



UNC

INSTITUTE FOR GLOBAL HEALTH
& INFECTIOUS DISEASES

IAS 2025 – What Matters Most



IAS 2025

IAS 2025, the 13th IAS Conference on HIV Science

A NATAP UPDATE

David Alain Wohl, MD

Professor of Medicine

Institute of Global Health and Infectious Diseases

The University of North Carolina at Chapel Hill

IAS 2025: What Matters Most

HIV TREATMENT

- Funding Loss
 - PrEP - Africa
 - ART - Mozambique
- Intermittent ART
 - Meta-analysis
 - BREATHER
- CAB/RPV
 - IMPALA
 - CARLOS
 - COMBINE-2
 - OPERA
- DOR/ISL switch – 184I/V
- Other New ART
 - MK-8507
 - Others

PREVENTION

- IM CAB
 - Adherence/persistence USA
 - Persistence in S Africa
 - Pregnancy
- SQ LEN
 - Pregnancy
 - Adolescents
 - Counterfactual calculation
- New PrEP
 - MK-8527

COMPLICATIONS/AGING/ CO-MORBIDITIES

- Predictors of Weight Gain
- Do It Study
- MODERATO Trial
- DM w and wo DTG [Africa]
- Falls
- Dermatologic Issues

Thank You!

Acknowledgement

The vast majority of practice-changing and life-enhancing data to be presented was generated or supported by the US Federal government through the NIH, CDC, USAID, and other agencies staffed by people dedicated to our health and well-being.

Thank you, Federal Workers, for your passionate commitment and for creating what has been the **greatest** engine of research in the world.





IAS 2025

Treatment

**“Drugs don’t work if
people don’t take them”**



- C. Everett Coop
former US Surgeon General



**“Drugs don’t work if
people **can’t get** them”**



- C. Everett Coop
former US Surgeon General



Impact of USG Funding Cuts for HIV PrEP

Modelling the impact of cuts in PEPFAR funding for HIV pre-exposure prophylaxis among key populations in sub-Saharan Africa

IAS 2025

(J. STONE)

Background



- PEPFAR accounts for > 90% of global initiations on to oral PrEP
 - Key populations account for a fifth of PEPFAR's provision of PrEP
- PEPFAR's provision of PrEP is in jeopardy due to the US government's recent stop-work order on all foreign aid at the end of January 2025¹.
- Waiver for providing PrEP for pregnant and breastfeeding women
 - All other PrEP services were put on pause until further notice^{2,3}
- No waiver was given for PrEP among key populations, with funding for PrEP services for these populations largely stopped³

Impact of USG Funding Cuts for HIV PrEP

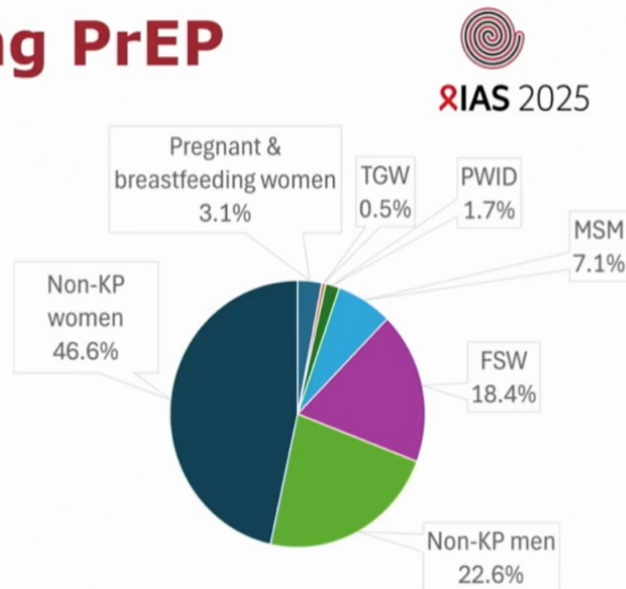
Modelling the impact of cuts in PEPFAR funding for HIV pre-exposure prophylaxis among key populations in sub-Saharan Africa

IAS 2025

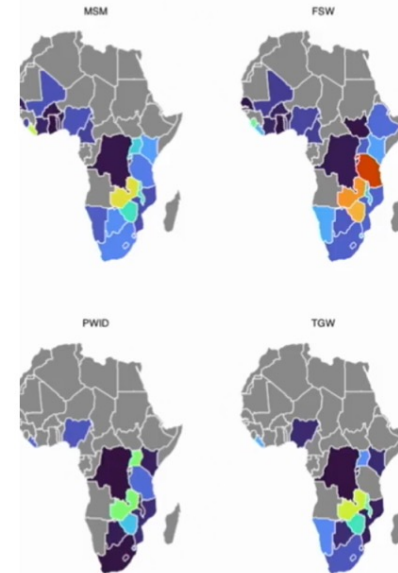
(J. STONE)

Numbers Receiving PrEP

- At the end of 2024, 742,136 individuals received PEPFAR-funded PrEP across 28 countries in Sub-Saharan Africa
 - 719,384 not covered by waiver
- 205,868 members of key populations
 - 3,666 TGW across 16 countries
 - 12,971 PWID across 15 countries
 - 52,548 MSM across 26 countries
 - 136,683 FSW across 28 countries



Coverage of PEPFAR Supported PrEP



- Among key population individuals, estimated coverage of 4.4% across countries providing PrEP
 - 2.6% among PWID
 - 2.7% among TGW
 - 4.0% among MSM
 - 5.0% among FSW
- 0.075% of HIV-negative non-key populations were receiving PrEP through PEPFAR
 - Coverage greatest in women aged 15-24 (0.15%)
- Considerable heterogeneity between countries

Impact of USG Funding Cuts for HIV PrEP

Modelling the impact of cuts in PEPFAR funding for HIV pre-exposure prophylaxis among key populations in sub-Saharan Africa

IAS 2025

(J. STONE)

Model



- We developed a static model to estimate the short-term impact of ceasing PEPFAR funding of PrEP for everyone except pregnant and breast-feeding women
- For different sub-populations, including each key population, the model estimates:
 1. Proportion of HIV-negative people receiving PrEP funded through PEPFAR ('coverage').
 2. Number of additional HIV infections that would occur over one year if PEPFAR-funded PrEP is suspended for one year – '*Primary Infections*'
 3. Number of *secondary infections* that could result from these primary infections over 5 years

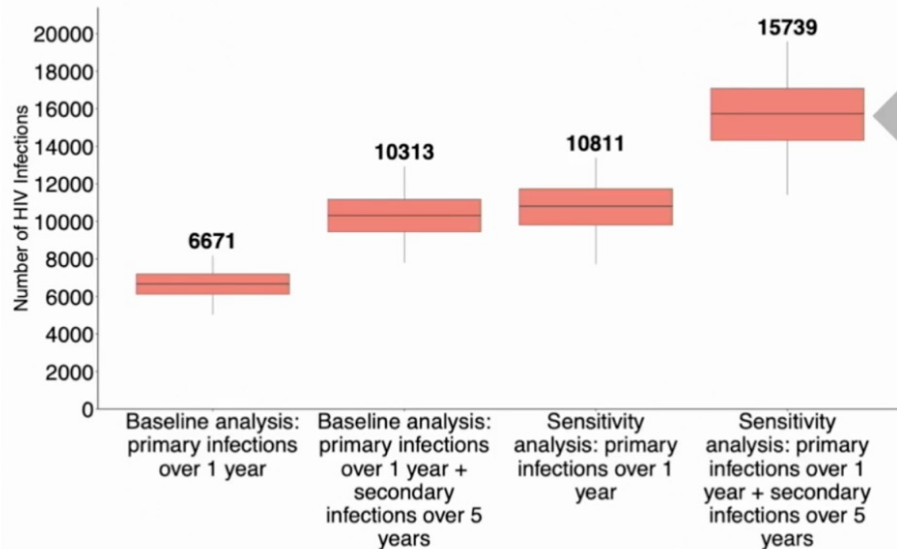
Impact of USG Funding Cuts for HIV PrEP

Modelling the impact of cuts in PEPFAR funding for HIV pre-exposure prophylaxis among key populations in sub-Saharan Africa

IAS 2025

(J. STONE)

Increase in new HIV infections



IAS 2025

Account for secondary infections & potential under-reporting of MSM

Summary



IAS 2025

- Ceasing PEPFAR's funding for PrEP in sub-Saharan Africa will remove approximately 700,000 individuals from using PrEP
 - Could lead to an estimated 6,671 additional HIV infections in the next year
 - 85% of these infections occurring among key populations.
- < 3% increase in HIV infections among key populations, due to low coverage
- Crucial that funding is found to not only continue PrEP services but to expand them
- Adds to growing evidence projecting considerable impact that cuts could have.
 - >Need to identify alternative sources of funding to offset these cuts.
 - >Ensure interventions are not vulnerable to political shifts and changing priorities of international donors

Impact of USG Funding Cuts for HIV Care

The impact of the U.S. funding interruption on HIV services and the HIV epidemic in Mozambique

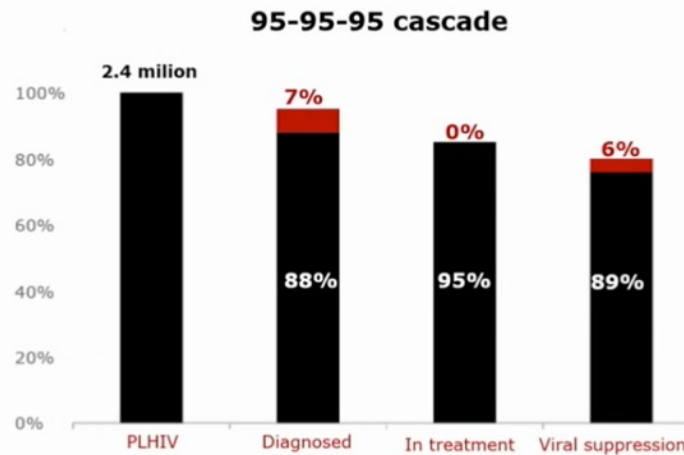
IAS 2025

(D. MOIANA UETELA)

IAS 2025

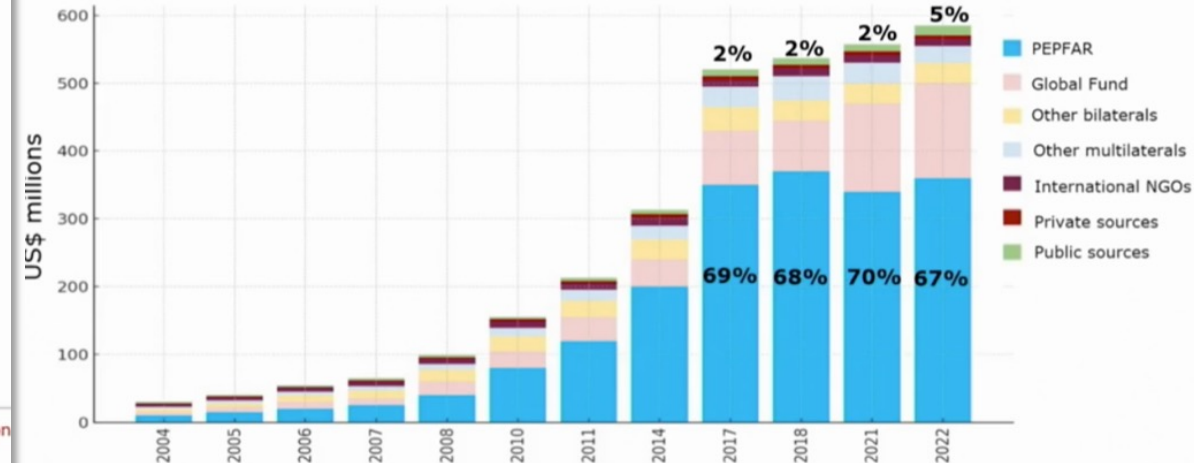
The Country's Epidemics and Progress

- Mozambique has the 3rd highest number of PLHIV globally and the 2nd highest number of new infections.
- ART is available since 2004, now offered in 97% of health facilities and serving approximately 2 million of the 2.4 PLHIV.



Source: National HIV Program, First Quarterly Report – 2025

Mozambique relies heavily on external funds for HIV response, with PEPFAR and the Global Fund being the major funders for over a decade



Source: CNCS, Megas (2008, 2010, 2014, 2016, 2020, 2023)

Impact of USG Funding Cuts for HIV Care

The impact of the U.S. funding interruption on HIV services and the HIV epidemic in Mozambique

IAS 2025

(D. MOIANA UETELA)

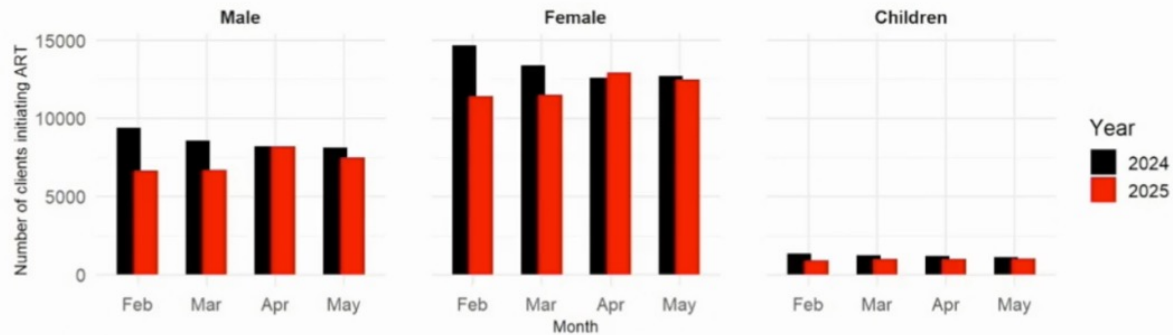


IAS 2025

Results

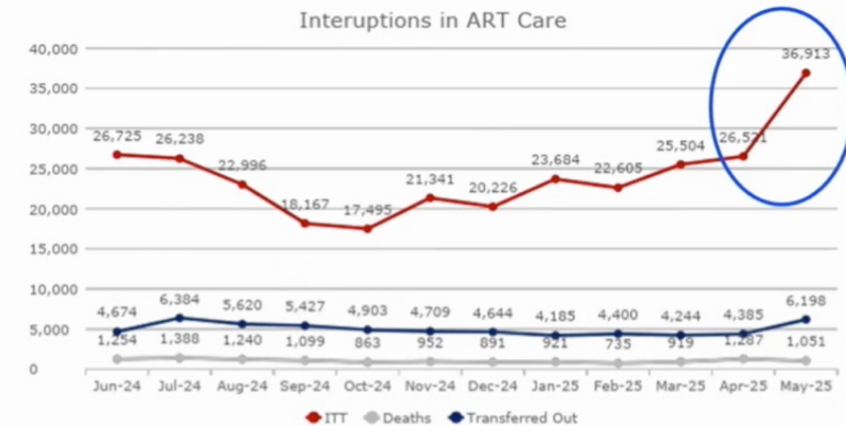
Treatment initiation

There was a 14% decrease (15,727) in ART initiations from February to May 2025



Interruption of treatment

There was a 39% (10,392) increase in interruption of treatment from April to May 2025



interruption defined as not picking up meds within 59 consecutive days of when was supposed to.

Impact of USG Funding Cuts for HIV Care

Systemic Review and Meta-Analysis of the Efficacy of Intermittent Antiretroviral Therapy dosing: a crisis response to the sudden cuts in USAID and PEPFAR funding

Cassandra Fairhead, Royal Free Hospital, London



Background

Uninterrupted person-centred ART access is essential

- However, individuals are already experiencing ART interruption

UNAIDS: supply chain disruption in **46% of surveyed countries**

Additional **1 to 3M HIV-related deaths and 4 to 11M new acquisitions** predicted over next 5 years

Could intermittent therapy safely extend supplies without risk of virological failure?



UNAIDS May 2025; UNAIDS
March 2025; Brink et al 2025

Methods



PubMed, MEDLINE, ClinicalTrials.Gov

Randomised controlled trials of triple ART 3-6 days/week versus daily

- Efficacy: HIV VL ≥ 50 copies/mL
Meta-analysis; Random Effects Model

Additional outcomes, where available:

- Viral suppression
- Highly-sensitive viral load
- Inflammation: interleukin-6, d-dimer, hsCRP
- Treatment-emergent drug resistance
- Adherence
- Acceptability

} Descriptive analysis

Impact of USG Funding Cuts for HIV Care

Systemic Review and Meta-Analysis of the Efficacy of Intermittent Antiretroviral Therapy dosing: a crisis response to the sudden cuts in USAID and PEPFAR funding

Cassandra Fairhead, Royal Free Hospital, London



XIAS 2025

Randomised trials

1346 individuals
22% female

	Location	Sample size	Length, weeks	Regimen	Median age, years	Average time on ART, years
BREATHER	11 countries	199	48	TDF/FTC/EFV	14	6.1
Reynolds et al	Uganda	113	72	EFV plus 2NRTI	38	1
Sun et al	Taiwan	60	52	BIC/FTC/TAF	ND	NR
Cohen et al	USA	60	24	TDF/FTC/EFV	44	NR
QUATUOR	France	636	48	Two NRTIs + PI or NNRTI or INSTI	50	7
ATAD	Italy	197	48	TDF/FTC/EFV	43	4.9
A-TRI-WEEK	Spain	61	24	TDF/FTC/EFV	49	NR
BETAF-RED	Spain	19	48	BIC/FTC/TAF	42	8

	Dosing	M	T	W	T	F	S	S
BREATHER	5 on, 2 off	✓	✓	✓	✓	✓	✗	✗
Reynolds et al	5 on, 2 off	✓	✓	✓	✓	✓	✗	✗
Sun et al	5 on, 2 off	✓	✓	✓	✓	✓	✗	✗
Cohen et al	5 on, 2 off	✓	✓	✓	✓	✓	✗	✗
QUATUOR	4 on, 3 off	✓	✓	✓	✓	✗	✗	✗
ATAD	Alternate	✓	✗	✓	✗	✓	✗	✓
A-TRI-WEEK	3 on, 4 off	✓	✗	✓	✗	✓	✗	✗
BETAF-RED	3 on, 4 off	✓	✗	✓	✗	✓	✗	✗

Impact of USG Funding Cuts for HIV Care

Systemic Review and Meta-Analysis of the Efficacy of Intermittent Antiretroviral Therapy dosing: a crisis response to the sudden cuts in USAID and PEPFAR funding

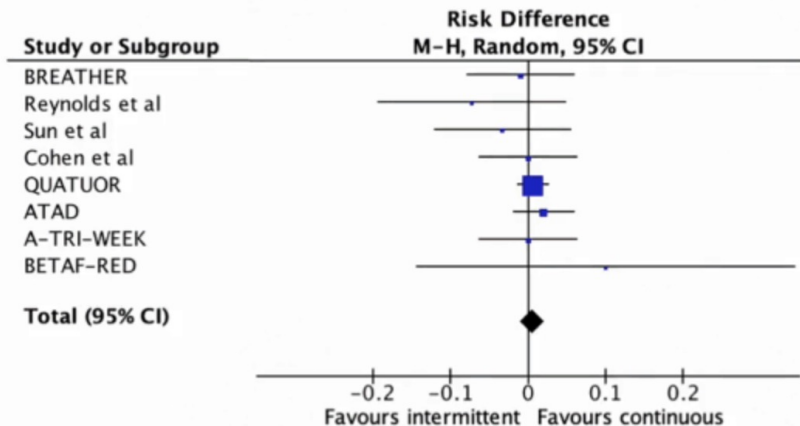
Cassandra Fairhead, Royal Free Hospital, London



Efficacy (HIV RNA ≥ 50 copies/mL*), ITT analysis

Risk Difference 0.00
95%CI -0.01 to 0.02

$p=0.54$



13 - 17 July • Kigali, Rwanda

ias2025.org

*A-TRI-WEEK: 37 copies/mL; Cohen and Reynolds et al: 400 copies/mL



IAS 2025

Treatment-emergent resistance

	TREATMENT-EMERGENT RESISTANCE	
	Intermittent	Continuous
BREATHER	2/3	5/6
REYNOLDS ET AL	4/4	4/5
QUATUOR	3/6	1/4
TOTAL	9/13 (69%) of genotypes 9/474 (1.9%) of participants	10/15 (67%) of genotypes 10/474 (2.1%) of participants

n/N = genotypes with resistance mutations/
successful genotypes in instances of virologic failure

Caveat: High adherence, virally suppressed at entry, and no prior failures or known resistance in setting of capacity to monitor viral load.

