2024 IAS Conference Review

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Disclosures

No conflicts of interest or relationships to disclose.

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Data Considerations

Data in this presentation offer a limited perspective of how systemic, social, and economic factors impact health. We recognize that racism, not race, creates and perpetuates health disparities.

To Learn More:
https://www.cdc.gov/minorityhealth/racism-disparities

Agenda

- Initial evaluation of injectable cabotegravir (CAB-LA) safety during pregnancy in the HPTN 084 open-label extension (abstract 12420)
- STI testing rates among PrEP users randomized to 3-monthly (standard of care) or 6-monthly monitoring within the EZI-PrEP trial, the Netherlands: preliminary results (abstract 3295)
- Twice-Yearly Lenacapavir or Daily Emtricitabine/Tenofovir Alafenamide for HIV Prevention in Cisgender Women: Interim Analysis Results from the PURPOSE 1 Study

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Initial evaluation of injectable cabotegravir (CAB-LA) safety during pregnancy in the HPTN 084 open-label extension

S Delany-Moretlwe, E Voldal, F Saidi, L Stranix-Chibanda, M Bhondai-Mhuri, P Mandima, N Mgodi, P Mukwekwerere, J Mpendo, P Nahirya Ntege, C Nakabiito, S Innes, D Kalonji, P Bock, C Mathew, R Panchia, N Singh, E Spooner, H Nuwagaba-Biribonwoha, S Dadabhai, J Makhema, V Mudhune, J Farrior, S Rose, E Piwowar-Manning, M Holt, L Soto-Torres, S Zwerski, J Rooney, A Rinehart, M Cohen, M Hosseinipour **on behalf of the HPTN 084 study team**

AIDS 2024, Munich

HPTN HIV Prevention Trials Network

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Background

- HPTN 084, a phase 3, randomized, double-blind, double-dummy, active-controlled superiority trial in 20 sites in seven African countries, showed long-acting injectable cabotegravir (CAB-LA) significantly reduces HIV acquisition compared to daily oral TDF/FTC in individuals female at birth.
- During randomized trial period, participants had to use a long-acting reversible contraceptive and participants with a positive pregnancy test had CAB-LA held.
- However, few data exist regarding the safety of CAB-LA during pregnancy.
- **The HPTN 084 label extension (OLE) sought to evaluate the safety of CAB-LA during pregnancy.**

Delany-Moretlwe S, et al. Initial evaluation of injectable cabotegravir (CAB-LA) safety during pregnancy in the HPTN 084 open-label extension. AIDS 2024 Conference. 22-26 July 2024. Munich, Germany and virtual. Abstract ID: 12420.

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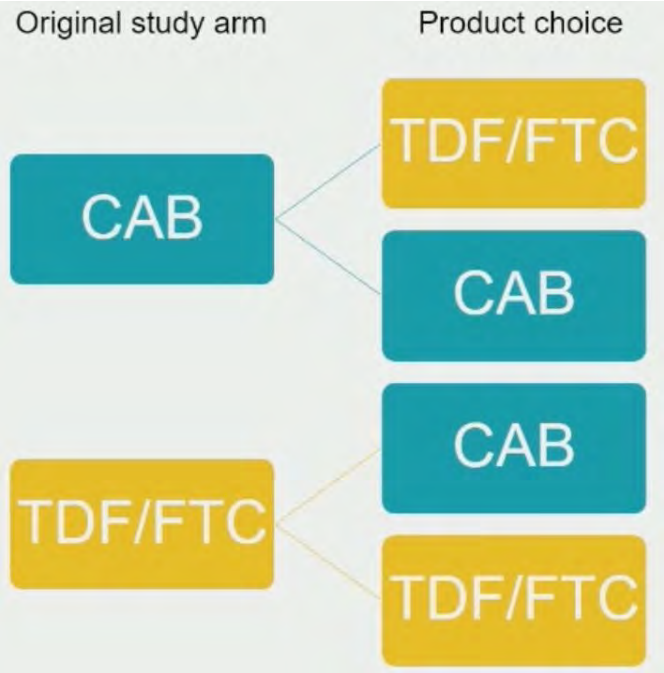
Methods



Ultrasound at Week 12

HIV testing and safety assessments at monthly visits through to pregnancy outcome

- **Population**: Persons assigned female at birth at 20 sites in seven African countries.
- **Design**: OLE in which eligible HPTN 084 participants were offered choice of open-label CAB-LA or TDF/FTC as PrEP, and the prior contraceptive restrictions were removed.

  Pregnancies categorized by exposure**:**
  1. CAB-LA **during pregnancy**
  2. CAB-LA **prior to pregnancy only**
  3. **No CAB-LA** (TDF/FTC group)
- **Study period**: Start of OLE in 2022 through 31 Dec 2023
- **Outcomes Monitored:**
  - Pregnancy incidence
  - Maternal adverse events (AEs)
  - Poor pregnancy outcomes
  - Infant outcomes

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Results

- 2472 HPTN 084 participants were enrolled in the OLE, among which there were 351 incident pregnancies among 334 participants over 3118 person years (incidence 11.3/100 person-years; 95% CI 10.1-12.5).

