virologic failure
Adapted from Blick G, et al. AIDS 2024. Presentation #SS0403LB.

Hepatitis B Core Antibody: Results Pooled from Phase 3/3b Studies

N=76 Patients from the GEMINI-1/-2, STAT, TANGO, and SALSA studies

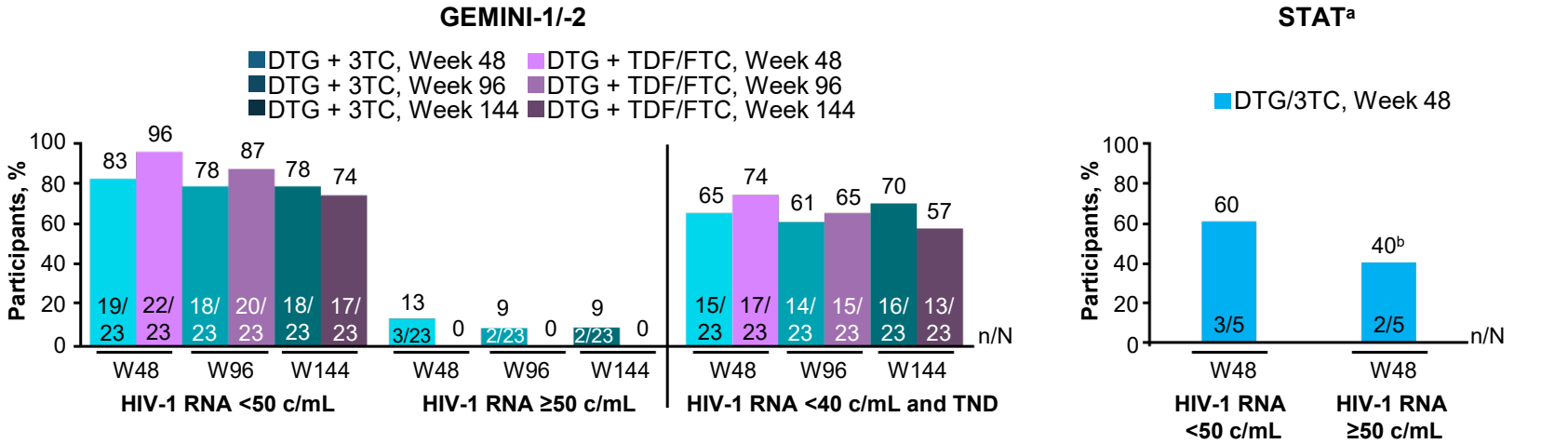
Demographics & Baseline Characteristics

Parameter		GEMINI-1 / -2		STAT	TANGO / SALSA	
		DTG + 3TC (n=23)	DTG + TDF/FTC (n=23)	DTG/3TC (n=5)	DTG/3TC (n=16)	CAR (n=9)
Female sex at birth, n (%)		2 (9)	1 (4)	0	0	3 (33)
Median age, years (range)		38 (24-55)	42 (25-64)	46 (28-58)	4 (31-66)	47 (33-35)
Age ≥50 years, n (%)		1 (4)	10 (43)	2 (40)	5 (31)	3 (33)
Race, n (%)	White	14 (61)	16 (70)	1 (20)	10 (63)	5 (56)
	Black / African	3 (13)	3 (13)	4 (80)	1 (6)	2 (22)
	Asian	4 (17)	3 (13)	0	3 (19)	2 (22)
	Other	2 (9)	1 (4)	0	2 (13)	0
Median BMI, kg/m^2		23.4	22.7	21.0	24.7	24.3

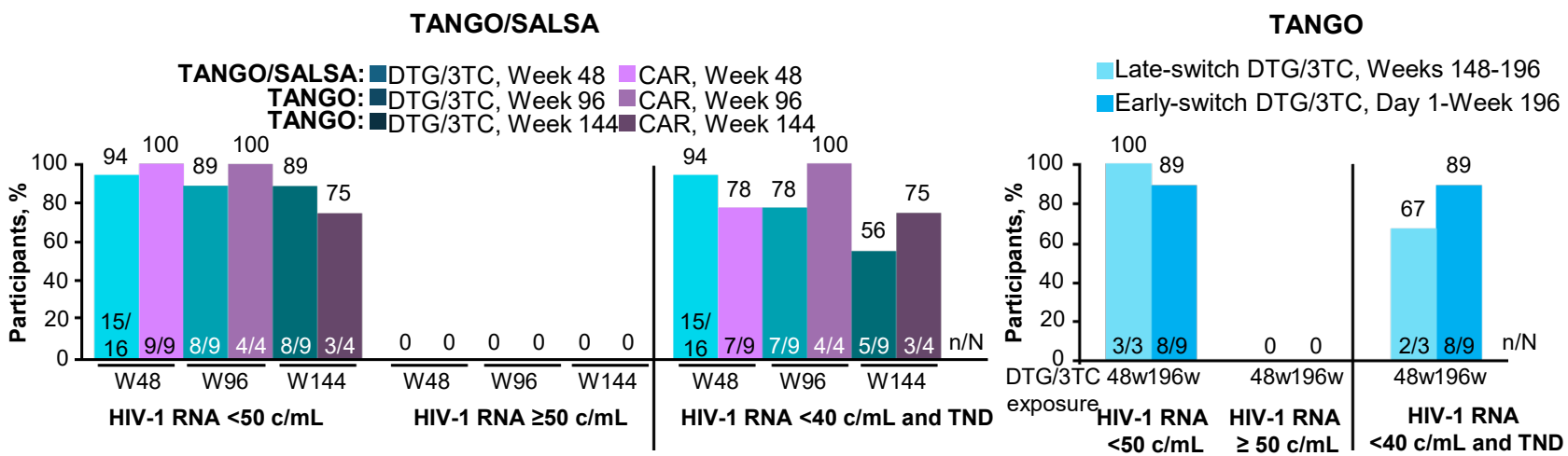
DTG/3TC in PWH with Isolated Reactive Hepatitis B Core Antibody: Results Pooled from Phase 3/3b Studies

N=76 Patients from the GEMINI-1/-2, STAT, TANGO, and SALSA studies

HIV virologic outcomes in ART-naïve patients



HIV virologic outcomes in patients with prior virologic suppression



[a]Data for HIV-1 RNA<40 c/mL and TND were not available for STAT. [b]In STAT, 1 participant who had HIV-1 RNA <50 c/mL at week 24 was considered as having HIV-1 RNA ≥50 c/mL at week 48 due to a change in ART after their week 24 assessment. This change in ART was not efficacy related (decision by participant or proxy/participant incarceration).
3TC, lamivudine; CAR, current antiretroviral regimen; DTG, dolutegravir; FTC, emtricitabine; TDF, tenofovir disoproxil; TND, target not detected
Adapted from Fox D, et al. AIDS 2024. Presentation #OAB0106LB.

DTG/3TC in PWH with Isolated Reactive Hepatitis B Core Antibody: Results Pooled from Phase 3/3b Studies

Safety: Summary of Maximum Post-baseline Emergent Liver Chemistry Test Elevations[a]

Parameter, n (%)	GEMINI-1 / -2		STAT	TANGO / SALSA[b]	
	DTG + 3TC (n=23)	DTG + TDF/FTC (n=23)	DTG/3TC (n=5)	DTG/3TC (n=16)	CAR (n=9)
Grade 1	6 (26)	4 (17)	0	2 (13)	1 (11)
Grade 2	2 (9)	2 (9)	0	1 (6)	1 (11)
Grade 3	0	1 (4)	0	0	0
Elevated serum or plasma AST	0	1 (4)	0	0	0
Grade 4	2 (9)	0	0	0	0
Elevated serum or plasma AST	2 (9)	0	0	0	0
Elevated serum or plasma ALT	1 (4)	0	0	0	0

- In the GEMINI studies, 2 pts receiving DTG/3TC had grade 4 elevations in AST (n=2) or ALT (n=1), and 1 participant receiving DTG + TDF/FTC had a grade 3 elevation in AST
  - All other liver chemistry test elevations were grade 1 or 2 in GEMINI-1/-2, TANGO and SALSA, and no liver chemistry test elevations were reported in STAT
- 1 participant receiving DTG + 3TC in GEMINI-1/-2 had hepatitis E virus and liver enzyme elevations that met liver-stopping criteria; they discontinued treatment at ~144 weeks and withdrew from the study

Across all studies, no instances of HBV reactivation were reported

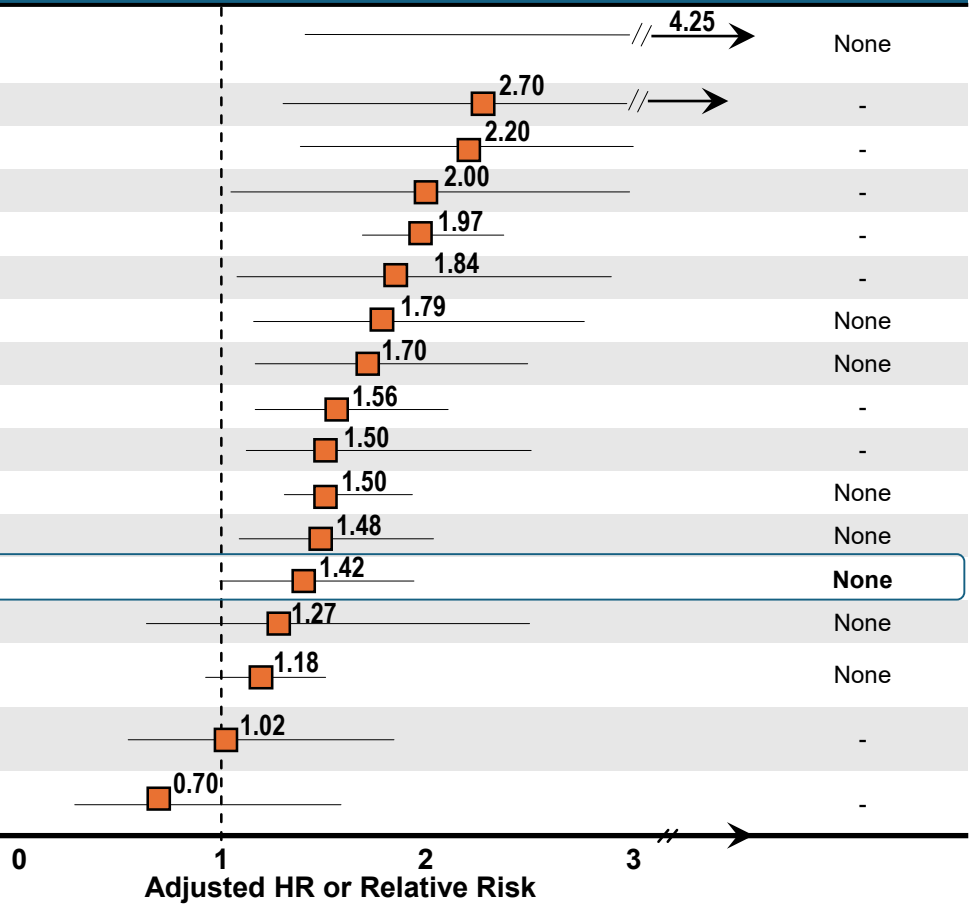
[a]Through end of study; includes serum or plasma albumin, ALP, ALT, AST, bilirubin and protein; [b]All grade 1 elevations were reported in TANGO, and all grade 2 elevations were reported in SALSA
3TC, lamivudine; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CAR, current antiretroviral regimen; DTG, dolutegravir; FTC, emtricitabine; PWH, people with HIV; TDF, tenofovir disoproxil
Adapted from Fox D, et al. AIDS 2024. Presentation #OAB0106LB.

Association of ABC and TDF Exposure With Chance of CV Events

Except REPRIEVE, data presented on this slide were not part of the AIDS 2024 program

This is not a cross-study comparison (each line represents a separate study) and no direct comparisons should be made of individual studies

Study	Reference	PY of Follow-Up	ABC Use	Event, n	ABC Association, Risk[a] of Event (95% CI)	TDF Association
SMART[1]	Strategies for Management of Anti-Retroviral Therapy/INSIGHT; DAD Study Groups. *AIDS*. 2008;22:F17-24	NR	Current	MI (19)	4.25 (1.39, 13.0)	None
North Carolina Medicaid[2]	Brouwer ES, et al. *Epidemiology*. 2014;25:406-17	6399[b]	Current	MI (38)	2.70 (1.24, 5.91)[h]	-
Kaiser[3]	Marcus JL, et al. *J Acquir Immune Defic Syndr*. 2016;73:39-46	31,211[b]	Current	CVD (178)	2.20 (1.4, 3.5)	-
Danish[4]	Obel N, et al. *HIV Med*. 2010;11:130-6	19,124[c]	Current	MI (67)	2.00 (1.07, 3.76)	-
D:A:D 2014 (post-2008)[5]	Sabin C, et al. *BMC Med*. 2016;14:61	157,309[c]	Current	MI (269)	1.97 (1.43, 2.72)[i]	-
NA-ACCORD Overall[6]	Elion R, et al. *J Acquir Immune Defic Syndr*. 2018;78:62-72	29,077[b]	Recent	MI (123)	1.84 (1.17, 2.91)	-
QPHID[7]	Durand M, et al. *J Acquir Immune Defic Syndr*. 2011;57:245-53	35,851	Any	MI (125)	1.79 (1.16, 2.76)	None
D:A:D[8]	Worm SW, et al. *J Infect Dis*. 2010;201:318-30	178,835[c]	Recent	MI (580)	1.70 (1.17, 2.47)	None
MAGNIFICENT[9]	Rotger M, et al. *Clin Infect Dis*. 2013;57:112-21	NA	Current	CVD event[d] (571)	1.56 (1.17, 2.07)	-
Swiss[10]	Young J, et al. *J Acquir Immune Defic Syndr*. 2015;69:413-21	80,004[c]	Recent	CVD event[d] (365)	1.50 (1.12, 2.00)	-
VA – Desai[11]	Desai M, et al. *Clin Infect Dis*. 2015;61:445-52	164,059[c]	Current	CVD event[e] (934)	1.50 (1.26, 1.79)	None
VA – Choi[12]	Choi AI, et al. *AIDS*. 2011;25:1289-98	59,578[c]	Recent	CVD event[f] (501)	1.48 (1.08, 2.04)	None
REPRIEVE[13]	**Fichtenbaum CJ, et al. AIDS 2024, Oral OAB3406LB**	**NR[c]**	**Recent**	**MACE (52)[g]**	**1.42 (1.00, 2.00)[j]**	**None**
French HD[14]	Lang S, et al. *Arch Intern Med*. 2010;170:1228-38	298,156[b]	Recent	MI (289)	1.27 (0.64, 2.49)[k]	None
VA – Bedimo[15]	Bedimo RJ, et al. *Clin Infect Dis*. 2011;53:84-91	76,376[c]	Cumulative	MI (278)	1.18 (0.92, 1.50)[l]	None
Ding meta-analysis[16]	Ding X, et al. *J Acquir Immune Defic Syndr*. 2012;61:441-7	Range: 42 to 1257	Current	MI (46)	1.02 (0.56, 1.84)	-
ALLRT/ACTG[17]	Ribaudo HJ, et al. *Clin Infect Dis*. 2011;52:929-40	17,404[b]	In initial regimen	MI (36)	0.70 (0.3, 1.6)	-