Impact of USG Funding Cuts for HIV Care

Short cycle antiretroviral therapy (ART) with weekends off is inferior to continuous ART in adolescents living with HIV receiving tenofovir disoproxil fumarate/lamivudine/dolutegravir (TLD) in sub-Saharan Africa: BREATHER Plus 96-week results

IAS 2025

(A. R. KEKITIINWA)

BREATHER Plus study design



- **Study design:** open-label non-inferiority (NI) RCT comparing SCT (5 days on/2 days off) to CT (daily ART) in adolescents
- Participants were aged 12-19, on ART ≥ 1 year, on TLD ≥ 1 month, had no history of treatment failure, virologically suppressed (VL <50 c/mL) for 12 months
- **Primary endpoint:** Confirmed viral rebound, defined as 2 consecutive HIV-RNA ≥ 50 copies/mL, by the week 96 assessment
- Visits were 8/12 weekly, real-time VLs were 6-12 monthly as per in-country monitoring guidelines, retrospective VLs were done at other visits
- Employed a 'smooth away from expected' (SAFE) non-inferiority margin¹: *CI and NI margin changed depending on the proportion of CT participants with confirmed viral rebound*

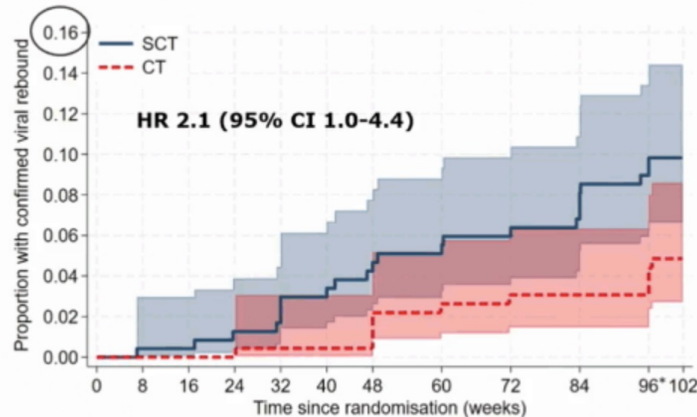
Impact of USG Funding Cuts for HIV Care

Short cycle antiretroviral therapy (ART) with weekends off is inferior to continuous ART in adolescents living with HIV receiving tenofovir disoproxil fumarate/lamivudine/dolutegravir (TLD) in sub-Saharan Africa: BREATHER Plus 96-week results

IAS 2025

(A. R. KEKITIINWA)

Primary efficacy endpoint: *Kaplan-Meier estimates for confirmed viral rebound*



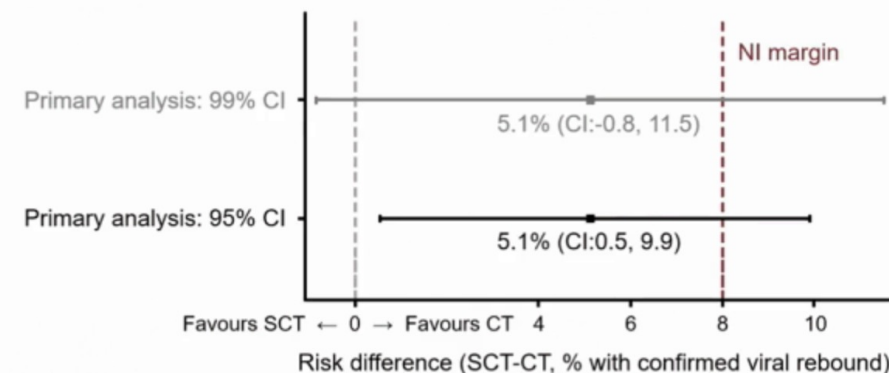
No heterogeneity in treatment effect by site or baseline age

Figure Kaplan–Meier estimates for confirmed viral rebound rate, stratified by treatment arm with 95% confidence intervals

13 – 1 *98% of participants met the primary endpoint or had ≥96 weeks follow-up

Slide 7

Primary efficacy endpoint: *inferiority*



SCT is significantly worse (inferior) than CT; p-value 0.034

13 – 17 July • Kigali, Rwanda

ias2025.org

*2 consecutive plasma HIV-RNA ≥50 copies/mL
Slide 6

CAB/RPV after oral ART suppression

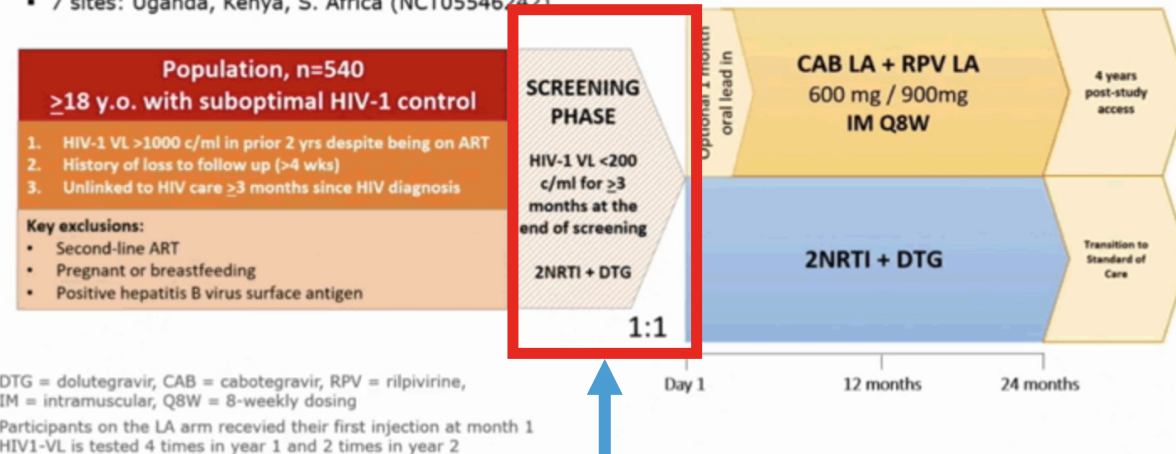
Long-acting cabotegravir and rilpivirine in adults with suboptimal HIV control in sub-Saharan Africa: the IMPALA trial 48-week results

F. CRESSWELL]

Study rationale and design

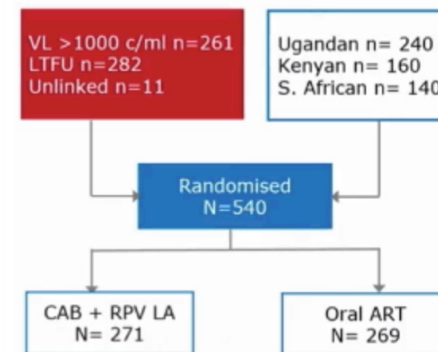


- Evidence gaps: sub-optimal HIV control in public health approach, prior HBV exposure (cAb+), women
- Phase 3b, open-label, non-inferiority trial
- 7 sites: Uganda, Kenya, S. Africa (NCT05546242)



Viral suppression required

Baseline characteristics



All participants had VL<200 prior to randomisation

- 4 withdrawals from study (2 LA, 2 oral)
- 1 participant choice after randomisation to oral arm
- 2 participant choice due to visit schedule (1 oral, 1 LA)
- 1 moved out of area, LA arm

	Total
Age, median years (IQR)	40 (33-48)
Cis-female, n (%)	324 (60%)
Black African, n (%)	538 (99.6%)
Hepatitis B core antibody positive	168 (31.1%)
Formal employment, n (%)	96 (17.8%)
BMI ≥ 30, N (%)	120 (22.2%)
CD4, median cells/μl (IQR)	629 (453-873)
ART duration, median yrs (IQR)	7.5 (4.6-10.8)
Prior AIDS-defining illness, n (%)	142 (26.3%)
Prior exposure to NNRTI, n (%)	411 (78.3%)

Next generation sequencing for archived baseline resistance and sub-type is ongoing. This is performed on proviral DNA extracted from baseline PBMCs and will be included in the manuscript.

All variables were well balanced between randomization arms

CAB/RPV after oral ART suppression

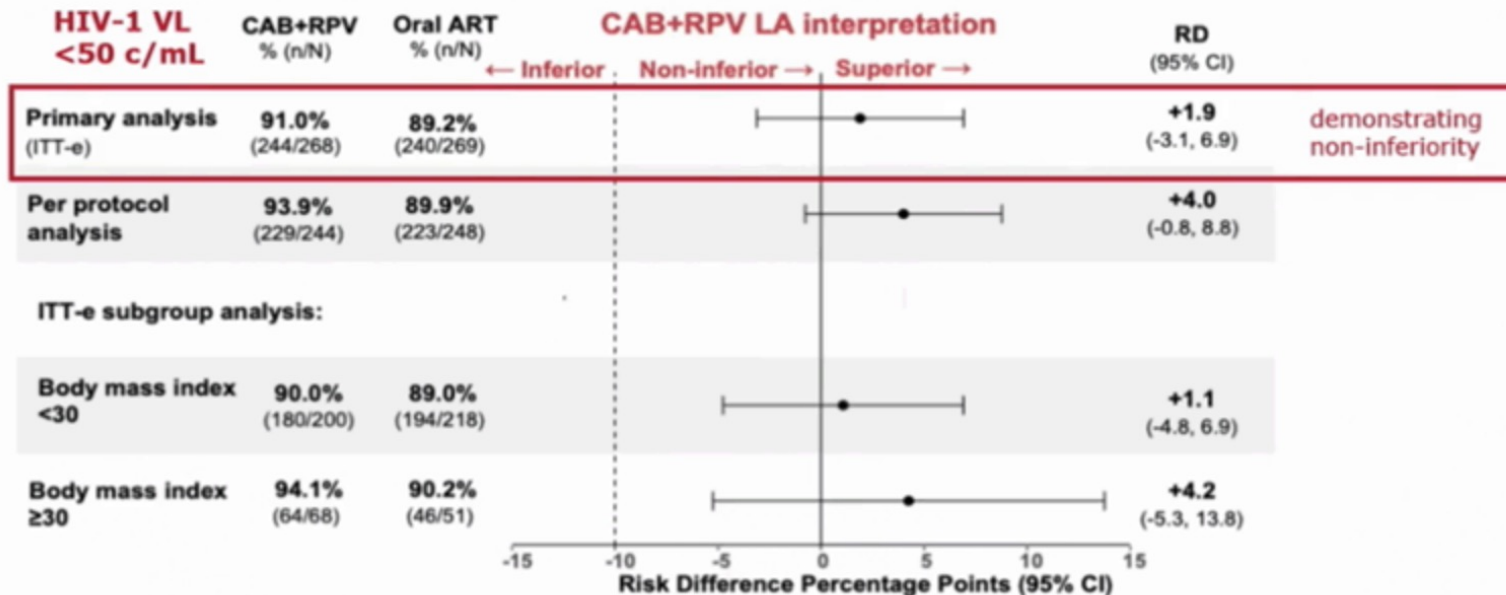
Long-acting cabotegravir and rilpivirine in adults with suboptimal HIV control in sub-Saharan Africa: the IMPALA trial 48-week results

F. CRESSWELL

Primary outcome at Week 48



- 99.0% retention. 98% of 2159 injections given within window



13 - 17 July • Kigali, Rwanda

ias2025.org



Injection site reactions: no ISR-related discontinuations

- 161 events from 100 (37%) participants, all grade 1 & 2

CAB/RPV after oral ART suppression

Long-acting cabotegravir and rilpivirine in adults with suboptimal HIV control in sub-Saharan Africa: the IMPALA trial 48-week results

F. CRESSWELL]

Confirmed virological failure



Number	1	2	3	4	5
Visit	Month 6	Month 8	Month 12	Month 12	Month 12
Sub-type	C	unknown	A1	C	A1
Baseline resistance [§]	Testing ongoing	Testing ongoing	NNRTI: K103S INSTI: none	NNRTI: L100I, K103N INSTI: L74I High level RPV	Testing ongoing
HIV VL at failure c/ml	3336	6303	36670	475	5232
Repeat HIV VL c/ml	1809	1888	96120	282	231
NNRTI RAMs at failure	Insufficient volume	E138K, Y188L	K103S, E138K, Y181C	K103N, V108I	E138K, Y181C
Resistance prediction	N/A	Low: ETR High: EFV, NVP, RPV	Intermediate: ETR High: RPV , EFV, NVP	Sensitive: RPV High: EFV, NVP	Intermediate: EFV, ETR High: RPV , NVP
INSTI RAMs at failure	Insufficient volume	E138K, Q148R	E138K, Q148R	Q148R	Q148R
Resistance prediction [§]	N/A	Intermediate: DTG , BIC High: CAB , RAL, EVG	Intermediate: DTG , BIC High: CAB , RAL, EVG	Low: DTG , BIC High: CAB , RAL, EVG	Low: DTG , BIC High: CAB , RAL, EVG
Identifiable risk factors or DDI	Herbal medicine	BMI 38.3 kg/m ²	Nil	RPV RAMs (L100I/K103N)	Nil
Current regimen	TLD	TLD	TLD	TDF/FTC + LPV/r	TLD
Most recent HIV VL*	<50 c/ml	<50 c/ml	<50 c/ml	<50 c/ml	<50 c/ml

§ archived resistance on HIV DNA from PBMC using NGS [§]prediction using Stanford algorithm. *Median duration of follow-up following switch to oral ART is 35 weeks.
TLD = tenofovir, lamivudine, dolutegravir. LPV/r = lopinavir/ritonavir. EFV = efavirenz. NVP = nevirapine, RPV = rilpivirine. ETR = etravirine. CAB = cabotegravir.
RAL = raltegravir. EVG = elvitegravir. BIC = bictegravir. TDF = tenofovir df. FTC = emtricitabine. DDI = drug-drug interaction.

CAB/RPV in Clinical Practice

High Virologic Suppression and few Virologic Failures with Long-Acting Cabotegravir + Rilpivirine in Treatment Experienced Virologically Suppressed Individuals from COMBINE-2 cohort in Europe

IAS 2025, the 13th IAS conference on HIV Science

Anton Pozniak,¹ Gayathri Sridhar,² Lambert Assoumou,^{1,3} Ana Gonzalez-Cordon,⁴ Eugenia Negredo,⁵ Nathalie De Castro,⁶ Carl Fletcher,⁷ Leigh Ragone,² Ajay Shah,⁸ Jean van Wyk,⁹ Vani Vannappagari²
¹The European treatment network for HIV, hepatitis and global infectious diseases (NEAT-ID), London, UK; ²ViiV Healthcare, Durham, NC, USA; ³Sorbonne Université, INSERM, Institut Pierre Louis d'Épidémiologie et de Santé Publique, Paris, France
⁴Hospital Clinic Barcelona, Barcelona, Spain; ⁵Hospital Germans Trias I Pujol, Fundació Lluita contra les Infeccions, Barcelona, Spain; ⁶Hospital Saint Louis, Paris, France, ⁷Research Organization (KC) Ltd., London, UK; ⁸GlaxoSmithKline, London, England, UK; ⁹ViiV Healthcare, London, England, UK

Methods

- Treatment experienced, virologically suppressed PWH with no history of resistance or virological failure with NNRTI and INSTI classes initiating CAB+RPV LA at NEAT-ID Network sites across seven European countries between December 2020 and May 2024 were included.
- VLs were assessed from first injection until discontinuation or time of analysis.
- Confirmed virologic failure (CVF; 2 VL ≥ 200 copies/mL or 1 VL ≥ 200 copies/mL + discontinuation) was assessed among those with follow-up VL.

Table 2. Virologic outcomes among individuals initiating CAB+RPV LA regimen

		Overall (N=956)
Duration of follow-up	Median months (IQR)	10.2 (7.1, 16.6)
On CAB+RPV LA at end of follow-up	n (%)	882 (92)
≥ 1 VL after first injection	n (%)	937 (98)
	Last VL <50 copies/mL, n (%)	925/937 (99)
	All VLs <50 copies/mL, n (%)	880/937 (94)
	VL <50 copies/mL at month 6, n (%)	841/871 (97)
	VL <50 copies/mL at month 12, n (%)	350/366 (96)
	VL <50 copies/mL at month 24, n (%)	46/49 (94)
Confirmed virologic failure	n (%)	5/937 (0.5)

4 of 5 with CVF had ART resistance detected

CAB/RPV in Clinical Practice

24-Month Outcomes of Cabotegravir Plus Rilpivirine Long-Acting Every 2 Months in a Real-World Setting: Effectiveness, Adherence to Injections, and Patient-Reported Outcomes From People With HIV-1 in the German CARLOS Study

13th IAS Conference on HIV Science; July 13–17, 2025; Kigali, Rwanda

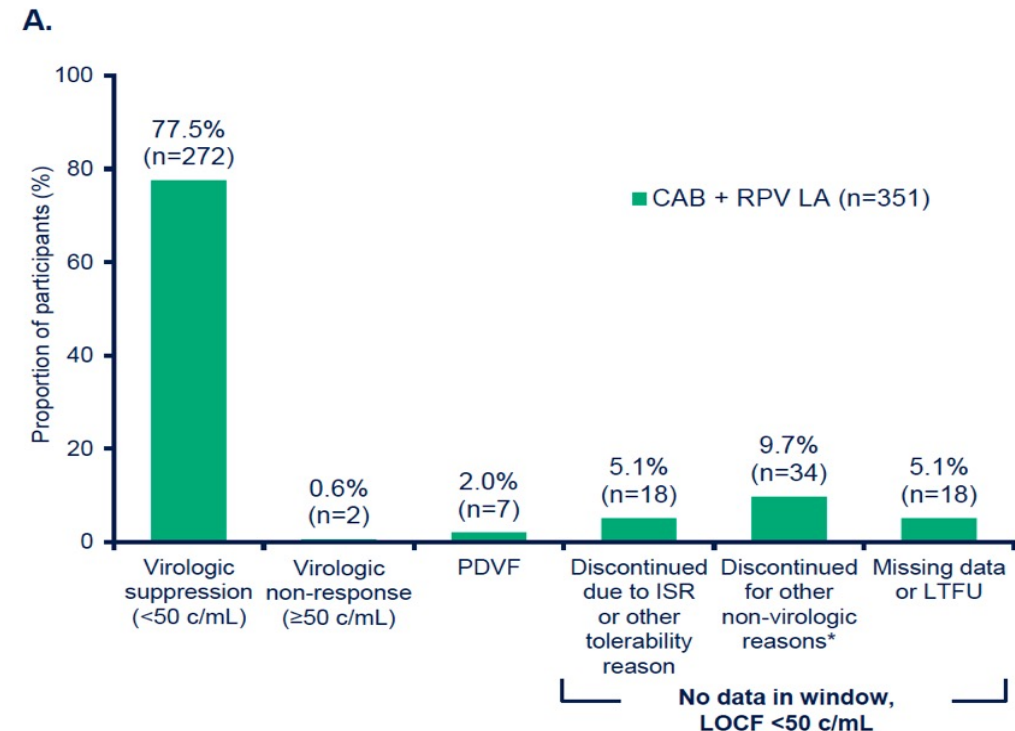
Christoph Wyen,¹ Sebastian Noe,² Celia Jonsson-Oldenbüttel,² Jan Borch,³ Kevin Ummard-Berger,⁴ Elena Rodríguez,⁵ Marcel Lee,⁶ Stefan Scholten,⁷ Martha Schneider,⁸ Kathrin M. Dymek,⁸ Bernd Westermayer,⁹ Jenny Scherzer⁸
¹Praxis am Ebertplatz, Cologne, Germany; ²MOVZ München am Goetheplatz, Munich, Germany; ³Praxis Goldstein, Berlin, Germany; ⁴UBN/Praxis, Berlin, Germany;
⁵Praxis Dr. Rump, Freiburg, Germany; ⁶MOVZ München am Isartorplatz, Munich, Germany; ⁷Praxis Hohenstaufenring, Cologne, Germany; ⁸ViiV Healthcare, Munich, Germany; ⁹GSK, Munich, Germany

Table 1. Baseline Characteristics

n (%) unless stated otherwise	CAB + RPV LA Q2M	n
Age		
Median years (IQR)	42 (35–50)	
<50 years	260 (74)	351
50–65 years	88 (25)	
>65 years	3 (<1)	
Sex at birth		
Male	332 (95)	351
Baseline risk factors		
BMI ≥30 kg/m ²	35 (13)	276
HIV-1 subtype A6/A1	3 (1)	214
Baseline resistance test		
No current/historical genotypic resistance test at baseline	103 (29)	351
Comorbidities with a prevalence of ≥25%		
Mental/behavioral disorders	143 (41)	351
Metabolic disorders	96 (27)	
HIV history		
Time on oral ART before switch, median years (IQR)	7.9 (4.3–11.4)	310
PWH with ≥3 prior ART regimens (excluding current daily oral)	145 (51)	284
ART regimen prior to switch (in ≥10% of participants)		
BIC/FTC/TAF	80 (23)	351
DTG/3TC	61 (17)	
DTG/3TC/ABC	36 (10)	

3TC, lamivudine; ABC, abacavir; BIC, bictegravir; BMI, body mass index; DTG, dolutegravir; FTC, emtricitabine; IQR, interquartile range; TAF, tenofovir alafenamide.

Figure 1. Virologic Outcomes at Month 24



CAB/RPV in Clinical Practice

24-Month Outcomes of Cabotegravir Plus Rilpivirine Long-Acting Every 2 Months in a Real-World Setting: Effectiveness, Adherence to Injections, and Patient-Reported Outcomes From People With HIV-1 in the German CARLOS Study

13th IAS Conference on HIV Science; July 13–17, 2025; Kigali, Rwanda

Christoph Wyen,¹ Sebastian Noe,² Celia Jonsson-Oldenbüttel,² Jan Borch,³ Kevin Ummard-Berger,⁴ Elena Rodríguez,⁵ Marcel Lee,⁶ Stefan Scholten,⁷ Martha Schneider,⁸ Kathrin M. Dymek,⁸ Bernd Westermayer,⁹ Jenny Scherzer⁸
¹Praxis am Ebertplatz, Cologne, Germany; ²MVZ München am Goetheplatz, Munich, Germany; ³Praxis Goldstein, Berlin, Germany; ⁴UBN/Praxis, Berlin, Germany;
⁵Praxis Dr. Rump, Freiburg, Germany; ⁶MVZ München am Isartorplatz, Munich, Germany; ⁷Praxis Hohenstaufenring, Cologne, Germany; ⁸ViiV Healthcare, Munich, Germany; ⁹GSK, Munich, Germany

- Five participants (n=5/351; 1.4%) met the PDVF criterion through Month 12 and have been reported previously.⁹
- For three participants, NNRTI resistance-associated mutations (RAMs; E138K, K101E, Y181C) and/or INSTI RAMs (Q148R, T97A, E138K, N155H) were observed at failure.
- Two additional participants met the PDVF criterion between Month 12 and Month 24 (**Table 2**).

Table 2. Summary of Participants With PDVF from Month 12 to 24*

	Participant 1	Participant 2
Sex at birth, age (year)	Male, 43	Male, 37
Baseline BMI (kg/m ²)	20	24
HIV-1 subtype	B	B
Historic resistance test available	No INI/NNRTI resistance reported at BL	No INI/NNRTI resistance reported at BL
Time to failure (months); injections received	15; 9 injections	17; 13 injections
Viral load at SVF/PDVF (c/mL)	667/10,200	421/446
RAMs at failure	NNRTI: K101P INSTI: E138K, Q148R	None
On time injections	Yes	Yes
ART following CAB + RPV LA discontinuation	DRV/COBI/FTC/TAF	NA; resuppressed on CAB + RPV LA

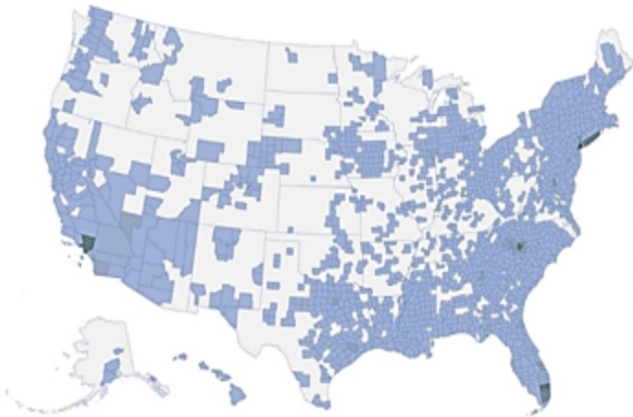
*Previously reported: One additional participant was excluded from the analysis population for off-label use of CAB + RPV LA (discovered *post hoc*; prior virologic failure with an agent of NNRTI class) had PDVF with NNRTI RAMs (K101E, Y181C, G190A) detected at failure. The participant had HIV-1 subtype C, a BMI of 20 kg/m², and on-time injections.¹³ COBI, cobicistat; DRV, darunavir; INI, integrase inhibitor; RAM, resistance-associated mutation; SVF, suspected virologic failure.