- **Maternal AEs:**
  - Any grade 2+ AE rate was higher in active CAB-LA group, but CIs overlapped
  - Pregnancy-related grade 2+ AE rates were similar across groups and CIs overlapped

	Active CAB-LA n (95% CI)	Prior CAB-LA n (95% CI)	No CAB-LA n (95% CI)
Any Grade 2+ AE incidence rate*	376 (337-417)	282 (208-374)	238 (168-326)
Pregnancy-related Grade 2+ AE incidence rate*	38 (27-53)	47 (20-93)	31 (10-73)
Gestational hypertension	9 (4-17)	6 (<1-33)	6 (<1-35)
Hyperemesis gravidarum	6 (2-14)	12 (1-42)	0 (0-23)
Afterbirth pain	6 (2-14)	6 (<1-33)	0 (0-23)
Pre-eclampsia	3 (1-9)	0 (0-22)	6 (<1-35)
Meconium-stained amniotic fluid	2 (<1-8)	0 (0-22)	0 (0-23)
Premature labour	1 (<1-6)	0 (0-22)	6 (<1-35)
Foetal distress	1 (<1-6)	6 (<1-33)	0 (0-23)
Post-partum haemorrhage	1 (<1-6)	6 (<1-33)	0 (0-23)
Cephalo-pelvic disproportion	0 (0-4)	6 (<1-33)	13 (2-45)

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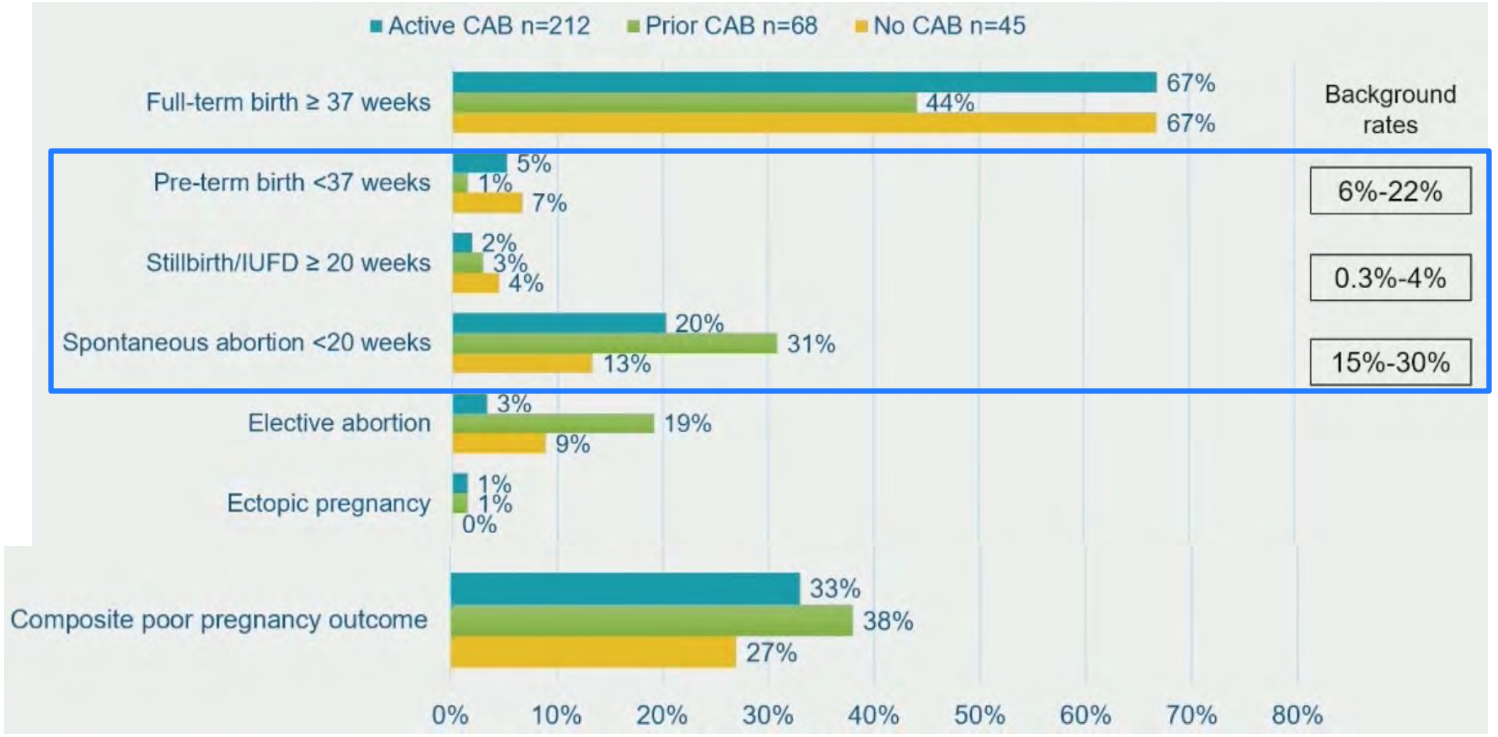
Results

- **Poor Pregnancy Outcomes:**
  - Poor pregnancy outcome rates relatively similar across groups*
  - Poor pregnancy outcome rates consistent with background rates
  - Composite poor pregnancy outcome rates similar across groups



*Spontaneous abortion rates should be interpreted with caution given elective abortions illegal in most countries where HPTN 084 was conducted.

