PrEP for HIV Prevention
Update from IAS 2025

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Disclosures

As of August 2025, the following medications are approved by the U.S. Food and Drug Administration (FDA) for use as HIV pre-exposure prophylaxis (though may not be approved for all populations):

2012: FTC/TDF (Truvada)
2019: FTC/TAF (Descovy)
2021: Long Acting Cabotegravir (CAB-LA, Apretude)
2025: Lenacapavir (as Yeztugo)

This talk will include discussion of non-FDA approved strategies for HIV prevention.

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Disclaimer

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AETC AIDS Education & Training Center Program Mountain West

Outline

- MK-8527
- Lenacapavir as PrEP - updates
- PrEP preferences
- Pregnancy and feeding outcomes with injectable PrEP
- AI and novel technologies

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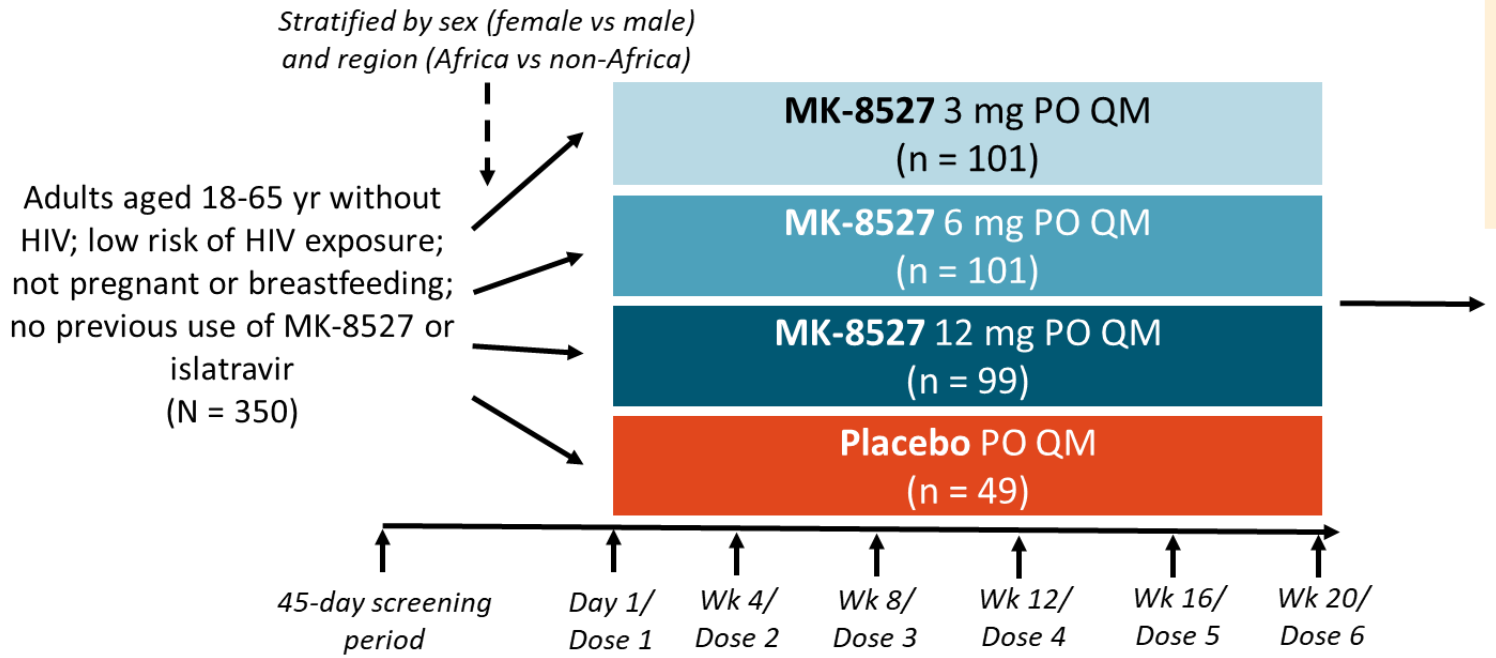
"Safety and pharmacokinetics of MK-8527 oral once-monthly: a Phase II study in adults at low risk of HIV-1 exposure"

- MK-8527 = oral Nucleoside Reverse Transcriptase Translocation Inhibitor (NRTTI)
- Phases
  - I: testing small numbers to assess safety and dosage
  - II: larger numbers to further assess safety and maybe efficacy
  - III: large scale efficacy trials
  - IV: post-marketing surveillance