CAB/RPV in Clinical Practice

Real-world Effectiveness of CAB+RPV LA in Individuals with HIV Viremia at Therapy Initiation

IAS 2025 July 13-17 Rwanda, oral today

Ricky K. Hsu, MD

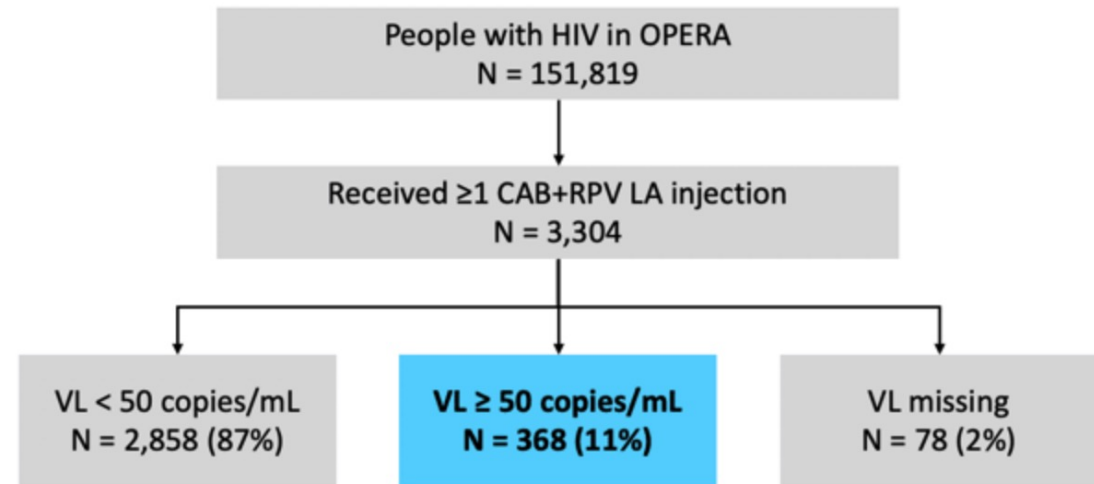


**Observational Pharmaco-Epidemiology
Research & Analysis**

>150K people with HIV in OPERA

~14% of people with HIV in the US

Results Study Population at Regimen Initiation



CAB/RPV in Clinical Practice

Real-world Effectiveness of CAB+RPV LA in Individuals with HIV Viremia at Therapy Initiation

IAS 2025 July 13-17 Rwanda, oral today

Ricky K. Hsu, MD

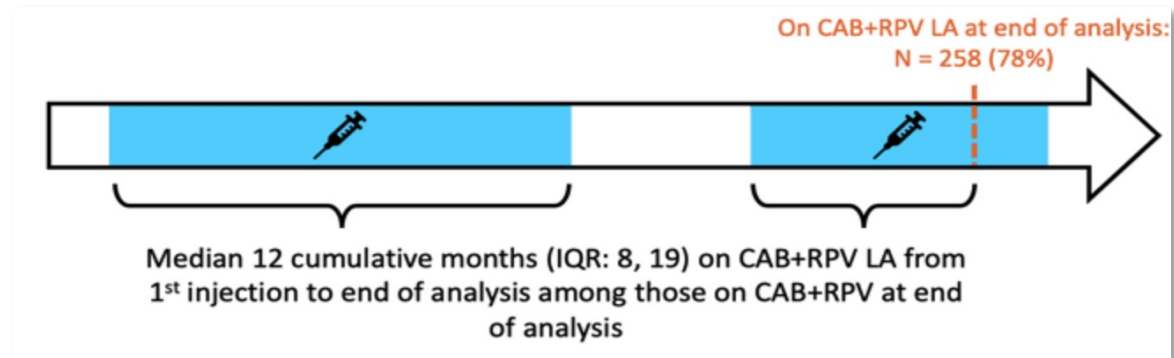
CAB+RPV LA users with viremia (N = 368)			
Age, ≥50 years, n (%)	101 (27%)	BMI, >30 kg/m ² , n (%)	106 (29%)
Female sex, n (%)	109 (30%)	Years since HIV diagnosis, median (IQR)	9 (3, 17)
Black race, n (%)	208 (57%)	History of AIDS-defined events, n (%)	126 (34%)
Hispanic ethnicity, n (%)	66 (18%)	HIV viral load, median copies/mL (IQR)	120 (61, 2535)
Single, n (%)	263 (71%)	HIV viral load ≥200 copies/mL, n (%)	148 (40%)
Men who have sex with men, n (%)	182 (49%)	CD4 cell count, median cells/μL (IQR)	578 (353, 808)
Southern USA, n (%)	233 (63%)	Any comorbidities, n (%)	295 (80%)

CAB/RPV in Clinical Practice

Real-world Effectiveness of CAB+RPV LA in Individuals with HIV Viremia at Therapy Initiation

IAS 2025 July 13-17 Rwanda, oral today

Ricky K. Hsu, MD



Adherence to Injection Schedule

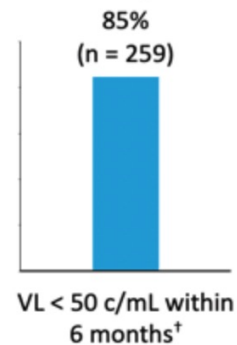
		Days between injection	n (%)
Initiation injection N = 368	Complete	Q1M & Q2M: ≤67 days	331 (90%)
	Incomplete	Q1M & Q2M: >67 days	37 (10%)
Maintenance injections N = 293	All on-time	Q1M: 23-67 days Q2M: 53-67 days	174 (59%)
	Delayed	Q1M: 38-52 days Q2M: 68-112 days	96 (33%) Median 1 delay (IQR: 1, 2)
	Missed	Q1M: 53-67 days Q2M: 113-127 days	38 (13%) Median 1 missed (IQR: 1, 1)

Q2M at initiation: n = 264 (80%)

Q2M at end of analysis or discontinuation: n = 307 (93%)

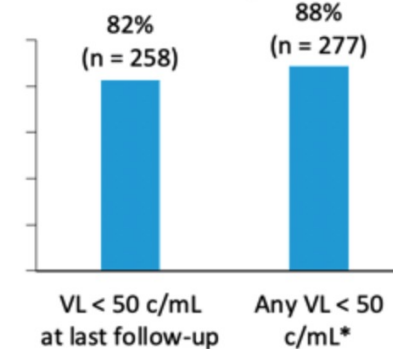
Virologic Outcomes

Complete initiators,
≥ 1 VL within 6 months (N = 306)



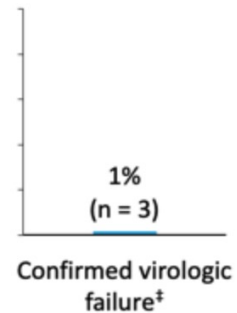
[†] + 30 days grace period

Complete initiators,
≥ 1 VL during follow-up (N = 313)



* 12% (n = 36) never suppressed to < 50 copies/mL

Complete initiators,
≥ 1 VL after suppression (N = 301)



[‡] 2 consecutive VLs ≥ 200 c/mL or 1 VL ≥ 200 c/mL + discontinuation within 2 (Q1M) or 4 (Q2M) months

CAB/RPV in Clinical Practice

Real-world Effectiveness of CAB+RPV LA in Individuals with HIV Viremia at Therapy Initiation

IAS 2025 July 13-17 Rwanda, oral today

Ricky K. Hsu, MD

Key Findings

368 individuals (11%) initiated CAB+RPV LA with viremia (off-label) in the OPERA cohort during the first 3 years of availability in the US

High persistence with moderate adherence on CAB+RPV LA

- 258 (78%) remained on CAB+RPV LA at the time of analysis
- 174 (59%) were fully adherent to injection schedule

CAB+RPV LA demonstrated high effectiveness in people with viremia

- 259 (85%) achieved suppression to <50 copies/mL by 6 months
- 3 (1%) experienced confirmed virologic failure, after which 2 had major NNRTI & INSTI resistance, 1 had no genotyping

New ART: Islatravir

Switching to Doravirine/Islatravir (100 mg/0.25 mg) Once-Daily Maintained Viral Suppression in the Presence of Archived M184I/V Resistance–Associated Mutations in Proviral DNA

IAS July 13-17 Rwanda

Tracy L. Diamond¹; Anjana Grandhi¹; Monica Fuszard¹; Yayun Xu¹; Uchechukwu Nwoke¹; Ying Zhang¹; Stephanie Klopfer¹; Karen Eves¹; Jaime Benner¹; Mengchun Li¹; Wayne Greaves¹; Rima Lahoulou²; Jason Kim¹; Michelle C. Fox¹; Ernest Asante-Appiah^{1*}
¹Merck & Co., Inc., Rahway, NJ, USA; ²MSD France, Puteaux, France

Study Designs for Phase 3 Studies of DOR/ISL (100 mg/0.25 mg) in Virologically Suppressed Adults

Comparator studies (P051 and P052)

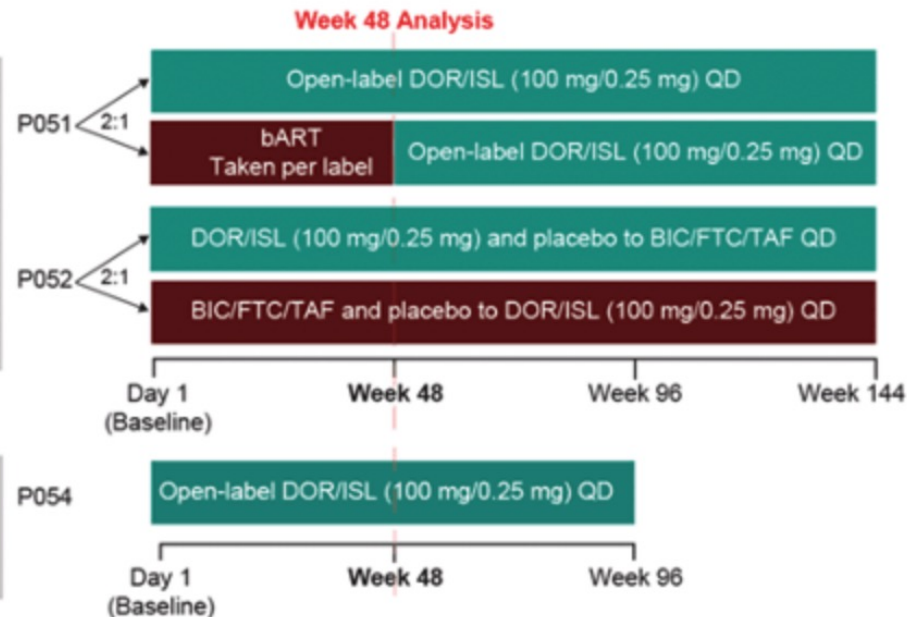
Population

- Virologically suppressed adults with HIV-1 (plasma RNA <50 copies/mL) for ≥3 months on stable ART
- CD4 T cell count ≥50 cells/mm³ or total lymphocytes ≥0.65×10⁹/L
- No history of treatment failure on any regimen
- No known resistance to DOR: V106A/M, V108I, Y188L, H221Y, P225H, F227C/L, M230I/L, L234I, P236L, or Y318F
- No active HBV infection

Single-arm study (P054)

Population

- Virologically suppressed adults that received DOR/ISL (100 mg/0.75 mg) in previous Phase 3 studies (except HTE) and considered to have derived clinical benefit



New ART: Islatravir

Baseline Resistance Analysis

Table 2. Prevalence of Preexisting RAMs Observed in >5% of Participants With Baseline Proviral DNA Data in Any Study Arm

Protein	RAM	P051		P052		P054	Pooled
		DOR/ISL (100 mg/0.25 mg)	Baseline ART	DOR/ISL (100 mg/0.25 mg)	Group 2: BIC/FTC/ TAF	DOR/ISL (100 mg/0.25 mg)	DOR/ISL (100 mg/0.25 mg)
		N = 322 n (%)	N = 166 n (%)	N = 309 n (%)	N = 152 n (%)	N = 596 n (%)	N=1227 n (%)
RT	Any NNRTI RAM	79 (24.5)	33 (19.9)	82 (26.5)	41 (27.0)	162 (27.2)	323 (26.3)
	K103N/R/S	34 (10.6)	11 (6.6)	38 (12.3)	16 (10.5)	53 (8.9)	125 (10.2)
	E138A/G/K/Q/R	21 (6.5)	7 (4.2)	18 (5.8)	9 (5.9)	39 (6.5)	78 (6.4)
	Any NRTI RAM	59 (18.3)	25 (15.1)	62 (20.1)	32 (21.1)	132 (22.1)	253 (20.6)
	V118I	20 (6.2)	11 (6.6)	18 (5.8)	10 (6.6)	49 (8.2)	87 (7.1)
	M184I/V	20 (6.2)	5 (3.0)	24 (7.8)	10 (6.6)	26 (4.4)	70 (5.7)
Integrase	Any INSTI RAM	124 (38.5)	68 (41.0)	88 (28.5)	37 (24.3)		
	M50I	91 (28.3)	53 (31.9)	49 (15.9)	23 (15.1)		
	E157K/Q	13 (4.0)	9 (5.4)	19 (6.1)	9 (5.9)		
Protease	Any PI RAM	280 (87.0)	149 (89.8)				
	M36I/L/V	166 (51.6)	87 (52.4)				
	V77I	86 (26.7)	44 (26.5)				
		*PI RAMS I62V, H69KR, L89I/M/V, A71T/V, L10F/I/R/V, and K20M/R/T were also present in both arms at >5%		Note: RAMs were sometimes present as mixtures with wild-type or other mutations within the same codon.			

- The prevalence of class-specific RAMs were comparable between studies and treatment groups
- Among 1,227 participants switched to DOR/ISL (100 mg/0.25 mg) across P051, P052, and P054, 323 (26.3%) had preexisting NNRTI RAMs and 70 (5.7%) had preexisting M184I/V
- K103N/R/S, E138K/Q, and M184I/V were the most prevalent major RAMs observed in RT at baseline
- Most of the RAMs observed in >5% of participants were minor RAMs that do not confer resistance to DOR or ISL

Table 3. Prevalence of Preexisting DOR RAMs

RAM	P051		P052		P054	Pooled
	DOR/ISL (100 mg/0.25 mg)	Baseline ART	DOR/ISL (100 mg/0.25 mg)	BIC/FTC/TAF	DOR/ISL (100 mg/0.25 mg)	DOR/ISL (100 mg/0.25 mg)
	N=322 n (%)	N=166 n (%)	N=309 n (%)	N=152 n (%)	N=596 n (%)	N=1,227 n (%)
Any DOR RAM	7 (2.2)	7 (4.2)	15 (4.9)	3 (2.0)	21 (3.5)	43 (3.5)
V108I	2 (0.6)	3 (1.8)	3 (1.0)	2 (1.3)	7 (1.2)	12 (1.0)
V106A/M	4 (1.2)	0 (0.0)	1 (0.3)	0 (0.0)	4 (0.7)	9 (0.7)
P225H	1 (0.3)	0 (0.0)	3 (1.0)	1 (0.7)	3 (0.5)	7 (0.6)
H221Y	0 (0.0)	1 (0.6)	4 (1.3)	1 (0.7)	3 (0.5)	7 (0.6)
M230I/L	0 (0.0)	0 (0.0)	2 (0.6)	0 (0.0)	2 (0.3)	4 (0.3)
F227C/L/V	1 (0.3)	1 (0.6)	0 (0.0)	0 (0.0)	2 (0.3)	3 (0.2)
Y188L	2 (0.6)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	2 (0.2)
Y318F	0 (0.0)	1 (0.6)	2 (0.6)	0 (0.0)	0 (0.0)	2 (0.2)
L234I	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.0)
P236L	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

- Preexisting DOR RAMs were rare, detected in 3.5% of participants that switched to DOR/ISL (100 mg/0.25 mg) across P051, P052, and P054
- V108I was the most prevalent DOR RAM; observed at <2% in all study groups

DOR

V106A/M, V108I, Y188L, F227C/L/V, M230I/L, L234I, Y318F

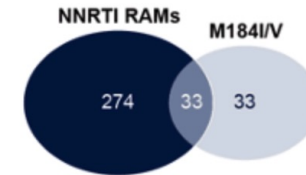
H221Y, P225H, P236L

New ART: Islatravir

Table 4: Week 48 Virologic Outcomes in Participants With Preexisting NNRTI RAMs or M184I/V in Proviral DNA

	P051*		P052		P054	Pooled
PARTICIPANTS WITH:	DOR/ISL (100/0.25 mg)	Baseline ART	DOR/ISL (100/0.25 mg)	BIC/FTC/TAF	DOR/ISL (100/0.25 mg)	DOR/ISL (100/0.25 mg)
Proviral DNA Data:	N = 322	N = 166	N = 309	N = 152	N=596	N=1227
Virologic Data at Week 48 n/N (%)	313/322 (97.2)	161/166 (97.0)	285/309 (92.2)	145/152 (95.4)	570/596 (95.6)	1168/1227 (95.2)
– HIV-1 RNA <50 c/mL at Week 48, m (%)	309 (98.7)	153 (95.0)	280 (98.2)	144 (99.3)	560 (98.2)	1149 (98.4)
– HIV-1 RNA ≥50 c/mL at Week 48, m (%)	4* (1.3)	8 (5.0)	5 (1.8)	1 (0.7)	10 (1.8)	19 (1.5)
→Discontinued w/ confirmed HIV-1 RNA ≥200 c/mL	3*	0	2	0	1	6*

Figure 2: Participants Treated With DOR/ISL With Preexisting NNRTI RAMs and M184I/V in Proviral DNA



- Among participants treated with DOR/ISL with virologic data at Week 48 and preexisting NNRTI RAMs (n=307) or M184I/V (n=66), 33 participants had both NNRTI RAMs and M184I/V
- 88% (29/33) of DOR/ISL participants with both NNRTI RAMs and M184I/V had HIV-1 RNA <50 copies/mL at Week 48 and only 1 discontinued with confirmed HIV-1 RNA ≥200 copies/mL

Table 5: Genotypic Analysis for DOR/ISL Participants That Discontinued With Confirmed HIV-1 RNA ≥200 copies/mL

Participant	Study	HIV-1 Subtype	Baseline RAMs in Proviral DNA ^a	HIV-1 RNA copies/mL at Sequencing (Study Week)	RAMs in Viral RNA	Treatment Emergent RAMs
Participants without post-baseline results due to assay failure						
1	P052	B	<u>NNRTI</u> : NONE <u>RTI</u> : NONE	287/486 (Week 36)	Assay Failed	ND
2	P054	AE	<u>NNRTI</u> : V179V/I <u>RTI</u> : NONE	332 (Week 12)	Assay Failed	ND
3 ^b	P054	Assay Failed	Assay Failed	227 (Week 48)	Assay Failed	ND
Participants who were later determined to be ineligible for enrollment						
4	P051	B	<u>NNRTI</u> : V106M, Y188L/W, F227L, K101A <u>RTI</u> : M41L, D67N, T69D, V118I, L210W, T215Y, K219R, E44A, V75M, M184T	38800 (Week 4)	<u>NNRTI</u> : V106M, F227L, K101A, Y188W <u>RTI</u> : M41L, D67N, T69D, V118I, L210W, T215Y, K219R, E44A, V75M, M184T	<u>NNRTI</u> : NONE <u>RTI</u> : NONE
5	P051	B	<u>NNRTI</u> : A98A/G, K103K/N, V106V/I, Y188Y/L <u>RTI</u> : M41M/L, E44E/D, D67D/N, K70K/R, V118V/I, M184M/I/V, L210L/W, T215T/N/S/Y, K219K/R	4780 (Week 12)	<u>NNRTI</u> : A98G, V106I, Y188L <u>RTI</u> : M41L, E44D, V118I, M184V, L210W, T215Y, K219R	<u>NNRTI</u> : NONE <u>RTI</u> : NONE
Participants with PK results indicating likely nonadherence						
6	P051	C	<u>NNRTI</u> : NONE <u>RTI</u> : NONE	2220 (Week 48)	<u>NNRTI</u> : NONE <u>RTI</u> : T215T/I	<u>NNRTI</u> : NONE <u>RTI</u> : T215T/I
7	P052	B	<u>NNRTI</u> : NONE <u>RTI</u> : T69T/N	83900 (Week 48)	<u>NNRTI</u> : NONE <u>RTI</u> : T69T/N	<u>NNRTI</u> : NONE <u>RTI</u> : NONE

Proviral DNA Data and Virologic Data at Week 48	N=313	N=161	N=285	N=145	N=570	N=1168
Any NNRTI RAMs at Baseline, n/N (%)	77/313 (24.6)	33/161 (20.5)	75/285 (26.3)	39/145 (26.9)	155/570 (27.2)	307/1168 (26.3)
– HIV-1 RNA <50 c/mL at Week 48, m (%)	74 (96.1)	31 (93.9)	73 (97.3)	39 (100.0)	150 (96.8)	297 (96.7)
– HIV-1 RNA ≥50 c/mL at Week 48, m (%)	3* (3.9)	2 (6.1)	2 (2.7)	0 (0.0)	5 (3.2)	10 (3.3)
→Discontinued w/ confirmed HIV-1 RNA ≥200 c/mL	2*	0	0	0	0	2*
M184I/V at Baseline, n/N (%)	20/313 (6.4)	4/161 (2.5)	20/285 (7.0)	8/145 (5.5)	26/570 (4.6)	66/1168 (5.7)
– HIV-1 RNA <50 c/mL at Week 48, m (%)	19 (95.0)	4 (100.0)	18 (90.0)	8 (100.0)	25 (96.2)	62 (93.9)
– HIV-1 RNA ≥50 c/mL at Week 48, m (%)	1* (5.0)	0 (0.0)	2 (10.0)	0 (0.0)	1 (3.8)	4 (6.1)
→Discontinued w/ confirmed HIV-1 RNA ≥200 c/mL	1*	0	0	0	0	1*

c/mL, copies/mL

*Two participants that discontinued with confirmed HIV-1 RNA ≥200 copies/mL in P051 were later determined to be ineligible for enrollment due to either previous history of virologic failure (n=1) or previous documentation of DOR resistance (n=1). Both had preexisting NNRTI RAMs (including Y188L) and 1 had preexisting M184I/V.

ND, not determined

^aDOR RAMs are shown in bold.