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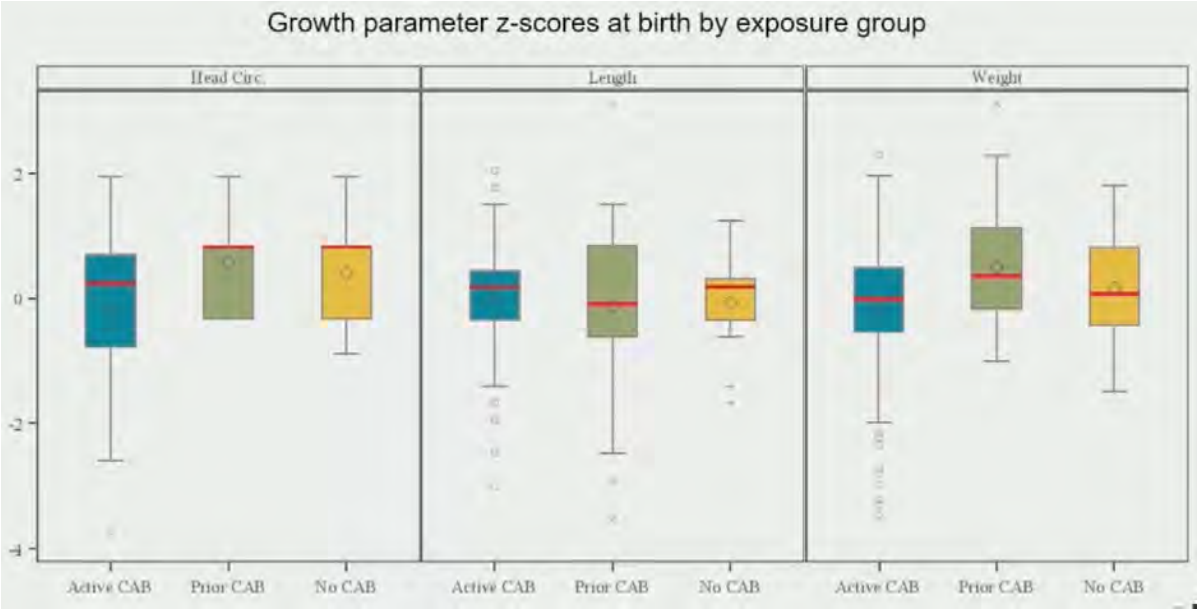
Results

- **Infant outcomes:**



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

1 death associated with major congenital anomaly, 3 deaths due to respiratory distress

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Conclusions

- **Maternal, pregnancy, and infant outcomes were similar across non-randomized exposure groups and consistent with expected background rates.**
  - No maternal deaths (or HIV infections - data not shown)
  - Similar rates of poor pregnancy outcomes
  - Infant growth parameters similar across exposure groups
- **CAB-LA was well tolerated in pregnant women.**
  - Pregnancy-related AE rates similar across groups

Initial data provide reassurance regarding use of CAB-LA in pregnancy, at least in populations where pregnancy and HIV incidence are high.

- Further accrual and evaluation of safety data is ongoing

Delany-Moretlwe S, et al. Initial evaluation of injectable cabotegravir (CAB-LA) safety during pregnancy in the HPTN 084 open-label extension. AIDS 2024 Conference. 22-26 July 2024. Munich, Germany and virtual. Abstract ID: 12420.

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GGD
Amsterdam

STI-testing rates and STI positivity among PrEP users randomized to 3- or 6-monthly monitoring

Preliminary analysis of the EZI-PrEP study , the Netherlands

Marije Groot Bruinderink
Maarten Schim van der Loeff & Udi Davidovich
Eline Wijstma

AIDS 2024

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Background

- Standard of care for PrEP monitoring for STIs involves visits every 3 months.
- Concerns with 3-monthly PrEP monitoring include that it may be a burden on PrEP users, costly, lead to over-treatment that could drive resistance, and may not impact STI prevalence.
- **The EZI-PrEP study sought to evaluate the impact of 6- vs 3-monthly PrEP STI monitoring on number of clinic visits and STIs diagnosed.**

Bruinderink M, et al. STI testing rates among PrEP users randomized to 3-monthly (standard of care) or 6-monthly monitoring within the EZI-PrEP trial, the Netherlands: preliminary results. AIDS 2024 Conference. 22-26 July 2024. Munich, Germany and virtual. Abstract ID: 3295.

Methods

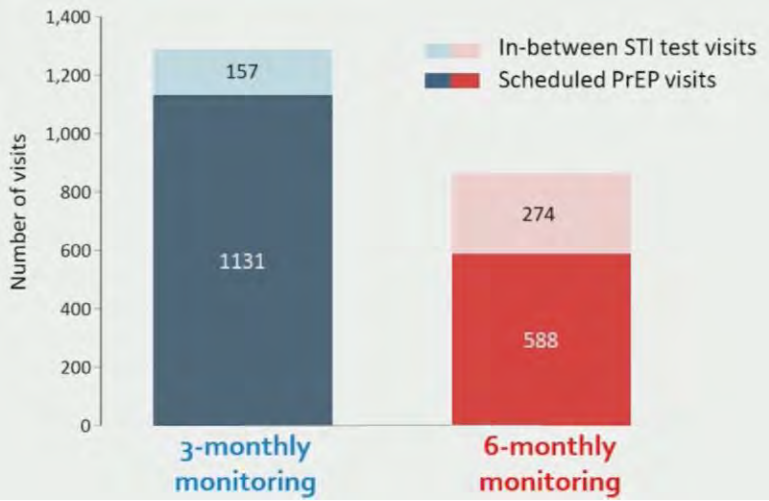
- **Population**: MSM at four sites in the Netherlands.
- **Design**: Randomized controlled trial on the non-inferiority of 6-monthly versus 3-monthly PrEP monitoring. Free in-between visit STI testing allowed.
- **Study period**: September 2021-March 2022
- **Outcomes**:
  - Overall visit rate (including in-between visits)
  - In-between STI test visit rate
  - Positive bacterial STI rate (chlamydia, gonorrhea, syphilis)

