3rd Long-Acting HIV Treatment and Prevention Conference

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Safety first:

Long-acting HIV prevention and treatme
in pregnancy and lactation

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Safety first: the framing

Long-acting options can prevent HIV acquisition and support treatment continuity. Pregnancy and lactation require a deliberate safety architecture.

1. Offer choice

Do not make pregnancy or breastfeeding a reason to withhold effective prevention when a person wants or needs PrEP.

2. Match evidence to product

Oral PrEP and ART have the deepest pregnancy safety record; CAB-LA and LEN have increasingly reassuring pregnancy/lactation data; LA ART treatment data remain limited.

3. Build surveillance

Safety-first programs include HIV testing, pregnancy registries, adverse event monitoring, infant follow-up, and clear plans for missed PrEP or ART pills, injections or discontinuation.

CLINICAL PRINCIPLE → IMPLEMENTATION PRINCIPLE → RESEARCH PRINCIPLE

Sources: HHS Perinatal HIV Guidelines 2026; Sullivan et al. AIDS 2026; Joseph Davey et al. AIDS 2024, WHO Guidelines 2025-6.

Why pregnancy and lactation cannot wait

HIV prevention has a maternal & an infant benefit in the same clinical encounter.

2x+

higher HIV acquisition risk reported during pregnancy/postpartum

45%

of new pediatric cases attributed to incident maternal infection in some estimates

6 mo

postpartum remains a high-risk period with lower clinic contact

1 visit

can combine ANC/PNC, HIV testing, STI care and prevention choice

1 **Periconception**
risk assessment
method choice

2 **Pregnancy**
nausea, side effects
routine visits

3 **Early postpartum**
caregiving load
fewer health visits

4 **Breastfeeding**
sustained protection
infant follow-up

Clinical implication
Prevention and treatment of HIV support must extend beyond antenatal initiation and be built for postpartum persistence & adherence.

Sources: Graybill et al. AIDS 2020; Mofenson J Infect Dis 2018; Joseph Davey et al. AIDS 2024; Lancet Global Health, 2025.

Ethical starting point: exclusion is not neutral

When pregnant and lactating people are excluded from trials, clinicians and patients still make decisions - just with weaker evidence.

Evidence gap risks

Misdosing, undetermined fetal/infant risks, provider hesitation, and restricted access.

Responsible inclusion

Pregnancy-specific PK, active safety follow-up, infant outcomes, community participation, and informed consent.

Reproductive justice

Pregnancy and lactation should not remove autonomy over HIV prevention or treatment decisions.

Protect through research - not from research.

A safety-first stance includes transparent uncertainty and rapid evidence generation.

Sources: Sullivan et al. AIDS 2026; PHASES Ethics Guidance, 2026; WHO antiretrovirals in pregnancy research toolkit.

Evidence landscape in 2026

Prevention products now have pregnancy/lactation-specific data; long-acting treatment remains cautious.

Product	Role	Interval	Pregnancy/lactation evidence	Safety-first posture
TDF/FTC oral	PrEP	Daily	Deepest evidence base	Recommended; safety benchmark
CAB-LA	PrEP	Every 2 months	HPTN 084 + OLE; emerging lactation	Offer/consider with shared decision-making
LEN	PrEP	Every 6 months	PURPOSE 1 pregnancy/lactation substudy	Accelerated access where available
DVR	PrEP	Monthly ring	DELIVER + B-PROTECTED	Option where approved; acceptability varies
CAB/RPV	ART treatment	Monthly/Q2M	Small PK/case data; RPV exposure concern	Expert consultation; avoid casual switching

