News from AIDS 2024 (Munich) on HIV Prevention and Cure, STIs, and Coinfections

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

Conflict of Interest: JKR

- **Honoraria for lectures and/or consultancies from Abbvie, Berlin Cures, Boehringer, Galapagos, Gilead, Janssen, MSD, and ViiV.**

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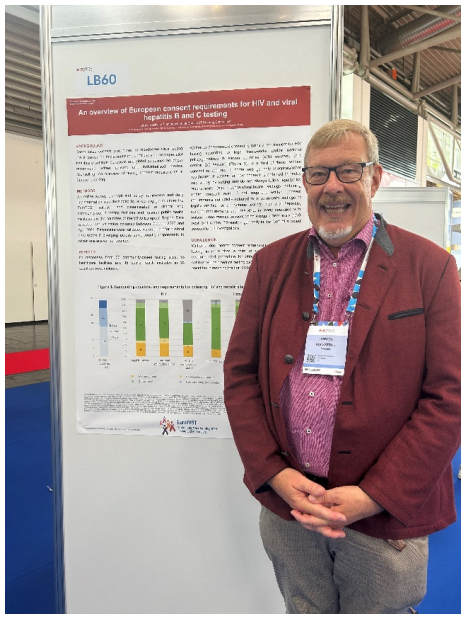
Munich IAS Conference 2024



AIDS 2024
22–26 July
Munich and virtual

Engage in this scientific analysis of data presented at AIDS 2024, with rapid postconference webinars by expert faculty on key HIV prevention and treatment studies, and new and investigational ART regimens.

This event is accredited for 1.00 CME/CPE/CE credit.

Monday, July 29, 2024

1:00 PM ET | 12:00 PM CT | 10:00 AM PT

Faculty: *Chloe Orkin, MBChB, FRCP, MD and Monica Gandhi, MD, MPH*

Register Now

Tuesday, July 30, 2024

12:00 PM ET | 11:00 AM CT | 9:00 AM PT

Faculty: *Daniel R. Kuritzkes, MD and Jürgen K. Rockstroh, MD*

Register Now

Federal Chancellor Scholz at the 25th International AIDS Conference in Munich

Monday, 22 July 2024 in München

Federal Chancellor Scholz at the 25th International AIDS Conference in Munich.
Photo: Federal Government/Guido Bergmann

- **– information and language also matter. Language changes how we perceive reality. A person labelled "AIDS-infected" is perceived differently from a person "living with HIV." That's why it is key to communicate in a people-centred way instead of putting the disease first.**
- **Seventy-five years on, that Article 1 has lost none of its power. In our country, every single person must be protected – no matter where they come from, no matter how healthy they are, no matter who they love.**

UNAIDS Statistics 2024

UNAIDS

FACT SHEET 2024

Global HIV statistics

- **39.9 million** [36.1 million–44.6 million] people globally were living with HIV in 2023.
- **1.3 million** [1 million–1.7 million] people became newly infected with HIV in 2023.
- **630 000** [500 000–820 000] people died from AIDS-related illnesses in 2023.
- **30.7 million** people [27–31.9 million] were accessing antiretroviral therapy in 2023.
- **88.4 million** [71.3 million–112.8 million] people have become infected with HIV since the start of the epidemic.
- **42.3 million** [35.7 million–51.1 million] people have died from AIDS-related illnesses since the start of the epidemic.

People living with HIV

- In 2023, there were 39.9 million [36.1 million–44.6 million] people living with HIV.
  - 38.6 million [34.9 million–43.1 million] adults (15 years or older).
  - 1.4 million [1.1 million–1.7 million] children (0–14 years).
  - 53% of all people living with HIV were women and girls.
- 86% [69–>98%] of all people living with HIV knew their HIV status in 2023.
- About 5.4 million people did not know that they were living with HIV in 2023.

» HIV Prevention

Long-acting PrEP

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*

ABSTRACT

BACKGROUND

There are gaps in uptake of, adherence to, and persistence in the use of preexposure prophylaxis for human immunodeficiency virus (HIV) prevention among cisgender women.

METHODS

We conducted a phase 3, double-blind, randomized, controlled trial involving adolescent girls and young women in South Africa and Uganda. Participants were assigned in a 2:2:1 ratio to receive subcutaneous lenacapavir every 26 weeks, daily oral emtricitabine–tenofovir alafenamide (F/TAF), or daily oral emtricitabine–tenofovir disoproxil fumarate (F/TDF; active control); all participants also received the alternate subcutaneous or oral placebo. We assessed the efficacy of lenacapavir and F/TAF by comparing the incidence of HIV infection with the estimated background incidence in the screened population and evaluated relative efficacy as compared with F/TDF.

RESULTS

Among 5338 participants who were initially HIV-negative, 55 incident HIV infections were observed: 0 infections among 2134 participants in the lenacapavir group (0 per 100 person-years; 95% confidence interval [CI], 0.00 to 0.19), 39 infections among 2136 participants in the F/TAF group (2.02 per 100 person-years; 95% CI, 1.44 to 2.76), and 16 infections among 1068 participants in the F/TDF group (1.69 per 100 person-years; 95% CI, 0.96 to 2.74). Background HIV incidence in the screened population (8094 participants) was 2.41 per 100 person-years (95% CI, 1.82 to 3.19). HIV incidence with lenacapavir was significantly lower than background HIV incidence (incidence rate ratio, 0.00; 95% CI, 0.00 to 0.04; P<0.001) and than HIV incidence with F/TDF (incidence rate ratio, 0.00; 95% CI, 0.00 to 0.10; P<0.001). HIV incidence with F/TAF did not differ significantly from background HIV incidence (incidence rate ratio, 0.84; 95% CI, 0.55 to 1.28; P=0.21), and no evidence of a meaningful difference in HIV incidence was observed between F/TAF and F/TDF (incidence rate ratio, 1.20; 95% CI, 0.67 to 2.14). Adherence to F/TAF and F/TDF was low. No safety concerns were found. Injection-site reactions were more common in the lenacapavir group (68.8%) than in the placebo injection group (F/TAF and F/TDF combined) (34.9%); 4 participants in the lenacapavir group (0.2%) discontinued the trial regimen owing to injection-site reactions.

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Dr. Das can be contacted at moupali.das@gilead.com or at Gilead Sciences, 333 Lakeside Dr., Foster City, CA 94404.

*The members of the PURPOSE 1 Study Team are listed in the Supplementary Appendix, available at NEJM.org.

This article was published on July 24, 2024, at NEJM.org.

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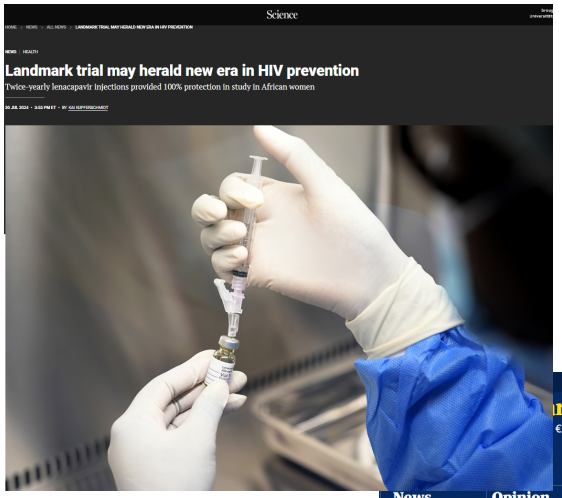

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About this content

Kat Lay, *Global health correspondent, in Munich*

Fri 26 Jul 2024 10.00 CEST

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Doctor behind trial of HIV prevention drug recounts breakthrough moment

Prof Linda-Gail Bekker receives ovation at Aids summit after presenting trial results of 'miracle' drug lenacapavir

Prof Linda-Gail Bekker presenting results of the lenacapavir trial at this week's Aids conference. It has been called a potential 'gamechanger'. Photograph: G Bell/International Aids Society

When the doctor behind the trial of a new HIV prevention drug heard the results, she could not contain her emotions. "I literally burst into tears," said Prof Linda-Gail Bekker

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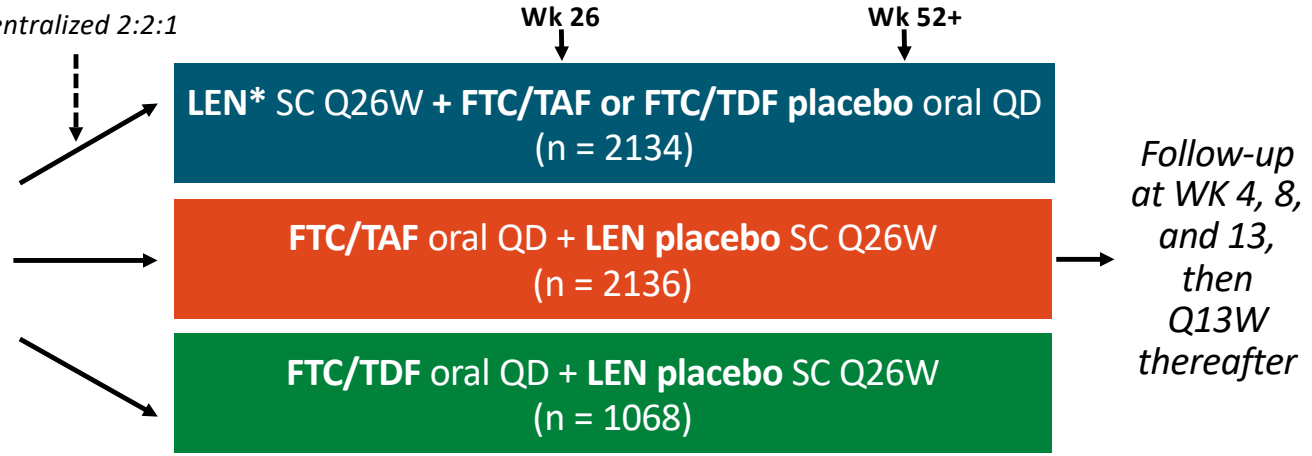
PURPOSE 1: Twice-Yearly LEN Injections vs Daily Oral Tenofovir as PrEP in Cisgender Women

- Randomized, double-blind phase III trial in South Africa and Uganda using counterfactual design

Cisgender women aged 16-25 yr; sexually active with cisgender men and >1 vaginal intercourse within last 3 mo (not pregnant); unknown HIV status; no prior HIV testing or PrEP/PEP use in last 3 mo; ≥35 kg body weight; eGFR ≥60 mL/min; no contraceptive requirement (N = 5368)



*Participants received a loading dose (300 mg tablets) on Day 1 and Day 2.

- Prespecified interim analysis when 50% of participants completed ≥52 wk
  - **Primary analysis**: LEN vs background HIV incidence, FTC/TAF vs background HIV incidence
  - **Secondary analysis**: LEN vs FTC/TDF HIV incidence, FTC/TAF vs FTC/TDF HIV incidence

Bekker. AIDS 2024. Abstr SS0407. Bekker. NEJM. 2024;[Epub].