Bruinderink M, et al. STI testing rates among PrEP users randomized to 3-monthly (standard of care) or 6-monthly monitoring within the EZI-PrEP trial, the Netherlands: preliminary results. AIDS 2024 Conference. 22-26 July 2024. Munich, Germany and virtual. Abstract ID: 3295.

Results

- 448 participants were 1:1 randomized to 3-monthly (n=225) or 6-monthly (n=223) scheduled testing, contributing a total of 560 person-years of follow-up.

- **Visit rates in 6- vs 3-monthly monitoring arm**



	Visit rate per py [95% CI]		Visit rate ratio [95% CI] (6-mo. vs 3-mo.)	*p*
	6-monthly monitoring arm	3-monthly monitoring arm		
Any visit	**3.1** [2.9-3.3]	**4.6** [4.3-4.8]	**0.68** [0.62-0.74]	<0.0001
Unscheduled, in-between STI visits	**0.99** [0.88-1.11]	**0.56** [0.47-0.65]	**1.78** [1.46-2.18]	<0.0001

Bruinderink M, et al. STI testing rates among PrEP users randomized to 3-monthly (standard of care) or 6-monthly monitoring within the EZI-PrEP trial, the Netherlands: preliminary results. AIDS 2024 Conference. 22-26 July 2024. Munich, Germany and virtual. Abstract ID: 3295.

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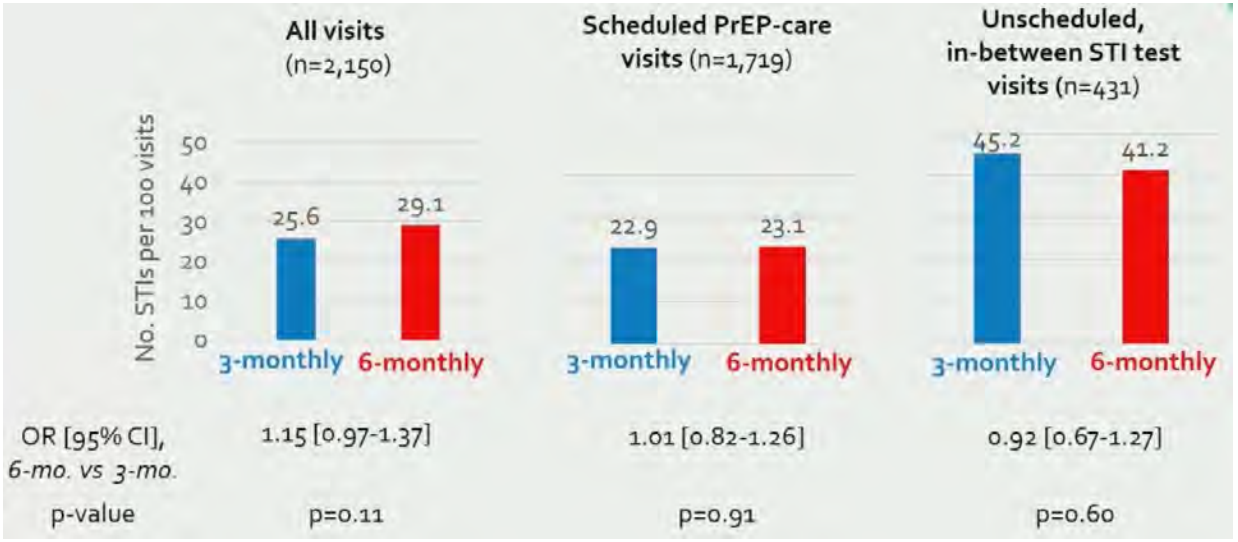
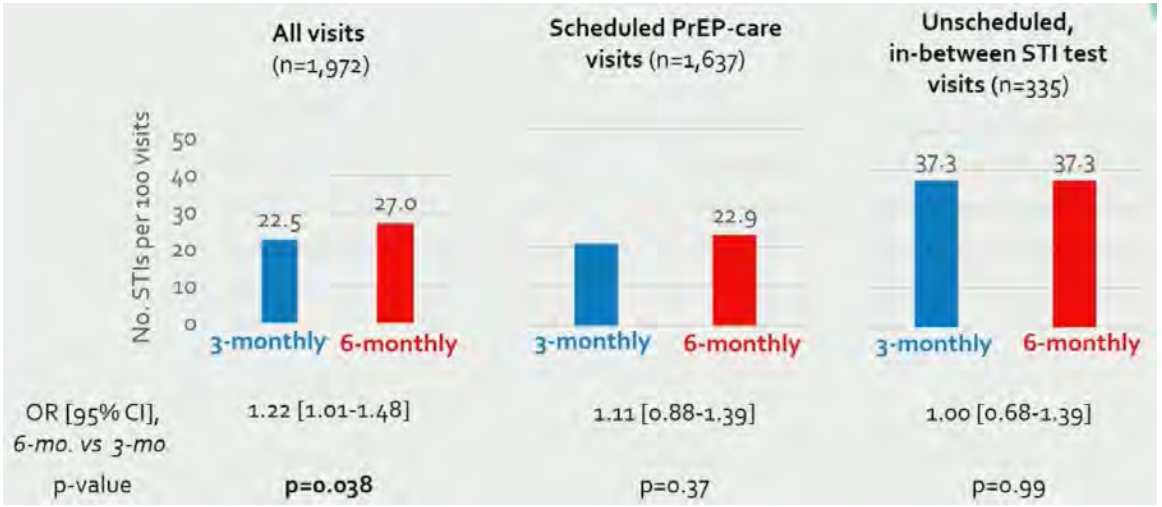
Results