[a]Risk reported is the adjusted risk as presented by each study; [b]All or majority of PWH were treatment naïve at ABC inclusion; [c]All or majority of PWH were treatment experienced at ABC initiation; [d]MI, unstable angina, PCI, CABG, fatal CAD; [e]MI, stroke, PCI, and CABG; [f]MI, unstable angina, CVA, PVD; [g]MI, TIA/stroke, revascularization, PAD and CV death; [h]Association compared with TDF (unadjusted); [i]Post-2008 association when PWH with moderate/high CVD risk were more likely to discontinue ABC; [j]Adjusted HR for risk of MACE with current ABC exposure; [k]Who did not use cocaine or IV drugs; [l]Adjusted for age, hypercholesterolemia, hypertension, type 2 diabetes and tobacco use. CABG, coronary artery bypass graft; CAD, coronary artery disease; CVA, cerebrovascular disease; CVD, cardiovascular disease; French HD, French Hospital Database; MACE, major adverse cardiovascular events; MI, myocardial infarction; NA, not available; NR, not reported; PAD, peripheral artery disease; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; PY, person-years; QPHD, Quebec's Public Health Insurance Database; TIA, transient ischemic attack

REPRIEVE: A randomized controlled trial

Association of ART With Major CV Adverse Events

N=7769

PWH aged 40–75 years, on ART for ≥180 days, CD4 count >100 cells/μL and low-moderate CVD risk[1]

Outcome
First MACE in REPRIEVE ITT population[1]

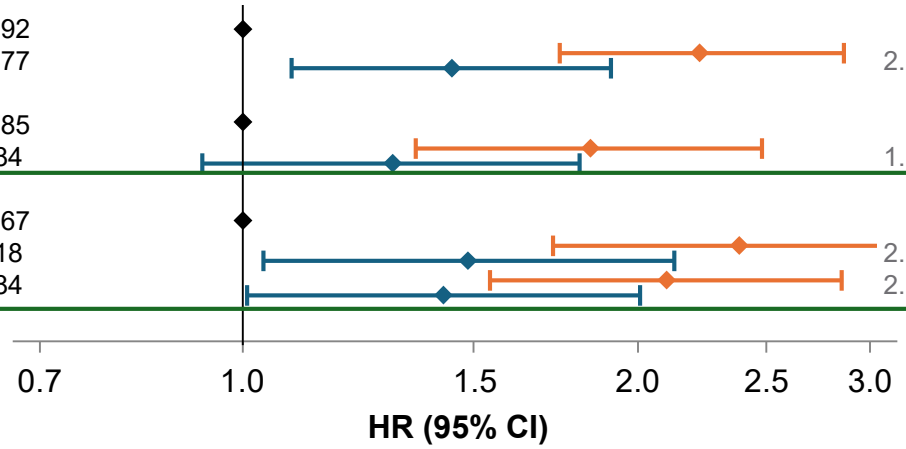
2015–2023[1]

Sex[1]: 31% female
Race[1]: 65% non-White
Median age[1]: 50 years
Fasting LDL[1]: 106 mg/dL
10-year ASCVD risk score[1]: 4.5%
CD4 count[1]: 621 cells/μL
VL <400 c/mL[1]: 98%
Median ART duration[2]: 9.5 years

Reported former/current exposure to[2]:
- ABC: 22% / 13%
- TDF: 86% / 61%
- AZT/d4T: 49% / 10%
- PIs: 47% / 26%

Effect of ABC Exposure on Incidence of MACE[1]

	No. of events	No. of individuals	Unadjusted HR (95% CI)	Risk factor adjusted HR (95% CI)
History of ABC exposure				
No	161	6092	Ref.	Ref.
Yes	96	1677	2.23 (1.73, 2.87)	1.44 (1.09, 1.91)
ABC use at randomization				
No	205	6785	Ref.	Ref.
Yes	52	984	1.83 (1.35, 2.48)	1.29 (0.93, 1.79)
ABC exposure				
Never	160	6067	Ref.	Ref.
Former	45	718	2.39 (1.71, 3.32)	1.50 (1.04, 2.15)
Current	52	984	2.10 (1.53, 2.87)	1.42 (1.00, 2.00)



Former and current use of ABC was associated with higher MACE incidence in the REPRIEVE trial; no other ARVs (including TDF) were associated with MACE[1]

ASCVD, atherosclerotic cardiovascular disease; CVD, cardiovascular disease; MACE, major adverse cardiovascular events; VL, viral load

1. Fichtenbaum CJ, et al. AIDS 2024, Oral OAB3406LB; 2. Fichtenbaum CJ, et al. AIDS 2024, Abstract OAB3406LB. https://programme.aids2024.org/Abstract/Abstract/?abstractid=11856 (accessed July 26, 2024)

NEURO-INSTI (SCOLTA project): Retrospective analysis of multicenter observational study

Neuropsychiatric AEs Among PWH Starting a New INSTI-Based Regimen

N=2922

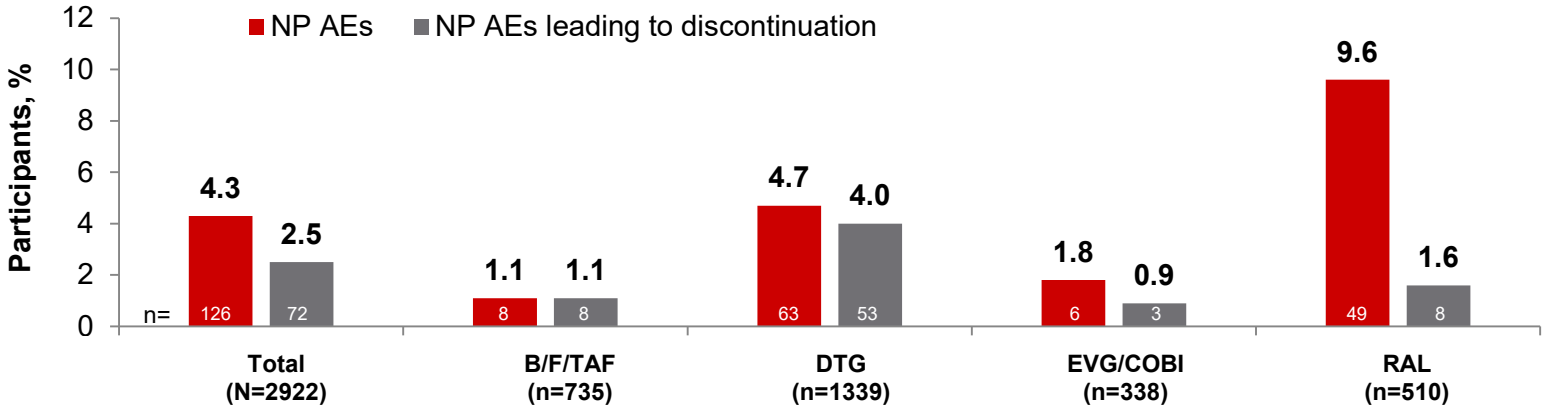
PWH starting a new INSTI

Outcomes

Incidence rates of NP AEs and related discontinuations

2007 onwards

NP AEs and NP AEs Leading to Discontinuation According to Treatment



	Total (N=2922)	B/F/TAF (n=735)	DTG (n=1339)	EVG/COBI (n=338)	RAL (n=510)
Adjusted incidence rate per 1000 PYFU (95% CI):					
NP AEs	15.9 (13.4, 19.0)	7.6 (3.4, 17.3)	25.4 (16.5, 39.0)	15.1 (6.1, 37.5)	60.5 (36.1, 101.4)
NP AEs leading to discontinuation	9.1 (7.2, 11.5)	13.4 (6.2, 29.0)	18.2 (13.3, 24.8)	8.2 (2.5, 26.5)	14.3 (6.6, 31.1)

- Median (IQR) observation time: **28 (14–45) months**
- Rate of discontinuation due to NP AEs across all cohorts **was low** (72 discontinuations)
- **Higher adjusted incidence rates** of NP AEs and NP AEs leading to discontinuation were seen in the following subgroups:
  - **Age ≥50 years** (vs. <50 years)
  - **ART naïve** (vs. ART experienced)
  - **History of IV drug use** (vs. no history)
  - **Regimens with ABC** (vs. without ABC)

B/F/TAF was associated with a low rate of treatment discontinuation due to NP AEs in a real-life setting, consistent with findings from clinical trials

A multivariate generalized linear model was used to calculate adjusted incidence rate based on selected baseline variables; observation was truncated at the first occurrence of NP AEs regardless of discontinuation. NP, neuropsychiatric; PYFU, person-years of follow-up; SCOLTA, Surveillance Cohort Long-Term Toxicity Antiretrovirals

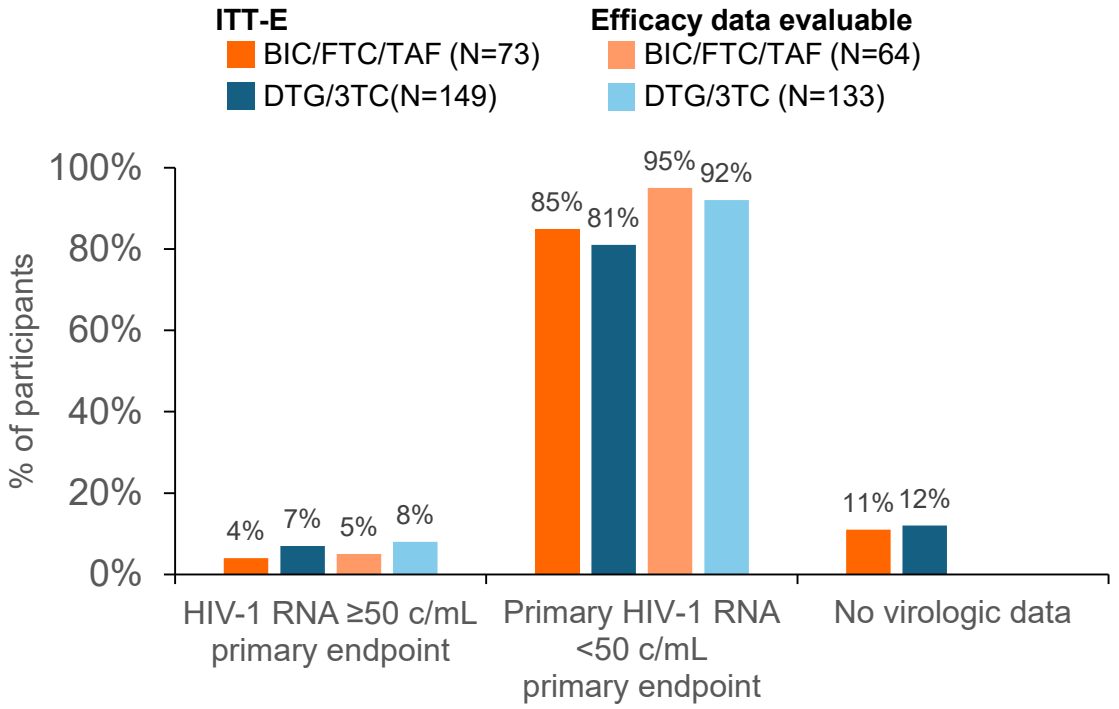
Squillace N, et al. AIDS 2024, Poster TUPEB082

Switch from BIC/FTC/TAF to DTG/3TC in Virologically Suppressed Adult PWH – DYAD Study 48-Week Results

Phase IV, Randomized, Open-label, Non-inferiority Study

- Single-centre study (Orlando, U.S.)
- N=222 adult PWH virologically suppressed on BIC/FTC/TAF
- Randomized to continue therapy (n=73) or switch to DTG/3TC (n=149)

Virologic Outcomes



Other Findings

Mean weight change from baseline was +0.2 kg for BIC/FTC/TAF and -1.0 kg for DTG/3TC (*p*=ns).