IAS 2025, Mayer et al, #OAS0106LB
Slideset available: https://clinicaloptions.com/activities/infectious-disease/mk-8527/106633/content

"Safety and pharmacokinetics of MK-8527 oral once-monthly: a Phase II study in adults at low risk of HIV-1 exposure"

- International, double-blind, randomized, dose-ranging phase IIa trial



- AEs, labs reviewed at each visit through 8 wk after final dose; HIV testing at screening, Day 1, and Q4W
- Plasma MK-8527 measured on Days 1-2, Wk 20, or final dose, and FU Day 1; MK-8527 TP in PBMCs in ~20 participants/ group at each visit

8 wk blinded follow-up (FU Wk 4, FU Wk 8)

*Participants left the study for any on-treatment decrease in total lymphocyte and/or CD4+ count (defined as <1.0 x 10^9/L and <500 cells/mm^3 decrease, respectively, with a ≥30% decline from BL, confirmed at 2 consecutive visits).

- **Coprimary endpoints**: safety, number of participants discontinuing treatment due to AE
- **Secondary endpoints:** $AUC_{0\text{-last}}$, C_{max} of MK-8527

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"Safety and pharmacokinetics of MK-8527 oral once-monthly: a Phase II study in adults at low risk of HIV-1 exposure"

Participants, n (%)	MK-8527 3 mg (n = 101)	MK-8527 6 mg (n = 101)	MK-8527 12 mg (n = 99)	Placebo (n = 49)
With 1 or more AE	62 (61.4)	69 (68.3)	66 (66.7)	31 (63.3)
With drug-related* AE	15 (14.9)	16 (15.8)	20 (20.2)	9 (18.4)
With grade 3-4 AE	5 (5.0)	2 (2.0)	4 (4.0)	4 (8.2)
With SAE	2 (2.0)	0 (0.0)	1 (1.0)	1 (2.0)
With drug-related SAE	1 (1.0)	0 (0.0)	0 (0.0)	1 (2.0)
Discontinued due to AE	0 (0.0)	2 (2.0)	1 (1.0)	2 (4.1)
Discontinued due to drug-related AE	0 (0.0)	1 (1.0)	1 (1.0)	0 (0.0)

*Determined by investigator.

IAS 2025, Mayer et al, #OAS0106LB
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Participants, n (%)	MK-8527 3 mg (n = 101)	MK-8527 6 mg (n = 101)	MK-8527 12 mg (n = 99)	Placebo (n = 49)
≥1 drug-related* AE	15 (14.9)	16 (15.8)	20 (20.2)	9 (18.4)
≥1 drug-related grade 3-4 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)

*Determined by investigator.

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"Safety and pharmacokinetics of MK-8527 oral once-monthly: a Phase II study in adults at low risk of HIV-1 exposure"

Conclusions

- MK-8527 was well tolerated and showed similar safety profile as placebo.
- MK-8527 exposure and levels were proportional to dose.
- Phase III trials to start enrollment in 2025
    - 11mg MK-8527 v FTC/TDF
    - EXPrESSIVE-10: women in sub-Saharan Africa
    - EXPrESSIVE-11: San Francisco, North Carolina, Texas

https://clinicaltrials.gov/study/NCT07071623 and NCT07044297

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Lenacapavir updates

- June 18, 2025: FDA approved.
- July 9: Global Fund secures agreement to obtain LEN for 2 million people at cost.
  - https://www.theglobalfund.org/en/news/2025/2025-07-09-global-fund-secures-access-breakthrough-hiv-prevention-drug-lenacapavir/
- July 14: WHO recommends LEN along with point-of-care HIV testing.
  - https://www.who.int/publications/i/item/9789240111608

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"Preference for twice-yearly injections vs daily oral pills for HIV PrEP in … people enrolled in PURPOSE 2"

Factor, n (%)	Daily Pills Preferred (n = 97)	Twice-Yearly Injections Preferred (n = 751)
Perceived risk and safety	15 (15.5)	23 (3.1)
Perceived efficacy	11 (11.3)	189 (25.2)
Adherence feasibility and forgetfulness	5 (5.2)	218 (29.0)
Routine integration	3 (3.1)	9 (1.2)
Convenience and logistic effort	24 (24.7)	417 (55.5)
Lifestyle compatibility or burden	3 (3.1)	46 (6.1)
Emotional response to mode	7 (7.2)	9 (1.2)

Factor, n (%)	Daily Pills Preferred (n = 97)	Twice-Yearly Injections Preferred (n = 751)
Affective forecasting, anticipated regret	3 (3.1)	84 (11.2)
Pain and discomfort	52 (53.6)	11 (1.5)
Body autonomy and control	1 (1.0)	7 (0.9)
Stigma and disclosure concerns	1 (1.0)	1 (0.1)
Trust in system and tech	0	2 (0.3)
Other	3 (3.1)	29 (3.9)

- Overall, **most favored twice-yearly injections** (78%) over daily pills (11%)

Mngadi. IAS 2025. Abstr OAC0502.