New ART: Islatravir + Ulonivirine

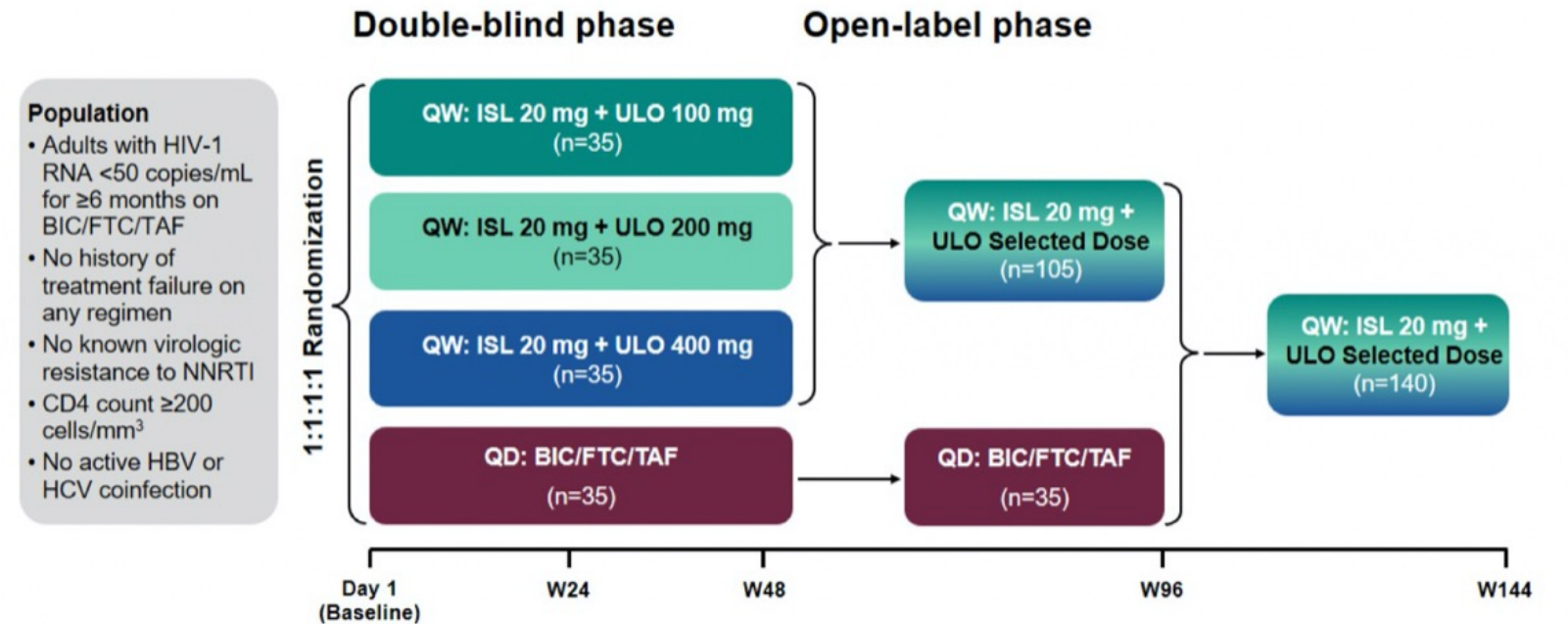
A Double-Blind, Active-Controlled, Phase 2b Study to Evaluate the Efficacy and Safety of Ulonivirine in Combination With Islatravir in Virologically Suppressed Adults Living With HIV-1

IAS 2025 July 13-17 Rwanda

Molina J-M, Ramgopal MN, Katlama C, Cunningham DL, Hagins DP, Braun DL, Osiyemi OO, Hofmann E, Dietz CA, Lin G, Beckey K, Rawlins S, Matthews RP, Greaves W

- Ulonivirine (ULO, MK-8507), an oral nonnucleoside reverse transcriptase inhibitor (NNRTI), is being assessed in combination with islatravir (ISL), an investigational nucleoside reverse transcriptase translocation inhibitor (NRTTI), as a once-weekly (QW) treatment for HIV-1.

Original Phase 2b Study Design



BIC/FTC/TAF, bictegravir/emtricitabine/tenofovir alafenamide. HBV, hepatitis B virus. HCV, hepatitis C virus. ISL, islatravir. NNRTI, non-nucleoside reverse transcriptase inhibitor. QD, once daily. QW, once weekly. ULO, ulonivirine.

New ART: Islatravir + Ulonivirine

A Double-Blind, Active-Controlled, Phase 2b Study to Evaluate the Efficacy and Safety of Ulonivirine in Combination With Islatravir in Virologically Suppressed Adults Living With HIV-1

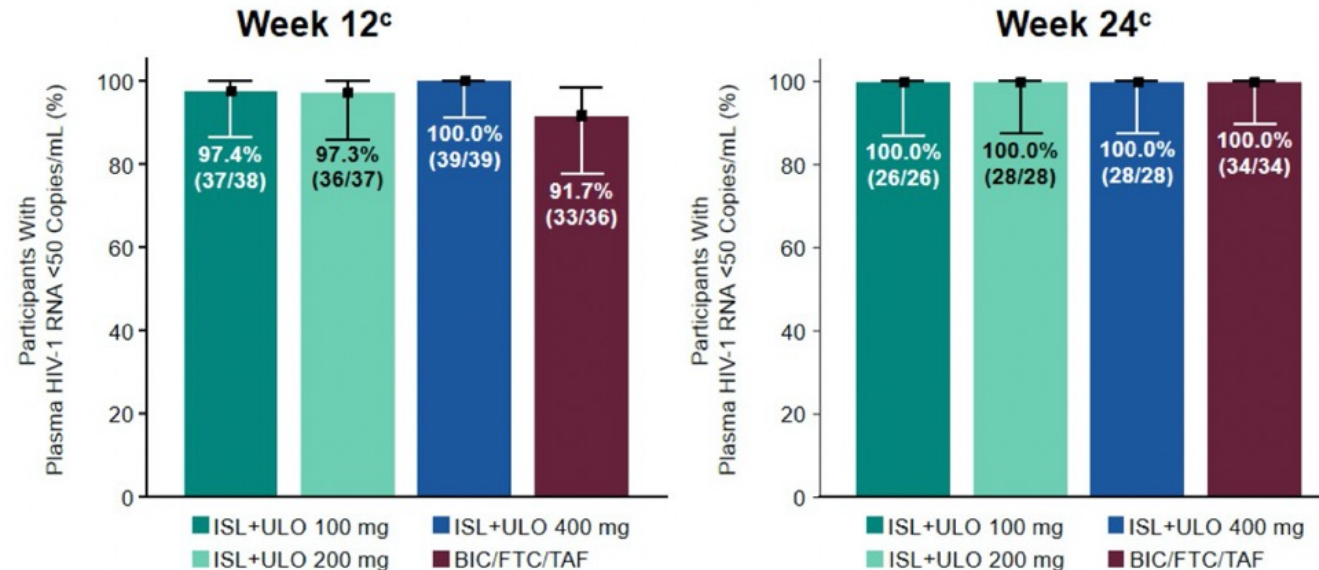
IAS 2025 July 13-17 Rwanda

Molina J-M, Ramgopal MN, Katlama C, Cunningham DL, Hagins DP, Braun DL, Osiyemi OO, Hofmann E, Dietz CA, Lin G, Beckey K, Rawlins S, Matthews RP, Greaves W

Virologic Suppression Was Maintained in All ISL+ULO Arms^a

There were no confirmed virologic failures^b in any treatment arm

All data are observed data



^aPercentage values with 95% confidence intervals. Based on available data for participants receiving double-blind study intervention at the respective timepoints; numerators and denominators exclude participants with missing data. ^bDefined as two consecutive (2-4 weeks apart) confirmed occurrences of HIV-1 RNA ≥ 200 copies/mL at any time during the study. ^cWeek 12 was prespecified as measurements taken between days 71 through 98 and Week 24 as measurements taken between day 127 through 210, both relative to the first day of double-blind study intervention (i.e., day 1).

New ART: Islatravir + Ulonivirine

A Double-Blind, Active-Controlled, Phase 2b Study to Evaluate the Efficacy and Safety of Ulonivirine in Combination With Islatravir in Virologically Suppressed Adults Living With HIV-1

IAS 2025 July 13-17 Rwanda

Molina J-M, Ramgopal MN, Katlama C, Cunningham DL, Hagins DP, Braun DL, Osiyemi OO, Hofmann E, Dietz CA, Lin G, Beckey K, Rawlins S, Matthews RP, Greaves W

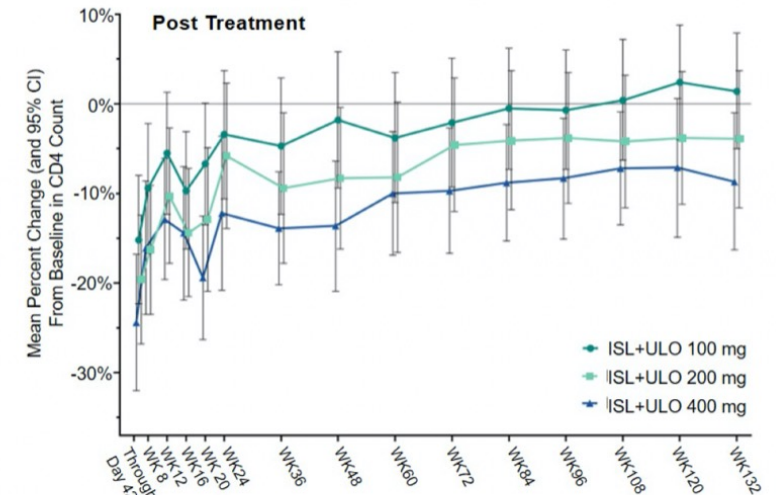
AE Profile Was Comparable to BIC/FTC/TAF (Double-blind Phase Through 42 Days Follow-up)

n (%) participants	ISL+ULO 100 mg N = 40	ISL+ULO 200 mg N = 41	ISL+ULO 400 mg N = 40	BIC/FTC/TAF N = 40
One or more AEs	30 (75.0%)	31 (75.6%)	32 (80.0%)	27 (67.5%)
Toxicity grade 3-4 AEs	2 (5.0%)	6 (14.6%)	3 (7.5%)	1 (2.5%)
Serious AEs	2 (5.0%)	3 (7.3%)	1 (2.5%)	0 (0.0%)
Discontinued due AEs	0 (0.0%)	2 ^a (4.9%)	1 ^b (2.5%)	0 (0.0%)
Drug-related ^c AEs	5 (12.5%)	10 (24.4%)	6 (15.0%)	4 (10.0%)
Discontinued due to drug-related ^c AEs	0 (0.0%)	2 ^a (4.9%)	1 ^b (2.5%)	0 (0.0%)

- Most frequently reported (>5%) AEs with ISL+ULO: COVID-19 (11.6%), fatigue (9.9%), diarrhea (8.3%), headache (8.3%), nausea (6.6%), accidental overdose^d (6.6%)
- Most frequently reported (>5%) AEs with BIC/FTC/TAF: accidental overdose (12.5%), COVID-19 (7.5%), nasopharyngitis (7.5%)

CD4 Count Recovery Towards Baseline Was Observed After Stopping ISL+ULO

- On-treatment declines in total lymphocyte and CD4 counts were observed in all ISL+ULO arms by 8-12 weeks¹
- Longer-term follow-up through Week 132 after stopping ISL+ULO demonstrated that the decreases in total lymphocyte and CD4 counts were generally reversible



CI, confidence interval. WK, week of safety follow-up monitoring phase.

¹Squires K, et al. CROI 2023. Oral abstract 192.

The 'post-treatment' period includes all measurements obtained at follow-up visits that occurred 42 days after the last dose of double-blind study intervention. For missing post-treatment data, the last post-treatment measurement prior to the missing measurement was carried forward to the timepoint(s) with missing data.

New ART: Ulonivirine

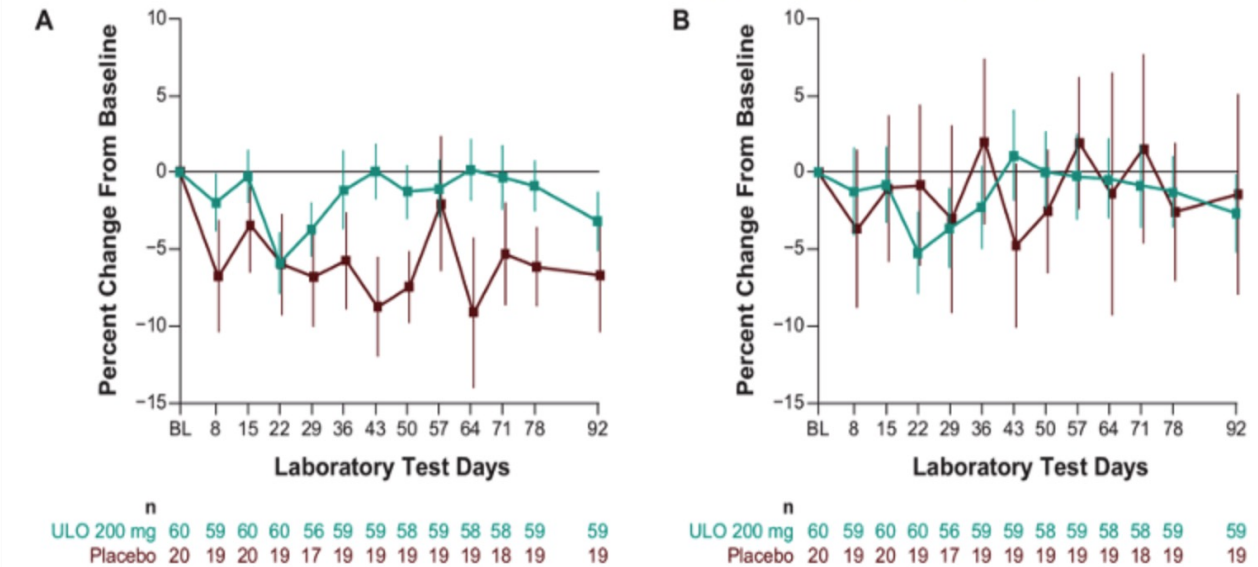
A Double-Blind, Placebo-Controlled, Phase 1 Study to Evaluate Extended Multiple Dosing of Ulonivirine (MK-8507) in Adults Without HIV

Table 1. Participant demographics and baseline characteristics

	ULO 200 mg n = 60	Placebo n = 20	Total N = 80
Female, n (%)	24 (40.0)	9 (45.0)	33 (41.3)
Age, median (range), years	33.5 (20-55)	33.5 (20-55)	33.5 (20-55)
Race, n (%)			
Asian	0	2 (10.0)	2 (2.5)
Black or African American	2 (3.3)	0	2 (2.5)
White	58 (96.7)	18 (90.0)	76 (95.0)
Ethnicity, n (%)			
Not Hispanic or Latinx	60 (100.0)	20 (100.0)	80 (100.0)
Weight, median (range), kg	74.4 (51.0-100.0)	72.2 (48.0-92.0)	74.4 (48.0-100.0)
BMI, median (range), kg/m ²	25.0 (18.9-30.2)	24.6 (18.7-28.4)	24.9 (18.7-30.2)

BMI, body mass index; ULO, ulonivirine.

Figure 2. Mean percent change ($\pm$ SE) from baseline for (A) total lymphocyte count and (B) CD4+ T-cell count after administration of 12 QW doses of ULO 200 mg (n = 60) or placebo (n = 20)



BL, baseline; QW, once weekly; SE, standard error; ULO, ulonivirine.

New ART: Islatravir + Ulonivirine

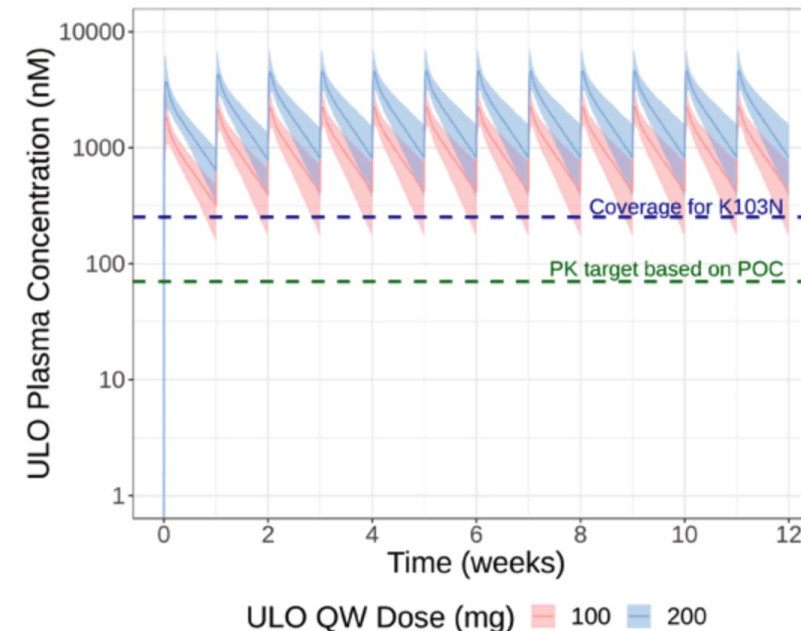
Phase 2 Once-Weekly Dose Optimization for Ulonivirine in Combination with Islatravir 2 mg

IAS 2025, the 13th IAS conference on HIV Science

Michelle Pham*, Gillian Gillespie, Tracy L. Diamond, Stephanie Klopfer, Randolph P. Matthews, Martin Johnson#, Ryan Vargo
Merck & Co., Inc., Rahway, NJ, USA

- Ulonivirine (ULO, MK-8507), an oral nonnucleoside reverse transcriptase inhibitor (NNRTI), is being assessed in combination with islatravir (ISL), an investigational nucleoside reverse transcriptase translocation inhibitor (NRTTI), as a once-weekly (QW) treatment for HIV-1
- Simulation of Phase 2 study of once weekly ISL and ULO.

Figure 2. Predicted ULO Concentrations Following ULO 100mg and 200mg QW Dosing



Solid lines: median predicted concentration;
Colored ribbons: 80% individual prediction interval;
ULO – ulonivirine; QW – once-weekly; PK – pharmacokinetic; POC – proof-of-concept

Rajesh Gandhi, MD
Massachusetts General Hospital

State of the ART Symposium

Antiretroviral Therapy (ART): What's Next



Weekly Oral Dosing

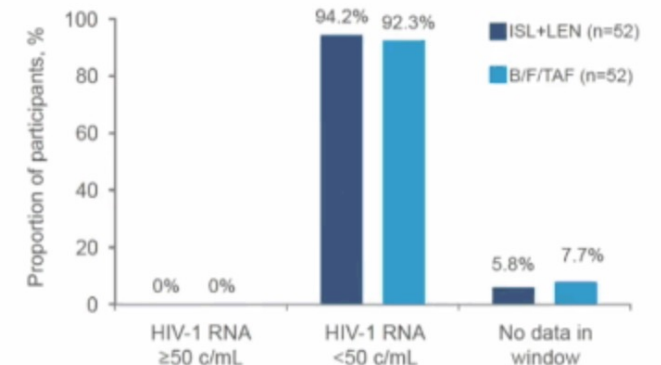
Switching to Oral Weekly Islatravir (ISL) + Lenacapavir (LEN) in Virologically Suppressed PWH

- PK of ISL and LEN support once weekly dosing
- Phase 2: switching virologically suppressed PWH to BIC/FTC/TAF daily or oral ISL 2 mg + oral LEN 300 mg weekly
- >90%: continued HIV suppression
- No differences in lymphocyte, CD4 counts

Phase 3: ISLEND-1 and -2
ISL/LEN (2 mg/300 mg): one tablet per week
(enrollment complete; results likely in 2026)

<https://clinicaltrials.gov/study/NCT06630286>

Week 48 HIV RNA results



Why we need
new ART

New drugs

How will use
new drugs?

Slide 10

Colson A, et al. ID Week 2024. Abstract 577.

Rajesh Gandhi, MD
Massachusetts General Hospital

State of the ART Symposium

Antiretroviral Therapy (ART): What's Next

Long-Acting Investigational Agents



- **MK-8527 (Nucleoside reverse transcriptase translocation inhibitor, NRTTI)**
 - Being studied for monthly oral pre-exposure prophylaxis (PrEP)
 - Phase 2 data (n=350): similar safety profile as placebo
 - Phase 3 clinical trials (EXPrESSIVE) starting soon
- **Cabotegravir (CAB) Ultra-long acting (ULA) (Integrase inhibitor). Phase 2**
 - Every 4-month intramuscular (IM) dosing
 - Being evaluated for PrEP (EXTEND 4 M; results expected in 3rd quarter 2026)
 - CAB ULA + RPV every 4 months for treatment trial planned
- **Islatravir Prodrug, GS 1614 (in combination with lenacapavir)**
 - GS 1614: Every 3 months dosing



Mayer K et al, IAS 2025 (Kigali), OAS0106LB
<https://www.merck.com/news/merck-to-initiate-phase-3-trials-for-investigational-once-monthly-hiv-prevention-pill/>
Han, et al. CROI 2024, Oral presentation 120
NCT06741397; NCT05418868; NCT06786520

Why we need
new ART

New drugs

How will use
new drugs?

Rajesh Gandhi, MD
Massachusetts General Hospital

State of the ART Symposium

Antiretroviral Therapy (ART): What's Next

Long-Acting Investigational Agents

- **VH-499: Capsid inhibitor**

- Treatment naïve PWH (oral dosing): mean maximum 2.2 log reduction in HIV RNA
- 1 out of 20 participants developed emergent capsid inhibitor mutation (Q67Q/H)
- Long-acting injectable formulations: phase 1 studies
- Also being developed for treatment

- **VH-184: Third generation integrase inhibitor**

- Active in vitro against HIV resistant to dolutegravir
- Treatment naïve PWH (oral dosing): HIV RNA declines >2 log
- Long-acting injectable formulations being evaluated in adults without HIV (phase 1)
- Also being developed for treatment

Why we need
new ART

New drugs

How will use
new drugs?

Griesel R et al, CROI 2025, Abstract 153. Rogg L et al, CROI 2025, Abstract 152. NCT06310551

Rajesh Gandhi, MD
Massachusetts General Hospital

State of the ART Symposium

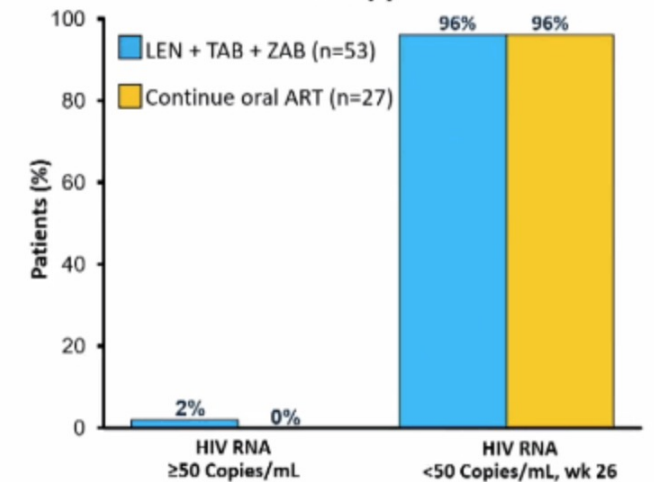
Antiretroviral Therapy (ART): What's Next



Every 6-month Dosing

- Broadly neutralizing antibodies (bNAb):
 - Lenacapavir (capsid inhibitor) + 2 bNAb, Teropavimab (TAB), Zinlirvimab (ZAB): Phase 2
 - 1 participant: virologic failure, LEN resistance, loss of ZAB susceptibility; Low LEN levels
 - Phase 3 trial planning in progress
 - N6LS every 6 months plus CAB LA every 2 months (EMBRACE part 2; enrolling)

PWH with virologic suppression who switched to LEN, TAB and ZAB or continued daily oral therapy



Ogbuagu O et al, CROI 2025, Abstract 151.

Why we need
new ART

New drugs

How will use
new drugs?