Individuals switched to DTG/3TC had higher rates of AEs and discontinuations due to AEs compared to those staying on BIC/FTC/TAF

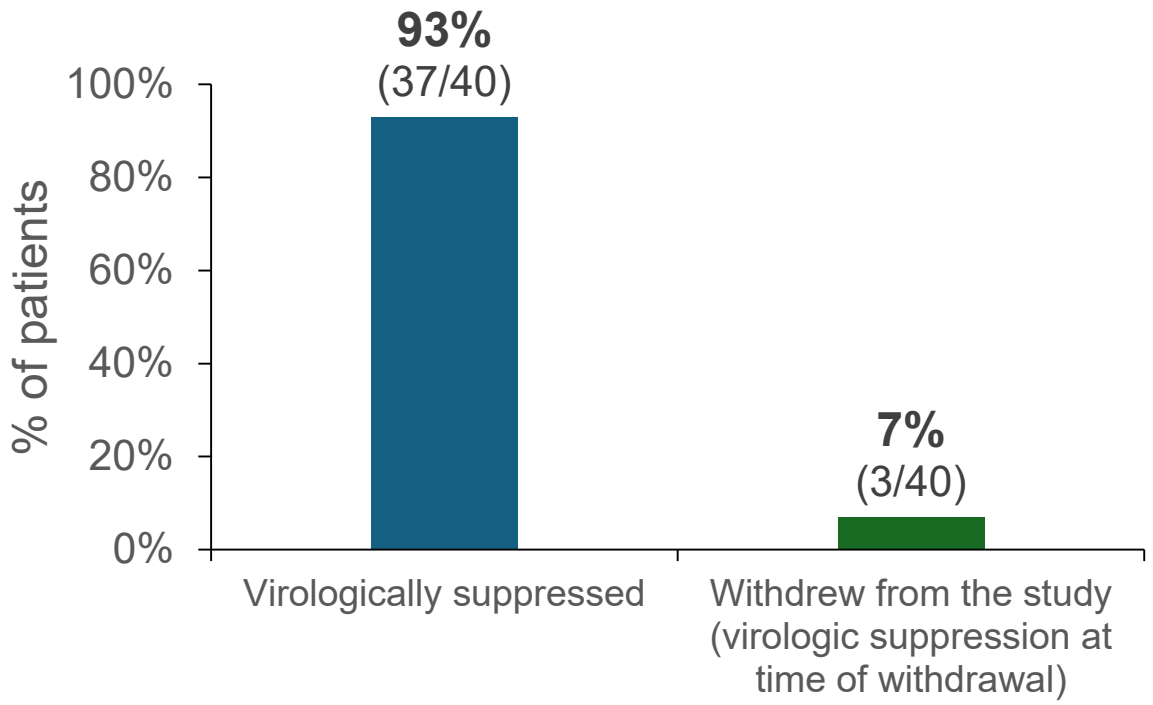
Investigators' key conclusions: **Switching to DTG/3TC was non-inferior to continuing BIC/FTC/TAF; this reinforces findings from TANGO and SALSA and supports the use of DTG/3TC as a switch option from contemporary 3-drug regimens**

3TC, lamivudine; BIC, bictegravir; DTG, dolutegravir; PWH, people with HIV; ITT-E, intention-to-treat exposed; FTC, emtricitabine; TAF, tenofovir alafenamide
Adapted from Hinestrosa F, et al. AIDS 2024. Poster #THPEB089.

Switch from BIC/FTC/TAF to DTG/3TC in Virologically Suppressed Adult PWH: 96-week Results from the SOUND Study

Open-label, Single-centre, Pilot Study: N=40 PWH virologically suppressed on BIC/FTC/TAF

Virologic Outcomes



NRTI & INSTI Mutations

(Retrospective proviral DNA on Baseline Samples*)

RAMs, n (%)		N (%)
NRTI	Total	6 (19)
	T69N	1 (3)
	M184M/V	5 (16)
	M184V	1 (3)
INSTI	Total	2 (6)
	S157S/G	1 (3)
	Q148Q/R	1 (3)

*32 participants had baseline samples

***Investigators' key conclusion*: These data support the efficacy and safety of switching to DTG/3TC for PWH virologically suppressed on BIC/FTC/TAF with unknown resistance history**

3TC, lamivudine; BIC, bictegravir; DTG, dolutegravir; PWH, people with HIV; FTC, emtricitabine; INSTI, integrase strand inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; TAF, tenofovir alafenamide

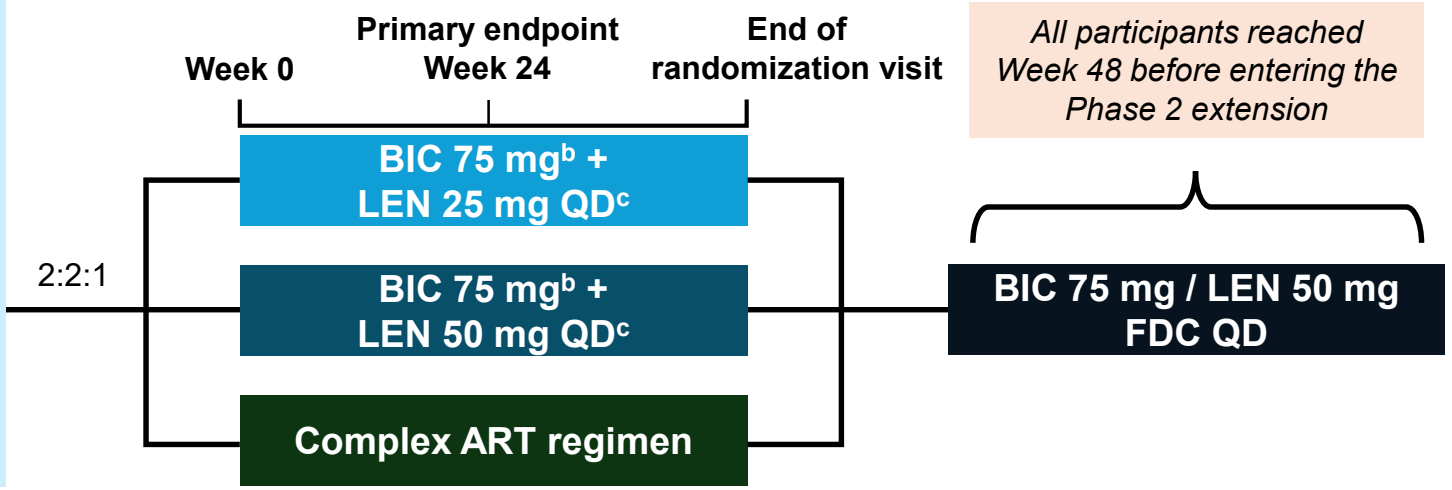
Adapted from Slim J, et al. AIDS 2024. Poster #THPEB092.

Bictegravir + Lenacapavir for Virologically Suppressed PWH on Complex ART: 48-week Outcomes from the ARTISTRY-1 Trial

Study Design

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

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

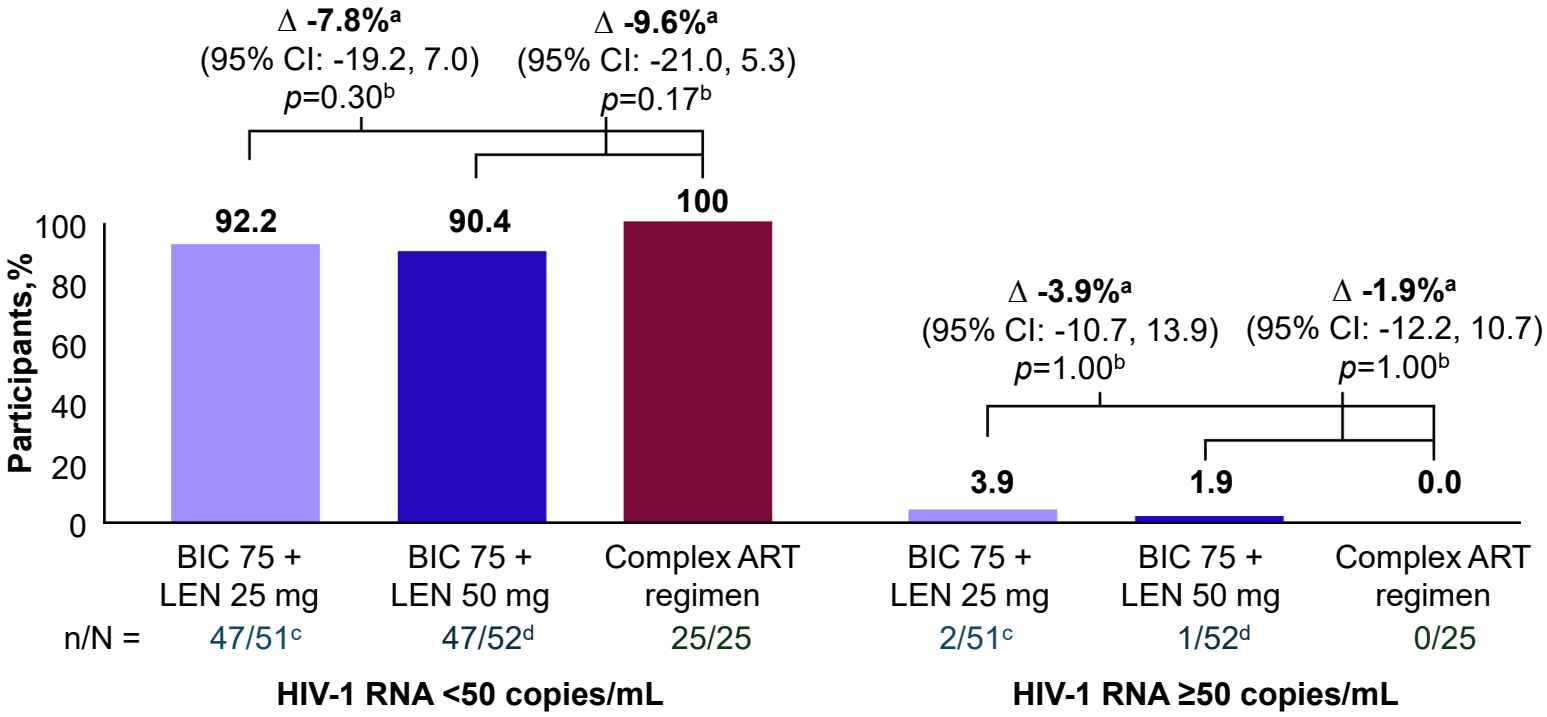
Endpoints at Week 48

- Proportions of participants with HIV-1 RNA <50 c/mL (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]BIC 75 mg single agent provides exposure consistent with BIC 50 mg as part of BIC/FTC/TAF. [c]All participants receiving BIC+LEN received an oral loading dose of LEN 600 mg on Days 1 and 2 of treatment; [d]Participants who switch from a complex antiretroviral regimen in the extension phase will receive the oral loading doses of LEN.
ART, antiretroviral therapy; BIC, bictegravir; FDC, fixed-dose combination; eGFR, estimated glomerular filtration rate; HBV, hepatitis B virus; LEN, lenacapavir; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; PWH, people with HIV; QD, once daily; STR, single-tablet regimen
Adapted from Segal-Maurer S, et al. AIDS 2024. Presentation #OAB2602.

Bictegravir + Lenacapavir for Virologically Suppressed PWH on Complex ART: 48-week Outcomes from the ARTISTRY-1 Trial

Virologic Suppression at Week 48, FDA Snapshot Analysis



Changes in CD4 cell count and % also comparable among groups

***Investigators' key conclusion*:**

- **BIC + LEN was highly effective and safe in participants switching from a complex regimen**
- **The findings support the continued evaluation of BIC + LEN**
- **A BIC 75 mg/LEN 50 mg STR will be assessed in the next phase of the study**

[a]Difference in % (95% CI): BIC + LEN - complex ART regimen calculated based on an unconditional exact method using two inverted one-sided tests; [b]Based on Fisher exact test; [c]Two participants had no virologic data in the Week 48 window as they discontinued study drug before Week 48 visit; one participant due to AE and one participant due to participant decision; [d]4 participants had no virologic data in the Week 48 window as they discontinued study drug before Week 48 visit due to AE, death, participant decision, and investigator decision (n=1 for each).
AE, adverse event; ART, antiretroviral therapy; BIC, bictegravir; LEN, lenacapavir; PWH, people with HIV
Adapted from Segal-Maurer S, et al. AIDS 2024. Presentation #OAB2602.

BICSTaR (subanalysis)

Switching to B/F/TAF in Older PWH With Comorbidities (1 of 3):

Study Design

BICSTaR

N=401

TE PWH ≥50 years of age, with ≥1 comorbidity, who switched to B/F/TAF

Outcomes

Virologic effectiveness, treatment persistence and safety through 24 months

Data cutoff date: Feb. 18, 2022

N=963
TE PWH switching to B/F/TAF

N=455
≥50 years of age

N=401
≥50 years of age
+
≥1 comorbidity

Baseline — 12 months: primary endpoint — 24 months

This study was conducted in:

- France
- Germany
- Ireland
- Italy
- Spain
- The Netherlands
- United Kingdom
- Canada
- Israel

24-month outcomes included:

- HIV-1 RNA <50 c/mL by key population (age, sex, race, complex medical history)
- CD4 cell count and CD4/CD8 ratio changes
- Treatment persistence
- AEs, DRAEs[a]
- Change in weight and BMI
- Change in laboratory parameters
- PROs (HIVTSQc score at 12 months)

BICSTaR is a large, multinational, prospective, observational cohort study; this subanalysis evaluated PWH aged ≥50 years with ≥1 comorbidity who switched to B/F/TAF

[a]Any HIV AE considered by the investigator to be related to B/F/TAF and occurring within 24 months after B/F/TAF initiation

DRAE, drug-related adverse event; HIVTSQc, HIV Treatment Satisfaction Questionnaire: change version; PRO, participant-reported outcome; TE, treatment-experienced