- **STI positivity in 6- vs 3-monthly monitoring arm**

STI positivity by monitoring frequency



Asymptomatic* STI positivity by monitoring frequency



* included only visits where the participant did not report any STI-related symptoms

Bruinderink M, et al. STI testing rates among PrEP users randomized to 3-monthly (standard of care) or 6-monthly monitoring within the EZI-PrEP trial, the Netherlands: preliminary results. AIDS 2024 Conference. 22-26 July 2024. Munich, Germany and virtual. Abstract ID: 3295.

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Conclusions

- **Monitoring every 6 months vs every 3 months leads to**:
  - More in-between STI test visits
  - Fewer scheduled PrEP monitoring visits
  - Fewer overall visits
- **Overall STI positivity similar in the two monitoring frequency groups**:
  - Slightly higher positivity of asymptomatic STIs in the 6-monthly arm

6-monthly monitoring as standard of care may reduce healthcare costs and burden on PrEP users without a resulting major increase in STIs.

- Dutch guidelines updated in 2024 to advise monitoring of PrEP users q6 months.

Bruinderink M, et al. STI testing rates among PrEP users randomized to 3-monthly (standard of care) or 6-monthly monitoring within the EZI-PrEP trial, the Netherlands: preliminary results. AIDS 2024 Conference. 22-26 July 2024. Munich, Germany and virtual. Abstract ID: 3295.

PURPOSE

Prevention with PURPOSE

AIDS 2024

Twice-Yearly Lenacapavir or Daily Oral Emtricitabine/Tenofovir Alafenamide for HIV Prevention in Cisgender Women: Interim Analysis Results from the PURPOSE 1 Study

Linda-Gail Bekker, MBChB, PhD, on behalf of the PURPOSE 1 Study Team

The Desmond Tutu HIV Centre, University of Cape Town, Cape Town, South Africa

Co-authors: Moupali Das, Quarraisha Abdool Karim, Khatija Ahmed, Joanne Batting, William Brumskine, Katherine Gill, Ishana Harkoo, Manjeetha Jaggernath, Godfrey Kigozi, Noah Kiwanuka, Philip Kotze, Limakatso Lebina, Cheryl E. Louw, Moelo Malahleha, Mmatsie Manentsa, Leila E. Mansoor, Dhayendre Moodley, Vimla Naicker, Logashvari Naidoo, Megeshinee Naidoo, Gonasagrie Nair, Nkosiphile Ndlovu, Thesla Palanee-Phillips, Ravindre Panchia, Saresha Pillay, Disebo Potloane, Pearl Selepe, Nishanta Singh, Yashna Singh, Elizabeth Spooner, Amy M. Ward, Zwelethu Zwane, Ramin Ebrahimi, Yang Zhao, Alexander Kintu, Chris Deaton, Christoph Carter, Jared M. Baeten, and Flavia Matovu Kiweewa

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Background

- Cisgender women account for about half of the 1.3 million new HIV infections that occur annually.
- The standard PrEP for cisgender women involves daily oral TDF/FTC (i.e., F/TDF), which is effective if taken as directed.
- However, women's poor uptake of, adherence to, and persistence in the use of oral PrEP remains limited worldwide, underscoring the need for new options.
- Lenacapavir, a novel, first-in-class, multi-stage HIV-1 capsid inhibitor, offers a novel, long-acting alternative with twice-yearly subcutaneous injections.
- **The PURPOSE 1 study sought to assess the efficacy of lenacapavir and F/TDF in preventing HIV acquisition.**

Bekker LG. Twice-Yearly Lenacapavir or Daily Emtricitabine/Tenofovir Alafenamide for HIV Prevention in Cisgender Women: Interim Analysis Results from the PURPOSE 1 Study. Co-Chairs' Choice Special Session. AIDS 2024 Conference. 22-26 July 2024. Munich, Germany and virtual.
Bekker LG et al. Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women. N Engl J Med. 2024 Jul 24. doi: 10.1056/NEJMoa2407001.