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"Updates on the evaluation of CAB-LA safety during pregnancy"

- Pregnancy was an exclusion criteria in HPTN 084. Participants who became pregnant had CAB stopped.
- In the HPTN 084 OLE, they were consented to continue.
- Safety data continues to accrue, PK analyses are pending.

IAS 2025, Delany-Moretiwe, #SY1904
Slideset available: https://www.natap.org/2025/IAS/IAS_44.htm

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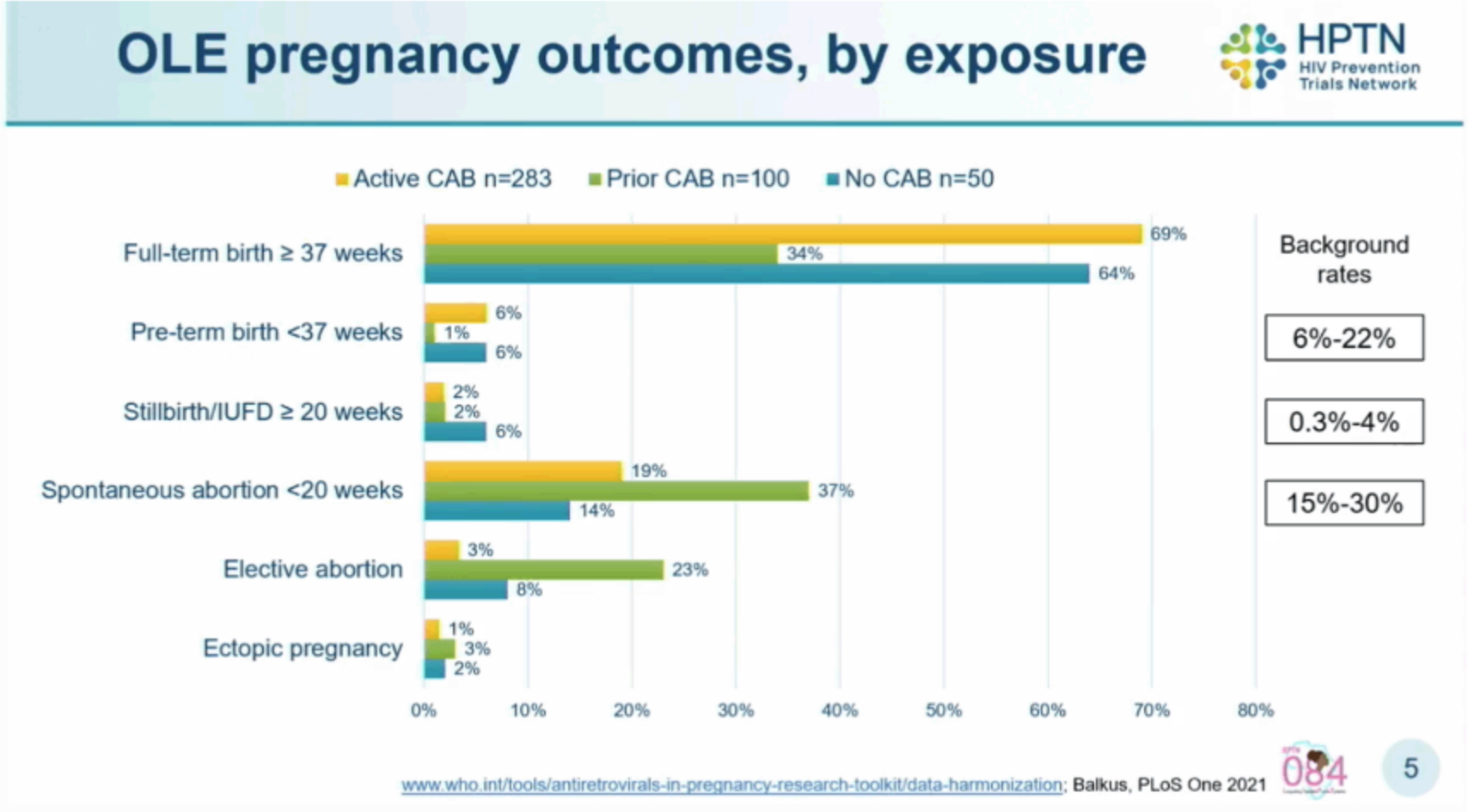
"Updates on the evaluation of CAB-LA safety during pregnancy"