Miralles C, et al. AIDS 2024, Poster TUPEB072

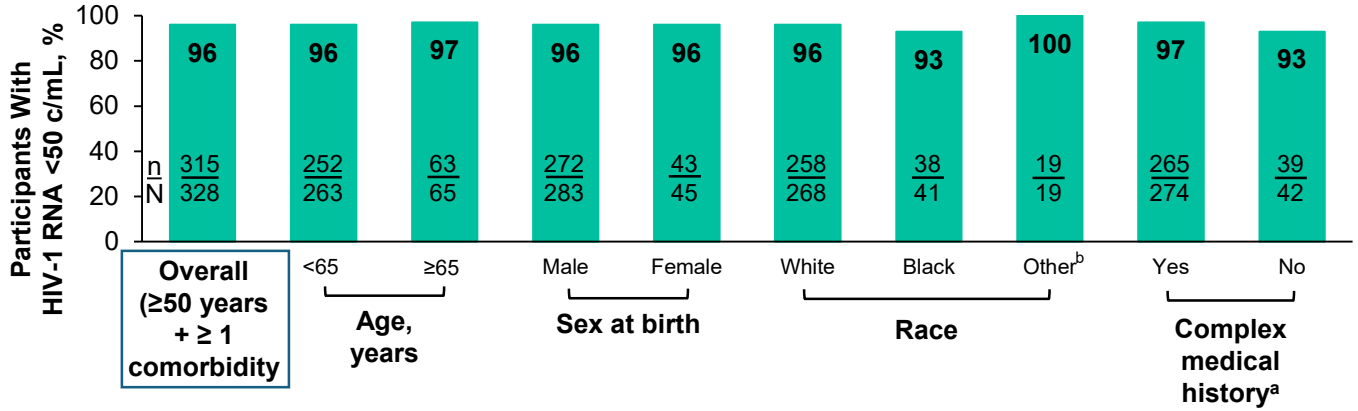
BICSTaR (subanalysis)

Switching to B/F/TAF in Older PWH With Comorbidities (2 of 3):

Baseline Characteristics and Efficacy Outcomes at 24 Months

Baseline Characteristics	N=401
Sex at birth, n (%)	
Male	344 (86)
Female	57 (14)
Age at B/F/TAF initiation, years, median (Q1, Q3)	**56 (53, 62)**
Age ≥65 years, n (%)	74 (18)
Complex medical history,[a] n (%)	335 (84)
Comorbidities, n (%)	
≤2	142 (35)
>2	259 (65)
>3	186 (46)
>4	131 (33)
Most frequent comorbidities by SOC (≥30%), n (%)	
Cardiovascular disorders	193 (48)
Metabolism and nutrition disorders	191 (48)
Infections and infestations	138 (34)
Psychiatric disorders	136 (34)
Polypharmacy (≥5 comedications), n (%)	87 (22)

Virologic Effectiveness Through 24 Months (M=E)



- **81% (13/16)[c]** of participants who were **not virologically suppressed at baseline** achieved **HIV-1 RNA <50 c/mL at 24 months** after switching to B/F/TAF
- **No treatment-emergent resistance** to the components of B/F/TAF was reported

Switching to B/F/TAF maintained high levels of effectiveness through 24 months in PWH aged ≥50 years with a high burden of comorbidities at baseline

[a]CD4 count <200 cells/μL or ≥2 comorbidities or ≥5 concomitant medications at switch to B/F/TAF; [b]American Indian or Alaska Native, Asian, Not Permitted and Other;
[c]16 participants with VL ≥50 c/mL at baseline had available data at 24 months
M=E, missing equals excluded; SOC, System Organ Class; TE, treatment-experienced; VL, viral load
Miralles C, et al. AIDS 2024, Poster TUPEB072

BICSTaR (subanalysis)

Switching to B/F/TAF in Older PWH With Comorbidities (3 of 3):

Safety and Other Outcomes up to 24 Months

BICSTaR

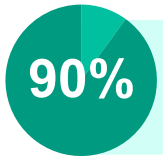
AEs at 24 Months	N=401
Participants with any DRAE, n (%)	**54 (13)**
Most common types of DRAE, n (%)[a]	
Weight increased	17 (22)
Headache[b]	6 (8)
Sleep disorder	4 (5)
Participants with any DRAE leading to B/F/TAF discontinuation, n (%)	**27 (7)**

Clinical Changes from Baseline at 24 Months

Median (Q1, Q3)		Baseline		Median (Q1, Q3) change at 24 months
eGFR, mL/min	n=204	**85** (74, 102)	→	**-5.0** (-13.7, 1.8)
ALT, U/L	n=263	**24** (19, 32)	→	**+1.0** (-4.0, 7.4)
LDL, mmol/L	n=167	**3** (2, 3)	→	**0.0** (-0.5, 0.5)
TC:HDL ratio	n=173	**4** (3, 5)	→	**-0.1** (-0.6, 0.5)
Weight, kg	n=229	**76** (66, 86)	→	**+1.0** (-1.3, 3.2)
BMI, kg/m^2	n=229	**25** (23, 28)	→	**+0.3** (-0.5, 1.2)

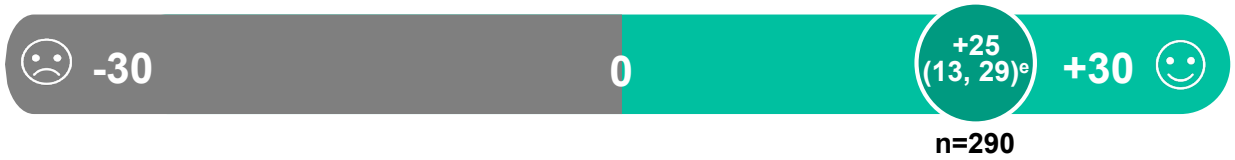
Renal, liver, lipid and weight parameters remained stable through 24 months

Treatment Persistence at 24 Months



90% of people were **still taking B/F/TAF at 24 months (359/401)[c]**

Treatment Satisfaction (HIVTSQc Score) at 12 Months[d]



Switching to B/F/TAF was generally well tolerated and maintained high rates of treatment persistence through 24 months, in PWH aged ≥50 years with a high burden of comorbidities at baseline

[a]Total number of DRAE reports: n=76; [b]2/6 in single participant; [c]Reasons for discontinuation, n (%): AE, 28 (7); death, 8 (2); investigator's discretion, 4 (1); lack of efficacy, 2 (1); new treatment available, 1 (<1); participant's decision, 3 (1); [d]HIVTSQc score ranges from -30 to 30, with higher scores indicating greater improvement in treatment satisfaction; [e]Median (Q1, Q3). DRAE, drug-related adverse event; HIVTSQc, HIV Treatment Satisfaction Questionnaire: change version; TC, total cholesterol

Miralles C, et al. AIDS 2024, Poster TUPEB072

BICTARG: Retrospective observational real-world subanalysis (Argentina)

B/F/TAF in PWH Who Are TE With a History of VF, M184V/I and other RAMs[1]

N=185

PWH who are TE starting B/F/TAF with[1]:

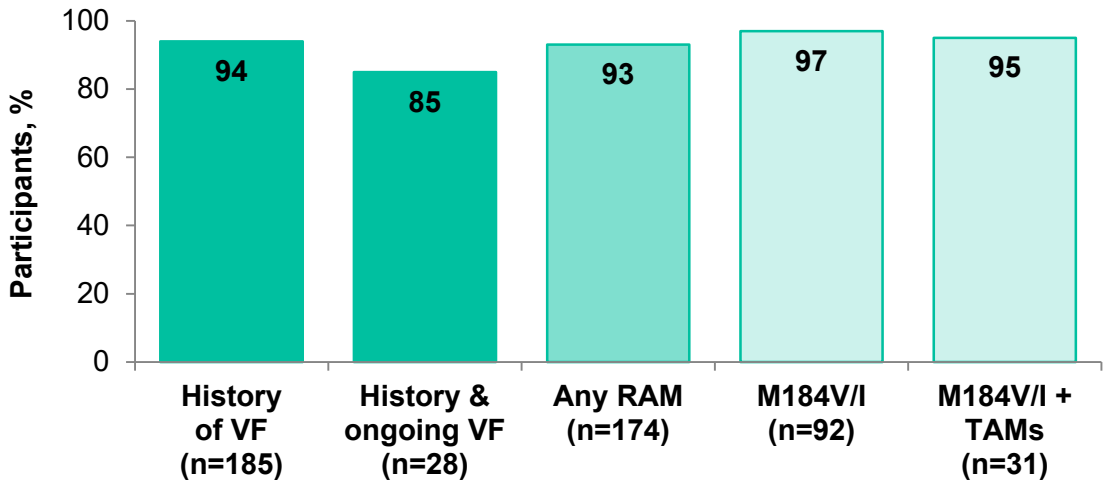
- A history of VF or ongoing VF
- Any documented RAM
- M184V/I mutation
- M184V/I + TAMs

Outcomes

VS (viral load <50 c/mL) by VF status, RAMs and GSS group[1]

October 2019–December 2021

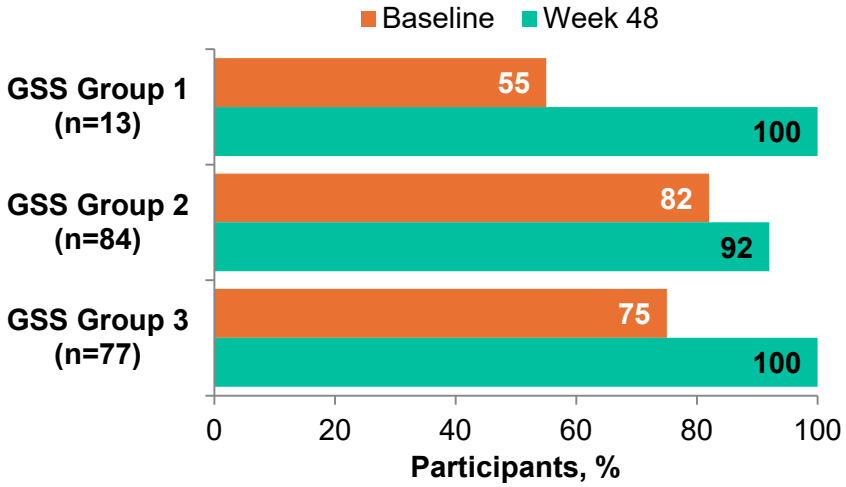
VS at Week 48 by VF Status and RAMs[1]



There was no emergence of new RAMs during follow-up[1]

B/F/TAF had high effectiveness, including in PWH with suboptimal GSS[1]

VS at Baseline and Week 48 by GSS Group[1,a]



In this real-world cohort, B/F/TAF achieved high levels of VS at 48 weeks in PWH with a history of VF, with or without M184V/I and other RAMs[1]

[a]B/F/TAF GSS was classed as 1–1.75 (Group 1), 2–2.75 (Group 2) or 3 (Group 3)[1]; According to the Stanford HIV Drug Resistance Database genotypic resistance interpretation system, lower GSS indicates higher resistance[2]

GSS, genotype sensitivity score; TAM, thymidine analog mutation; TE, treatment experienced; VF, virologic failure; VS, virologic suppression

1. Lamaizón C, et al. AIDS 2024, Poster TUPEB097; 2. Gonzalez-Serna A, et al. J Antimicrob Chemother 2017;72:496-503

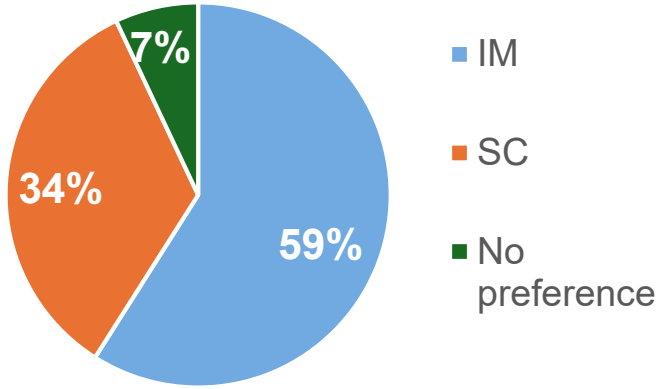
Subcutaneous injections of CAB + RPV LA in Virally Suppressed Adult PWH: Substudy of the Phase 3 FLAIR study

Good Efficacy and Safety, But More Patients Prefer the IM Formulation

Key Findings

- CAB and RPV PK parameters were similar with SC and IM gluteal injections
- Efficacy results were consistent with the overall FLAIR study
- SC injections led to a higher incidence and longer duration of ISRs
  - Resulted in lower acceptability of, and satisfaction with, SC injections compared with IM injections

"Which injection site do you prefer?" (1 week following 3rd SC injection, n=85)



Most common reasons for preferences:

- **IM**: Less injection site swelling (58%), nodules (58%), and pain (54%)
- **SC**: Convenience (86%), injections not interfering with daily activities (59%)

CAB, cabotegravir; IM, intramuscular; LA, long-acting; PK, pharmacokinetic; PWH, people with HIV; RPV, rilpivirine; SC, subcutaneous
Adapted from D'Amico R, et al. AIDS 2024. Presentation #OAB2604.

Diagnosis and Prevention Data

App, website and telehealth study (Canada)

Reaching First-Time Testers and Key Populations With HIV Self-Testing

N=9340

Canadians aged >18 years who ordered ≥1 HIV self-test kit via "I'm Ready" mobile app

Outcomes

Diagnosis rate, demographic characteristics of participants

June 2021–July 2024

Participant Characteristics

Characteristic	N=9340
<35 years of age	70%
Cisgender male	67%
More than high school education	75%
From ≥1 key population[a]	78%
Employed full-time	53%
Very large urban areas (population >200,000)	60%

App: Profile, surveys, order HIV tests, submit test results
Telehealth platform: Connect to peer navigator
Website: Pathways for care/treatment

41 new diagnoses

- From **3241** people who provided information about their test results
- **29%** were first-time testers
- Diagnosis rate of **1.3%**

Characteristics of First-Time Testers (n=2952)[b]

2.8 times more likely to be under 24 years of age (n=1076)

3.2 times more likely to identify as straight, bisexual or other sexual orientations[c] (n=1885)

1.4 times more likely to live in a rural area (n=725)

1.5 times more likely to identify as female (n=823)

1.8 times more likely to have a high school education or less (n=752)

1.8 times more likely to be a student (n=674)

The program was an effective way to reach undiagnosed individuals who had not previously been linked to care. The self-test population contained a high proportion of people testing for the first time

[a]MSM, Black individuals, Indigenous peoples, people who inject drugs, and women; [b]Compared with people who are not first-time testers; [c]Includes heteroflexible, questioning, and pansexual

Galli R, et al. AIDS 2024, Poster THPEC267

Performance Characteristics of HIV RNA Screening With CAB LA PrEP in the HPTN 083 Study

Objective: To evaluate whether prospective HIV RNA testing at each CAB LA injection could reliably identify HIV infection earlier

Key Assessments:

- Positive predictive value (PPV) and false positive rate (FPR) of isolated positive RNA results
- Sensitivity of HIV RNA screening

Population Characteristics

		Participants	# of visits with an RNA screening test	Person-years of follow-up
Overall		2,619	26,528	3,892
Per participant median (min-max)		--	12 (1-22)	--
Randomization arm	Cabotegravir	1,334	13,268	1,998
	TDF/FTC	1,285	13,260	1,894
Region	Africa	72	519	141
	Asia	525	5,716	801
	Latin America	1,213	11,831	1,733
	United States	809	8,462	1,217
Participants choosing CAB in OLE		2,483		
w/ visits with CAB LA in past 6m		2,461	23,300	3,684
w/ visits with no CAB LA in past 6m		1,925	3,228	209

PrEP, pre-exposure prophylaxis; CAB, cabotegravir; FTC, emtricitabine; HPTN, HIV Prevention Trials Network; LA, long-acting; OLE, open-label extension; TDF, tenofovir disoproxil
Adapted from Landovitz R, et al. AIDS 2024. Presentation #OAE0406LB.