Methods

- **Population**: Adolescent girls and young women from 28 sites in South Africa and Uganda.
- **Design:** Phase 3, double-blind, randomized controlled trial comparing twice-yearly subcutaneous lenacapavir, daily oral F/TAF, and daily oral F/TDF (active control).
- **Study period**: August 2021– August 2023
- **Outcomes**:
  - HIV incidence in each group
  - Adherence to PrEP regimens
  - Safety profiles, including injection-site reactions

Bekker LG. Twice-Yearly Lenacapavir or Daily Emtricitabine/Tenofovir Alafenamide for HIV Prevention in Cisgender Women: Interim Analysis Results from the PURPOSE 1 Study. Co-Chairs' Choice Special Session. AIDS 2024 Conference. 22-26 July 2024. Munich, Germany and virtual.
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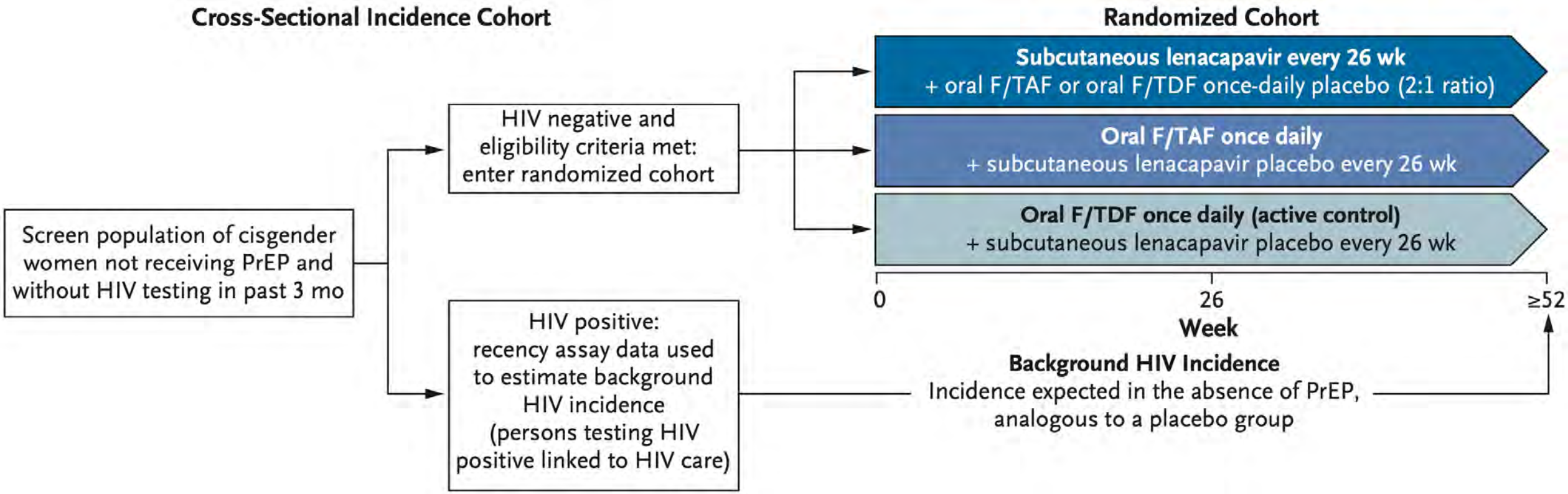
Methods

- Trial design



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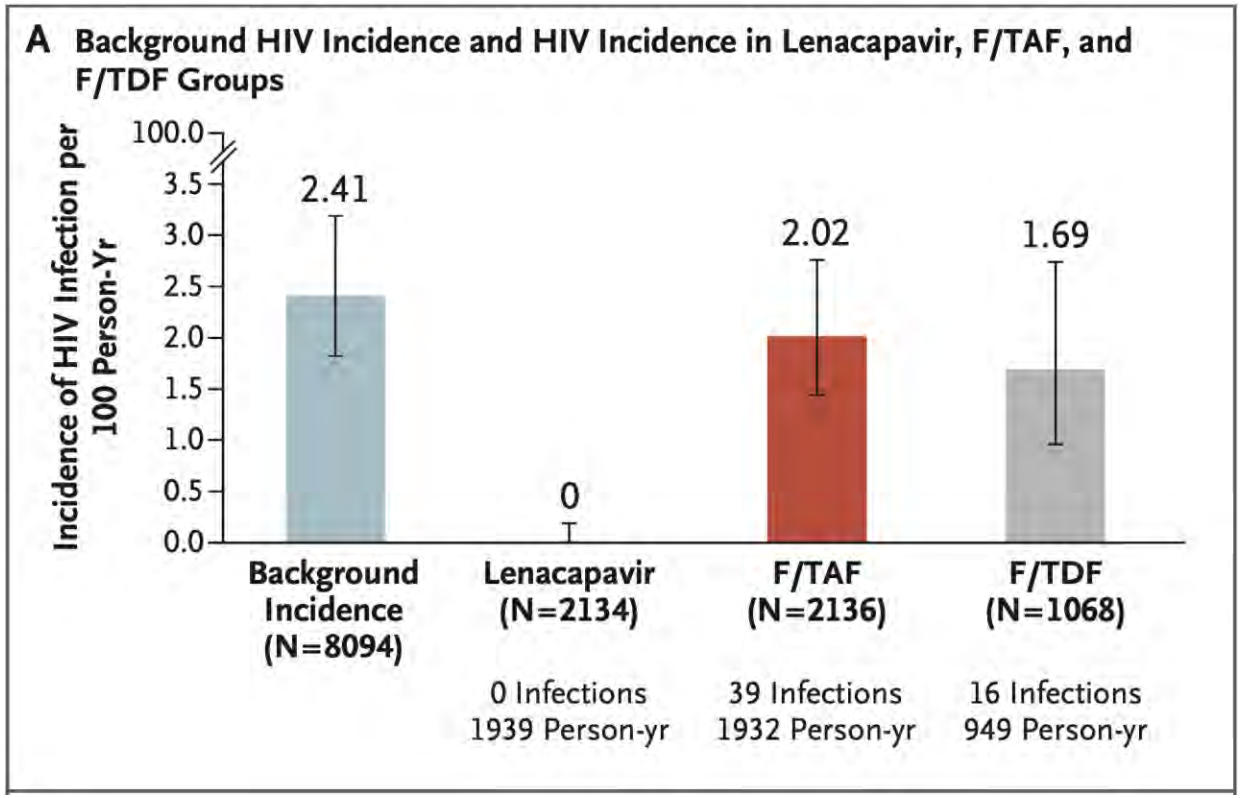
Results