Slide credit: clinicaloptions.com

Baseline Characteristics

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 race,[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

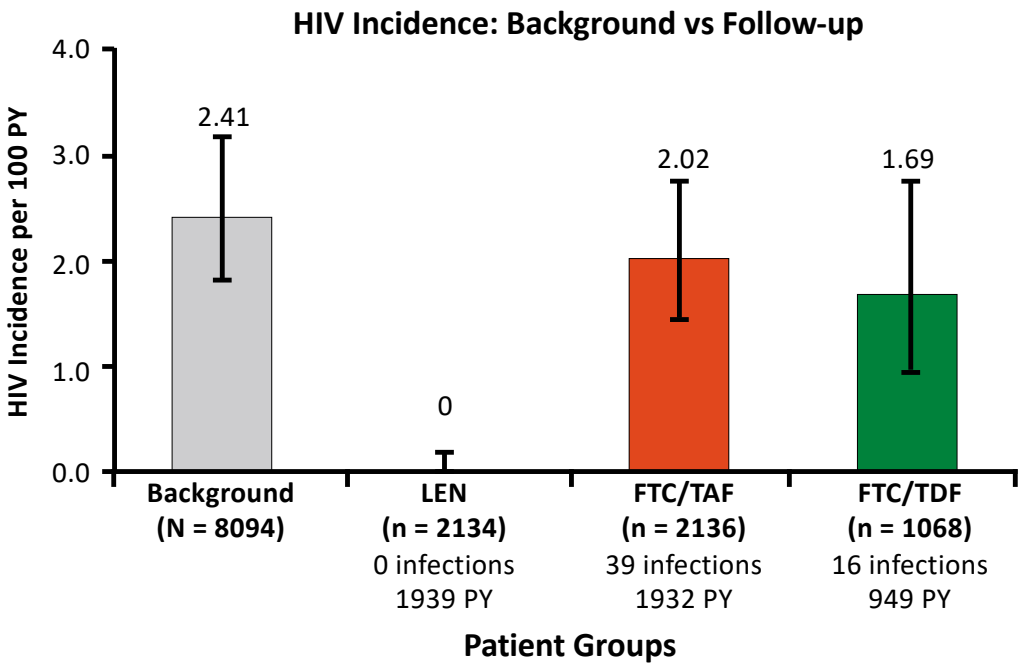
84.3%
South Africa

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
Q, quartile; STI, sexually transmitted infection.

PURPOSE 1: HIV Incidence in mITT Population at Interim Analysis



- At baseline, median age 21 yr, 23%-56% aged 16-18 yr, ~25% with any STI

Comparison	HIV Incidence Rate Ratio (95% CI)*	*P* Value
LEN vs background HIV incidence	0 (0.04)	<.0001
FTC/TAF vs background HIV incidence	0.84 (0.55-1.28)	.21
LEN vs FTC/TDF HIV incidence	0 (0.10)	<.0001
FTC/TAF vs FTC/TDF HIV incidence	1.20 (0.67-2.14)	--

*People found to have HIV at study entry excluded from analysis.

- **Zero HIV infections occurred in cisgender women receiving LEN**
- In oral FTC/TAF arm, HIV incidence no different from background and treatment adherence was poor

Bekker. AIDS 2024. Abstr SS0407. Bekker. NEJM. 2024;[Epub].

HIV Test Results for Participants who had HIV at Baseline

Table S6. HIV Test Results for Participants Adjudicated to Have HIV at Baseline.

Case	Group	Week	Rapid Antibody/antigen	Central Antibody/antigen	Ab differentiation	Viral load (copies/mL)
1	LEN	Baseline	negative	positive	negative	4,540,000
		Day 8	positive	ND	ND	26,500
		Day 29	ND	ND	ND	195
		Day 91	ND	ND	ND	<20
2	LEN	Baseline	negative	positive	negative	105,000,000
		Day 9	negative	positive	positive	227,000
3	LEN	Baseline	negative	positive	negative	80,500,000
		Day 29	positive	ND	ND	ND
		Day 75	ND	positive	positive	ND
4	LEN	Baseline	negative	negative	ND	129,000
		Day 15	ND	ND	ND	269,000
		Day 29	ND	ND	ND	353
		Day 95	ND	ND	ND	none detected
5	F/TAF	Baseline	negative	positive	negative	36,200,000
		Day 9	ND	ND	ND	191,000
		Day 41	ND	ND	ND	22,900
6	F/TDF	Baseline	negative	negative	ND	47,500
		Day 7	negative	negative	ND	59,000
		Day 13	positive	positive	positive	187,000
		Day 49	ND	ND	ND	67,100
		Day 96	ND	ND	ND	37,600
7	F/TDF	Baseline	negative	positive	negative	512,000
		Day 15	ND	ND	ND	1,130
		Day 43	ND	positive	positive	62
		Day 49	ND	ND	ND	43
		Day 100	ND	ND	ND	none detected

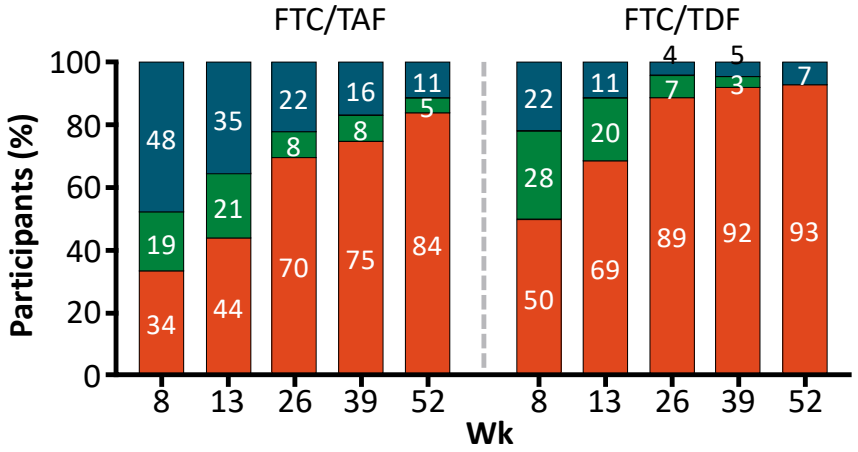
All results through 100 days of follow-up are presented. ND, not done

Bekker LG et al. N Engl J 2024

PURPOSE-1: Adherence

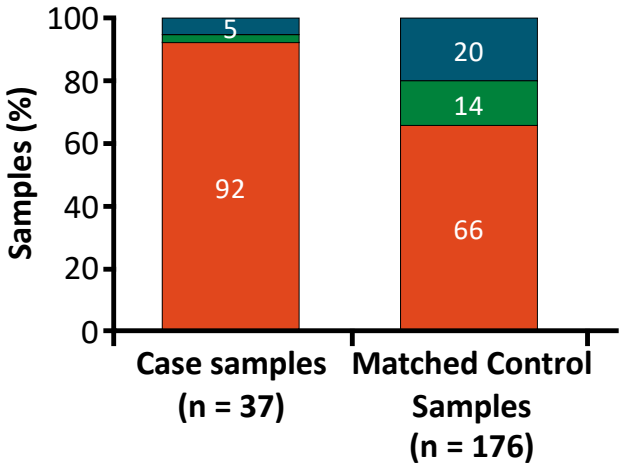
- On-time injections were similar across all groups: 91.5% at Wk 26 and 92.8% at Wk 52
- Adherence to oral therapy was low for most FTC/TAF and FTC/TDF participants and decreased over time

Adherence to FTC/TAF and FTC/TDF



Patients at Risk, n	200	204	192	171	182	106	103	101	86	43

FTC/TAF Adherence-Efficacy Association



- Lower odds of HIV infection with medium or high FTC/TAF adherence vs low adherence (OR: 0.11; 95% CI: 0.01 to 0.49)

Bekker. AIDS 2024. Abstr SS0407. Bekker. NEJM. 2024;[Epub].

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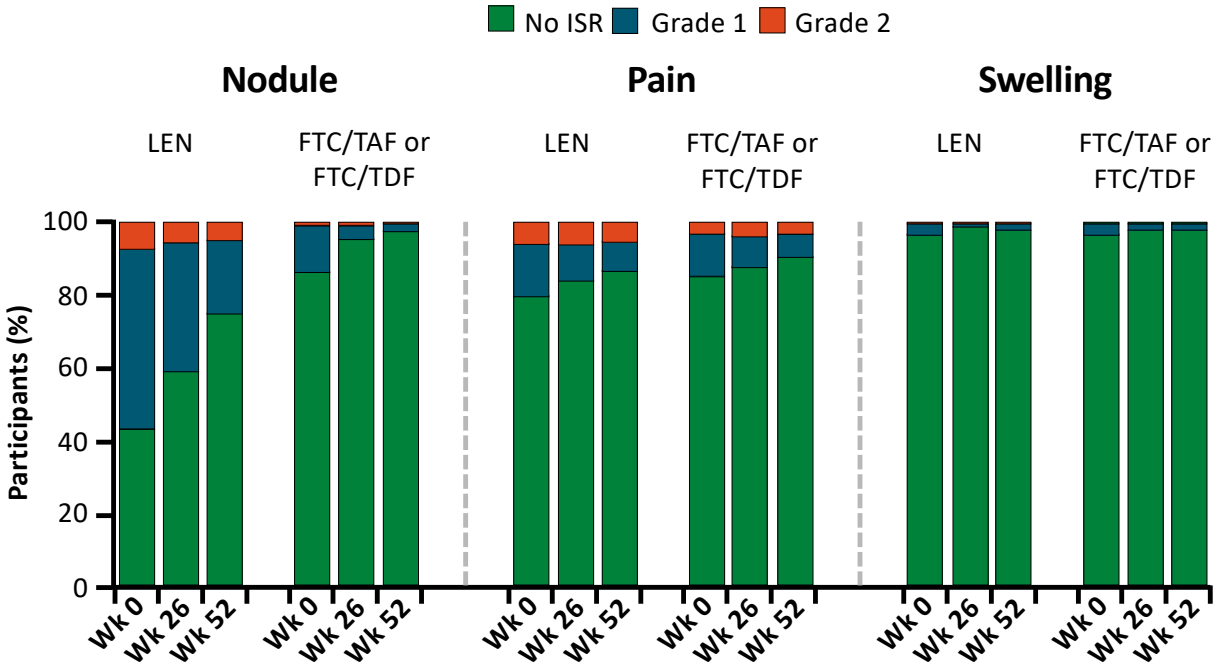
PURPOSE 1: LEN Treatment Adherence and ISRs

- Injections given on time in
  - 91.5% (4545/4967) at Wk 26
  - 92.8% (2025/2181) at Wk 52
- On-time injection rate similar for LEN and placebo
- **Adherence to oral tablets was low** based on TDF-DP concentration for both FTC/TAF and FTC/TDF, declined over time
- Pregnancies were common and outcomes were similar to those expected for the population



*LEN n: baseline, 2138; Wk 26, 1930; Wk 52, 862. Placebo (FTC/TAF + FTC/TDF) n: baseline, 3206; Wk 26, 2883; Wk 52, 1274

- Among 25,329 injections, 4 ISRs led to treatment discontinuation

Bekker. AIDS 2024. Abstr SS0407. Bekker. NEJM. 2024;[Epub].