Rajesh Gandhi, MD
Massachusetts General Hospital

State of the ART Symposium

Antiretroviral Therapy (ART): What's Next

Every 12-month Dosing Lenacapavir in People without HIV



- Formulations with 5 or 10% ethanol.
- Intramuscular (IM) injection
- Dose, volume higher than every 6-month approved dose (5000 mg vs. 927 mg) → achieved high trough levels
- Phase 3 single arm trial with 3000 mg LEN IM (PURPOSE-365). n=300. (not yet recruiting)

Jogiraju V et al, Lancet 2025;
<https://clinicaltrials.gov/study/NCT07047716?aggFilters=phase:4%203,studyType:int>

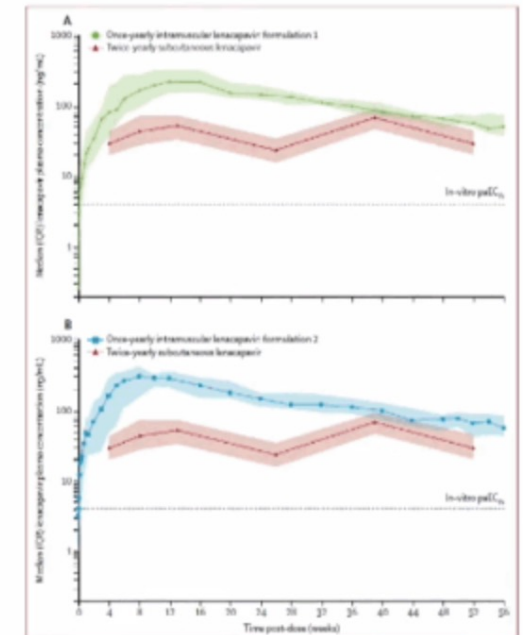


Figure 1: Median (PQ) plasma concentration-time profiles of once-yearly intramuscular lenacapavir versus twice-yearly subcutaneous lenacapavir for formulation 1 (A) and formulation 2 (B)

Why we need
new ART

New drugs

How will use
new drugs?



IAS 2025

Prevention

HIV PrEP – Long-Acting CAB in Practice

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

13th IAS Conference on HIV Science; July 13-17, 2025; Kigali, Rwanda

Aimee A. Metzner,¹ Gabrielle Herman,¹ Shana Walko,¹ Dora Martinez,¹ Catherine Nguyen,² Raj Desai,³ Sherry Shi,⁴ Leili Young-Xu,³ Maral DerSarkissian²
¹ViiV Healthcare, Durham, NC, USA; ²Analysis Group, Inc, Los Angeles, CA, USA; ³Analysis Group, Inc, Boston, MA, USA; ⁴Groupe d'analyse, Ltée, Montréal, Canada

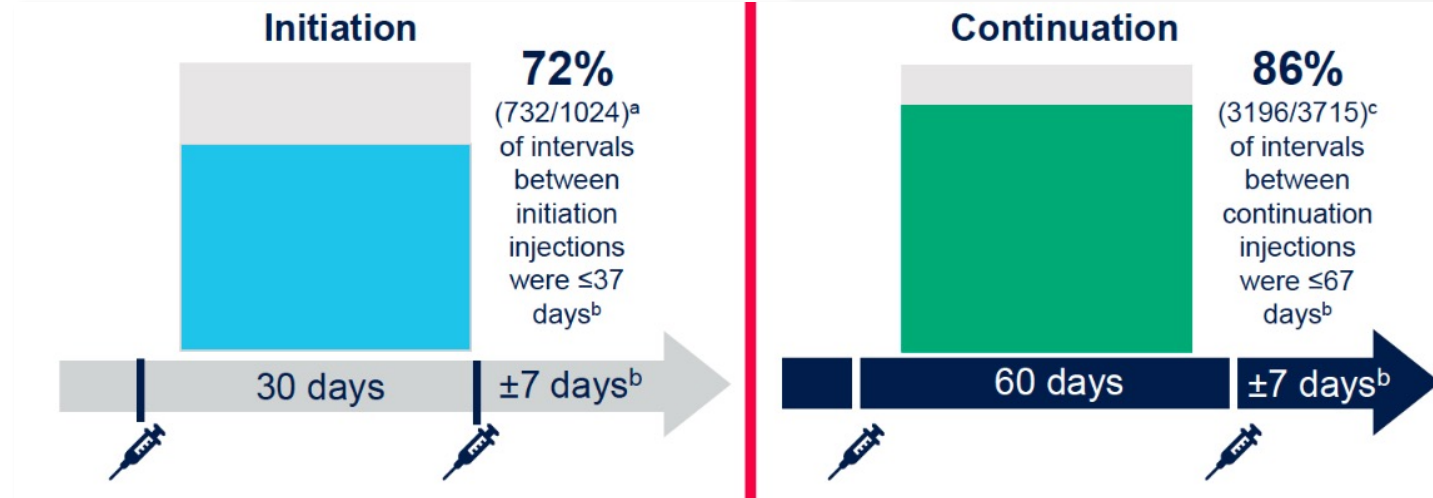
Results

Demographic Characteristics

- PrEPFACTS included 1202 individuals utilizing 3 main insurance types (commercial, 59%; Medicare, 4%; Medicaid, 37%) (Table)
- Most individuals were male (83%; recorded by payer) and mostly White (31%), Black or African American (22%), and Hispanic or Latin American (18%)

CAB LA Utilization

- Eligible individuals had a median (IQR) follow-up of 325 (242-423) days and 85% received >1 CAB LA injection
- Most intervals between continuation injections were within 90 days (96%), the majority of which were within 67 days (86%; Figure 3)
- The majority of intervals between initiation injections were within 37 days (72%)



HIV PrEP – Long-Acting CAB in Practice

Characteristics of early non-persistors on Cabotegravir long-acting (injectable PrEP) compared to persistent users in the PrEPared to Choose study, Cape Town, South Africa.

IAS 2025 Kigali, Rwanda | July 2025

Pike C, Lebelo K, Rousseau, E. Macdonald Mapukata Vanto O, Bekker LG. Desmond Tutu Health Foundation, Cape Town, South Africa.

METHODS

PrEPared to Choose (PtC), a phase 3B clinical trial, tracked uptake and persistence of three PrEP products

- ❖ daily oral PrEP
- ❖ monthly intra-vaginal DapiRing
- ❖ injectable PrEP – 8 weekly CAB LA

amongst 1164 South African adolescents and young people (age ≥ 15 years) via a nurse-driven, integrated sexual and reproductive health (SRH) service from two community-based sites (mobile clinic; government clinic) in Cape Town, South Africa.

Real world simulation of PrEP choice

- Free of charge PrEP service → no research-related reimbursement (*one of the first real-world implementation studies to simulate standard of care*).
- Non-randomised cohort: free, supported choice between the three PrEP products
 - Unlimited option to switch products at any future study visit.
 - Structured, comprehensive choice counselling at baseline with an HIV counsellor (30-minute session supported by a self-administered PrEP quiz and PrEP readiness assessment). *Pike et al., HIVR4P 2024 poster TUPE092.*

Who were the PrEPared to Choose participants?

- 1164 participants enrolled between February and August 2024 (70% **mobile clinic**; 30% community health clinic).
- Baseline **injectable PrEP** uptake (74%) exceeded that of shorter-acting agents (**oral PrEP** 25%; **DapiRing** 1%).
- Participants were predominantly **young women** (67%, 779/1164) and **PrEP inexperienced** (59%, 691/1164).
- PrEP product preference was most influenced by **compatibility with lifestyle**. $\geq 80\%$ reported high product interest and high confidence in ability to use it as intended.

HIV PrEP – Long-Acting CAB in Practice

Characteristics of early non-persistors on Cabotegravir long-acting (injectable PrEP) compared to persistent users in the PrEPared to Choose study, Cape Town, South Africa.

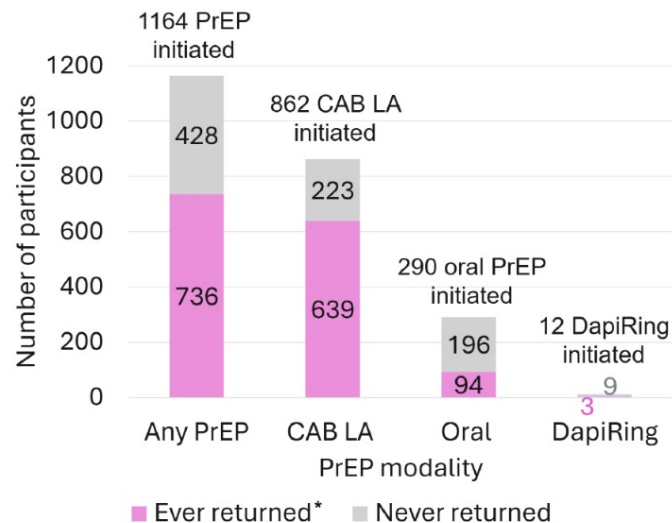
IAS 2025 Kigali, Rwanda | July 2025

Pike C, Lebelo K, Rousseau, E. Macdonald Mapukata Vanto O, Bekker LG. Desmond Tutu Health Foundation, Cape Town, South Africa.

Over a third (37%) of 1164 PrEP initiated participants did not return after the first visit.

26% of CAB LA initiators, **68%** of oral PrEP initiators, and **75%** of DapiRing initiators did not return for subsequent PrEP visits.

The odds of CAB LA initiators ever returning was **6.06 (95% CI: 4.55; 8.06)** compared to initiators on shorter acting agents (oral PrEP or DapiRing).



11% of CAB LA initiators that ever returned, returned >28 days from their scheduled visit and were required to restart the CAB-LA regimen.

CAB LA user characteristics associated with an increased probability of return:

CAB LA initiating participants were more likely to ever return if they had these characteristics compared to never returned CAB LA initiators:

- **Age:** Older participants, >19 years were 50% more likely to ever return (OR 1.5, CI 1.09-2.30).
- **PrEP experience:** Participants with prior PrEP experience (OR 2.4, CI 1.53-4.09) were more likely to ever return.
- **Prior PrEP disclosure:** Participants that had disclosed their PrEP use (OR 2.59, CI 1.48-3.69) were more likely to ever return.
- **Location of PrEP access:** Participants that accessed PrEP from the mobile clinic were 42% more likely to ever return (OR 1.42, CI 1.04-1.95).

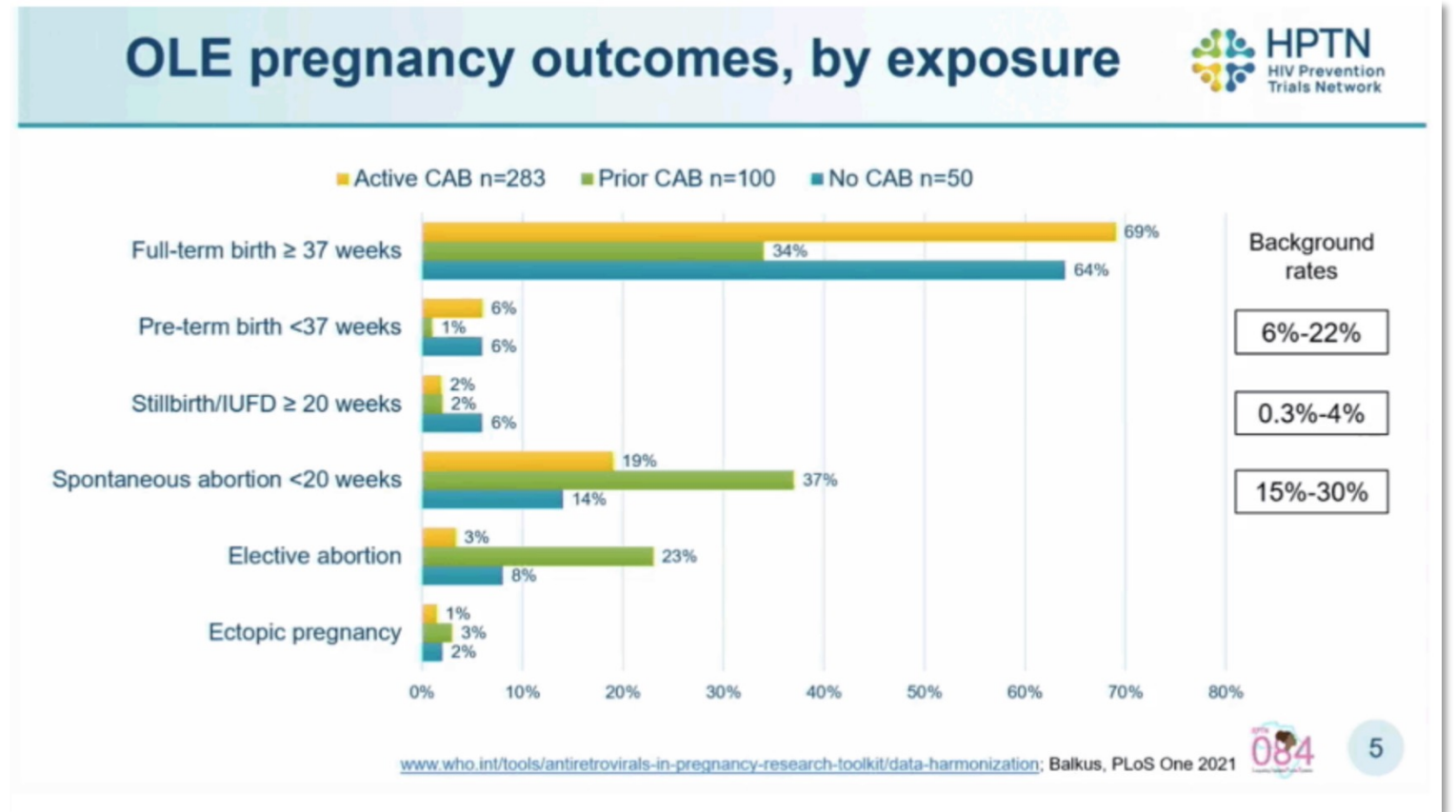
HIV PrEP – Long-Acting CAB in Pregnancy



HPTN 084
Long-acting Injectable For the Epidemic

Updates on the evaluation of CAB-LA safety during pregnancy

S Delany-Moretlwe
On behalf of the HPTN 084 study team
IAS 2025, Kigali



HIV PrEP – Long-Acting LEN

The New York Times

Regulators Approve a Twice-Yearly Shot to Prevent H.I.V. Infection

The drug could change the course of the AIDS epidemic. But the Trump administration has gutted the programs that might have paid for it in low-income countries.

Listen to this article · 6:18 min [Learn more](#)

Share full article

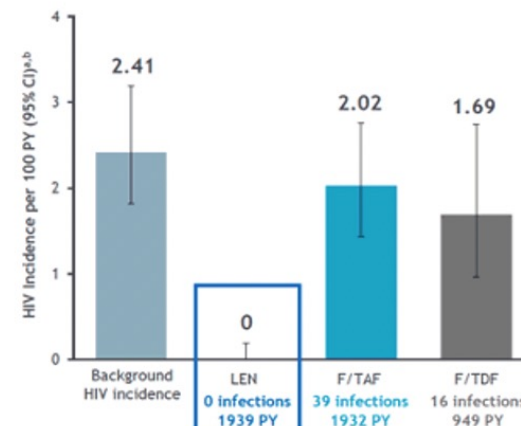


Lenacapavir is already sold as a treatment for H.I.V. infections that are resistant to other medications. Nardus Engelbrecht/Associated Press



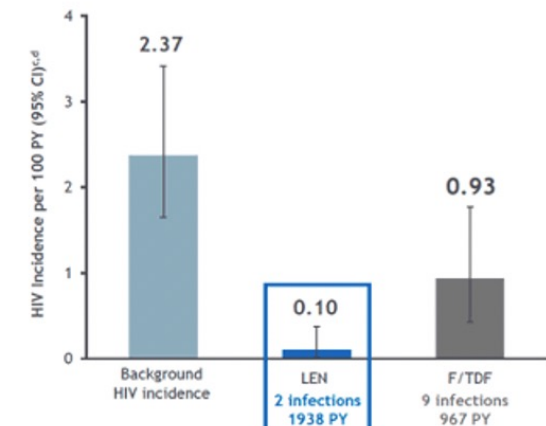
By Apoorva Mandavilli

PURPOSE 1: Zero HIV Infections in Cisgender Women Receiving LEN



Median follow-up duration: 44.0 weeks

PURPOSE 2: Two HIV Infections in Participants Receiving LEN



Median follow-up duration: 39.4 weeks

^aOverall n: background HIV incidence group, 809; LEN, 2134; F/TAF, 2136; F/TDF, 1068. ^b95% CI: background HIV incidence group, 1.62-3.19; LEN, 0-0.19; F/TAF, 1.44-2.76; F/TDF, 0.96-2.74. ^cOverall n: background HIV incidence group, 4634; LEN, 2179; F/TDF, 1086. PY, person-years.

HIV PrEP – Long-Acting LEN

The New York Times

Regulators Approve a Twice-Yearly Shot to Prevent H.I.V. Infection

The drug could change the course of the AIDS epidemic. But the Trump administration has gutted the programs that might have paid for it in low-income countries.

Listen to this article · 6:18 min [Learn more](#) [Share full article](#)

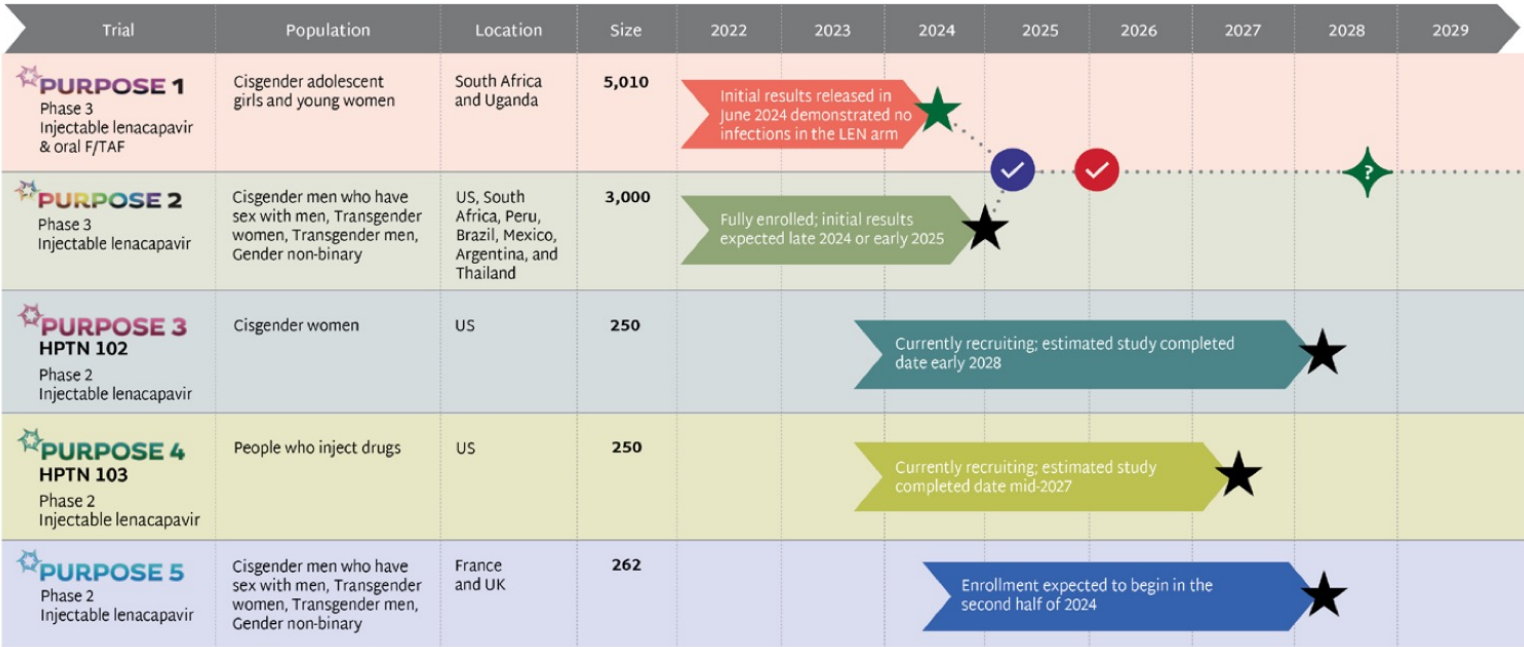


Lenacapavir is already sold as a treatment for H.I.V. infections that are resistant to other medications. Nardus Engelbrecht/Associated Press

 By Apoorva Mandavilli

Overview of Lenacapavir (LEN) for PrEP Trials

- ★ Initial data
- ★ Possible data
- ✓ Possible earliest regulatory submissions
- ✓ Possible earliest regulatory approval and market entry with product from Gilead
- ◆ Possible earliest generic manufacturer(s)



HIV PrEP – Long-Acting LEN

The New York Times

Regulators Approve a Twice-Yearly Shot to Prevent H.I.V. Infection

The drug could change the course of the AIDS epidemic. But the Trump administration has gutted the programs that might have paid for it in low-income countries.

Listen to this article · 6:18 min [Learn more](#)

[Share full article](#)



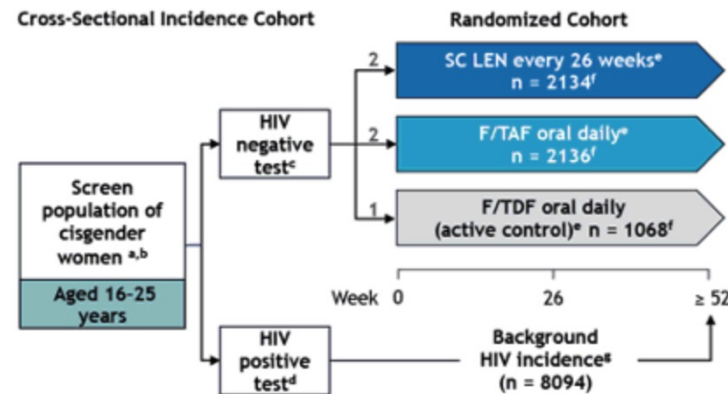
Lenacapavir is already sold as a treatment for H.I.V. infections that are resistant to other medications. Nardus Engelbrecht/Associated Press



By Apoorva Mandavilli

PURPOSE 1 and 2 Study Designs

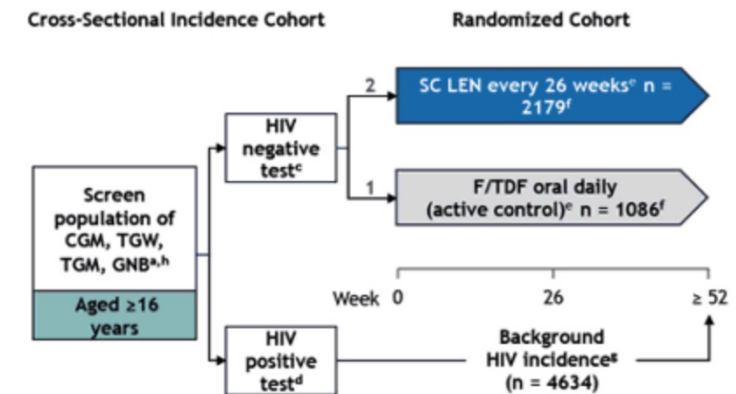
PURPOSE 1



ClinicalTrials.gov: NCT04994509

^aNot receiving PrEP and without HIV testing in past 3 months; ^bThe 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; ^cParticipants also met eligibility criteria (including weight ≥ 35 kg, eGFR ≥ 60 mL/min, not pregnant); ^dRecency assay data were used to estimate background HIV incidence (persons testing HIV positive were referred to HIV care); ^ePlus the alternative SC/oral placebo; ^fn numbers represent the full analysis set for efficacy analyses; ^gBackground HIV incidence is the incidence expected without PrEP that would have been expected in a placebo group (the counterfactual HIV incidence); ^hThe first participant was screened in June 2021, the 50th percentile participant was randomized in August 2023, and the last participant was randomized in December 2023. CGM, cisgender men; eGFR, estimated glomerular filtration rate; F/TAF^g, emtricitabine/tenofovir alafenamide; F/TDF^g, emtricitabine/tenofovir disoproxil fumarate; GNB^{a,h}, gender-nonbinary; LEN^a, lenacapavir; PrEP, pre-exposure prophylaxis; SC, subcutaneous; TGM, transgender men; TGW, transgender women.