- 5338 initially HIV-negative participants randomized 2:2:1 to lenacapavir (n=2148), F/TAF (n=2147), or F/TDF (n=1073).
- **Incidence of HIV infection:**



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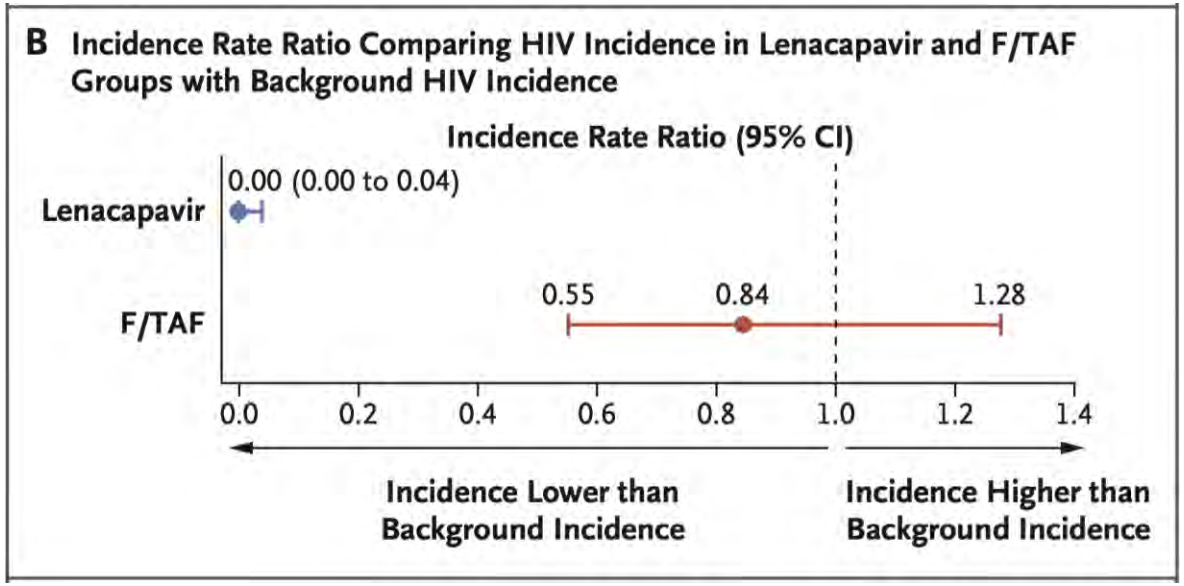
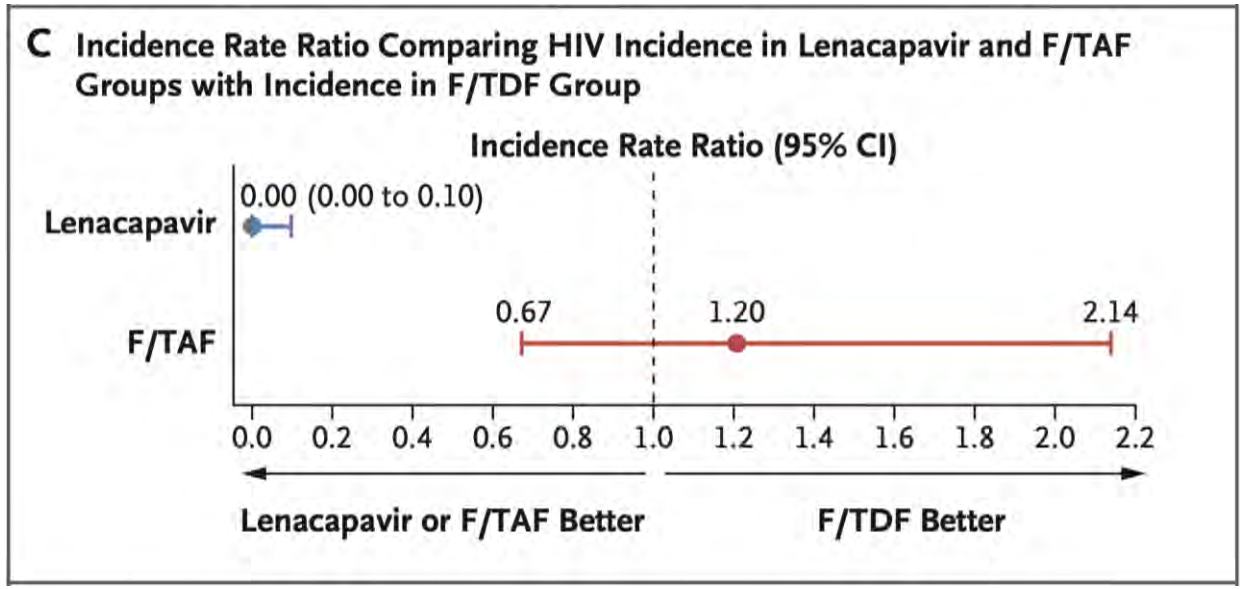
Results