HIV RNA Screening: High Proportion of False Positive Results

26,528
Visits with an RNA screening test at sites

73 (One or more reactive/positive HIV test result)

+RNA or +RNA or -RNA

42

2

29

22
+RNA
False positive

27
Isolated RNA-positive visits

5
+RNA
True positive

All occurrences of isolated positive RNA test but below limit of quantification (200 c/mL) were false positives

Isolated positive RNA tests could be confirmed as false positive if repeat RNA and Ag/Ab negative

5 cases that were confirmed positives initially had non-reactive HIV rapid and Ag/Ab tests

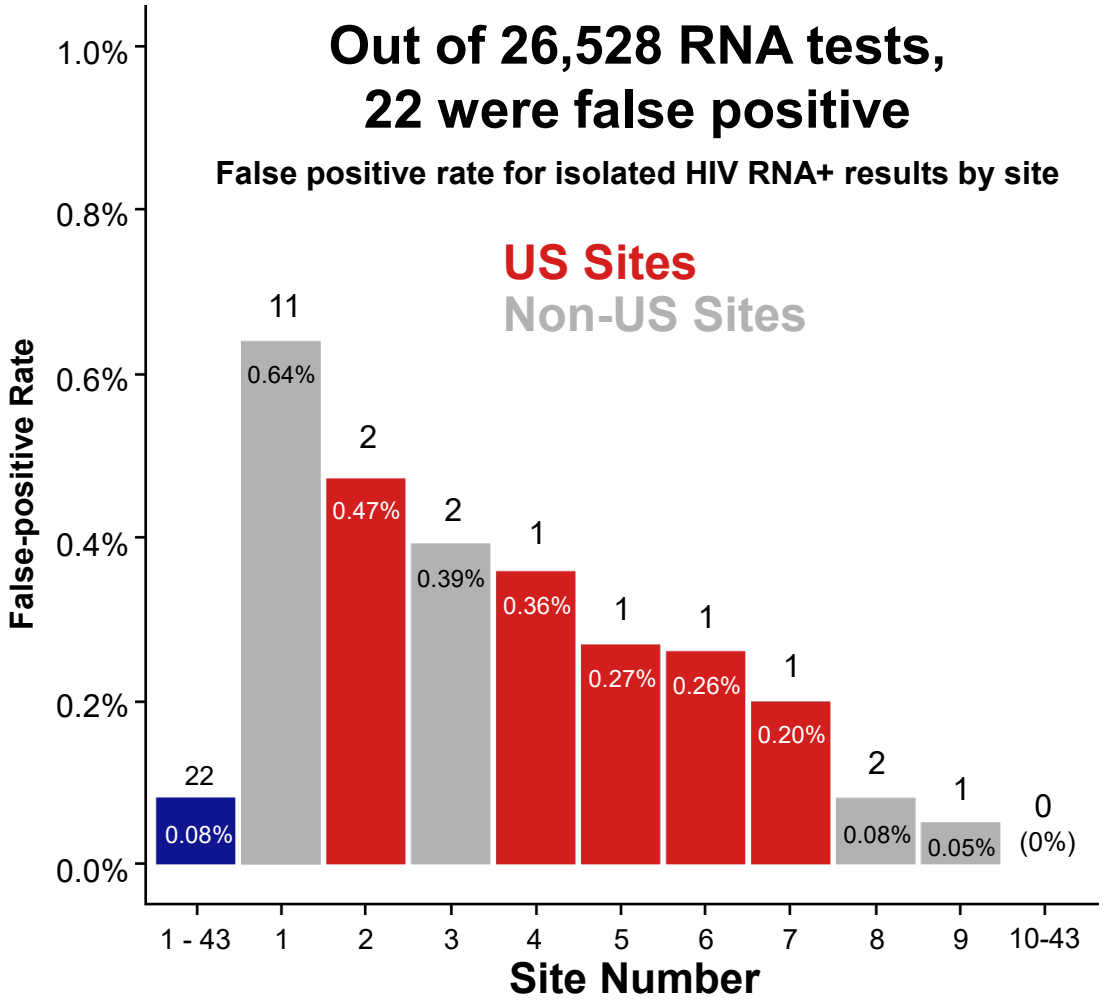
3 2 17 7

AJUDICATED NEGATIVE | AJUDICATED POSITIVE | ADJUDICATION STATUS NOT DETERMINED | POSITIVE HIV RNA TEST | NEGATIVE HIV RNA TEST | POSITIVE NON-RNA HIV TEST | NEGATIVE NON-RNA HIV TEST | NO CAB-LA W/ IN THE LAST 6 MONTHS | CAB-LA W/ IN THE LAST 6 MONTHS

CAB, cabotegravir; LA, long-acting
Adapted from Landovitz R, et al. AIDS 2024. Presentation #OAE0406LB.

Performance Characteristics of HIV RNA Screening

		PPV (95% CI)*	FPR (95% CI)*	Sensitivity (95% CI)†
Overall		**18.5%** (7.0%, 38.7%)	**0.08%** (0.05%, 0.13%)	**96.4%** (79.8%, 99.8%)
CAB LA within the last 6 mos?	**Yes**	**9.1%** (1.6%, 30.6%)	**0.09%** (0.05%, 0.14%)	**87.5%** (46.7%, 99.3%)
	No	**60%** (17%, 92.7%)	**0.06%** (0.01%, 0.25%)	**100%** (80%, 100%)



*Isolated positive RNA results; †RNA screening with other tests
CAB, cabotegravir; FPR, false positive rate; LA, long-acting; PPV, positive predictive value
Adapted from Landovitz R, et al. AIDS 2024. Presentation #OAE0406LB.

STI Testing Rates and Positivity Among PrEP Users Undergoing 6-Monthly Versus 3-Monthly PrEP Monitoring[1]

EZI-PrEP: Randomized controlled non-inferiority trial (Netherlands)

N=448

MSM and transgender/ gender-diverse persons eligible for PrEP

- 3-monthly (SoC) PrEP monitoring[a]
- 6-monthly PrEP monitoring[a]

Outcomes

- Number of visits per person-year[b]
- Positive STI tests per 100 visits[c]

September 2021–March 2024

Incidence Rate of Visits

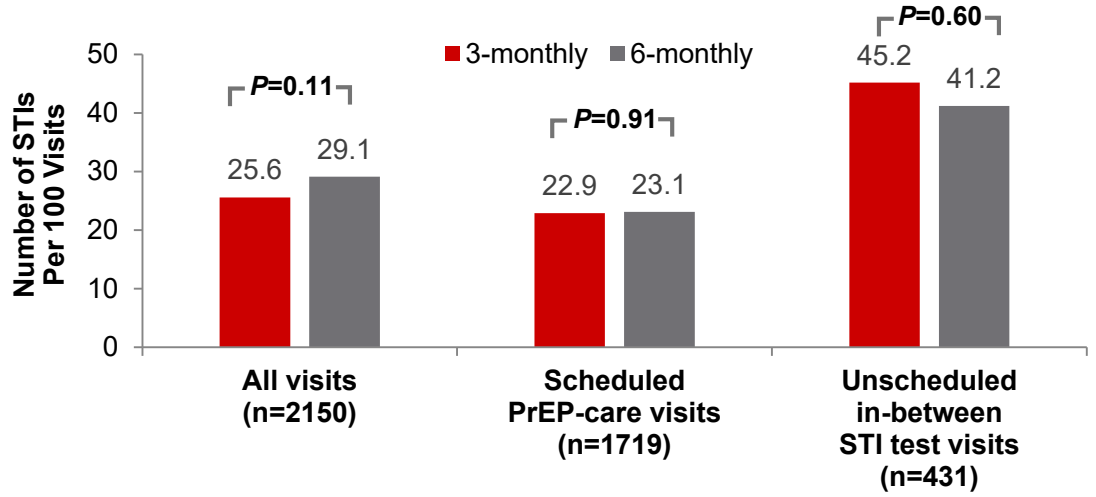
	Visit rate per person-year (95% CI)		Visit rate ratio (95% CI) (6- vs. 3-monthly)	*P*-value
	6-monthly monitoring	3-monthly monitoring		
Any visit	3.1 (2.9–3.3)	4.6 (4.3–4.8)	**0.68 (0.62–0.74)**	<0.0001
Unscheduled in-between STI test visits	0.99 (0.88–1.11)	0.56 (0.47–0.65)	**1.78 (1.46–2.18)**	<0.0001

Baseline STI rates[2]:

- Gonorrhea 10%
- Chlamydia 9%
- Syphilis 2%

No differences in STI rates between study arms at baseline

STI Positivity by Monitoring Frequency[d]



	All visits (n=2150)	Scheduled PrEP-care visits (n=1719)	Unscheduled in-between STI test visits (n=431)
OR (95% CI) (6- vs 3-monthly)	1.15 (0.97–1.37)	1.01 (0.82–1.26)	0.92 (0.67–1.27)

Preliminary data suggest implementing 6-monthly PrEP monitoring as SoC could reduce total visit numbers without resulting in major increases in STI positivity

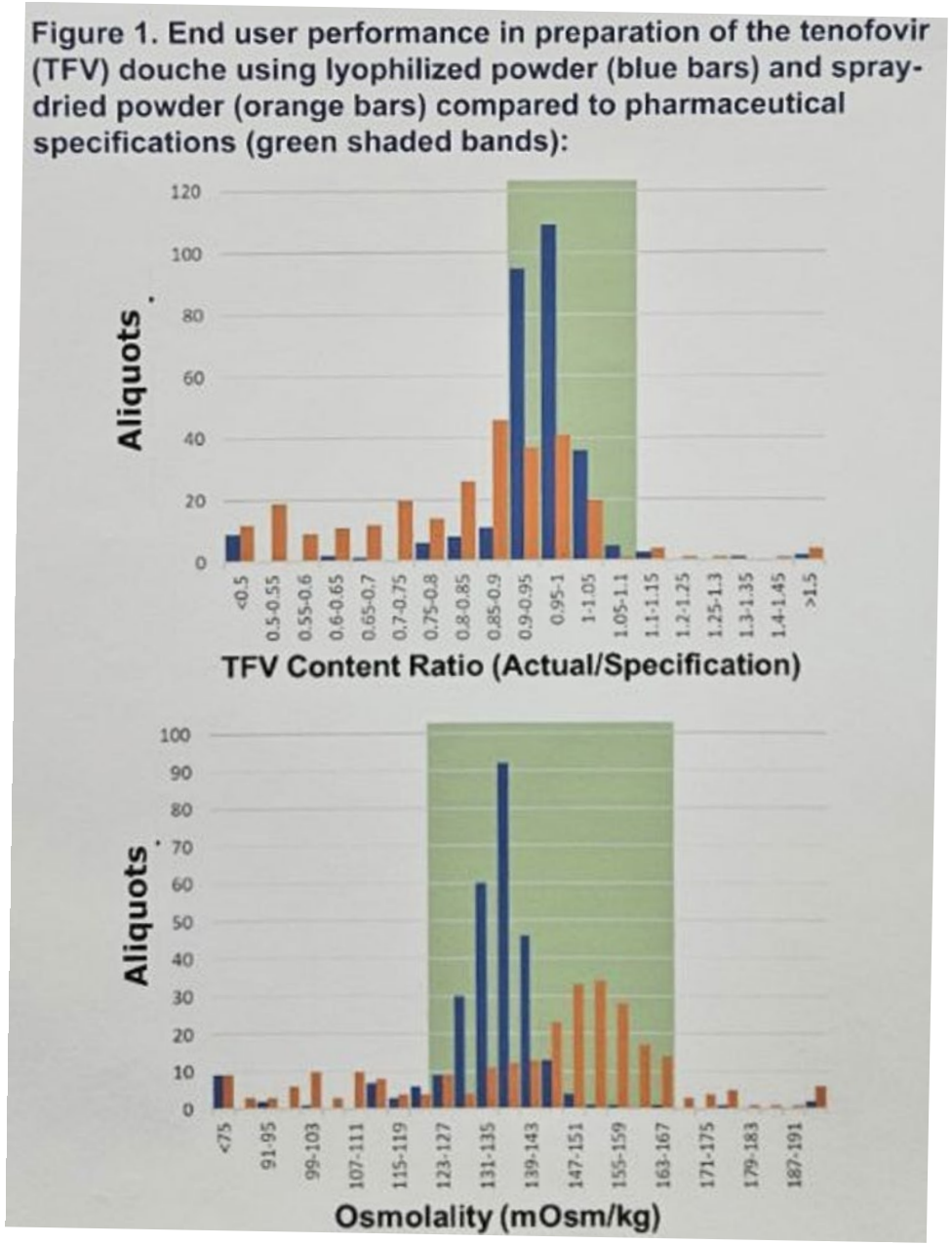
[a]Participants can get tested for STIs between monitoring visits; [b]Overall visit rate (PrEP visits plus in-between STI test visits) and in-between STI test visit rate; [c]Chlamydia, gonorrhea and infectious syphilis; [d]Changes in incidence were not assessed; baseline STI positivity was similar across treatment arms at baseline.[2] OR, odds ratio; SoC, standard of care

1. Groot Bruinderink ML, et al. AIDS 2024, Oral OAE3902; 2. Data on file. Gilead Sciences, Inc.

HIV pre-exposure prophylaxis for receptive anal intercourse: end user feasibility evaluation of tenofovir rectal microbicide douche

Study Design

- Cisgender adult men with a history of RAI-related douching were consented, screened, and enrolled
- Twenty-one participants were randomized 1:1 to the order of douche product preparation. Participants received written instructions on how to prepare a douche with the sachet powder.