PURPOSE 2



ClinicalTrials.gov: NCT04925752

HIV PrEP – Long-Acting LEN in Pregnancy



Pregnancy with PURPOSE

Inclusion with intention in the PURPOSE 1 trial of lenacapavir for PrEP

Moupali Das, MD, MPH
Vice President, HIV Prevention and Virology Pediatrics
Gilead Sciences
www.purposestudies.com

PURPOSE 1 Pregnancies Were Common and Outcomes Similar to Expected Rates in the Population

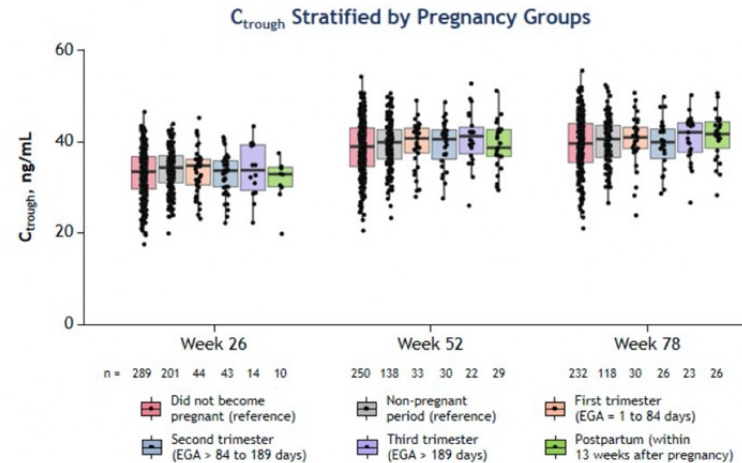
Participants and Pregnancies, n (%)	LEN n = 2138	F/TAF n = 2137	F/TDF n = 1070
Participants with confirmed pregnancies	184	208	95
Confirmed pregnancies	193	219	98
Completed pregnancies	105 (54.4)	119 (54.3)	53 (54.1)
Ongoing pregnancies	88 (45.6)	100 (45.7)	45 (45.9)
Births ^a	55 (28.5)	45 (20.5)	21 (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:^{1,2}

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

Available pregnancy outcomes were similar to those expected for the population³

PURPOSE 1 Efficacy, Safety, and PK Support LEN Use in Pregnancy and During Breastfeeding



- LEN is efficacious, safe, and well-tolerated during pregnancy and postpartum
- ZERO HIV infections among 184 participants with 193 pregnancies on LEN
- Pregnancy outcomes similar to regional background rates¹⁻⁴
- LEN safety similar in pregnant and non-pregnant people
- No dose adjustment required for pregnancy or post-partum⁵
- Minimal infant exposure through breastmilk

Intentional inclusion of pregnant and lactating people provided data to guide use in these vulnerable populations at the time of LEN for PrEP approval

HIV PrEP – Long-Acting LEN in Adolescents

PURPOSE
Prevention with PURPOSE

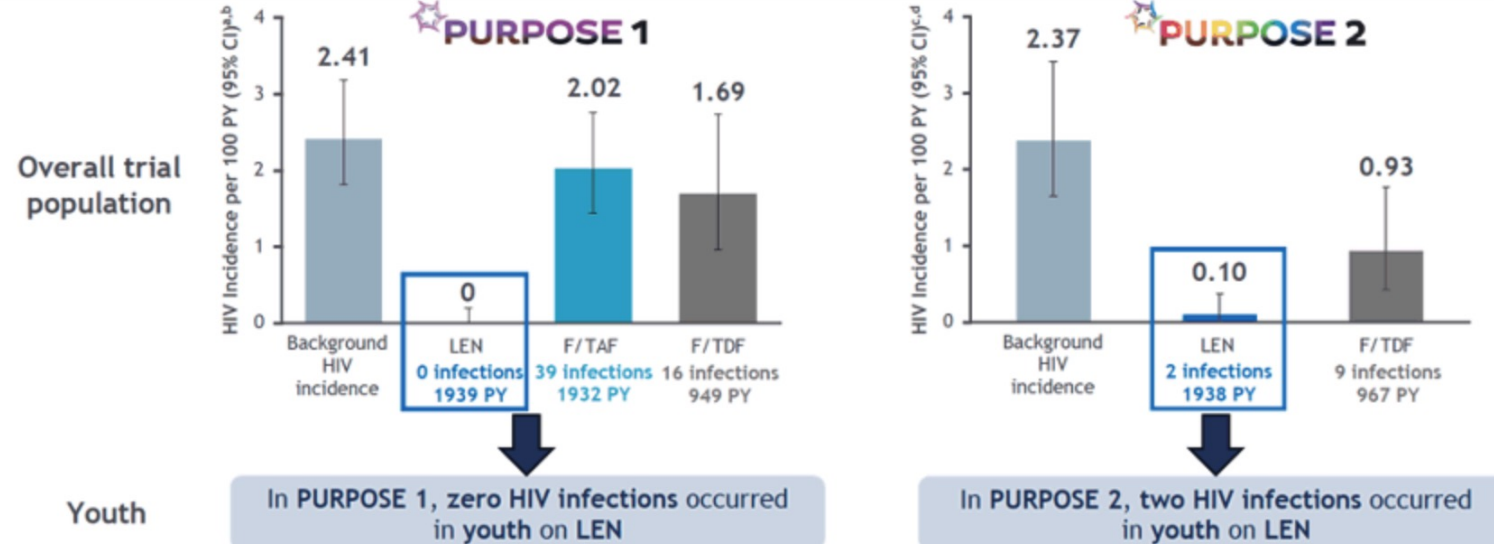
Efficacy, Safety, and Pharmacokinetics of Twice-Yearly Subcutaneous Lenacapavir for PrEP Among Adolescents and Young People in the Phase 3 Trials PURPOSE 1 and PURPOSE 2

Katherine Gill¹, Quarraisha Abdool Karim², Suvaporn Anugulruengkitt³, Linda-Gail Bekker¹, Jorge A Gallardo-Cartagena⁴, Aditya Gaur⁵, Mmatsie Manentsa⁶, Megeshinee Naidoo², Disebo Potloane², Yashna Singh¹, Alexander Kintu⁷, Pamela Wong⁷, Yang Zhao⁷, Priyanka Arora⁷, Renu Singh⁷, Lillian B Brown⁷, Christoph C Carter⁷, Moupali Das⁷, Allison Agwu⁸

¹The Desmond Tutu HIV Centre, University of Cape Town, Cape Town, South Africa; ²Centre for the AIDS Programme of Research in South Africa, University of KwaZulu-Natal, Durban, South Africa; ³Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand; ⁴Centro de Investigaciones Tecnológicas, Biomédicas y Medioambientales, Universidad Nacional Mayor de San Marcos, Lima, Peru; ⁵St. Jude Children's Research Hospital, Memphis, TN, USA; ⁶The Aurum Institute, Johannesburg, South Africa; ⁷Grifed Sciences, Inc., Foster City, CA, USA; ⁸Division of Infectious Diseases, Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD, USA

13th International AIDS Society (IAS) Conference on HIV Science; July 13-17, 2025; Kigali, Rwanda

Only Two HIV Infections in Youth on LEN From PURPOSE 1 and 2



LEN demonstrated efficacy for HIV prevention in youth^{1,2}

^aOverall n: background HIV incidence group, 8094; LEN, 2134; F/TAF, 2136; F/TDF, 1068. ^b95% CI: background HIV incidence group, 1.82-3.19; LEN, 0.0-0.19; F/TAF, 1.44-2.76; F/TDF, 0.96-2.74. ^cOverall n: background HIV incidence group, 4634; LEN, 2119; F/TDF, 1066.

^d95% CI: background HIV incidence group, 1.65-3.42; LEN, 0.01-0.37; F/TDF, 0.40-1.77.

CI, confidence interval; F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; LEN, lenacapavir; PY, person-years.

1. Bekker L-G, et al. *N Engl J Med*. 2024;391:1179-92. 2. Kelley CF, et al. *N Engl J Med*. 2025;392:1261-76.

HIV PrEP – Long-Acting LEN Trials: Counterfactual

 **PURPOSE**
Prevention with PURPOSE

 IAS 2025

Estimation of the Counterfactual HIV Incidence in the PURPOSE Trials

Colleen Kelley¹, Flavia Matovu Kiweewa², Onyema Ogbuagu³, Shelley Facente⁴, Eduard Grebe⁵, David V Glidden⁶, Yongwu Shao⁷, Yang Zhao⁷, Stephanie Cox⁷, Alexander Kintu⁷, Lillian B Brown⁷, Christoph C Carter⁷, Moupali Das⁷, Linda-Gail Bekker⁸

¹Division of Infectious Diseases, Emory University School of Medicine and Grady Health System, Atlanta, GA, USA; ²Makere University-Johns Hopkins University Research Collaboration, Kampala, Uganda; ³School of Medicine, Yale University, New Haven, CT, USA; ⁴School of Public Health, University of California, Berkeley, CA, USA; ⁵Vitalant Research Institute, San Francisco, CA, USA; ⁶Department of Epidemiology and Biostatistics, University of California, San Francisco, CA, USA; ⁷Gilead Sciences, Inc., Foster City, CA, USA; ⁸The Desmond Tutu HIV Centre, University of Cape Town, Cape Town, South Africa

13th International AIDS Society (IAS) Conference on HIV Science; July 13-17, 2025; Kigali, Rwanda

Challenges in HIV Prevention Clinical Trial Design

Superiority to placebo

- Placebo use is unethical¹

Superiority to active comparator

- May not be reasonable to assume superiority to the active comparator²

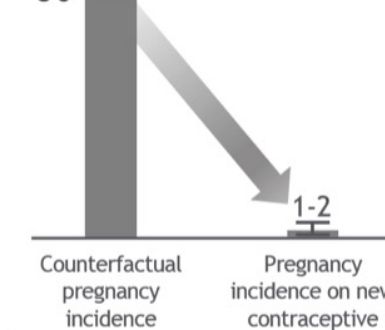
Noninferiority to active comparator

- Large cohort sizes with long duration³
- Infeasible in certain populations¹

Counterfactual incidence is used in contraceptive trials

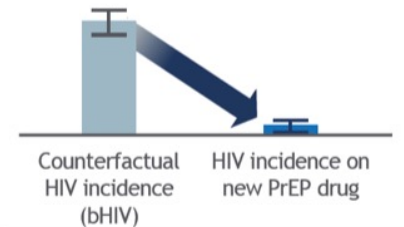
Pearl Index: Pregnancies/100 PY

~80



Counterfactual incidence design was chosen for the PURPOSE trials

Counterfactual bHIV:
HIV infections/100 PY



Counterfactual HIV incidence design was used in the PURPOSE 1 and 2 trials^{4,5} to address these challenges

HIV PrEP – Long-Acting LEN Trials: Counterfactual

 **PURPOSE**
Prevention with PURPOSE

 IAS 2025

Estimation of the Counterfactual HIV Incidence in the PURPOSE Trials

Colleen Kelley¹, Flavia Matovu Kiweewa², Onyema Ogbuagu³, Shelley Facente⁴, Eduard Grebe⁵, David V Glidden⁶, Yongwu Shao⁷, Yang Zhao⁷, Stephanie Cox⁷, Alexander Kintu⁷, Lillian B Brown⁷, Christoph C Carter⁷, Moupali Das⁷, Linda-Gail Bekker⁸

¹Division of Infectious Diseases, Emory University School of Medicine and Grady Health System, Atlanta, GA, USA; ²Makerebe University-Johns Hopkins University Research Collaboration, Kampala, Uganda; ³School of Medicine, Yale University, New Haven, CT, USA; ⁴School of Public Health, University of California, Berkeley, CA, USA; ⁵Vitalant Research Institute, San Francisco, CA, USA; ⁶Department of Epidemiology and Biostatistics, University of California, San Francisco, CA, USA; ⁷Gilead Sciences, Inc., Foster City, CA, USA; ⁸The Desmond Tutu HIV Centre, University of Cape Town, Cape Town, South Africa

13th International AIDS Society (IAS) Conference on HIV Science; July 13-17, 2025; Kigali, Rwanda

Different Methods to Estimate Counterfactual HIV Incidence

HIV incidence from prior clinical trials; run-in cohorts¹

HIV surveillance data²

Rectal gonorrhea-HIV incidence relationship³

Acute HIV infections between screening and baseline⁴

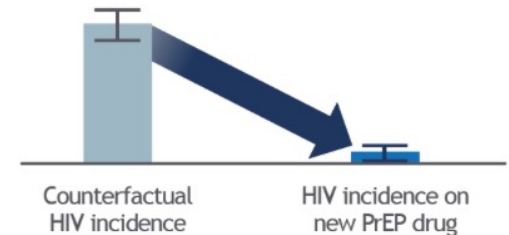
VOICE risk score⁵

F/TDF adherence-efficacy relationship⁴

Recency assay and RITA

Optimal approach to estimating the counterfactual background HIV incidence (bHIV) using a RITA

Counterfactual bHIV:
HIV infections/100 PY



This analysis compares the RITA-estimated bHIV from PURPOSE 1 and PURPOSE 2 primary analyses to the estimated bHIV using alternative RITA parameters and to other counterfactual methods

HIV PrEP – Long-Acting LEN Trials: Counterfactual

 **PURPOSE**
Prevention with PURPOSE

 IAS 2025

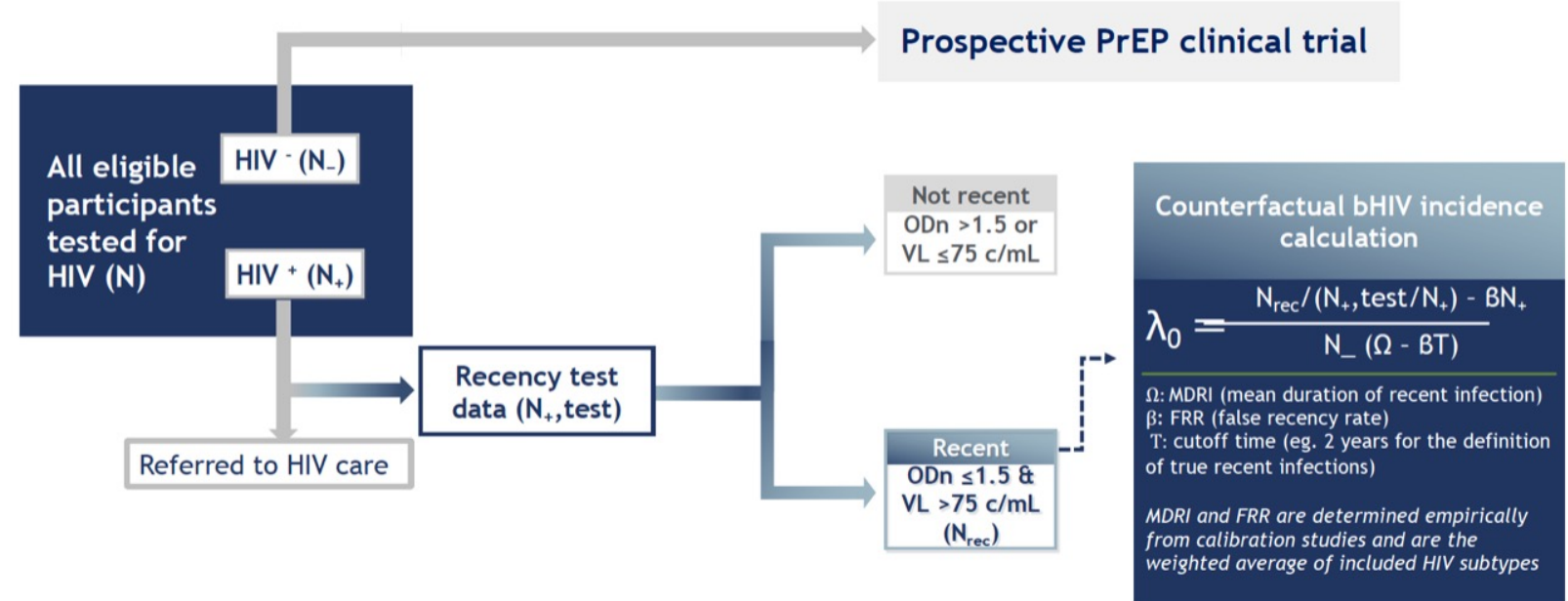
Estimation of the Counterfactual HIV Incidence in the PURPOSE Trials

Colleen Kelley¹, Flavia Matovu Kiweewa², Onyema Ogbuagu³, Shelley Facente⁴, Eduard Grebe⁵, David V Glidden⁶, Yongwu Shao⁷, Yang Zhao⁷, Stephanie Cox⁷, Alexander Kintu⁷, Lillian B Brown⁷, Christoph C Carter⁷, Moupali Das⁷, Linda-Gail Bekker⁸

¹Division of Infectious Diseases, Emory University School of Medicine and Grady Health System, Atlanta, GA, USA; ²Makere University-Johns Hopkins University Research Collaboration, Kampala, Uganda; ³School of Medicine, Yale University, New Haven, CT, USA; ⁴School of Public Health, University of California, Berkeley, CA, USA; ⁵Vitalant Research Institute, San Francisco, CA, USA; ⁶Department of Epidemiology and Biostatistics, University of California, San Francisco, CA, USA; ⁷Gilead Sciences, Inc., Foster City, CA, USA; ⁸The Desmond Tutu HIV Centre, University of Cape Town, Cape Town, South Africa

13th International AIDS Society (IAS) Conference on HIV Science; July 13-17, 2025; Kigali, Rwanda

Applying a RITA to Estimate bHIV in a PrEP Clinical Trial^{1,2}



bHIV, background HIV; c/mL, copies per mL; FRR, false recency rate; MDRI, mean duration of recent infection; ODn, normalized optical density; PrEP, pre-exposure prophylaxis; RITA, recent infection testing algorithm; VL, viral load.

1. Kassanjee R, et al. *Epidemiology*. 2012;23:721-8. 2. Gao F, et al. *Stat Commun Infect Dis*. 2021;13:20200009.

HIV PrEP – New Agents

Safety and Pharmacokinetics of MK-8527 Oral Once-Monthly: A Phase 2 Study in Adults at Low Risk of HIV-1 Exposure, oral

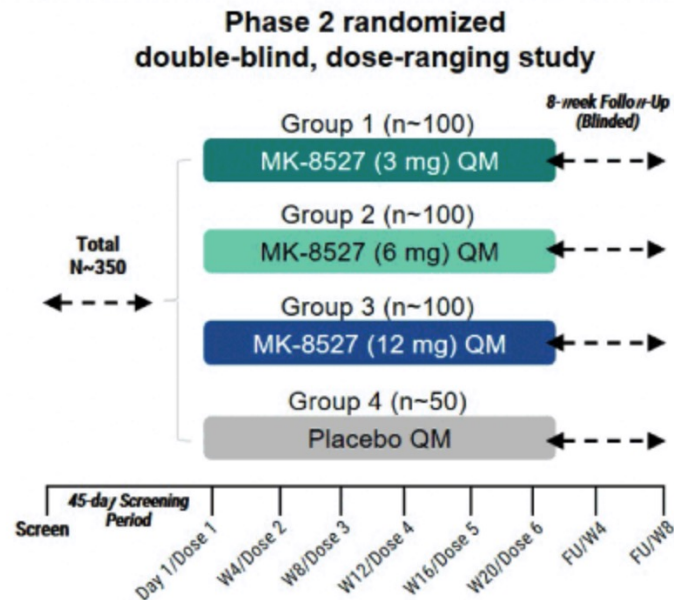
IAS 2025 July 13-17 Rwanda

Mayer K, Kotze P, Lombaard J, Caraco Y, Peer A, Poovan N, Khalsa S, Khetan S, Shapiro AE, Rassool M, Gonzalez A, Singh Y, Sinclair G, Riddler S, Buchbinder S, Vesay M, Homony B, Evans B, Grandhi A, Zhang C, Skataric M, Robertson MN, Kapoor Y, Matthews RP, Plank RM

MK-8527-007 Study Design

Key Inclusion Criteria

- 18-65 years old without HIV
 - Low likelihood of HIV exposure
 - Not pregnant or breastfeeding
 - No prior use of islatravir or MK-8527
- Participants randomized (2:2:2:1) to receive oral monthly doses of MK-8527 (3, 6, or 12 mg) or placebo for up to 6 consecutive months (1 dose every 4 weeks) from Day 1 to Week 20
 - Randomization was stratified by sex (female, male) and region (Africa, non-Africa)
 - The study was conducted in Israel, South Africa, and the United States



Baseline Characteristics

		MK-8527 3 mg N=101	MK-8527 6 mg N=101	MK-8527 12 mg N=99	Placebo N=49
Sex at birth:	Male	43 (42.6)	42 (41.6)	41 (41.4)	20 (40.8)
	Female	58 (57.4)	59 (58.4)	58 (58.6)	29 (59.2)
Age (years), median (IQR)		27.0 (23, 33)	28.0 (24, 34)	28.0 (23, 34)	28.0 (24, 34)
Race:	White	49 (48.5)	54 (53.5)	51 (51.5)	26 (53.1)
	Black	44 (43.6)	40 (39.6)	40 (40.4)	21 (42.9)
	Asian	3 (3.0)	2 (2.0)	3 (3.0)	0 (0.0)
	Other	5 (5.0)	5 (5.0)	5 (5.1)	2 (4.1)
Ethnicity:	Hispanic/Latino	18 (17.8)	13 (12.9)	14 (14.1)	11 (22.4)
Country:	United States	42 (41.6)	48 (47.5)	45 (45.5)	21 (42.9)
	South Africa	35 (34.7)	34 (33.7)	34 (34.3)	16 (32.7)
	Israel	24 (23.8)	19 (18.8)	20 (20.2)	12 (24.5)