Green: use with routine monitoring

Amber: shared decision + surveillance

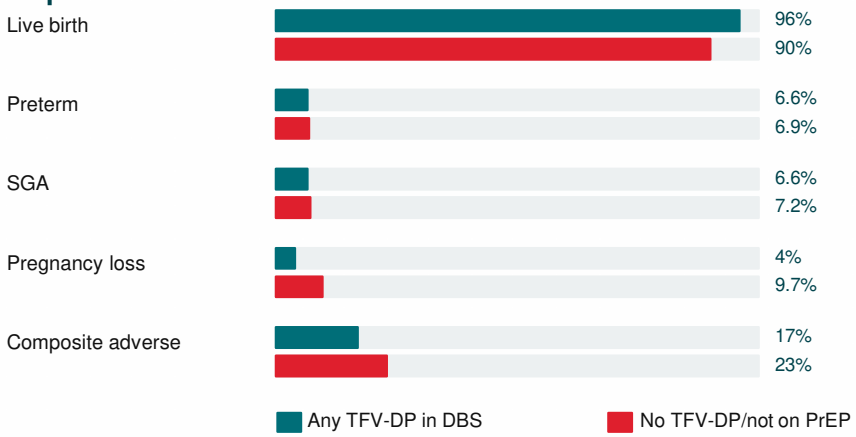
Red: specialist ART planning

Sources: HHS Perinatal HIV Guidelines 2026; WHO LEN guidance 2025; HPTN 084; PURPOSE 1; DELIVER/B-PROTECTED; Sunagawa et al. OFID 2025.

Oral PrEP: the safety benchmark

South African PrEP-PP data with objective TFV-DP exposure showed no signal for adverse pregnancy or birth outcomes.

PrEP-PP pregnancy/birth outcomes by objective TFV-DP exposure



What this establishes

- TDF/FTC has reassuring pregnancy safety data
- Objective adherence measurement matters
- 12-month child follow-up data are increasingly reassuring
- Remaining gap: first trimester/periconception and early losses

Clinical translation

Use oral PrEP evidence to normalize HIV prevention in ANC/PNC while offering long-acting choices.

Sources: Joseph Davey et al. AIDS 2024; Gómez et al. Lancet Glob Health 2025; Joseph Davey & Bunge Lancet GH Comment 2025.

CAB-LA PrEP: strong efficacy, reassuring pregnancy PK/safety

CAB-LA every 2 months reduces the adherence burden; pregnancy-specific data are emerging and reassuring.

HPTN 084 pregnancy analysis

57 pregnancies
30 CAB-LA vs 27 TDF/FTC
81% live births
No congenital anomalies observed

Safety signal

Grade 2+ maternal adverse events and composite poor pregnancy outcomes did not differ significantly by arm.

PK signal

CAB apparent terminal half-life was comparable in pregnant and non-pregnant women after injection cessation.

Safety-first implementation questions

Rule out acute HIV before initiation and at follow-up.
Create a missed-injection and oral bridging plan.
Document pregnancy/lactation exposure and infant outcomes.

Sources: Delany-Moretlwe et al. J Int AIDS Soc 2025; HHS Perinatal HIV Guidelines 2026; NIH CAB-LA pregnancy release 2024.

Lenacapavir PrEP: twice-yearly prevention with fast-moving evidence

LEN changes the implementation equation: two subcutaneous injections per year with pregnancy/lactation data from PURPOSE 1.

PURPOSE efficacy

No HIV acquisitions in the LEN arm of PURPOSE 1 among cisgender AGYW; WHO cites high-certainty evidence across PURPOSE 1 and 2.

Pregnancy/lactation substudy

509 pregnancies (184 on LEN)
Adverse events balanced across groups (TDF/TAF and LEN)
Injection-site reactions were grade 1-2 and did not lead to discontinuation.

PK and infant exposure

No clinically significant exposure differences by trimester/postpartum;

Infant plasma exposure via breastmilk was minimal.

Counseling balance: very high efficacy and low dosing burden, with explicit counseling on injection-site reactions, delayed HIV detection/resistance safeguards, and pregnancy/infant pharmacovigilance.

Sources: Bekker et al. Lancet HIV 2026; WHO LEN guidance 2025; HHS Perinatal HIV Guidelines 2026; LactMed 2025.

Dapivirine vaginal ring: safe data, but acceptability and approvals matter

The ring is monthly, user-controlled and discreet - but pregnancy approval and user preference vary by setting.

DELIVER pregnancy

DVR and oral PrEP were studied from pregnancy through delivery; adverse pregnancy outcomes and complications were uncommon.

B-PROTECTED lactation

DVR and oral PrEP in mother-infant pairs showed reassuring safety and very low infant exposure.

Preference reality

In southern African qualitative and DCE work, vaginal insertion was often least acceptable, driven by unfamiliarity and discomfort.

Safety-first does not mean product-first. Offer available options, then let client values drive the method.

Sources: Bunge et al. JAIDS 2024; Noguchi et al. Lancet HIV 2025; Fairlie et al. Lancet HIV 2025; Chen-Charles et al. AIDS Behav 2025; de Vos et al. AIDS Behav 2025.