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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**

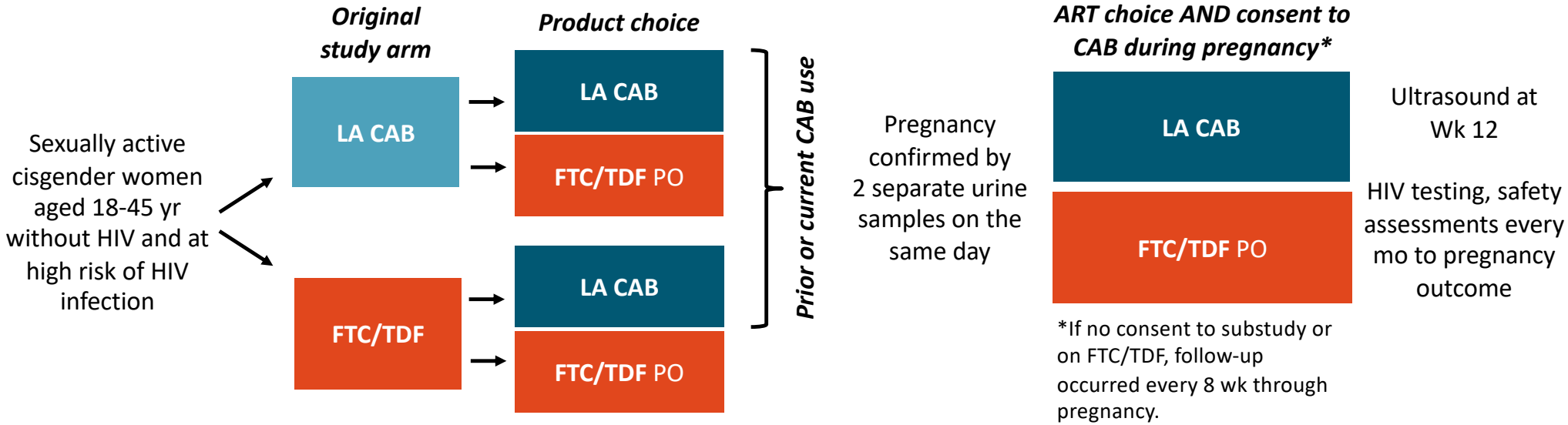
Available pregnancy outcomes were similar to those expected for the population[3]

[a]Completed uninterrupted pregnancies which includes live births and 8 still births: 3 in the LEN group, 4 in the F/TAF group, and 1 in the F/TDF group. [b]Spontaneous miscarriage defined as occurring at < 20 weeks' gestation.

1. ACOG Committee on Practice Bulletins—Gynecology. *Obstet Gynecol*. 2018;132(5):e197-e207. **2.** Wilcox AJ, et al. *N Engl J Med*. 1988;319:189-94. **3.** Mugo NR, et al. *JAMA*. 2014;312(4):362-71.

HPTN 084 Open-Label Extension: Safety Evaluation of LA CAB During Pregnancy

- International, randomized, double-blind phase III trial, with evaluation of OLE in pregnant individuals offered the choice of LA CAB or FTC/TDF from 2022 onwards



- **Primary outcomes:** pregnancy incidence, maternal AE incidence, individual and composite pregnancy outcomes: birth that includes spontaneous abortion <20 wk or IUFD; stillbirth ≥20 wk or premature birth <37 wk or small gestational age; infant outcomes

Delany-Moretlwe. AIDS 2024. Abstr SY2503.

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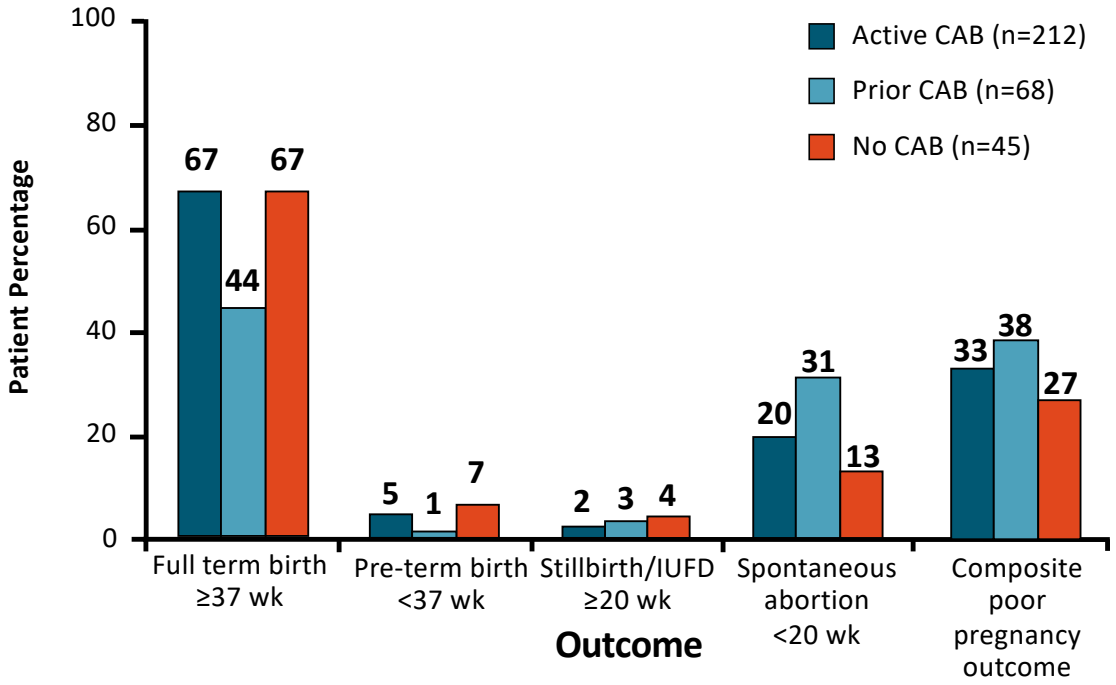
HPTN 084 OLE: Pregnancy Outcomes By CAB Exposure



- Across non-randomized exposure CAB groups, pregnancy outcomes were consistent with expected background rates of pre-term birth, stillbirth/IUFD, spontaneous abortion
- Composite of poor pregnancy outcomes rates were similar across groups and driven by spontaneous abortion rates

- Interpret spontaneous abortion with caution given the non-legal status of abortion in many of the countries participating in this study

Delany-Moretlwe. AIDS 2024. Abstr SY2503.

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HPTN 084 OLE: Infant Outcomes by CAB Exposure

Outcome	Active CAB	Prior CAB	No CAB
Live infants, n	157	31	35
Median gestational age at delivery, wk (IQR)	39 (37-40)	38 (36-40)	37 (37-39)
Median birth weight, kg (IQR)	3 (3-3)	3 (3-4)	3 (3-4)
Size for gestational age, n (%)			
▪ Small	17 (10)	2 (6)	3 (9)
▪ Appropriate	104 (66)	15 (48)	15 (43)
▪ Large	21 (13)	10 (32)	9 (26)
▪ No data	15 (10)	4 (13)	8 (23)
Neonatal death within 28 days, n	4	0	0

- Infant growth was similar across CAB exposure groups, and the 10% small size for gestational age in the active CAB group was lower than previously reported background rates for similar populations
- All neonatal deaths were considered by investigators to be unrelated to PrEP, and 2.5% prevalence rate was consistent with background rates of neonatal deaths, which can range from 1%-4% in this population

Delany-Moretlwe. AIDS 2024. Abstr SY2503.

HPTN 083: HIV-1 RNA Screening in People With HIV Receiving LA CAB for PrEP

- LA CAB vs FTC/TDF for PrEP in cisgender men and transgender women[1,2]
- In original study, HIV detection with antigen/antibody testing was delayed compared with qualitative HIV-1 RNA testing for both arms[2]

Delays in Diagnosis, Median Days[3,4]	Baseline Infections	Incident Infections
LA CAB for PrEP	62	98
Oral FTC/TDF for PrEP	34	31

- Based on these results, 2021 CDC guidelines recommend using HIV-1 RNA assays for monitoring people on both oral and LA injectable PrEP[5]
- Current analysis of OLE participants (LA CAB only) through November 30, 2023, calculated positive predictive value and false positive rates of isolated positive RNA results and assessed screening sensitivity[1]

1. Landovitz. AIDS 2024. Abstr OAE0406LB. 2. Marzinke. CROI 2021. Abstr 153. 3. Marzinke. J Infect Dis. 2021;224:1581.
4. Delany-Moretlwe. Lancet. 2022;399:1779. 5. cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf.

HPTN 083: HIV-1 RNA Testing Results

- Out of 26,528 HIV-1 RNA tests, 22 were false positives
  - Of these, 7 resulted in subsequent LA CAB administration delays
- A single, isolated positive HIV-1 RNA result was uncommon, but when it occurred, was frequently a false positive
- Repeat HIV-1 RNA testing can clarify whether the initial positive result is indeed an HIV infection

Results From Isolated Positive HIV-1 RNA Tests

Patient Group	PPV, % (95% CI)	FPR, % (95% CI)
Overall	18.5 (7.0-38.7)	0.08 (0.05-0.13)
No LA CAB in last 6 mo	60 (17-92.7)	0.06 (0.01-0.25)
LA CAB in last 6 mo	9.1 (1.6-30.6)	0.09 (0.05-0.14)

- HIV-1 RNA assay performance was better in those who had not received LA CAB in the past 6 mo

Landovitz. AIDS 2024. Abstr OAE0406LB.

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» Sexually Transmitted Infections (STIs)

DOXY PEP in Canada

Methods: MSM living with HIV with previous syphilis were randomized 1:1 to receive 48 weeks of daily doxycycline 100mg orally versus placebo in this double-blind pilot study in Toronto and Vancouver

Results: 52 participants were randomized. The bacterial STI incidence rate at week 48 b<y study arm is summarized in table 1. There were no between-arm differences in sexual behaviors, adverse events or tetracycline resistance to S. aureus.

	Total STIs per arm		Incidence rate (95% CI), per 100 PY		Rate ratio* (95% CI)	p
	DoxyPrEP	Placebo	DoxyPrEP	Placebo		
Syphilis	1	5	3.95 (0.96, 16.28)	19.26 (10.23, 36.28)	0.21 (0.04, 0.97)	**0.04**
Chlamydia	1	13	3.97 (0.69, 22.77)	50.09 (30.86, 81.30)	0.08 (0.01, 0.49)	**0.01**
Gonorrhea	4	13	15.88 (6.61, 38.15)	50.09 (30.81, 81.44)	0.32 (0.12, 0.86)	**0.02**
TOTAL	6	31	23.71 (9.93, 56.66)	119.44 (81.42, 175.20)	0.20 (0.08, 0.51)	**<0.001**

Abbreviations: CI, confidence interval; doxyPrEP, doxycycline pre-exposure prophylaxis; PY, person-years; STI, sexually transmitted infection. ***Rate ratio <1** suggests lower incidence rate in doxycycline arm.