C. Diniz1 , C. Bagia2 , R. Giguere3,4, L. Wang2 , S. Abdul Massih1 , V. Bui1 , S. Beselman1 , R. Bakshi1 , M. Marzinke1 , E. Fuchs1 , L. Rohan2 , C. Hendrix1 1 Johns Hopkins University School of Medicine, Baltimore, United States, 2 University of Pittsburgh, Magee-Womens Research Institute, Pittsburgh, United States, 3 Columbia University and NY State Psychiatric Institute, HIV Center for Clinical and Behavioral Studies, New York, United States, 4 Florida State University College of Medicine, Center for Translational Behavioral Science, Tallahassee, United States

PURPOSE 1

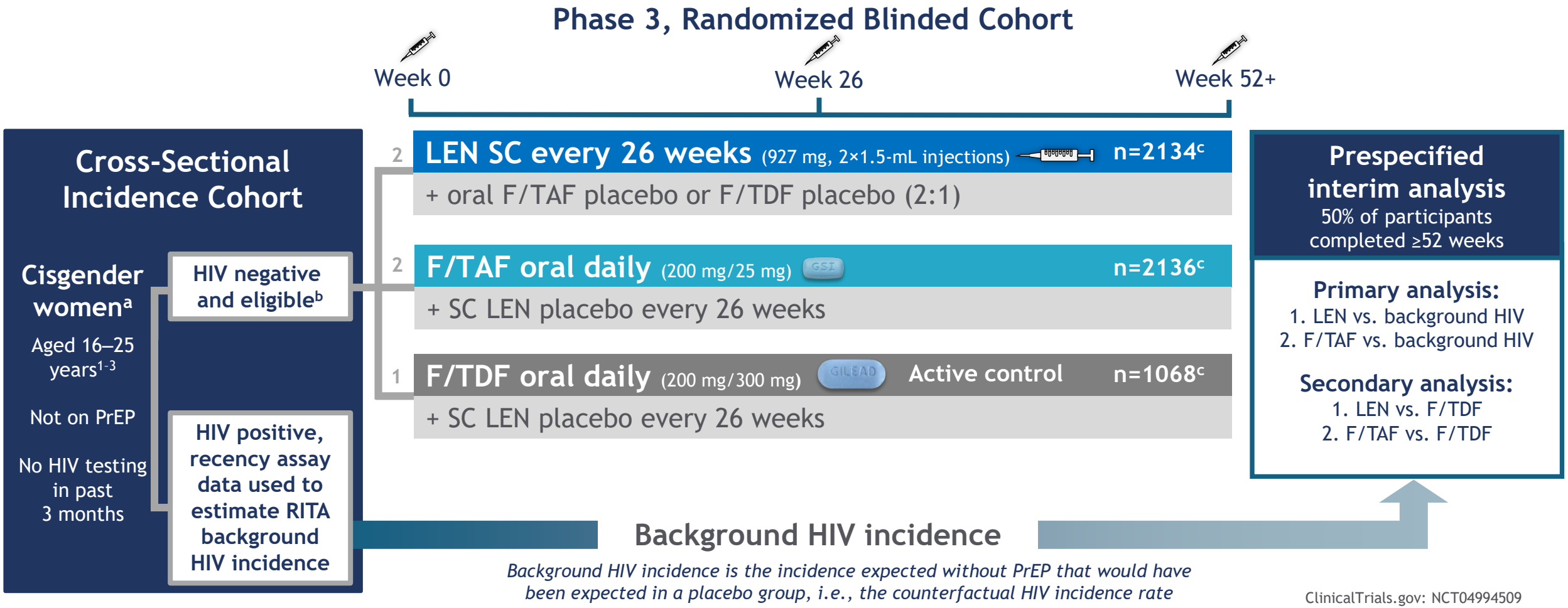
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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*

PURPOSE 1 Study Design and Efficacy Outcomes[1,2]



[a]The first participant was screened in August 2021, the 50th percentile participant was randomized in May 2023, and the last participant was randomized in September 2023. [b]Eligibility criteria included: weight ≥35 kg, eGFR ≥60 mL/min, not pregnant. [c]n numbers represent the full analysis set for efficacy analyses. **1.** Bekker LG, et al. AIDS 2024, Oral SS0407. **2.** Bekker LG, et al. *N Engl J Med*. 2024;10.1056/NEJMoa2407001. **3.** NCT04994509. https://clinicaltrials.gov/study/NCT04994509?intr=NCT04994509 (accessed July 16, 2024)

Baseline Demographics and Clinical Characteristics[1,2]

Characteristic	LEN, n=2138	F/TAF, n=2137	F/TDF, n=1070
Age, years, median (range)	21 (16–25)	21 (16–26)[a]	21 (16–25)
Age 16 to <18, years, n (%)	56 (2.6)	45 (2.1)	23 (2.1)
Black,[b] n (%)	2135 (99.9)	2136 (100)	1068 (99.8)
Highest education level college/university,[c] n (%)	183 (8.6)	198 (9.3)	109 (10.2)
Marital status, n (%)			
Married	26 (1.2)	30 (1.4)	17 (1.6)
Living with primary partner	148 (6.9)	132 (6.2)	73 (6.8)
STIs, n (%)			
Chlamydia trachomatis	520 (24.3)	562 (26.3)	263 (24.6)
Neisseria gonorrhoeae	197 (9.2)	178 (8.3)	90 (8.4)
Trichomonas vaginalis	154 (7.2)	165 (7.7)	82 (7.7)
Syphilis	57 (2.7)	63 (2.9)	29 (2.7)
Any prior use of PrEP, n (%)	143 (6.7)	121 (5.7)	71 (6.6)
Any prior HIV testing, n (%)	1713 (80.1)	1731 (81.0)	860 (80.4)
Median time since last HIV test, months (Q1, Q3)	6.8 (4.7, 11.5)	6.6 (4.8, 11.0)	6.5 (4.6, 11.0)

Participants

84.3%
South Africa

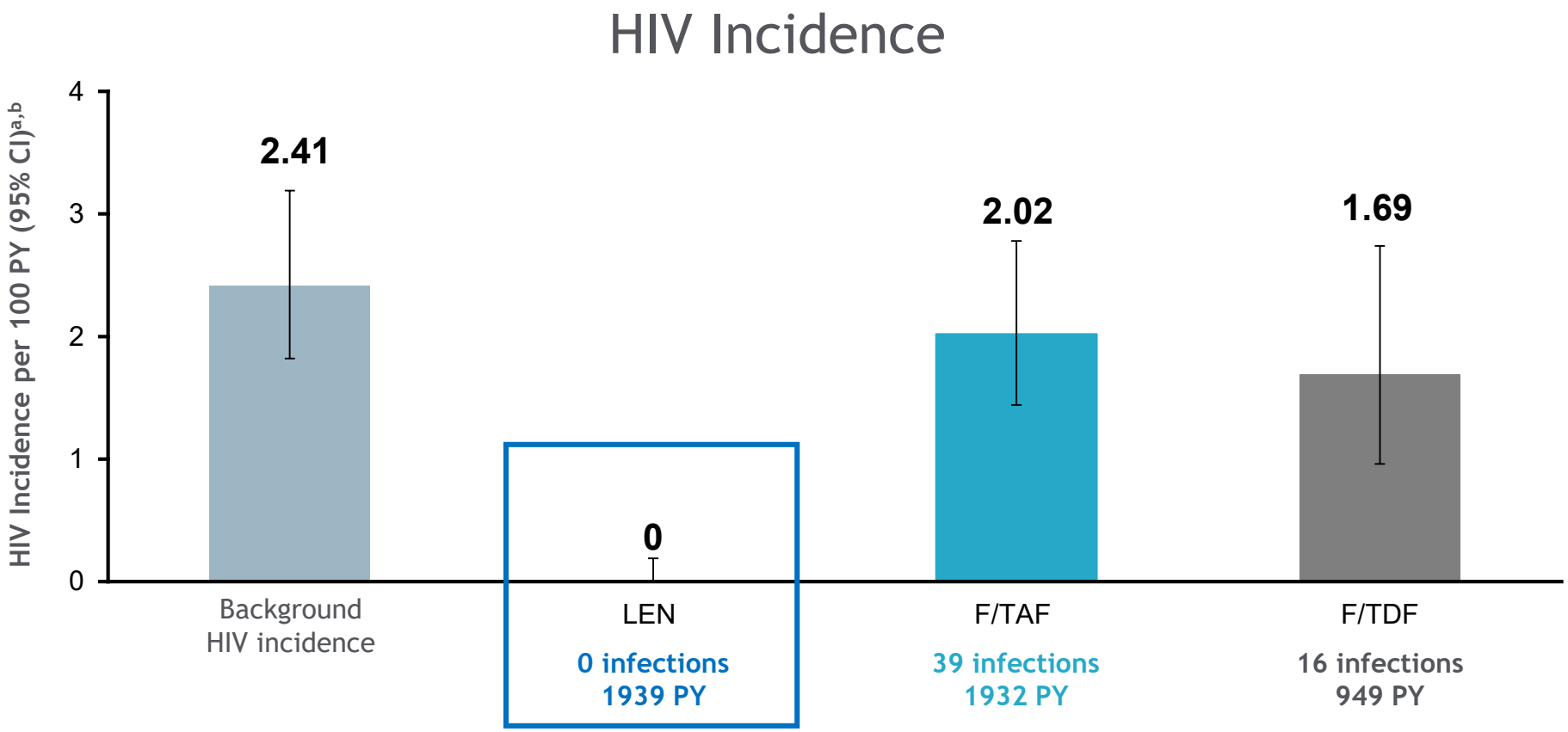
15.7%
Uganda

Baseline demographics and clinical characteristics were balanced across randomized groups

Seven participants were subsequently determined to have had HIV infection at the time of randomization, and thus 5338 were included in the modified intention-to-treat efficacy analysis. [a]One participant was aged 25 years at screening but turned 26 by randomization—this was not a violation of eligibility criteria. [b]All non-Black participants were multiracial. [c]Sample size: LEN 2136, F/TAF 2134, F/TDF 1069

1. Bekker LG, et al. AIDS 2024, Oral SS0407. **2.** Bekker LG, et al. *N Engl J Med.* 2024;10.1056/NEJMoa2407001

HIV Incidence[1,2]



No incident HIV acquisitions were observed in the LEN group.
HIV incidence on F/TAF was not different from background HIV incidence

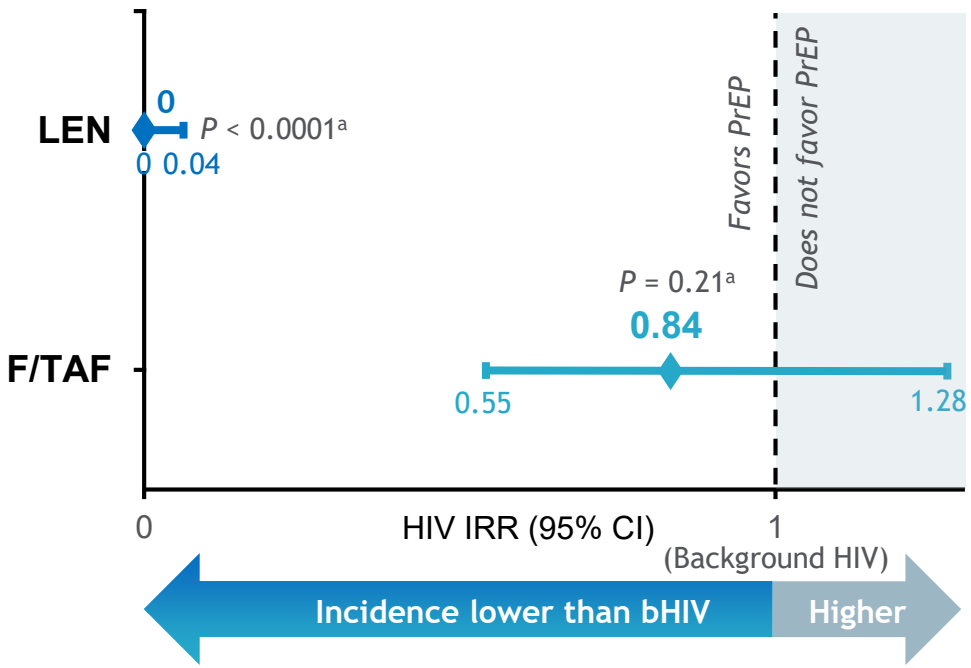
[a]Overall n: background HIV incidence group 8094, LEN 2134, F/TAF 2136, F/TDF 1068. [b]95% CIs: background HIV incidence group 1.82, 3.19, LEN 0, 0.19, F/TAF 1.44, 2.76. F/TDF 0.96, 2.74
PY, person-years

1. Bekker LG, et al. AIDS 2024, Oral SS0407. **2.** Bekker LG, et al. *N Engl J Med.* 2024;10.1056/NEJMoa2407001

HIV Incidence Rate Ratios in Primary and Secondary Analyses[1,2]