HIV PrEP – New Agents

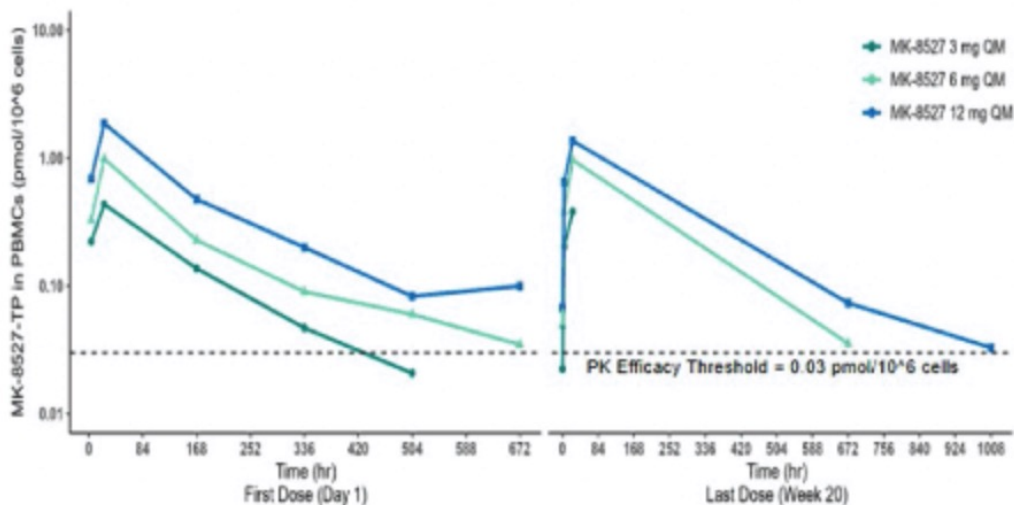
Safety and Pharmacokinetics of MK-8527 Oral Once-Monthly: A Phase 2 Study in Adults at Low Risk of HIV-1 Exposure, oral

IAS 2025 July 13-17 Rwanda

Mayer K, Kotze P, Lombaard J, Caraco Y, Peer A, Poovan N, Khalsa S, Khetan S, Shapiro AE, Rassool M, Gonzalez A, Singh Y, Sinclair G, Riddler S, Buchbinder S, Vesay M, Homony B, Evans B, Grandhi A, Zhang C, Skataric M, Robertson MN, Kapoor Y, Matthews RP, Plank RM

MK-8527-TP in PBMCs

Concentration vs Time Profiles (semi-log scale)



Drug-Related[†] AEs were Similar Across MK-8527 and Placebo Groups

Number (%) of participants	MK-8527 3 mg N=101	MK-8527 6 mg N=101	MK-8527 12 mg N=99	Placebo N=49
with one or more drug-related [†] AE	15 (14.9)	16 (15.8)	20 (20.2)	9 (18.4)
with toxicity grade 3-4 drug-related [†] AE	1 (1.0)	0 (0.0)	1 (1.0)	1 (2.0)
Most common drug-related [†] AEs (>2% in any MK-8527 group)				
Headache	4 (4.0)	5 (5.0)	2 (2.0)	1 (2.0)
Nausea	3 (3.0)	4 (4.0)	2 (2.0)	1 (2.0)
CD4 lymphocytes decreased	2 (2.0)	1 (1.0)	3 (3.0)	1 (2.0)
Lymphocyte count decreased	0 (0.0)	1 (1.0)	4 (4.0)	1 (2.0)
Fatigue	0 (0.0)	3 (3.0)	2 (2.0)	1 (2.0)

[†] Relationship to study drug was determined by the investigator.

- Most drug-related AEs were DAIDS toxicity Grade 1 or 2 and were reported as resolved during the study
- Two participants had confirmed CD4 and/or lymphocyte count declines that met protocol-specified discontinuation criteria, which resolved within 11 weeks
 - MK-8527 6 mg: lymphocyte nadir $0.80 \times 10^9/L$ (36.5% ↓), CD4 nadir 313 cells/mm³ (grade 1; 51.4% ↓)
 - MK-8527 12 mg: lymphocyte nadir $0.61 \times 10^9/L$ (grade 1; 54.1% ↓)

No Meaningful Change in Total Lymphocyte Count or CD4 Count for MK-8527 Doses up to 12 mg oral QM

HIV PrEP – New Agents

Safety and Pharmacokinetics of MK-8527 Oral Once-Monthly: A Phase 2 Study in Adults at Low Risk of HIV-1 Exposure, oral

IAS 2025 July 13-17 Rwanda

Mayer K, Kotze P, Lombaard J, Caraco Y, Peer A, Poovan N, Khalsa S, Khetan S, Shapiro AE, Rassool M, Gonzalez A, Singh Y, Sinclair G, Riddler S, Buchbinder S, Vesay M, Homony B, Evans B, Grandhi A, Zhang C, Skataric M, Robertson MN, Kapoor Y, Matthews RP, Plank RM

MK-8527 Phase 3 Program for PrEP





IAS 2025

Complications/ Aging/ Co-morbidities

Complications – Weight

- What we know for sure:
 - TDF and EFV lead to attenuation of weight gain.
 - Switch from or stopping of these agents leads to a jump in weight
 - PWH starting ART often gain weight
 - Especially if CD4 cell count is low, HIV RNA is high
 - PWH starting BFTAF or ISL/DOR experienced similar weight gain
- What we don't know:
 - Whether or not TAF cause weight gain
 - Whether or not INSTI cause weight gain

Complications – Weight

Predictors of Weight Gain Among People with HIV over 3-Year Period

IAS 2025 July 13-17 Rwanda

Richard A Elion¹, Joshua Gruber², Janna Radtchenko¹, Paul E. Sax³, Megan Dunbar², Joseph J. Eron⁴, Cal Cohen², Grace McComsey⁵



IAS 2025

Data Source and Study Design

- TRIO HIV Research Network Database
 - Electronic medical records (EMR) data from 12 geographically distributed health clinics in the US.
- Retrospective **case-control** design
 - Case: significant weight gain
 - Gain $\geq 10\%$ with concurrent shift to a higher Body Mass index (BMI) category;
 - Gain $\geq 10\%$ among those identified as obese at baseline
 - Control: minimal weight gain
 - Gain $>0\%$ up to $<5\%$.

Methods

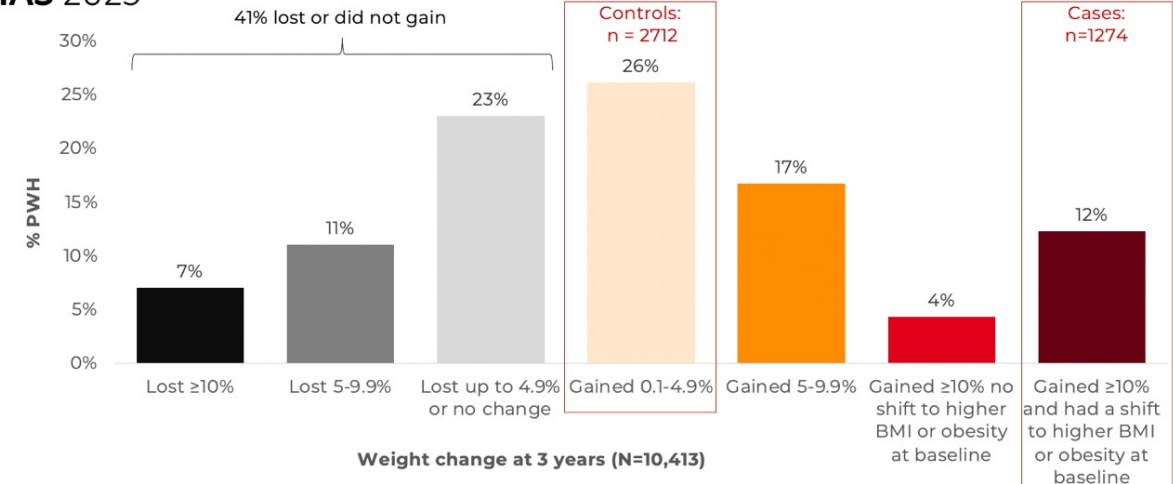
Inclusion Criteria

- Adult people with HIV (age ≥ 18)
- In care between Jan 2015 – Aug 2023
- **Virally suppressed at baseline:**
 - If on first ART, HIV RNA < 200 copies/mL for ≥ 6 mo, ≥ 12 mo since first ART initiation
 - If with ≥ 1 prior regimen, HIV RNA < 200 copies/mL at regimen initiation
- **Virally suppressed at 3 years since baseline** (HIV RNA < 200 copies/mL)
- With weight measurements at baseline and 3 years (± 3 mo)
- No evidence of participation in clinical trial during study period.



IAS 2025

Distribution of Weight Change at 3 Years



Complications – Weight



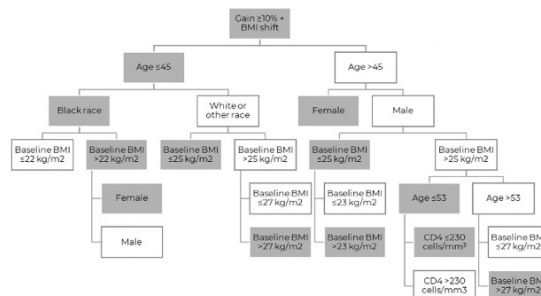
IAS 2025

Key Predictors of Significant Weight Gain: CART

- CART: a **machine learning** approach that creates intuitive decision trees to **predict outcomes** by splitting data into subgroups based on **individual characteristics**.
- Variables associated with significant weight gain ($\geq 10\%$ with BMI shift):
 - baseline BMI
 - younger baseline age
 - female gender
 - Black race
 - lower baseline CD4 count.
- No ART factors were identified as significant predictors of weight gain.**

Key Predictors of Significant Weight Gain

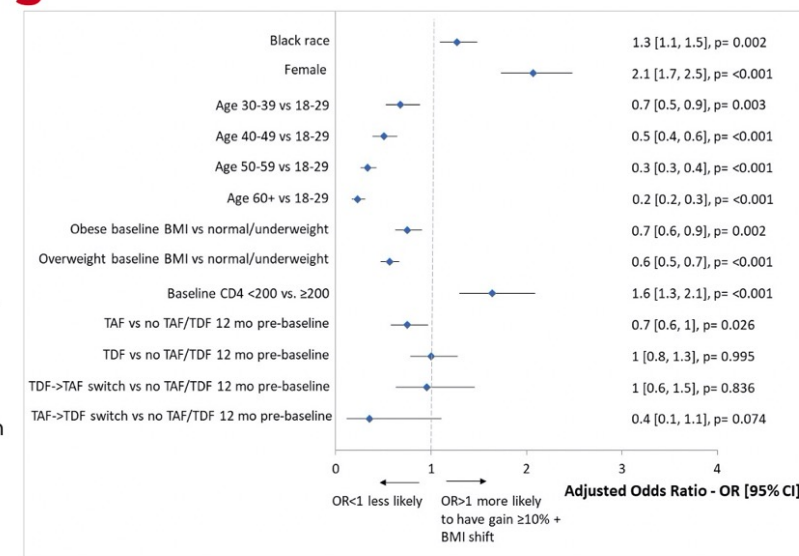
Independent Variable	Importance to the model	Normalized Importance
Baseline BMI	0.015	100%
Age	0.015	99.1%
Gender	0.007	42.5%
Race	0.004	27%
Baseline CD4	0.001	9.2%



IAS 2025

Key Predictors of Significant Weight Gain: Logistic Regression

- Key significant predictors:
 - Black race,
 - female gender,
 - baseline age 18-29,
 - normal baseline BMI,
 - CD4 <200 cells/mm³,
 - no TAF/TDF exposure 12 months pre-baseline (vs. TAF exposure).
- Non-Significant Predictors:**
 - NRTI usage during 3-year observation
 - INSTI, PI, NNRTI usage during 3-year observation or prior to baseline.



Complications – Weight

ACTG A5391: A Randomized Multicenter 3-arm Controlled Trial for People with Obesity on Integrase Inhibitors and Tenofovir Alafenamide switching to Doravirine, with or without Tenofovir Disoproxil Fumarate (The DO-IT Trial)

IAS 2025 July 13-17 Rwanda

John Koethe, MD



IAS 2025

Study Design

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

	Week 0	Week 48
Obese (BMI >30 kg/m ²) persons on RAL, DTG, or BIC + TAF/FTC	Arm 1: Switch to DOR+TAF/FTC	
	Arm 2: Switch to DOR+TDF/FTC	
	Arm 3: Continuation of INSTI+TAF/FTC	



IAS 2025

Results

- From July 2021 to November 2023, 145 participants from 25 sites in the US randomized to DOR+TAF/FTC (n=47), DOR+TDF/FTC (n=49), or to continue their INSTI+TAF/FTC regimen (n=49) initiated study treatment.
- Forty-nine percent were female, 53% Black, and 18% Hispanic/Latino.
- At entry, median age was 49 years; BMI 34.9 kg/m²; waist circumference 111 cm, and CD4⁺ T cell count 688 cells/ μ l.
- Median time on current INSTI+TAF/FTC was 3.4 years; 86% were taking BIC, 13% DTG, and 1% RAL, all with TAF/FTC.
- Sixty-five percent of participants had a $>10\%$ weight gain in the first 1-3 years of INSTI-based ART.

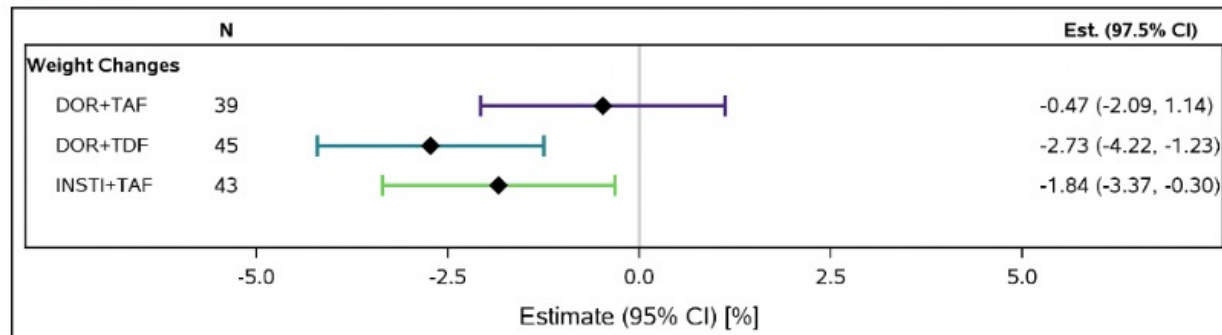
"Median time on current INSTI+TAF/FTC was 3.4 years; 86% were taking BIC, 13% DTG, and 1% RAL, all with TAF/FTC."

Complications – Weight

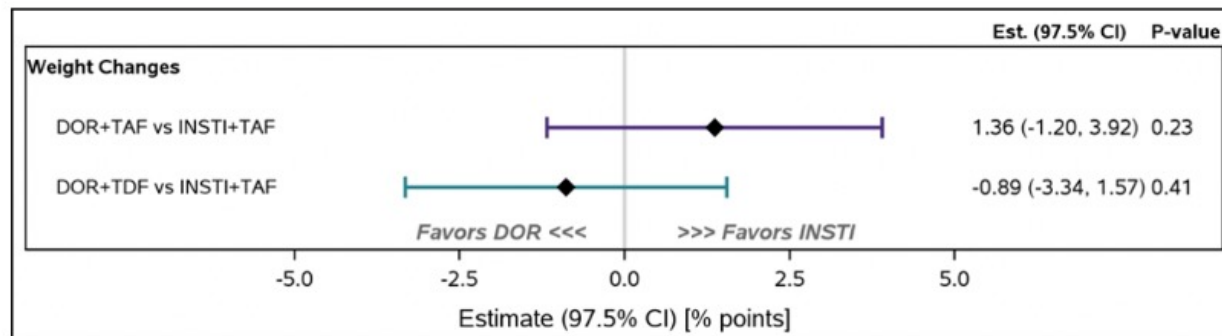


Primary Outcome: Weight Change at 48 Weeks

Within Arm:



Pairwise Treatment Arm Comparisons:



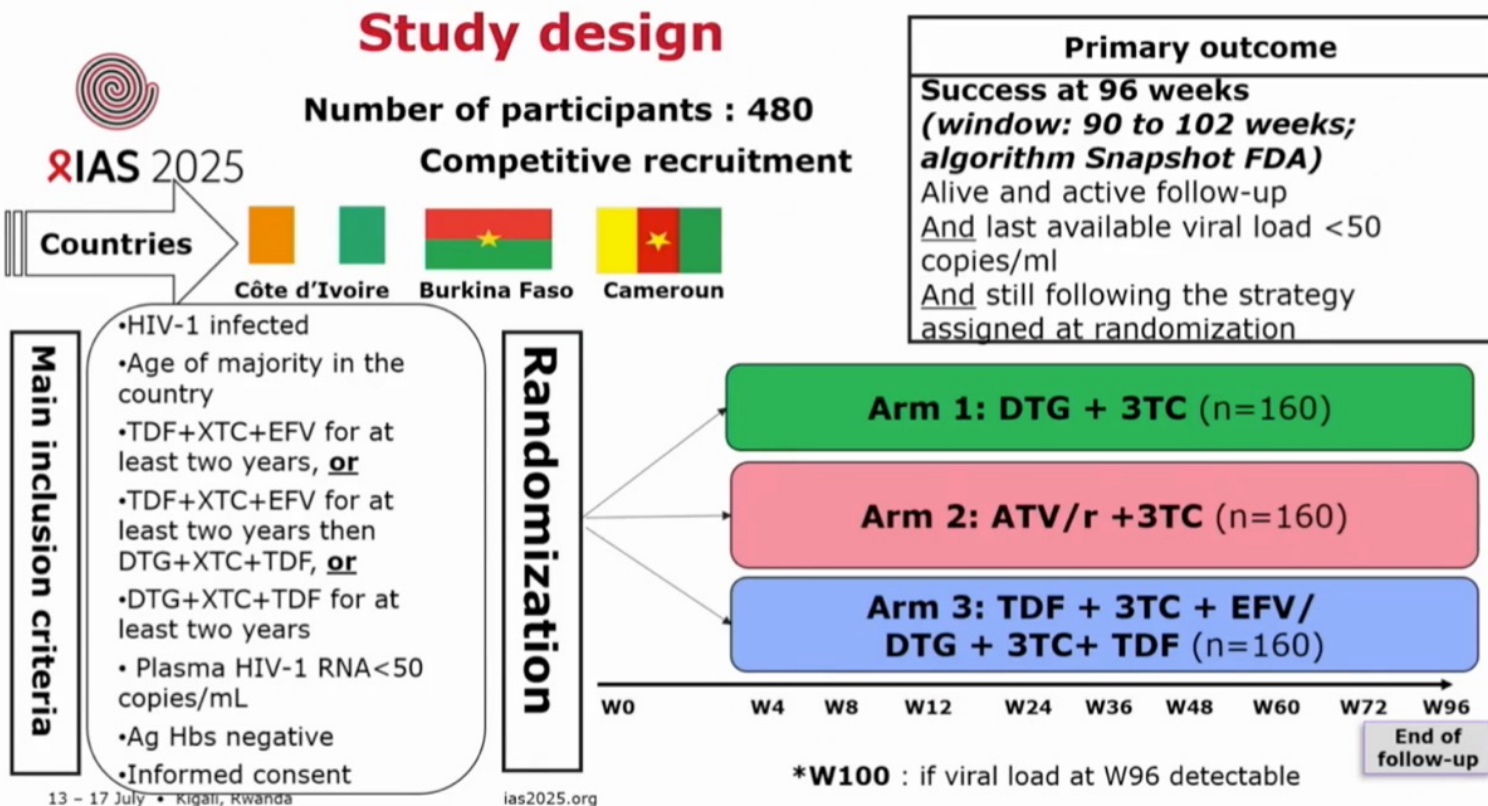
All study arms lost weight. There was no evidence that a switch to DOR affected 48-week changes in weight compared to continued INSTI + TAF/FTC, and 97.5% confidence intervals were <5 percentage points

Complications – Weight

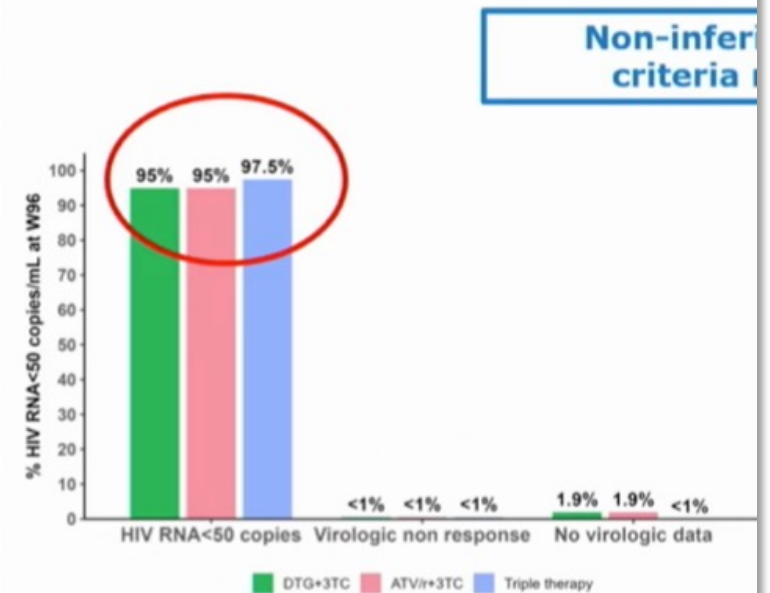
First experience of dual antiretroviral maintenance regimen in West and Central Africa compared with continuing 3-drug current antiretroviral regimens (CARs): week 96 results from the MODERATO trial (ANRS -MIE 12372)

IAS 2025 July 13-17 Rwanda

(F. FADIGA)