DOX PREP PREVENTS STIS WITHOUT AFFECTING VAGINAL BACTERIAL FLORA IN FSW

- **Before DoxyPrEP, the overall STI incidence rate was 232.3 per 100 person-years. After initiating DoxyPrEP, the overall STI incidence rate declined to 79.2 per 100 person-years**

Incidence for each infection before and after starting DoxyPEP

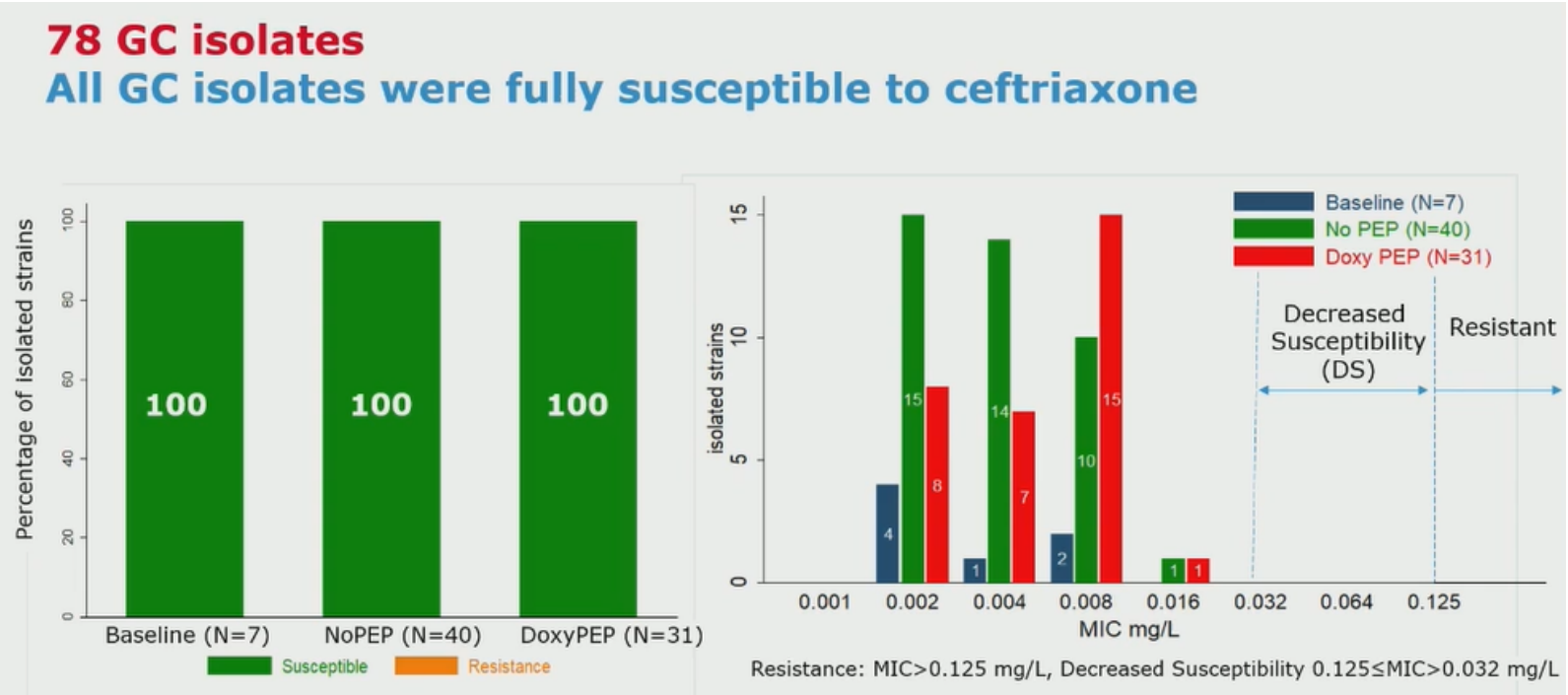
	Before DoxyPrEP			After starting DoxyPrEP			
	Number of Diagnosis	PYs	IR (/100 PYs)	Number of Diagnosis	PYs	IR (/100 PYs)	IRR(95%CI)
Overall STIs (N=40)	108	46.5	232.3	18	22.7	79.2	0.33(0.13-0.84) p=0.020
Chlamydia (N=40)	74	46.5	159.2	13	22.7	57.2	0.35(0.12-1.03) p=0.056
Gonorrhea (N=40)	26	46.5	55.9	5	22.7	22.0	0.45(0.15-1.29) p=0.136
Syphilis (N=40)	8	46.5	17.2	0	22.7	0	–
Bacterial Vaginosis(N=27)	36	34.2	105.2	23	16.7	137.7	1.19(0.72-1.94) p=0.499
Vulvovaginal candidiasis(N=27)	18	34.2	52.6	12	16.7	71.8	1.52(0.62-3.70) p=0.358

Abbreviations: PYs : Person-Years, IR : Incidence Rates, IRR : Incidence Rate Ratio, 95% CI: 95% Confidence Interval

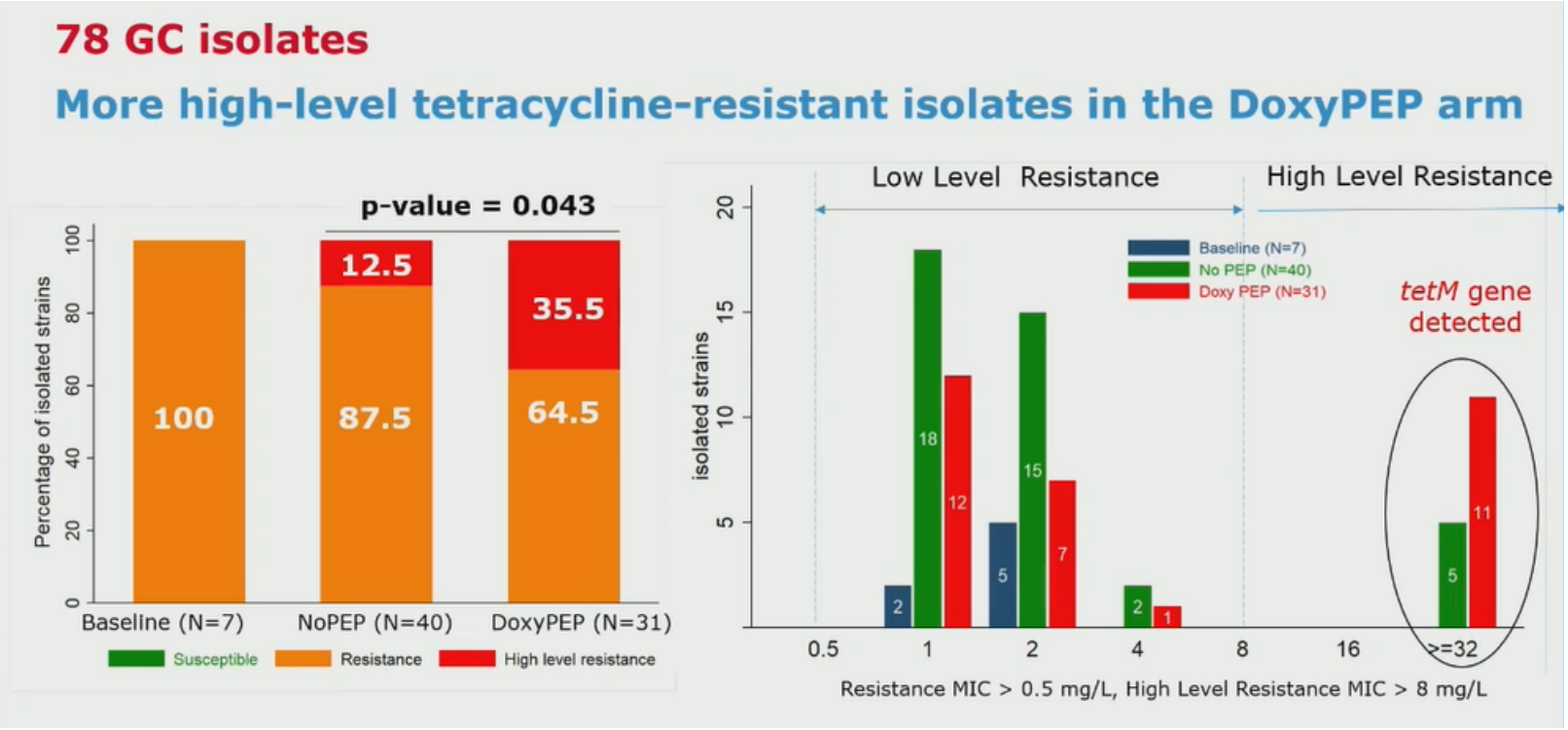
Antimicrobial resistance in Neisseria gonorrhoeae infections among MSM on DOXYPEP

- 450 samples (278 patients) were GC-positive by NAAT.

Susceptibility to ceftriaxone, MIC distribution



Antimicrobial resistance in Neisseria gonorrhoeae infections among MSM on DOXYPEP



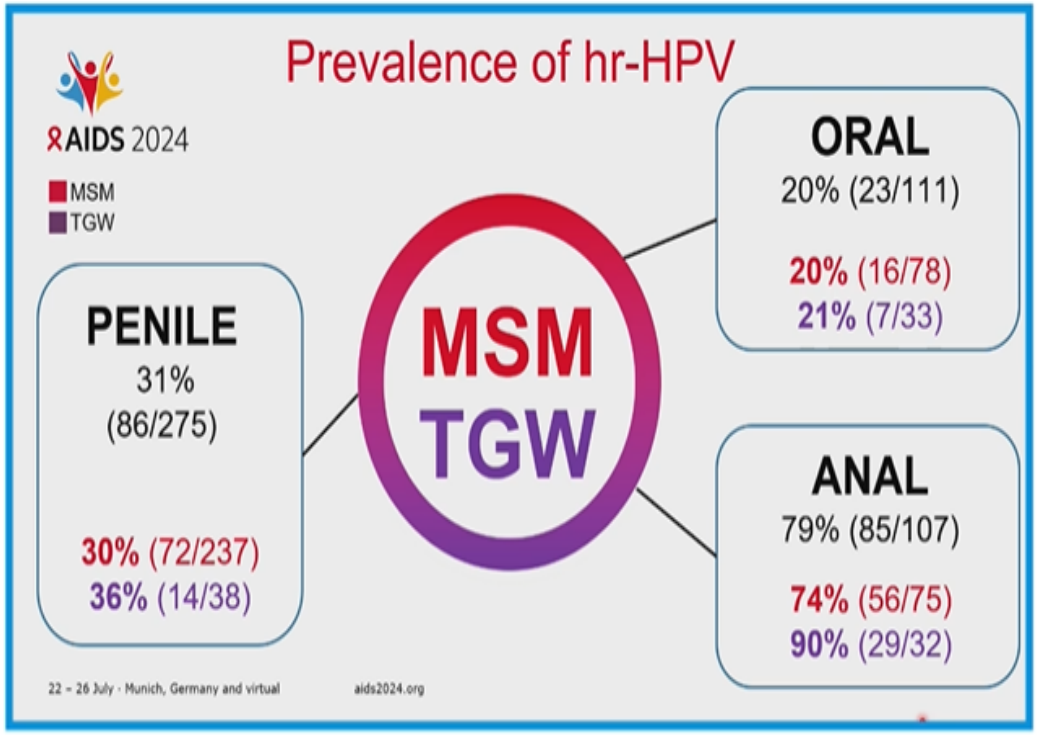
Béatrice BERCOT, et al. IAS 2024, Co-chair Special Session Wednesday: SS0404LB

Prevalence of high risk penile human papillomavirus MSM and TGW).