IAS 2025, Delany-Moretiwe, #SY1904
Slideset available: https://www.natap.org/2025/IAS/IAS_44.htm

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"Updates on the evaluation of CAB-LA safety during pregnancy"

Infant outcomes, by exposure

HPTN HIV Prevention Trials Network

	Active CAB-LA N (% or IQR)	Prior CAB-LA	No CAB-LA
Live infants	218	35	37
Median gestational age at delivery (weeks)	39 (38-40)	39 (37-40)	37 (38-39)
Median birth weight (kg)	3 (3-3)	3 (3-4)	3 (3-4)
Small for gestational age (≤10%)	23 (11)	2 (6)	4 (11)
Major congenital anomalies*	2	0	0
Neonatal death with 28 days**	7 (3)	0	0
Respiratory distress	5	-	-
Exomphalos	1	-	-
Not specified	1	-	-

* Exomphalos, trisomy 21
**data available for 201 active CAB, 34 prior CAB, 35 no CAB

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IAS 2025, Delany-Moretiwe, #SY1904
Slideset available: https://www.natap.org/2025/IAS/IAS_44.htm

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Pregnancy and lactation "in the PURPOSE 1 study: efficacy, safety, and pharmacokinetics"

- Pregnancy was an exclusion criteria at baseline. Participants who became pregnant were re-consented.
- PK substudy at wk 0, 4, 8, 13, 26, 39, 52, 65, and 78.
- Infant plasma and breast milk samples obtained at weeks 52/65 or 65/78.

Bekker et al., IAS 2025, abstract #OAC0504
Slide credit: clinicaloptions.com

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Pregnancy and lactation "in the PURPOSE 1 study: efficacy, safety, and pharmacokinetics"

Outcome	LEN (n = 184)	FTC/TAF (n = 208)	FTC/TDF (n = 95)
Confirmed pregnancy(ies), n	193	218	98
Pregnancy status, n (%)			
▪ Completed	186 (96.4)	207 (95.0)	97 (99.0)
▪ Unknown	7 (3.6)	11 (5.0)	1 (1.0)
Live births,* n (%)	128 (66.3)	119 (54.6)	56 (57.1)
Pregnancy losses, n (%)	60 (31.1)	89 (40.8)	41 (41.8)
▪ Stillbirth	5 (2.6)	6 (2.8)	3 (3.1)
▪ Induced abortion†	35 (18.1)	50 (22.9)	23 (23.5)
▪ Spontaneous miscarriage‡	20 (10.4)	33 (15.1)	15 (15.3)
Congenital abnormalities, n	6	4	--

*Data include 3 pregnancies with 2 outcomes due to twins. †Fetal death at ≥20 wk gestation. ‡Occurring at <20 wk gestation.

Bekker et al., IAS 2025, abstract #OAC0504
Slide credit: clinicaloptions.com

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Pregnancy and lactation "in the PURPOSE 1 study: efficacy, safety, and pharmacokinetics"

- PKs were similar in pregnancy v non pregnant, abdomen v thigh.
- LEN was present in breast milk (median 52% of plasma levels, IQR 38-77).
- Median LEN concentrations in infant plasma was 2% of maternal plasma (1-5%).

- Conclusions: LEN was effective, safe, and well-tolerated in pregnant and lactating participants.

Bekker et al., IAS 2025, abstract #OAC0504
Slide credit: clinicaloptions.com

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Artificial intelligence

- Innovative use of mobile digital chest-xray equipped with artificial intelligence to improve TB diagnosis among people living with HIV at primary health centres (PHCs) in Lagos, Nigeria. Udunze et al. #OAE0604
- AI-powered preventive intervention for stigma and suicidal ideation in HIV self-management: development, evaluation, and user testing of the MARVIN chatbot's integrated mental health management module. Villanueva et al. #0AD0602
- Self-care from anywhere: usability of an AI-Driven HIV testing and care toolkit for AGYW and clinicians in South Africa. Bokolo et al. #LB49

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