Primary Analysis

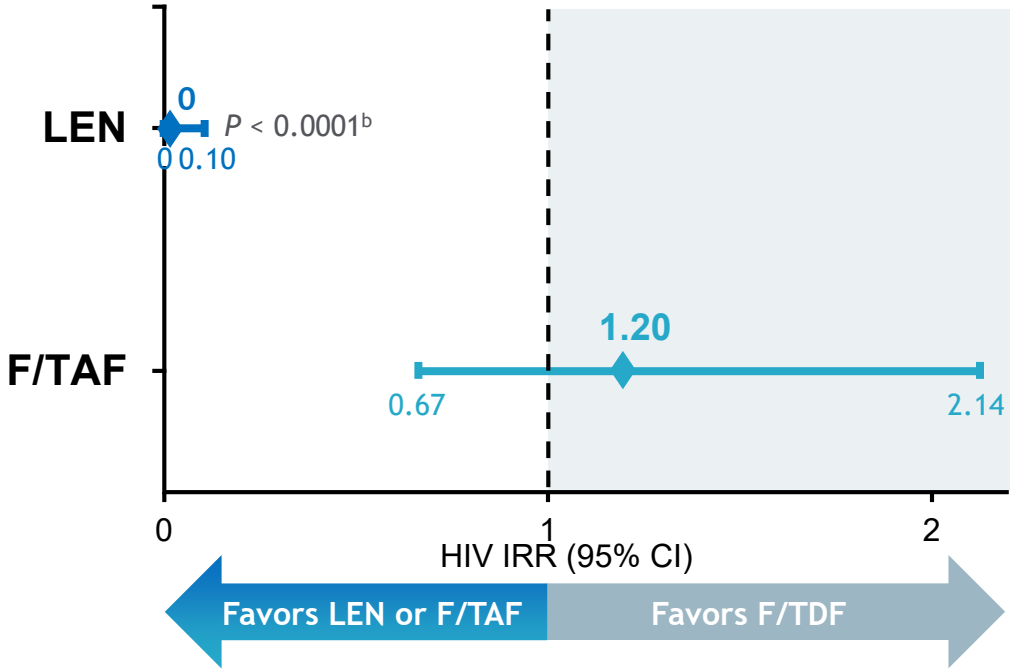
Efficacy Compared With Background HIV Incidence



LEN reduced HIV incidence by 100% compared with background HIV; HIV incidence with F/TAF was not different from background HIV incidence

Secondary Analysis

Relative Efficacy Compared With F/TDF



LEN was superior to F/TDF with 0 cases of HIV; F/TAF had numerically similar incidence to F/TDF

[a]HIV IRR LEN vs. background HIV assessed using a likelihood ratio test (LEN, due to zero infections) and a Wald test (F/TAF).[3,4] [b]HIV IRR LEN vs. F/TDF assessed using an exact conditional Poisson regression model (due to zero infections).

1. Bekker LG, et al. AIDS 2024, Oral SS0407. **2.** Bekker LG, et al. *N Engl J Med*. 2024;10.1056/NEJMoa2407001. **3.** Shao Y, Gao F. *Stat Commun Infect Dis*. 2024;16:20230004. **4.** Gao F, et al. *Stat Commun Infect Dis*. 2021;13:20200009

Adherence and Matched Case-Control Analysis[1,2]

Adherence to Injections

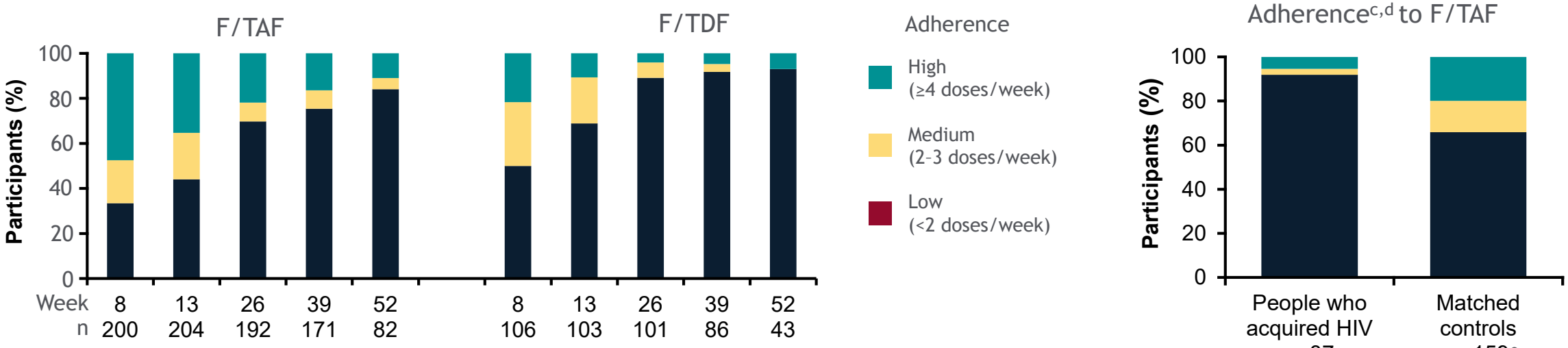
Injections were on time[a] for:

- **91.5% (4545/4967) at Week 26**
- **92.8% (2025/2181) at Week 52**

On-time injection similar on LEN and placebo (F/TAF and F/TDF)

Within the F/TAF group, those with medium or high adherence had a significantly lower likelihood of acquiring HIV than those with low adherence (odds ratio: 0.11; 95% CI: 0.012, 0.49; *P*=0.0006)

Adherence[b,c] to F/TAF and F/TDF



Matched Case-Control Analysis of Adherence[c,d] to F/TAF

On-time adherence to injections was high. Most participants in both the F/TAF and F/TDF groups overall had low adherence to oral tablets and adherence declined over time. Most infections on F/TAF occurred in those with low adherence

[a]Adherence to LEN defined as on-time injection (<28 weeks from the last injection) and participants who presented late required negative HIV testing to reinitiate study product which included reloading with oral LEN or placebo. [b]Preselected 10% sample of participants. [c]By TFV-DP DBS levels (adherence cutoffs for F/TAF: low <450, medium ≥450 to <900, high ≥900 fmol/punch and F/TDF: low <350, medium ≥350 to <700, high ≥700 fmol/punch); [d]Missing DBS concentrations imputed for participants with HIV infection based on last concentration prior to HIV diagnosis and decay rate based on the median half-life. [e]Available data shown in stacked bar
DBS, dried blood spot; TFV-DP, tenofovir diphosphate. **1.** Bekker LG, et al. AIDS 2024, Oral SS0407. **2.** Bekker LG, et al. *N Engl J Med.* 2024;10.1056/NEJMoa2407001

Safety Results[1,2]

Adverse Events,[a] n (%)	LEN n=2138	F/TAF n=2137	F/TDF n=1070
Any	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)
SAEs	59 (2.8)	85 (4.0)	35 (3.3)
AEs leading to discontinuation of study drug	5 (0.2)[b]	2 (<0.1)[c]	0
AEs occurring in ≥10% of participants, n (%)			
Headache	285 (13.3)	352 (16.5)	155 (14.5)
Urinary tract infection	307 (14.4)	305 (14.3)	163 (15.2)
Genitourinary chlamydia infection	300 (14.0)	317 (14.8)	129 (12.1)
Upper respiratory tract infection	271 (12.7)	274 (12.8)	121 (11.3)
Nausea	144 (6.7)	234 (10.9)	142 (13.3)
Vomiting	125 (5.8)	235 (11.0)	107 (10.0)
Laboratory abnormalities, n with ≥1 baseline result	2126	2113	1054
Any Grade ≥1, n (%)	1929 (90.7)	1904 (90.1)	959 (91.0)

Six deaths[d] all in the F/TAF group; none related to study drug per investigator

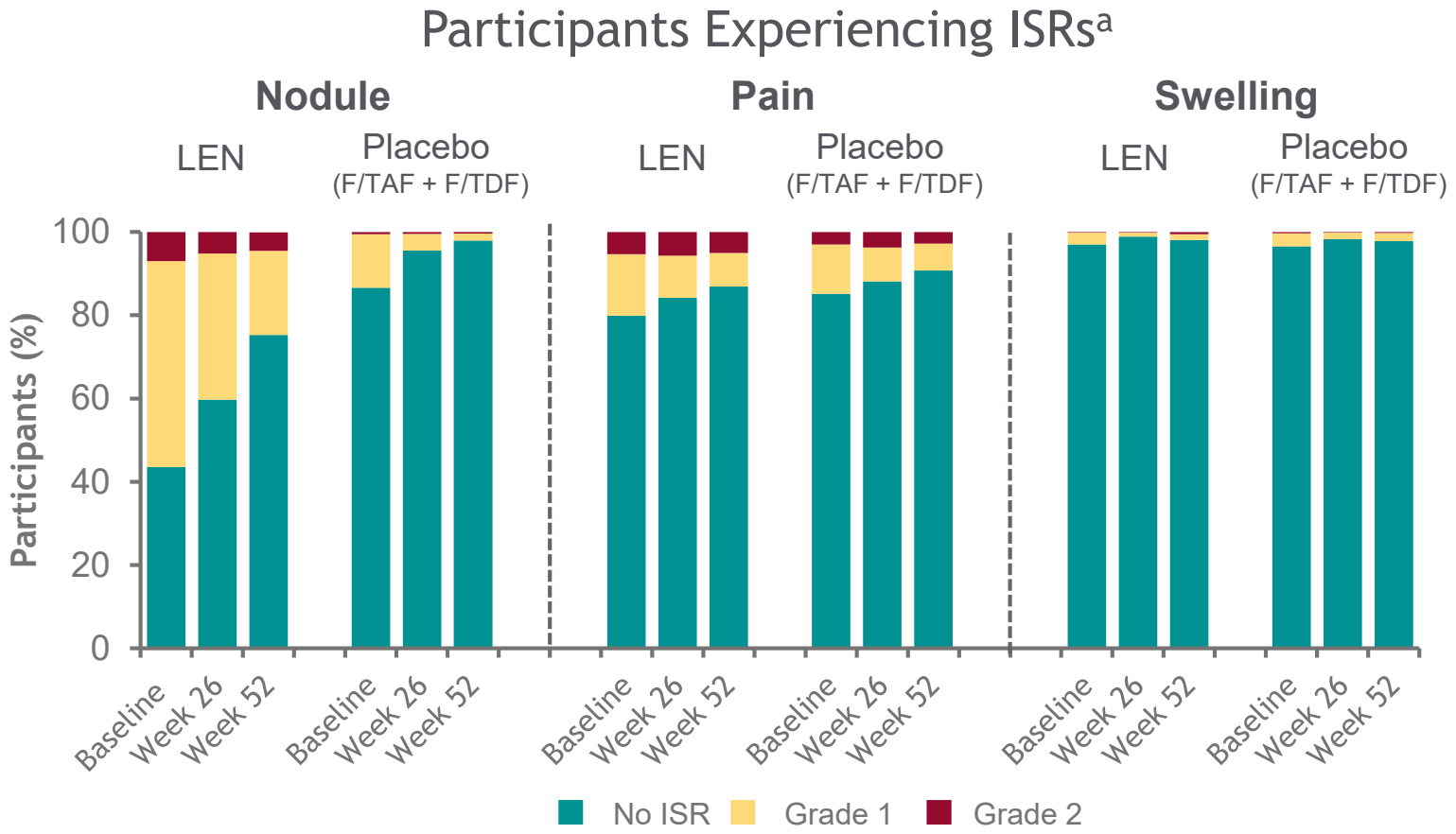
Adverse events were consistent with prior LEN, F/TAF and F/TDF trials[1-6]

[a]AEs are treatment emergent in persons who received at least one dose of study drug; AEs exclude injection-site reactions; AEs coded according to Medical Dictionary for Regulatory Activities, version 27.0, and graded by the Division of AIDS Table for Grading the Severity of Adult and Pediatric AEs, Version 2.1. [b]n=1 for each of: nausea, decreased creatinine renal clearance, increased hepatic enzyme, spontaneous miscarriage, suicide attempt/major depression. [c]n=1 for each of: suicide attempt/depressive symptoms/drug overdose, angioedema. [d]Asphyxia secondary to strangulation, non-accidental burns, knife stab to chest, hemorrhage due to traffic accident, autopsy-confirmed ischemic cardiomyopathy, and ovarian cancer

1. Bekker LG, et al. AIDS 2024, Oral SS0407. 2. Bekker LG, et al. *N Engl J Med.* 2024;10.1056/NEJMoa2407001. 3. Gupta SK, et al. *Lancet HIV*. 2023;10:e15-e23. 4. Ogbuagu O, et al. *Lancet HIV*. 2023;10:e497-e505. 5. Mayer KH, et al. *Lancet*. 2020;396:239-54. 6. Baeten JM, et al. *N Engl J Med*. 2012;367:399-410

Injection-Site Reaction Frequency[1,2]

- LEN is injected into the SC space and forms a drug depot that may be palpable under the skin but is usually not visible
- As the drug elutes over time, the depot gets smaller and the nodules resolve or reduce in size substantially prior to the next injection
- ISRs, including nodules, decreased with subsequent doses (also observed in HIV treatment[3])



Among 25,329 injections, only 4 ISRs led to discontinuation

[a]Grade 1 and 2 ISRs are shown. ISR, injection-site reaction

1. Bekker LG, et al. AIDS 2024, Oral SS0407. **2.** Bekker LG, et al. *N Engl J Med.* 2024;10.1056/NEJMoa2407001. **3.** Kumar P, et al. AIDS 2022, Poster EPB184

Pregnancy Outcomes[1,2]

Participants and pregnancies,[a] n (%)	LEN n=2138	F/TAF n=2137	F/TDF n=1070
Participants with confirmed pregnancies	184	208	95
Confirmed pregnancies	193	219	98
Completed pregnancies	105 (54.4)	119 (54.3)	53 (54.1)
Ongoing pregnancies	88 (45.6)	100 (45.7)	45 (45.9)
Births[a]	55 (28.5)	45 (20.5)	21 (21.4)
Interrupted pregnancies	50 (25.9)	74 (33.8)	32 (32.7)
Induced abortion	30 (15.5)	40 (18.3)	20 (20.4)
Spontaneous miscarriage[b]	20 (10.4)	34 (15.5)	12 (12.2)