» **This study aimed to evaluate the prevalence of penile HPV among MSM and TGW populations from Buenos Aires, Argentina. The study involved 246 MSM and 43 TGW.**

- **HIV diagnosis and lifetime sex work were identified as significant predictors of detecting any penile hr-HPV.**

Prevalence of hr-HBV by risk group and site of examination.

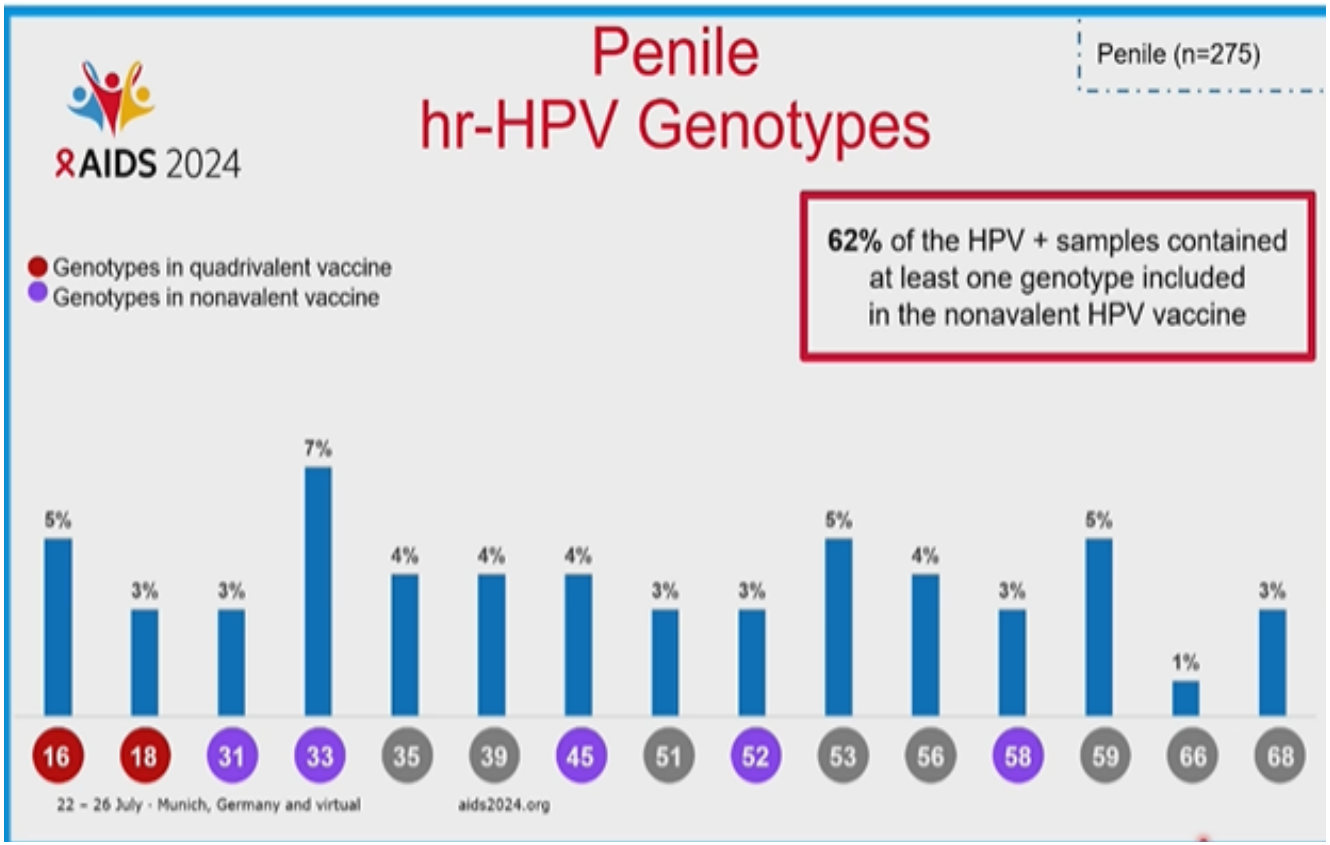


Diego Salusso et al., IAS 2024;
Oral Abstract session: OAB0103

Prevalence of high risk penile human papillomavirus MSM and TGW).

- **The prevalence of penile hr-HPV was 31%, with no statistical difference between MSM and TGW.**
- **A high proportion of penile samples with detectable HPV contained at least one genotype included in the nonvalent HPV vaccine.**

Distribution of hr-HPV genotypes



Diego Salusso et al., IAS 2024;
Oral Abstract session: OAB0103

European consent requirements for HIV and viral hepatitis B and C testing

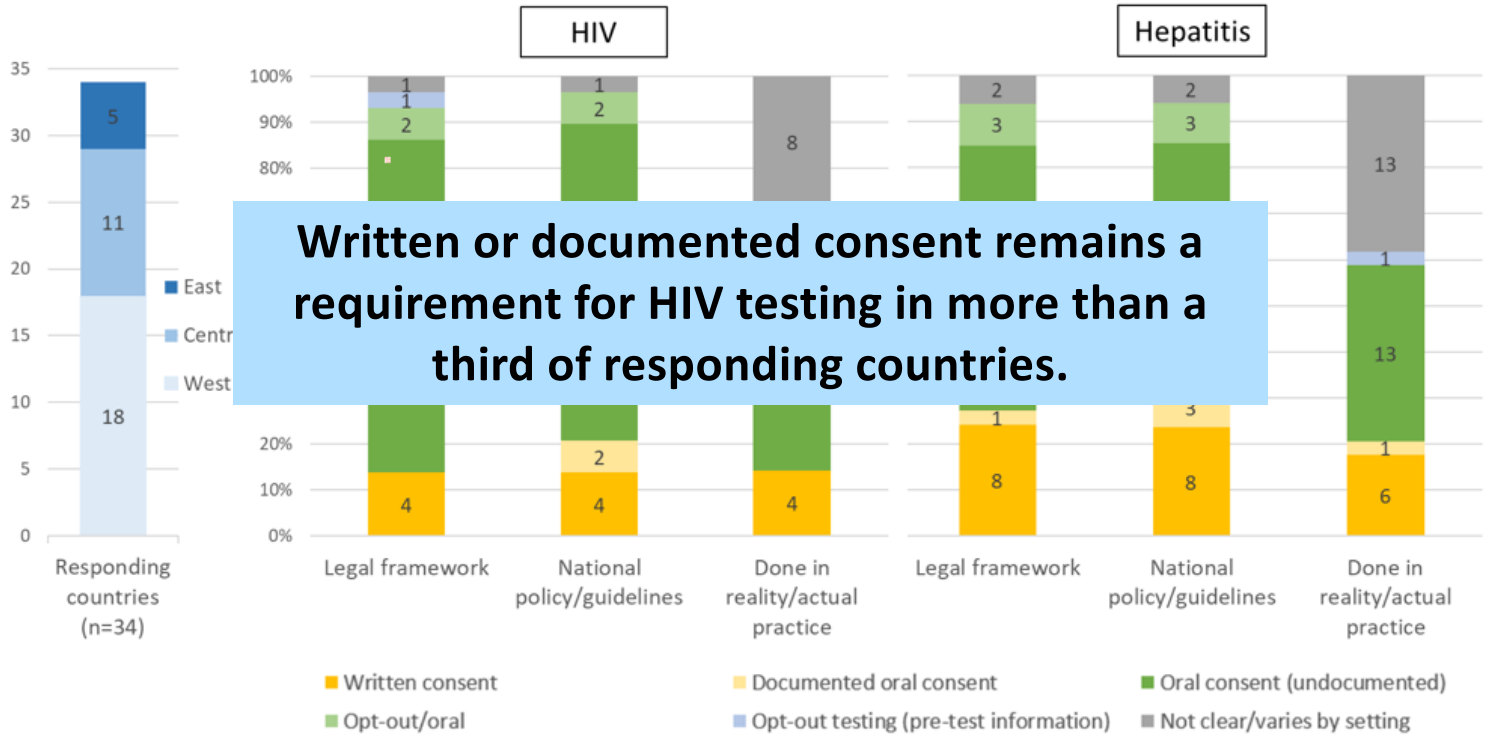
- **An online survey on legal and policy frameworks and daily implementation was developed by a working group under the EuroTEST Initiative and disseminated to clinical and community-based testing facilities and national public health institutions in the countries of the WHO European Region. Data collection and validation occurred between October 2023 and April 2024.**

- **84 responses from 36 community-based testing sites, 33 healthcare facilities and 15 public health institutes in 34 countries were included**

Rockstroh J et al. IAS 2024; Poster LB60

European consent requirements for HIV and viral hepatitis B and C testing

Responding countries and requirements for obtaining HIV and hepatitis testing consent.



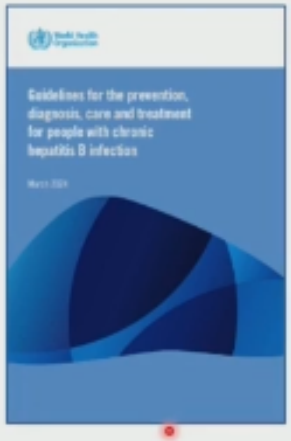
» Coinfections

2024 WHO Guidelines for Prevention, Diagnosis, Care, and Treatment of People with CBH Infection

AIDS 2024

Key topics

- Non-invasive fibrosis assessment
- Who to treat
- First-line antiviral therapies
- PMTCT
- Simplifying diagnosis
- Simplifying service delivery



Chan P, et al. AIDS 2024 (SY0902)

New HBV WHO guidelines

5. Who to treat among people with CHB

5.1 Recommendations

New recommendations – who to treat

Treatment is recommended for all adults and adolescents (aged ≥12 years) with CHB[a] (including pregnant women and girls and non-pregnant women of reproductive age) with:

1. Evidence of significant fibrosis (≥F2)[b] based on an APRI score of >0.5 or transient elastography[c] value of >7 kPa or evidence of cirrhosis (F4) (based on clinical criteria (or an APRI score of >1 or transient elastography value of >12.5 kPa[b]), regardless of HBV DNA or ALT levels.

(adults: strong recommendation, moderate-certainty evidence; adolescents: strong recommendation, low-certainty evidence)

OR

2. HBV DNA >2000 IU/mL and an ALT level above the upper limit of normal (ULN) (30 U/L for men and boys and 19 U/L for women and girls). For adolescents, this should be based on ALT>ULN on at least two occasions in a 6- to 12-month period.[d]

(adults: strong recommendation, high-certainty evidence [HBV DNA >20 000 IU/mL] and low-certainty evidence [HBV DNA 2000–20 000,]; adolescents: conditional recommendation, low-certainty evidence)

OR

3. Presence of **coinfections** (such as HIV, hepatitis D or hepatitis C); **family history** of liver cancer or cirrhosis; **immune suppression** (such as long-term steroids, solid organ or stem cell transplant); **comorbidities** (such as diabetes or metabolic dysfunction—associated steatotic liver disease); or **extrahepatic manifestations** (such as glomerulonephritis or vasculitis), regardless of the APRI score or HBV DNA or ALT levels.