- **Incidence of HIV infection:**





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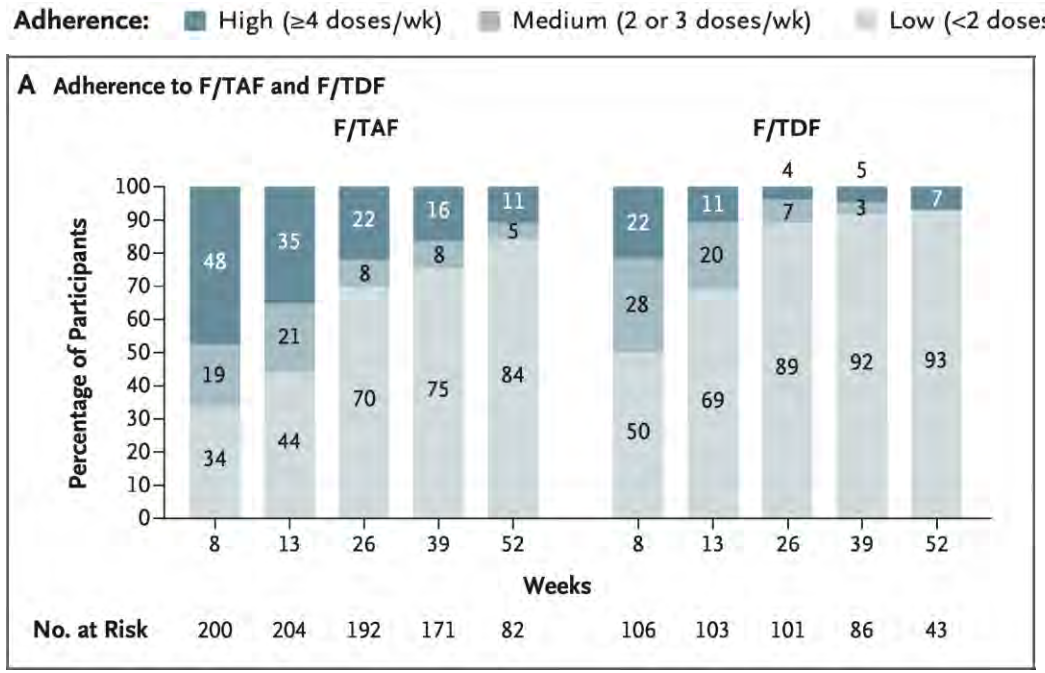
Results

- **Adherence to PrEP:**
  - 92% adherence to lenacapavir
  - Adherence much lower for oral PrEP



- **Safety**
  - Injection-site reactions more common in 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 trial regimen owing to injection-site reactions.

Bekker LG. Twice-Yearly Lenacapavir or Daily Emtricitabine/Tenofovir Alafenamide for HIV Prevention in Cisgender Women: Interim Analysis Results from the PURPOSE 1 Study. Co-Chairs' Choice Special Session. AIDS 2024 Conference. 22-26 July 2024. Munich, Germany and virtual.
Bekker LG et al. Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women. N Engl J Med. 2024 Jul 24. doi: 10.1056/NEJMoa2407001.

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Conclusions

- **No participants receiving twice-yearly lenacapavir acquired HIV infection.**
  - HIV incidence with lenacapavir was significantly lower than background HIV incidence and HIV incidence with F/TDF.
- **Adherence**: Low adherence was observed to both daily oral F/TAF and F/TDF.
- **Safety**: No major safety concerns, but higher injection-site reactions were seen with lenacapavir (68.8%) compared to placebo (34.9%).

Twice-yearly lenacapavir offers a highly efficacious and discreet option to potentially improve PrEP use among women.

- Evaluations of efficacy & safety in other populations and long-term, as well as real-world effectiveness, are ongoing

Bekker LG. Twice-Yearly Lenacapavir or Daily Emtricitabine/Tenofovir Alafenamide for HIV Prevention in Cisgender Women: Interim Analysis Results from the PURPOSE 1 Study. Co-Chairs' Choice Special Session. AIDS 2024 Conference. 22-26 July 2024. Munich, Germany and virtual.
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Summary

- HPTN 084 open-label extension (Sub-Saharan Africa) has provided reassuring data regarding the use of CAB-LA in pregnancy, at least among populations where pregnancy and HIV incidence are high.

- EZI-PrEP study (Netherlands) suggested that STI monitoring every 6 months instead of every 3 months as standard of care may reduce healthcare costs and burden on PrEP users without a resulting major increase in STIs.

- PURPOSE 1 study (South Africa, Uganda) provided compelling evidence that the twice-yearly lenacapavir offers a highly efficacious option to potentially improve PrEP use among cisgendered women.

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Q&A, Discussion

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Acknowledgment

This Mountain West AIDS Education and Training (MWAETC) program is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of award 1 TR7HA53202-01-00 totaling $2,982,063 with 0% financed with non-governmental sources.

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