What pregnant and breastfeeding women say they want

Acceptability data are consistent: people want protection that fits their lives, bodies, privacy needs, and postpartum routines.

Preferred features

Discretion
Convenience
Reduced dosing
Minimal discomfort
Ability to switch

Common concerns

Pain
Side effects
Partner reaction
Implant mistrust
Vaginal insertion

Support needed

Reminders
Provider clarity
Community transparency
Privacy in care
Nonjudgmental counseling

Discrete choice experiment in pregnant women using oral PrEP

- 43% delivery seekers (want PrEP in community, easy to collect)
- 25% physical/physiological prioritizers (scared of side effects)
- 32% vaginal insertion avoiders (prefer oral or injectable PrEP)

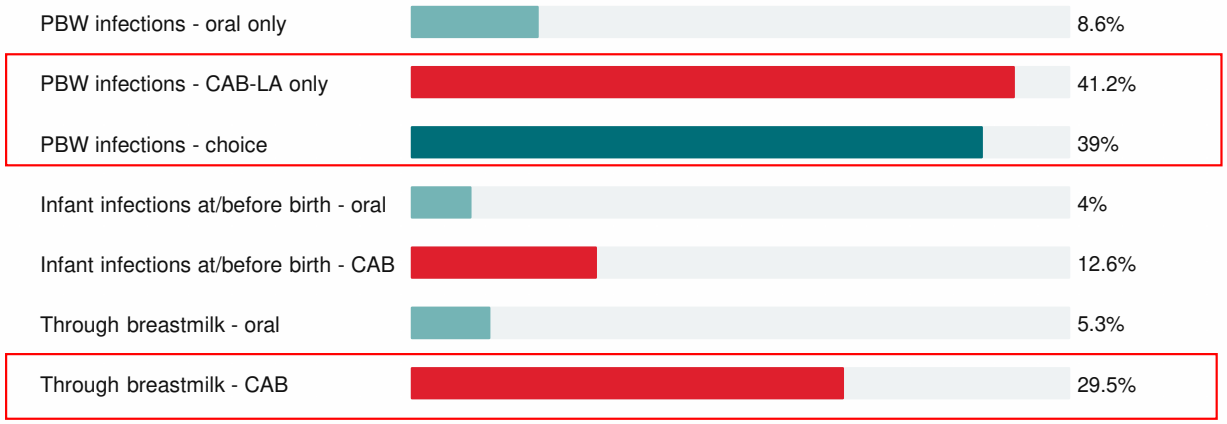
Choice architecture = product choice + delivery choice + permission to change methods

Sources: Chen-Charles et al. AIDS Behav 2025; de Vos et al. AIDS Behav 2025; Joseph Davey et al. Curr Opin HIV AIDS 2024.

Projected public-health payoff in South Africa

Modeling suggests LA PrEP for pregnant and breastfeeding women could avert substantially more maternal and infant infections than oral PrEP alone if uptake and retention are achieved.

Estimated % reduction in HIV cases versus no PrEP for PBW



Interpretation

Model quantifies the cost of delay: preventing maternal HIV acquisition can also prevent infant HIV at birth and through breastfeeding.

CAB-LA & Choice in products have largest potential impact on preventing HIV in PBF

Program implication

Access, price, delivery capacity and follow-up determine whether efficacy becomes impact.

Source: Johnson et al. AIDS 2024 mathematical model of CAB-LA in pregnant/breastfeeding women in South Africa.

LEN scale-up: cost-effectiveness lens for pregnancy and lactation

The economic case for LEN is strong. but in pregnancy/lactation, value depends on targeted delivery, persistence, and safeguarding treatment budgets.

Model & scope

Thembisa v4.8; South Africa
2026–2045; government perspective
Included AGYW, FSW, MSM, heterosexual men and PBFW

National impact

LEN to 1.7–2.9 million people/year
averted 19–31% of infections
and reached <0.1% incidence 10–14 years earlier

Value vs PrEP alternatives

$2,301–$3,567 per life-year saved
Oral TDF/FTC: $8,143/LYS
CAB: $11,114–$16,118/LYS

PBFW-specific scenario

PBFW-only rollout averted ~106,000 infections
$2,220/LYS and $3,149 per infection averted

Initial allocation

Highest-impact 500k PY allocation prioritized AGYW and key populations
PBFW-inclusive allocations had comparable impact

Safety-first translation

Do not read economic prioritization as exclusion
Integrate LEN into ANC/PNC;
Where risk, choice and continuity are highest

Policy message: LEN is cost-effective for South Africa; pregnancy/lactation scale-up should be risk-informed, choice-based, and paired with safety surveillance.