(adults: strong recommendation, moderate-certainty evidence; adolescents: conditional recommendation, low-certainty evidence)

OR

In the absence of access to an HBV DNA assay:

4. Persistently abnormal ALT levels (defined as two ALT values above the ULN at unspecified intervals during a 6- to 12-month period), regardless of APRI score.[e]

(adults and adolescents: conditional recommendation, very-low-certainty evidence)

a Defined as the presence of HBsAg on at least one occasion, and for adolescents and children, persistence of HBsAg for six months or more.
b The thresholds of non-invasive tests (APRI and transient elastography) for diagnosis of significant fibrosis or cirrhosis and treatment recommendation are based on extrapolating data from adults and have not yet been fully validated for adolescents or children.
c Clinical features of decompensated cirrhosis: portal hypertension (ascites, variceal haemorrhage and hepatic encephalopathy), coagulopathy or liver insufficiency (jaundice). Other clinical features of advanced liver disease and cirrhosis may include: hepatomegaly, splenomegaly, pruritus, fatigue, arthralgia, palmar erythema and oedema.
d The ULN for ALT have been defined as <30 U/L for men and boys and <19 U/L for women and girls for consistency. Some guidelines use different ULN ALT levels for adolescents and children (<22 U/L for girls and women and <25 U/L for boys and men). Raised ALT may normalize in pregnancy and is therefore not a good marker for deciding about long-term treatment in pregnancy. Pregnant women should be reassessed after delivery.
e Persistently normal or abnormal may be defined as two ALT values below or above the ULN at unspecified intervals during a 6- to 12-month period. ALT levels fluctuate with CHB and require longitudinal monitoring to determine the trend.

The 2024 guidelines include 11 updated chapters with new recommendations:

Expanded treatment eligibility and antiviral prophylaxis

- use of non-invasive tests for staging of liver disease (Chapter 4);
- who to treat among people with CHB (Chapter 5);
- first-line antiviral therapies for CHB (Chapter 6);
- preventing mother-to-child transmission of hepatitis B using antiviral prophylaxis (Chapter 7);
- treatment of adolescents and children with CHB (Chapter 8);

Hepatitis B DNA and HDV infection diagnostics

- measurement of HBV DNA to guide treatment eligibility and monitor response (Chapter 9);
- HBV DNA reflex testing (Chapter 10);
- HDV testing - who to test and how to test, including reflex testing for hepatitis delta coinfection (Chapters 12–14);

HBV Service Delivery

- Eight approaches to promote access and delivery of high-quality health services for CHB (no new recommendations but includes existing recommendation on strategies to promote linkage to care) (Chapter 15).

There are also updates to five chapters relating to monitoring with unchanged recommendations from the 2015 guidelines, but these have been updated with new context, additional studies and research gaps. These chapters are:

- second-line antiviral therapies for managing treatment failure (Chapter 9);
- monitoring for treatment response (Chapter 16) and treatment side effects (Chapter 17)
- surveillance for HCC (Chapter 18);
- when to stop and restart antiviral therapy (Chapter 19).

7. Preventing mother-to-child transmission of hepatitis B using antiviral prophylaxis

7.1 Recommendations

Antiviral prophylaxis among pregnant women and adolescent girls *(3)*

Updated recommendation

In settings where HBV DNA or HBeAg testing is available, prophylaxis with tenofovir disoproxil fumarate (TDF) is recommended for all HBV-positive (HBsAg-positive) pregnant women with HBV DNA ≥200 000 IU/mL or positive HBeAg[a] (preferably from the second trimester of pregnancy until at least delivery or completion of the infant HBV vaccination series), to prevent the mother-to-child transmission (MTCT) of HBV.

(strong recommendation, moderate-certainty evidence)

New recommendation

In settings where neither HBV DNA nor HBeAg testing[b] is available, prophylaxis with tenofovir disoproxil fumarate (TDF)[c] for all HBV-positive (HBsAg-positive) pregnant women may be considered (preferably from the second trimester of pregnancy until at least delivery or completion of the infant HBV vaccination series), to prevent MTCT of HBV.

(conditional recommendation, low-certainty evidence)

All interventions should be given in addition to at least three doses of hepatitis B vaccination for all infants, including a timely birth dose.

Note: All pregnant women and adolescent girls should be assessed first for eligibility for long-term treatment for their own health. For women of childbearing age planning additional pregnancies, TDF prophylaxis can also be maintained after delivery and during subsequent pregnancies, according to women's choice (Table 7.1).

a The use of the HBeAg recommendation represents an additional option for determining eligibility, but HBeAg RDTs have poor diagnostic performance, which limits their routine use in low- and middle-income countries.

b The use of the HBeAg recommendation represents an additional option for determining eligibility, but HBeAg RDTs have poor diagnostic performance, which limits their routine use in low- and middle-income countries.

c TAF may be considered for people (including pregnant women) with impaired kidney function and/or osteoporosis but is not yet approved for hepatitis B treatment in pregnancy (see Chapter 6). TAF is not recommended if eGFR is <15 m l/min.

New HBV WHO guidelines

DTG/3TC in People With HIV With Isolated Reactive Anti-HBc in Phase III/IIIb Trials

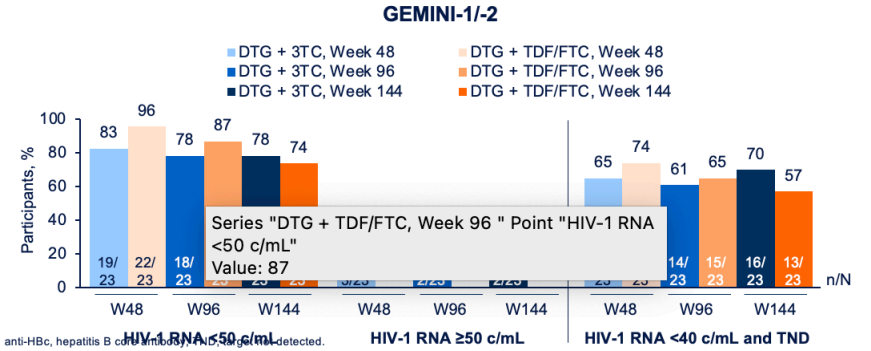
Trial	Isolated anti-HBc (n)	Study population	Design	Treatment
GEMINI-1/ GEMINI-2	46	ART-naive adults with HIV-1 RNA 1000-500,000 c/mL	Randomized, double-blind, phase III, non-inferiority trials	DTG + 3TC vs DTG + FTC/TDF
STAT	5	ART-naive adults	Single-arm study in test-and-treat setting (DTG/3TC started ≤14 days after diagnosis without baseline lab results)	DTG/3TC
TANGO SALSA	13 12	Adults with virologic suppression (HIV-1 RNA <50 c/mL) for >6 mo	Randomized, open-label, parallel-group, phase III, non-inferiority trials	Switch to DTG/3TC vs continue CAR

- Participant demographics and baseline characteristics were generally comparable between treatment groups across studies
- Studies did *not* proactively collect data on HBV vaccination

Fox. AIDS 2024. Abstr OAB0106LB.

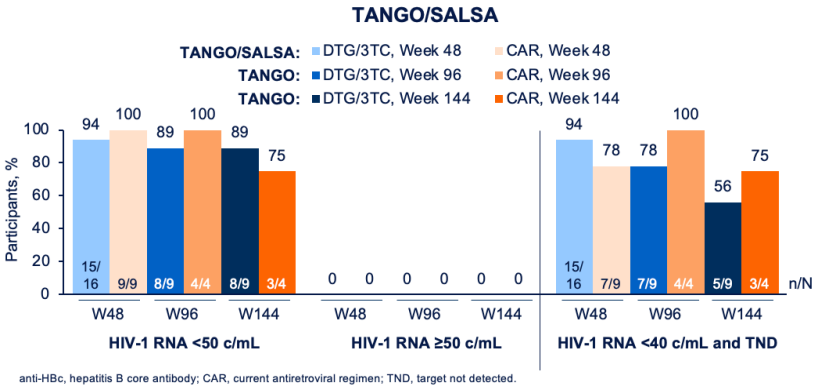
Slide credit: clinicaloptions.com

DTG/3TC in People With HIV-1 With Isolated Reactive Anti-HBc: Virologic Suppression

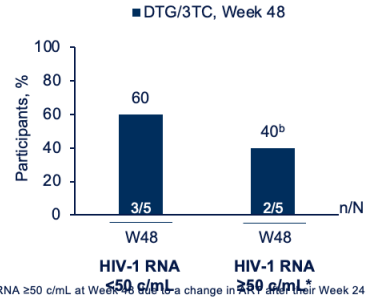


anti-HBc, hepatitis B core antibody; TND, target not detected.

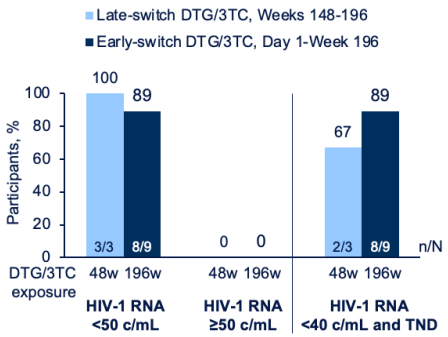
[a]Data for HIV-1 RNA <40 c/mL and TND were not available for STAT. [b]In STAT, 1 participant who had HIV-1 RNA <50 c/mL at Week 24 was considered as having HI assessment. This change in ART was not efficacy related (decision by participant or proxy/participant incarceration).



anti-HBc, hepatitis B core antibody; CAR, current antiretroviral regimen; TND, target not detected.



-1 RNA ≥50 c/mL at Week 48 due to a change in ART after their Week 24



Fox. AIDS 2024. Abstr OABC

DTG/3TC in People With HIV With Isolated Reactive Anti-HBc: Safety

Emergent Liver Chemistry Test Elevations, n (%)	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)
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/plasma AST	0	1 (4)	0	0	0
Grade 4	2 (9)	0	0	0	0
▪ Elevated serum/plasma AST	2 (9)	0	0	0	0
▪ Elevated serum/plasma ALT	1 (4)	0	0	0	0

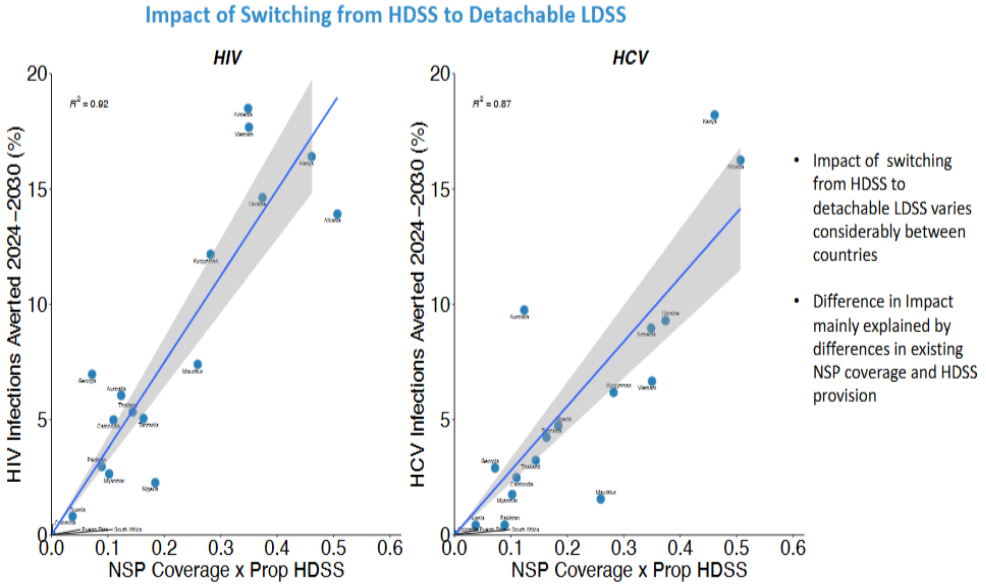
- 1 participant receiving DTG + 3TC in GEMINI-1/-2 discontinued treatment at ~Wk 144 and withdrew from study due to hepatitis E virus and liver enzyme elevations that met liver-stopping criteria
- **No instances of HBV reactivation** reported in any study
- Proportions of participants with HIV-1 RNA <50 c/mL or HIV-1 RNA <40 c/mL and target not detected were generally high and comparable between treatment groups across all studies

Fox. AIDS 2024. Abstr OAB0106LB.