Expected spontaneous miscarriage rate[3,4]:

- **10–20% of clinically recognized pregnancies**
- **~30% of biochemically detected pregnancies**

Available pregnancy outcomes were similar to those expected for the population[5]

[a]Completed uninterrupted pregnancies which includes lives births and eight still births: three in the LEN group, four in the F/TAF group, one in the F/TDF group. [b]Spontaneous miscarriage defined as occurring at <20 weeks' gestation

1. Bekker LG, et al. AIDS 2024, Oral SS0407. **2.** Bekker LG, et al. *N Engl J Med.* 2024;10.1056/NEJMoa2407001. **3.** ACOG Committee on Practice Bulletins—Gynecology. *Obstet Gynecol.* 2018;132:e197-e207. **4.** Wilcox AJ, et al. *N Engl J Med.* 1988;319:189-94. **5.** Mugo NR, et al. *JAMA.* 2014;312:362-71

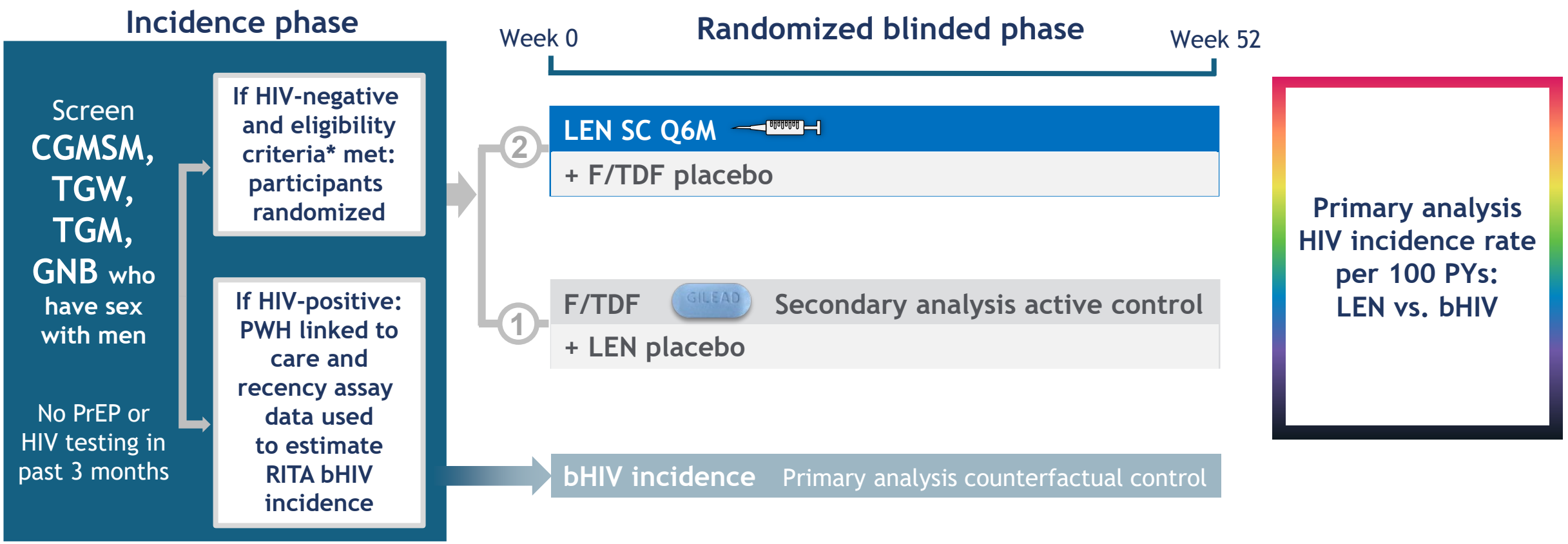
PURPOSE 1 Conclusions

- There were zero HIV infections in cisgender women receiving twice-yearly LEN for HIV prevention
  - LEN HIV prevention efficacy was superior to both background HIV incidence and F/TDF
- HIV incidence with F/TAF for cisgender females was not statistically significantly different compared with background HIV incidence, but was numerically similar to F/TDF
- Daily oral F/TAF and F/TDF adherence was poor
  - HIV protection was strongly associated with F/TAF adherence
- LEN, F/TAF, and F/TDF were generally well tolerated
- All trial participants are being offered open-label LEN
- This novel study design creates a path forward for future PrEP options or HIV vaccine trials

Bekker LG, et al. AIDS 2024, Oral SS0407

PURPOSE 2 Design: Randomized Blinded Phase

LEN for PrEP, prevention of rectal HIV acquisition



*High-level eligibility criteria: eGFR=> 60 mL/min, ≥35 kg

bHIV, background HIV; CGMSM, cisgender men who have sex with men; GNB, gender nonbinary individuals; PY, person-year; Q6M, every six months; RITA, recent-infection testing algorithm; TGM, transgender men, TGW, transgender women

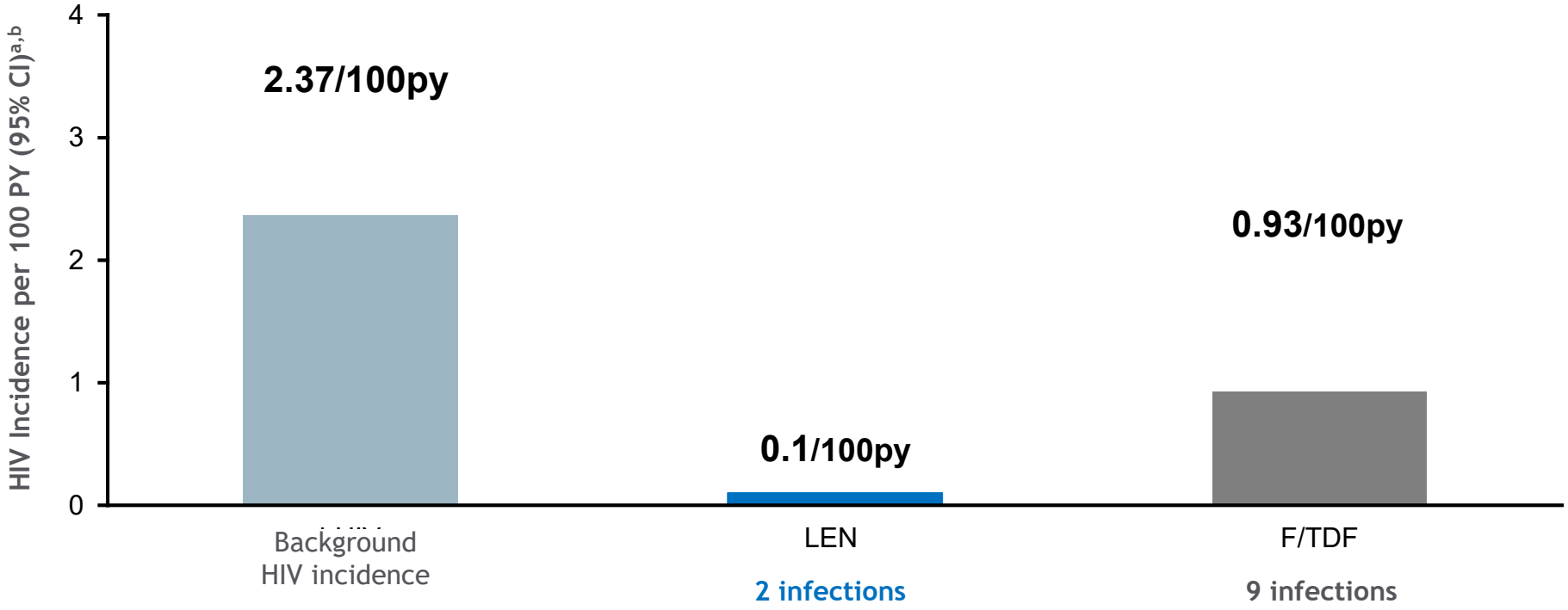
ClinicalTrials.gov identifier: NCT04925752

Slides presented at Das et al, et al. IAS 2023, Symposium SY05; and Das et al, et al. IAS 2023, Satellite SAT050

PURPOSE 2

HIV Incidence

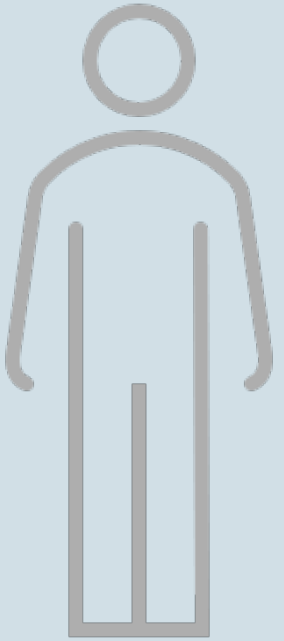
3,200 cisgender men, transgender men, transgender women and gender non-binary individuals aged 16 years or older who have sex with partners assigned male at birth



Two incident HIV acquisitions were observed in the LEN group.
96% RR reduction over bHIV, 89% more effective than F/TDF

** unpublished data from press release

Berlin Patient 2



Case study (Berlin, Germany)

Sustained HIV Remission Exceeding 5 Years Without ART Following CCR5 WT/Δ32 aHSCT: The Next Berlin Patient[1,2]

N=1

Individual in HIV remission following receipt of CCR5 WT/Δ32 aHSCT for AML

Outcomes

- HIV RNA, HIV DNA, viral tropism, CCR5 expression, viral outgrowth, ART levels and HIV-specific immune responses

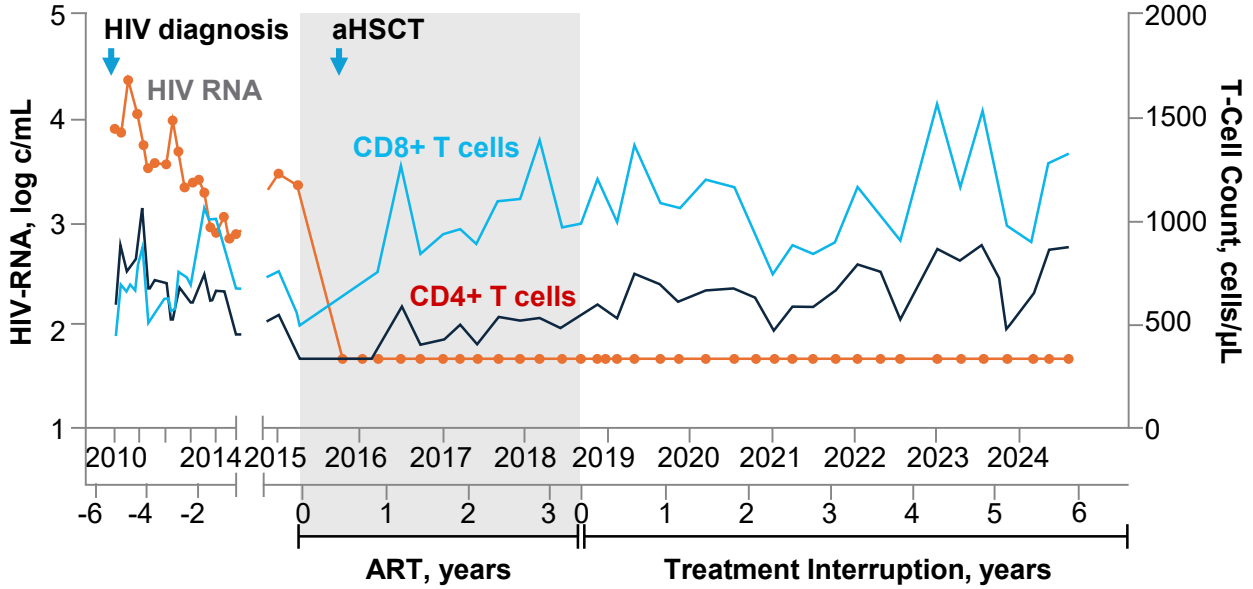
2009–2024

Characteristics and Timeline

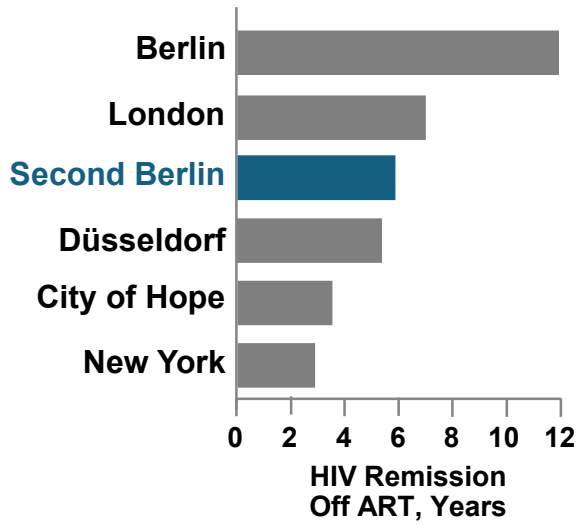
- White, Male
- Born 1964

- HIV diagnosis: 2009
- Genotype: CCR5 WT/Δ32
- No ART until 2015[a]
- RAL + ABC/3TC
- April 2015: AML diagnosis
- October 2015: aHSCT
- ART interrupted in 2018

HIV Remission



HIV Cure Cases



A cure case with CCR5 heterogeneity showed effective reservoir reductions, durable HIV remission and that potential cure can be achieved; allogeneic immunity fundamentally contributes to HIV eradication

[a]Due to treatment guidelines at the time

aHSCT, allogeneic hematopoietic stem cell transplant; AML, acute myeloid leukemia; CCR5, C-C chemokine receptor 5; WT, wild type

1. Gaebler C, et al. AIDS 2024, Oral SS0402LB; 2. Sáez-Cirión A, et al. IAS 2023, Oral OALBA0504