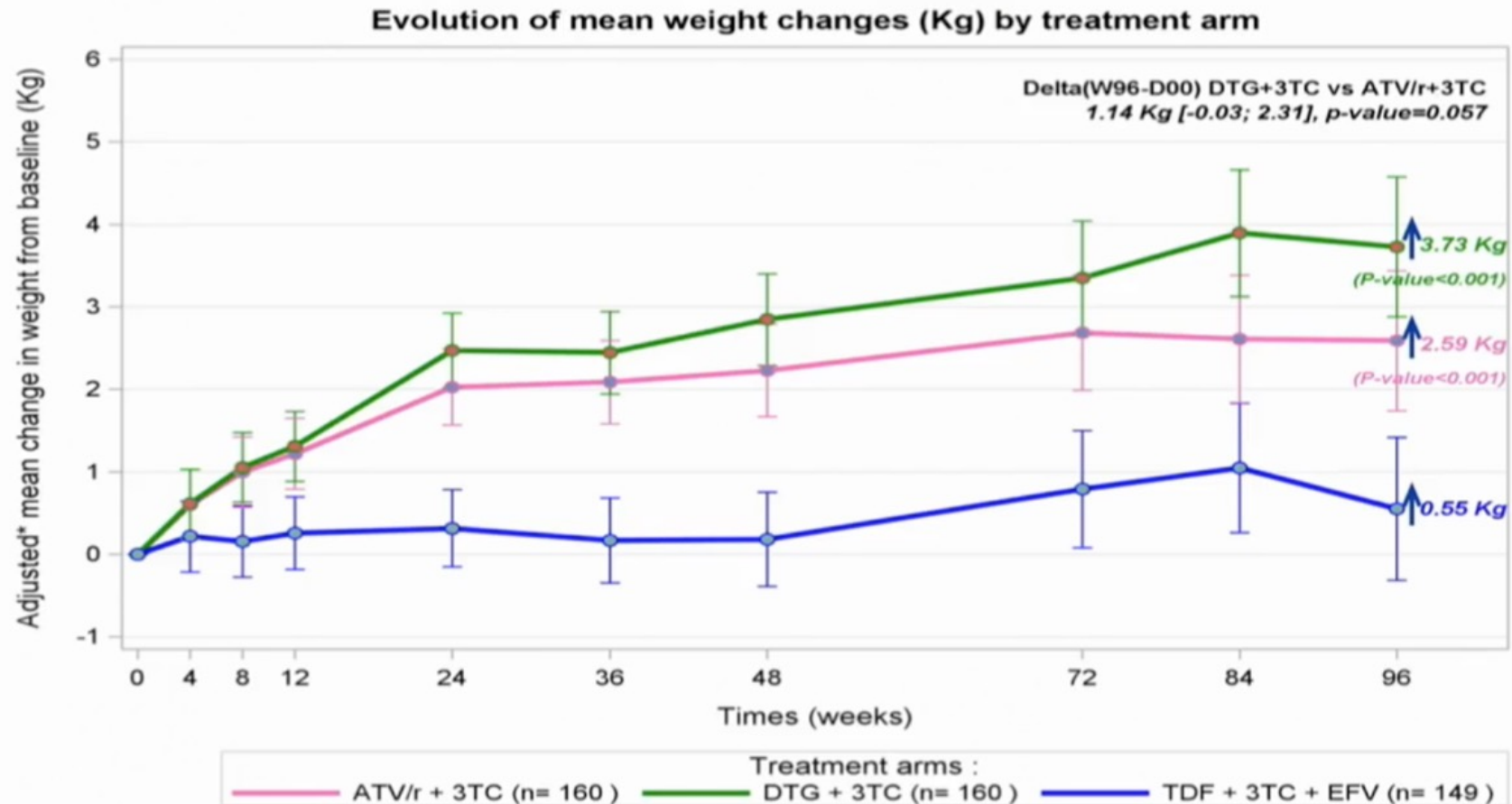


Primary endpoint :
HIV RNA <50 copies/mL
at W96 (FDA snapshot)



Complications – Weight

Evolution of weight changes



*Estimated mean change from baseline was calculated using mixed-model repeated measures adjusting for visit, baseline weight (continuous), initial BMI, treatment arm, gender, age (continuous), initial CD4 cells count (continuous), ART treatment duration, and interaction between treatment arm and visit, and between baseline weight (continuous) and visit

Complications – Diabetes

EXPLORING THE RELATIONSHIP BETWEEN DOLUTEGRAVIR & DIABETES USING PROGRAMMATIC DATA OF CLIENTS ON ART IN LUBOMBO & MANZINI

S. Haumba^{1,2} T. Maseko¹ F. Khumalo¹ S. Ojoo^{1,2}



1. Center for Global Health Practice and Impact, Georgetown University, Clinical Services, Mbabane, Eswatini
2. Center for Global Health Practice and Impact, Georgetown University Medical Center,



1. Center for Global Health Practice and Impact, Georgetown University, Clinical Services, Mbabane, Eswatini
2. Center for Global Health Practice and Impact, Georgetown University Medical Center,

S. Haumba^{1,2} T. Maseko¹ F. Khumalo¹ S. Ojoo^{1,2}

Study Design & Population



RESULTS

- 70955 participants were included in the analysis, and overall T2DM prevalence was 1.1% [0.8-1.4%].
- The prevalence was higher among clients on a non-DTG based regime (2.7% [2.2-3.4]) compared to those on a DTG-based regimen (1.0% [0.7-1.2]).
- A higher prevalence was also observed among clients who never transitioned to a DTG-based regimen (1.9% [1.3-2.4]) compared to those who transitioned (1.2% [0.7-1.6]).
- Predictors of T2DM were age >40 years (aOR:3.3 (2.4-4.7; p<0.001); BMI (aOR:1.1 (1.05-1.09); p<0.001) and duration on ART (aOR=1.0 (1.00-1.01), p<0.001).
- Being on DTG (aOR:1.1 (1.05-1.09), p<0.001) was protective from T2DM.

Complications – Diabetes

EXPLORING THE RELATIONSHIP BETWEEN DOLUTEGRAVIR & DIABETES USING PROGRAMMATIC DATA OF CLIENTS ON ART IN LUBOMBO & MANZINI

S. Haumba^{1,2} T. Maseko¹ F. Khumalo¹ S. Ojoo^{1,2}



1. Center for Global Health Practice and Impact, Georgetown University, Clinical Services, Mbabane, Eswatini
2. Center for Global Health Practice and Impact, Georgetown University Medical Center,



1. Center for Global Health Practice and Impact, Georgetown University, Clinical Services, Mbabane, Eswatini
2. Center for Global Health Practice and Impact, Georgetown University Medical Center,

S. Haumba^{1,2} T. Maseko¹ F. Khumalo¹ S. Ojoo^{1,2}

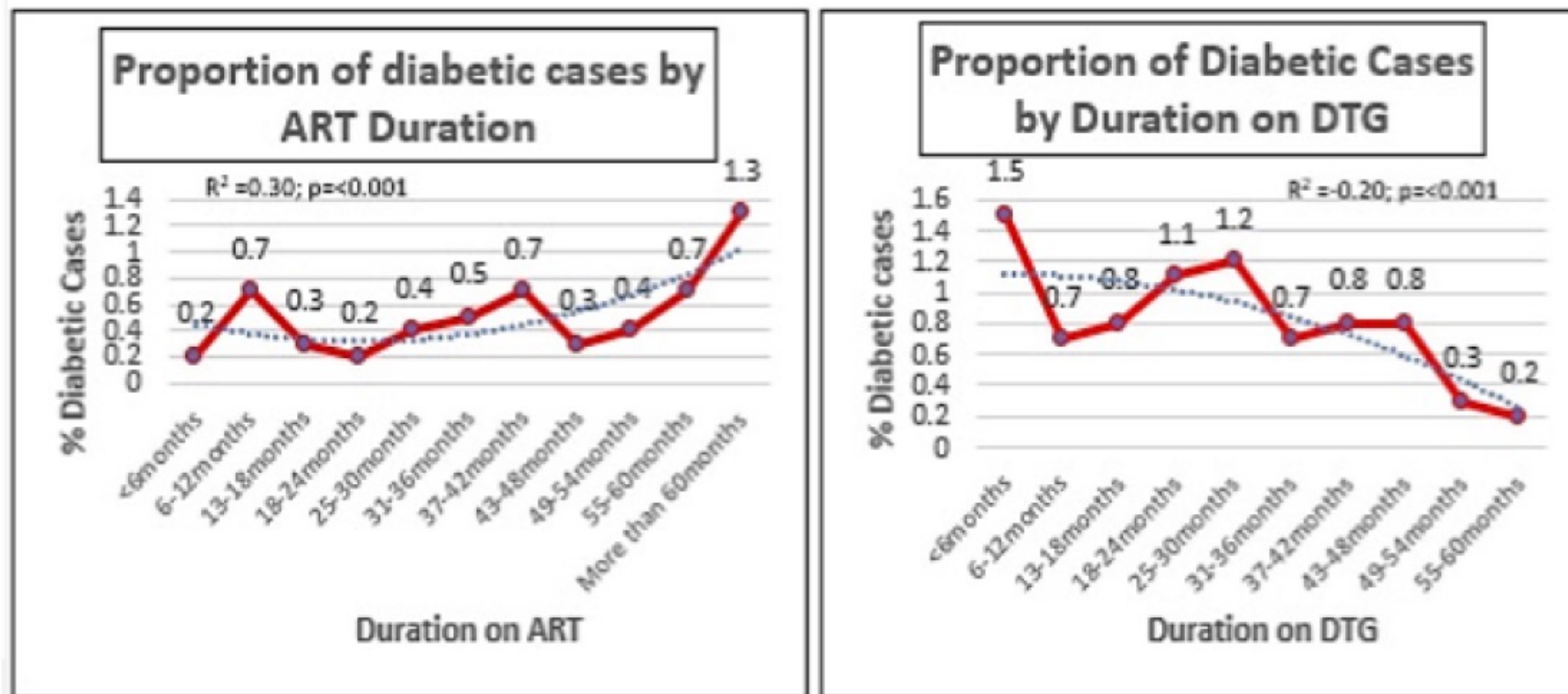


Figure 3: Comparison of T2DM cases between duration on ART and duration on DTG.

Complications – Falls

Recurrent falls as a marker for frailty in virologically suppressed PLWH in Salvador, Brazil: 17% Falls Prevalence, 5.4% Recurrent Falls: 52 Med Age

IAS 2025 July 13-17 Rwanda

S. Amaral¹, A. Tolentino¹, D. Zeballos¹, I. Montañó-Castellón¹, M. Arriaga¹, K. Page², C. Brites¹

RESULTS

A total of 222 people living with HIV were evaluated. The prevalence of falls in one year was 17.1%, while the prevalence of recurrent falls was 5.4%. Most participants were male (60.4%), with a mean age of 52,7 ($\pm 10,7$) years, had more than 8 years of schooling (64.4%), and self-identified as Black or mixed race (89.0%). The median current CD4 T lymphocyte count was 672 cells/ μ L (IQR 473-831), while the median nadir CD4 count was 199 cells/ μ L (IQR 74-318), additionally, 57.6% of participants had a history of AIDS.

In the logistic regression, any falls were associated with female sex, the use of central nervous system medications, and being single. For recurrent falls, female sex, the use of benzodiazepines, and frailty were associated factors.

Table 1: Logistic regression with any falls and recurrent falls as the outcomes among the study sample of PLWH with undetectable VL, Salvador - Brazil.

Variable	Sig.	Adjusted OR	95% CI
Any falls (outcome)			
Female sex	0.001	3.94	(1.73 - 8.94)
Status civil (single)	0.016	0.33	(0.13 - 0.81)
Status civil (divorced/widowed)	0.26	0.54	(0.19 - 1.56)
CNS medications use	0.04	3.90	(1.05 - 14.42)
Recurrent falls (outcome)			
Female sex	0.036	4.23	(1.10 - 16.20)
Frailty	0.024	6.53	(1.28 - 33.36)
Pre-frailty	0.64	0.70	(0.16 - 3.07)
Benzodiazepines use	0.022	10.22	(1.40 - 74.79)

Complications – Dermatologic

THE GEORGE
WASHINGTON
UNIVERSITY
WASHINGTON, DC



THE DC COHORT
Advancing HIV Care and Treatment in the District of Columbia

Prevalence, Incidence, and Risk Factors for Dermatologic Conditions in People with HIV in the Modern Antiretroviral Era: A Cohort Study in Washington, DC

Yagiz Matthew Akiska, BSE^{1,2}; Morgan Byrne, MPH²; Mana Nasser, BS¹;
Adeline Koay, MBBS, MSc³; Michael A. Horberg, MD, MAS^{4,5}; Anne Monroe, MD²;
Adam Friedman, MD^{6*}; Natella Rakhmanina, MD, PhD^{1,7,8*}

On Behalf of the DC Cohort Executive Committee | *Co-senior authors with equal contributions

Methods

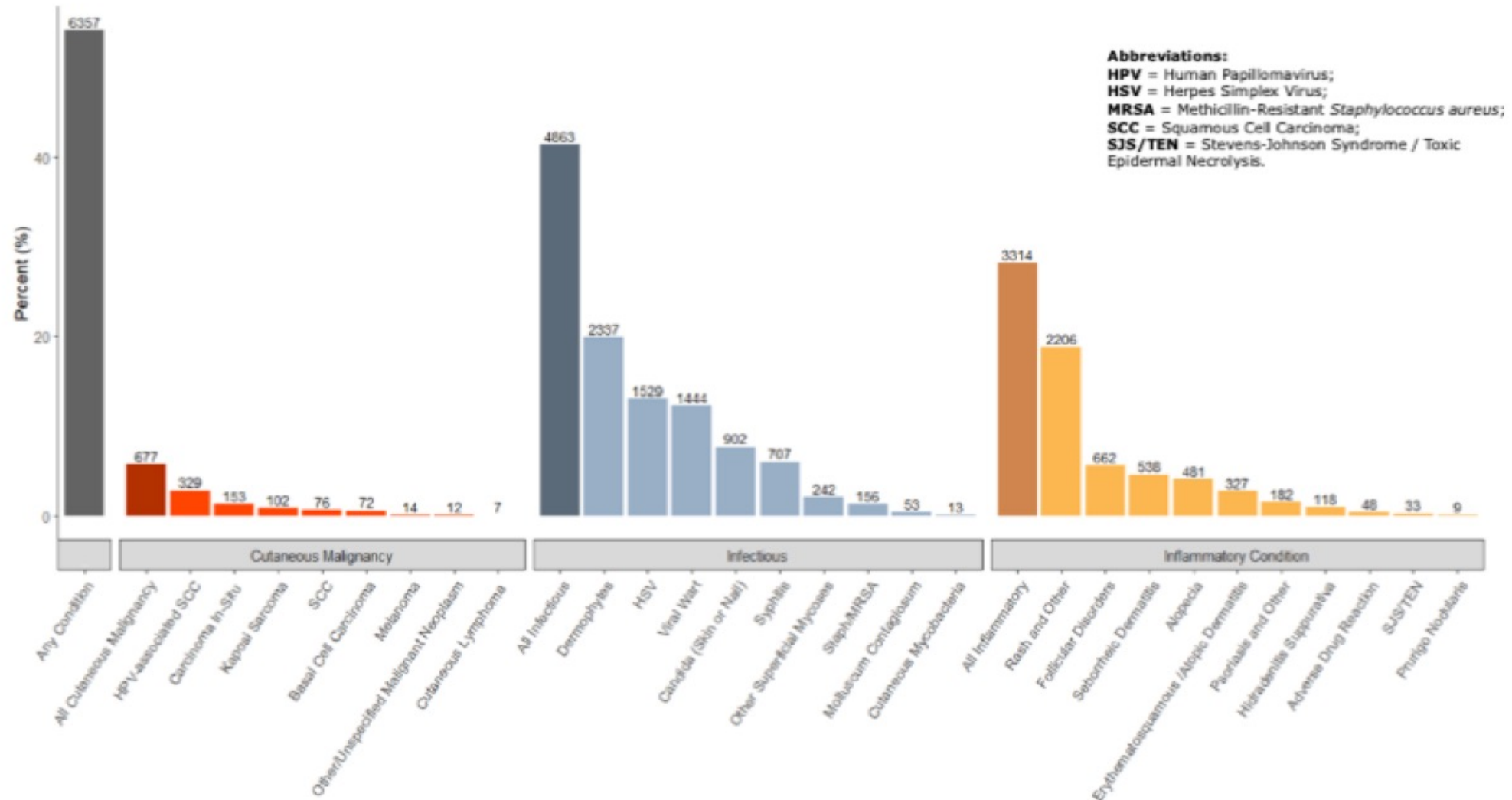
- Longitudinal study of 11,738 adults with HIV (≥ 18 years) receiving care at 14 sites in Washington, DC (2011–2024)⁵; participants enrolled by 9/30/2023 with ≥ 1 CD4 count and ≥ 2 HIV-related visits, followed through last visit or 12/31/2024.
- Dermatologic diagnoses were identified using ICD-9/10 codes and categorized as infectious, inflammatory, or cutaneous malignancies (CM).
- Prevalence was assessed in the full cohort and incidence trends were analyzed among participants newly diagnosed with HIV within 12 months of enrollment and without baseline skin disease.
- Multivariable logistic was used to assess factors associated with the presence of infectious, inflammatory, or malignant dermatologic conditions adjusting for demographics, immune status, site type, and behavioral factors.

Results

- Among 11,738 PWH, **49.3%** had ≥ 1 dermatologic diagnosis (Figure 1):
 - **Infectious DDs:** 41.5% (most common: dermatophytosis 19.9%, HSV 13.0%, viral warts 12.3%)
 - **Inflammatory DDs:** 28.2% (follicular disorders 5.6%, seborrheic dermatitis 4.6%, alopecia 4.1%)
 - **CM:** 5.8% (HPV-SCC 2.8%, carcinoma in situ 1.3%, Kaposi sarcoma 0.9%)
- **Incidence declined** from 2011 to 2024 for all categories: Infectious: 388 $\rightarrow$ 34 per 1,000, Inflammatory: 306 $\rightarrow$ 60 per 1,000, Malignant: 31 $\rightarrow$ 6 per 1,000 (Figure 2, $p < 0.001$);

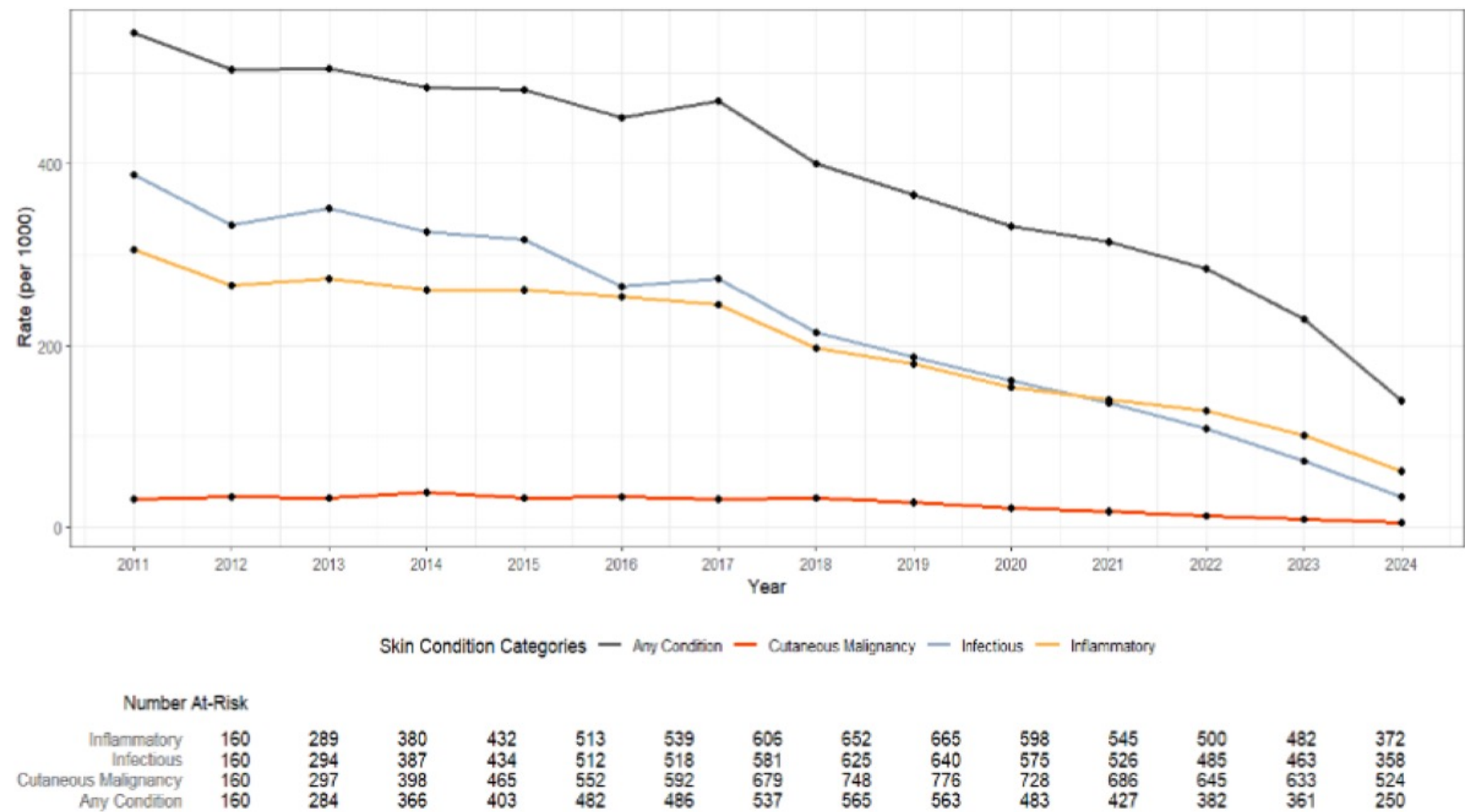
Complications – Dermatologic

Figure 1. The Number and Frequency of Dermatologic Conditions (N=11,738).



Complications – Dermatologic

Figure 2: Incidence Trends of Dermatologic Conditions among Newly Diagnosed PWH between 2011 and 2024.



Complications – Dermatologic

THE GEORGE
WASHINGTON
UNIVERSITY
WASHINGTON, DC



THE DC COHORT
Advancing HIV Care and Treatment in the District of Columbia

Prevalence, Incidence, and Risk Factors for Dermatologic Conditions in People with HIV in the Modern Antiretroviral Era: A Cohort Study in Washington, DC

Yagiz Matthew Akiska, BSE^{1,2}; Morgan Byrne, MPH²; Mana Nasser, BS¹;
Adeline Koay, MBBS, MSc³; Michael A. Horberg, MD, MAS^{4,5}; Anne Monroe, MD²;
Adam Friedman, MD^{6*}; Natella Rakhmanina, MD, PhD^{1,7,8*}

On Behalf of the DC Cohort Executive Committee | *Co-senior authors with equal contributions

- **Multivariable risk factors (Table 1):**
 - **CM:** older age (aOR 1.15), cisgender female (aOR 6.57), public insurance (aOR 1.44), male-to-male sexual contact (aOR 1.52)
 - **Inflammatory conditions:** cisgender female (aOR 1.30), higher CD4 (aOR 1.37), public insurance (aOR 1.45), community site care (aOR 1.26), MSM (aOR 1.24), and alcohol use (aOR 1.14)
 - **Infectious conditions:** history of opportunistic infections (aOR 4.04), lower CD4 (aOR 1.88), public insurance (aOR 1.33), community care (aOR 1.28), MSM (aOR 1.24), alcohol use (aOR 1.17), smoking (aOR 1.15).