Slide credit: clinicaloptions.com

Evaluating the impact of increased provision of low dead space syringes on HIV and HCV transmission among people who inject drugs: a modelling analysis for 19 countries

- **Low dead space syringes (LDSS) may reduce HIV and HCV transmission risk among people who inject drugs (PWID) compared to high dead space syringes (HDSS). The potential impact of introducing detachable LDSS into needle and syringe programs (NSPs) across 19 countries was evaluated.**
- **Replacing HDSS with detachable LDSS could avert 2.6% of new HCV infections and 2.9% of new HIV infections between 2024 and 2030.**

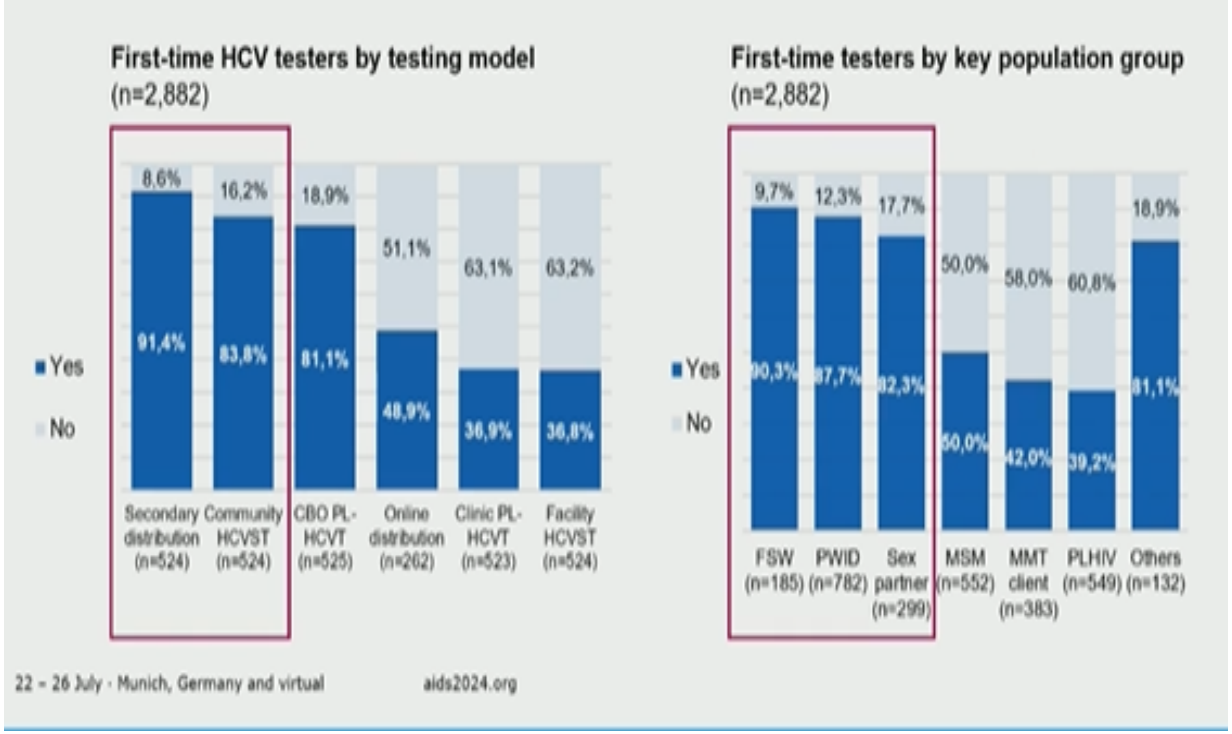


Kara Chew et al. IAS 2024: LB Poster Session: LB21

Integrating HCV self-testing into HIV and harm reduction services

» **Study aim: To compare Community-based HCV self-testing (HCVST) delivery models to provider-led HCV testing (PL-HCVT, that is, standard-of-care facility-based HCV testing, SOC-HCVT) and HCV testing by community-based organizations (CBO-HCVT).**

First-time HCV testers by testing model and by key population



Bao Vu et al. IAS 2024; OAE2005

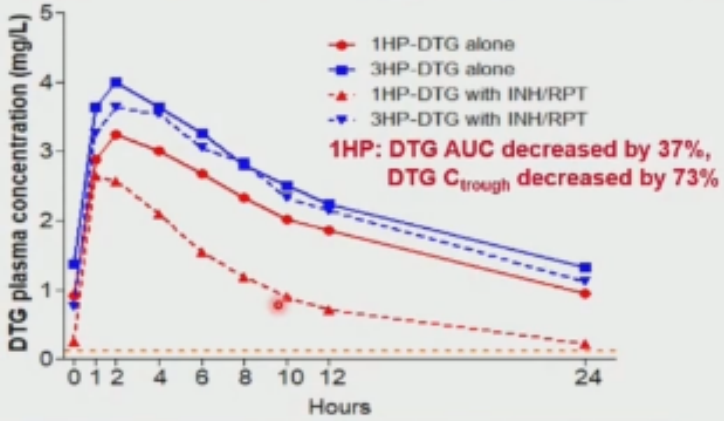
Pharmacokinetics and HIV viral load suppression of 1HP for TB preventive therapy among PWH taking standard dolutegravir

- **Ultrashort 1-month of daily rifapentine600/isoniazid 300 mg (1HP) is an effective and attractive Tuberculosis Preventive Therapy (TPT) regimen. However, co-administration of 1 HP and Dolutegravir (DTG) based ART is limited due mainly to potential suboptimal DTG concentrations. Recent findings from A5372 and Taiwanese HIV cohort suggest the potential concomitant use of 1 HP with standard dose DTG in Asian people with HIV (PWH). We therefore assessed safety, pharmacokinetics and HIV viral load suppression of once daily tenofovir disoproxil fumarate/lamivudine/DTG (TLD) when co-administration with 1HP in ARV naïve and ARV experienced PWH.**

Avihingsanon A et al. IAS 2024; OAB1702

Standard DTG-based Regimens in Adults with HIV Taking 1HP for TB Preventive Therapy

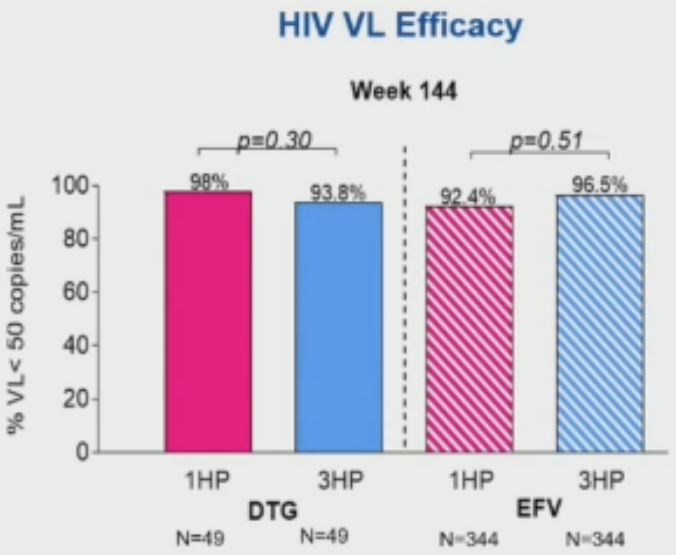
AIDS 2024



DTG C_{trough}, mg/L	1HP (N=27)		3HP (N=32)	
	Day 0	Day 28	Day 0	Day 28
	DTG alone	DTG+1HP	DTG alone	DTG+3HP
Geometric mean (95% CI)	0.56 (0.27-1.16)	0.15 (0.09-0.24)	0.98 (0.80-1.21)	0.86 (0.43-1.74)
>0.064 mg/L, N (%)*		25 (92.6%)		31 (96.9%%)

*protein-binding-adjusted IC_{90}

Avihingsanon A, et al. AIDS 2024 (OAB17021)

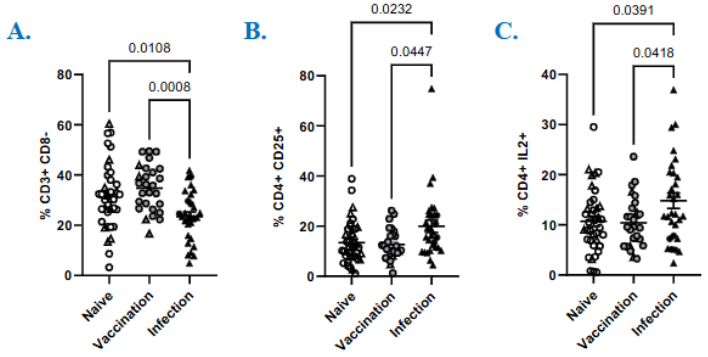


Immune response against Mpox

- **Objective: This study analyzed the immune response developed after mpox vaccination in comparison with mpox infection.**
- **People infected with mpox (mpox+) (n=30), people vaccinated against mpox (n=24; 4 of which were also previously vaccinated against smallpox), and people who were not in contact with mpox or smallpox (naive) (n=38) were recruited for this study.**

Quantification of CD4+ T lymphocytes, activation markers and cytokine production

A. Levels of CD4+ T cells of people infected with mpox were reduced compared to vacinnated and naïve individuals (p=0,0008 y p=0,0108, respectively).
B. Stimulation of CD4+ T cells with mpox peptides induced 1.5-fold more activation (CD25+) in mpox+ than in people vaccinated (p=0.0447) and naïve (p=0.0232).
C. CD4 expressed 1.4-fold higher levels of IL-2 in mpox+ than vaccinated (p=0.0.418) and naïve (p=0.0391) in response to mpox peptides.



O. de la Calle-Jiménez et al IAS 2024; THPEA017

W.H.O. Declares Global Emergency Over New Mpox Outbreak

RAPID RISK ASSESSMENT

Risk assessment for the EU/EEA of the mpox epidemic caused by monkeypox virus clade I in affected African countries

16 August 2024

Summary

Epidemiological situation

The monkeypox virus (MPXV) clade I epidemic that has been affecting the Democratic Republic of the Congo (DRC) since November 2023 has recently spread to several other African countries including Burundi, Rwanda, Uganda and Kenya. The size of these outbreaks could be larger than reported due to under-ascertainment and under-reporting.

On 15 August 2024, one case of MPXV clade Ib was reported in the EU/EEA and more imported MPXV clade I cases will likely occur. It is therefore important for European countries to be prepared to handle such imported cases and prevent secondary transmission.

In countries reporting clade I cases, human-to-human transmission through close physical contact and through both sexual and non-sexual transmission has been documented. Although all age groups are represented among cases infected with MPXV clade I, preliminary data show that infections by clade Ib virus concern mostly the adult population, whereas infections by clade Ia concern mostly children. To date, there are still significant uncertainties about the main transmission routes, transmissibility, severity, and natural disease history, and whether these differ between the two circulating subclades of clade I MPXV.

Mpox symptoms usually appear 6–13 days (up to 21 days) after infection. The clinical manifestation of the disease includes general febrile symptoms, a distinct rash (papules) on the skin and sores on the mucosa, back pain and muscle aches. The rash may spread quickly throughout the body within three days of experiencing the initial symptoms. Most people experience mild to moderate symptoms that usually last two to four weeks, followed by a full recovery.

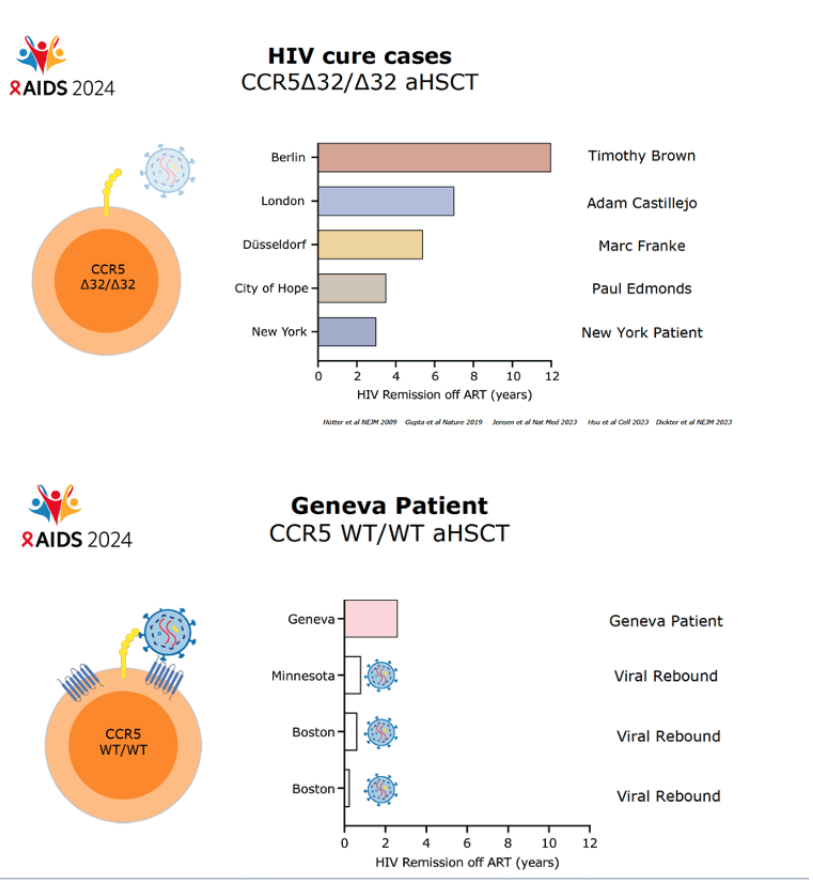
Risk assessment

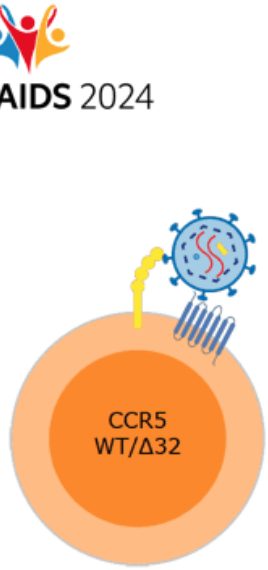
In the affected areas in the African continent:

The likelihood of infection with MPXV clade I for EU/EEA citizens travelling to or living in the affected areas and having close contact with affected communities is high, while the likelihood of infection is low when contacts with affected communities are avoided. The severity of the disease is expected to be low. Overall, the risk for these populations is **moderate** and **low**, respectively.

» HIV Cure

The next HIV Cure





The next Berlin Patient
CCR5 WT/Δ32 aHSCT

- Male, *1964, White
- Genotype: CCR5 WT/Δ32
- HIV diagnosed 2009, last neg. test 2008
- No ART until April 2015, then RAL/ABC/3TC
- AML diagnosis April 2015
- aHSCT October 2015 CCR5 WT/Δ32 donor
- Reduced Intensity Conditioning
- Acute GVHD (skin I°), topical steroids
- Full Donor Chimerism <1Month

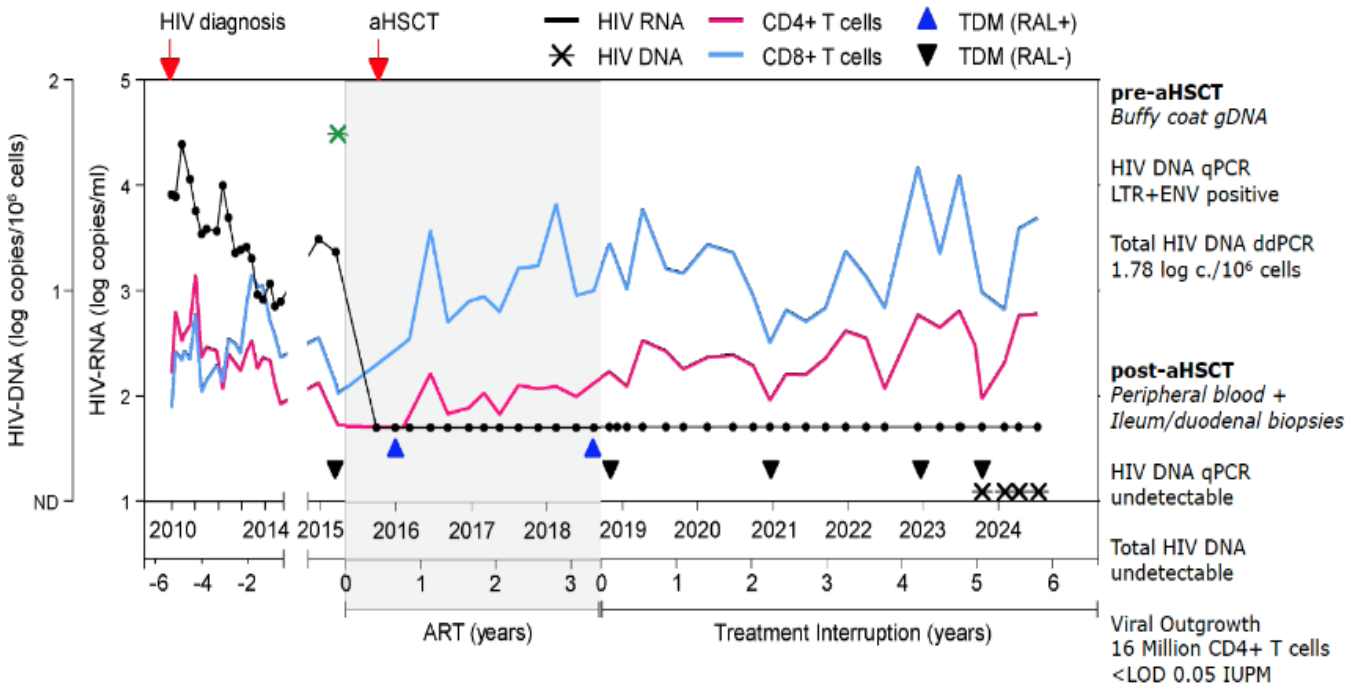
Donor and Recipient – HLA-identical

HLA-A	02:01, 02:01	HLA-DRB1	04:01, 16:01
HLA-B	15:01, 40:02	HLA-DQB1	03:01, 05:02
HLA-C	02:02, 03:04		

Gaebler. IAS 2024. Abstr SS0402LB.

HIV Remission After Heterozygous Allogeneic Hematopoietic Stem Cell Transplantation

- White male born in 1964, diagnosed with HIV in 2009
  - Viremic plasma sample from 2014 demonstrated CCR5 WT/Δ32 tropism
- Did not receive ART until April 2015 → initiated on RAL/ABC/3TC
- Diagnosed with AML April 2015 → aHSCT in October 2015 with reduced intensity conditioning
  - HLA-identical donor, CCR5 WT/Δ32
  - Full donor chimerism <1 mo



Gaebler. IAS 2024. Abstr SS0402LB.

Slide credit: clinicaloptions.com

The next HIV Cure

Conclusions

Prolonged HIV remission induced by aHSCT is not restricted to the use of homozygous CCR5Δ32/Δ32 donors

AIDS 2024

1. Prolonged HIV remission > five years without ART following heterozygous CCR5 WT/Δ32 aHSCT
2. HIV RNA and total HIV DNA were detected pre-aHSCT

→ no detectable HIV DNA or viral outgrowth post-aHSCT

3. Waning HIV-specific antibody and T cell immunity post-aHSCT

Effective reservoir reductions, durable HIV remission and potential cure can be achieved with functional viral co-receptors

→ **allogeneic immunity fundamentally contributes to HIV eradication.**

? Role of underlying CCR5 heterozygosity

? Innate/NK cell contribution to reservoir depletion

„Der Gesunde hat viele Wünsche, der Kranke nur einen."

"A healthy person has many wishes, a sick person only one."

The next Berlin Patient

Gaebler. IAS 2024. Abstr SS0402LB.

Summary

- The PURPOSE 1 trial has demonstrated 100% efficacy of lenacapavir, a twice-yearly injectable, in preventing new HIV infections among African cisgender women and adolescent girls.
- Initial data provide reassurance regarding use of CAB in pregnancy.
- DoxyPrEP significantly decreased rates of syphilis, chlamydia and gonorrhea compared to placebo, and was well-tolerated in MSM living with HIV.
- All GC were resistant to tetracycline but rate of high-level resistance mediated by the tetM gene were higher with Doxy-PEP. No impact of Doxy-PEP on Ceftriaxone susceptibility.
- Written or documented consent remains a requirement for HIV testing in more than a third of responding EU countries.
- The 2024 WHO HBV guidelines prioritize simplified treatment criteria for adults and adolescents and expanded eligibility for antiviral prophylaxis for pregnant women to prevent mother-to-child transmission of HBV.
- DTG/3TC in People With HIV With Isolated Reactive Anti-HBc showed no difference in efficacy endpoints; also no HBV reactivations were noted.
- HIV remission achieved after allogeneic hematopoietic stem cell transplantation.


Thank You for Your Attendance!
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