Sources: Jamieson et al., PLoS Med 2026; Thembisa v4.8; Tables 2–4. LEN=lenacapavir; PBFW=pregnant and breastfeeding women; LYS=life-years saved.

Long-acting ART treatment: promise with a higher caution bar

For treatment in pregnancy, the objective is sustained viral suppression. The evidence base for LA CAB/RPV remains limited compared with PrEP.

Why attractive?

May support adherence for people with pill fatigue, disclosure concerns, mobility, or structural barriers.

Why cautious?

Small pregnancy PK datasets; rilpivirine exposures can fall in pregnancy
Bimonthly dosing may be subtherapeutic in models/cases.

Safety-first approach

Do not switch casually in pregnancy. Use expert consultation, viral-load monitoring, therapeutic drug monitoring where available, and plan oral backup.

Bottom line: LA ART may be feasible in selected cases, but it is not yet a routine pregnancy simplification strategy.

Sources: Sunagawa et al. Open Forum Infect Dis 2025; Atoyebi et al. Br J Clin Pharmacol 2025; Rakhmanina et al. Br J Clin Pharmacol 2026; HHS Perinatal Guidelines.

Long-acting ART treatment: studies to date

Cabotegravir/rilpivirine in pregnancy: early insights from clinical practice

Michaeline McGuinty[a], Pierre Giguère[b] and Jonathan B. Angel[a]

Limited case studies to date
7 Women in Canadian study;
All had undetectable VL at time of delivery
2 women had CAB/RIL below PK target

Table 1. Characteristics of women receiving CAB/RPV through pregnancy

	Country of birth	Age (years)	GTPAL	First dose of CAB/ RPV	ART prior to CAB/RPV	GA at last dose of CAB/ RPV (weeks)	Interruption of CAB/RPV schedule	CAB/RPV regimen in pregnancy	GA at first dose of oral therapy (weeks)	Oral therapy initiated in pregnancy	Drug levels		
											CAB[a]	RPV[b]	GA (weeks)
1	Burma	42	G3T0P0A0L2	5 weeks pre conception	EVG/COBI/FTC/ TAF	7	Y	q2m	14	BIC/FTC/TAF			
2	Ukraine	38	G4T3P0A0L3	13 weeks gestation	BIC/FTC/ TAF	18	Y	q2m	24	BIC/FTC/TAF			
3	Liberia	47	G4T3P0A0L3	54 weeks pre conception	BIC/FTC/ TAF	12	Y	q2m	21	BIC/FTC/TAF			
4	Cameroon	44	G5T3P0A1L3	7 weeks pre conception	DTG/TDF/ 3TC	32	N	q2m	36	BIC/FTC/TAF	857	45	40
5	Nigeria	30	G2T1P0A0L1	120 weeks pre conception	EVG/COBI/FTC/ TAF	39	N	q2m	35	BIC/FTC/TAF	2619	74	36
6	Cote d'Ivoire	25	G1T0P0A0L0	25 weeks gestation	BIC/FTC/ TAF	37	N	q1m	N/A	N/A			
7	Democratic Republic of Congo	37	G6T5P0A0L5	7 weeks gestation	BIC/FTC/ TAF	31	N	q2m	35	BIC/FTC/TAF			

Author recommendations:
If woman is unwilling or unable to take oral ART, CAB/RPV can be administered monthly starting before 28w gestation to improve PK of rilpivirine.
CAB/RPV can be continued every 2m with oral ART supplementation from 34-36w gestation.

Long-acting ART treatment: studies to date (2)

1015

Long-Acting Cabotegravir/Rilpivirine in Pregnancy

William R. Short[1], Matty Zimmerman[2], Mariam Aziz[3] Jillian Baron[1], Phillip Bolduc[4], Eric Farmer[5], Naima Joseph[6], Stephen Kohlhoff[7], Florence Momplaisir[1], Alexander Nelson[8], Natalie Nielsen[9], Dimple Patel[10], Stephen Pagkalinawan[11], Mireya Wessolossky[4], Rachel K. Scott[12]

Multi-center study presented at CROI 2025

- N=23 women who initiated during pregnancy (26%) or were on CAB/RPV prior to pregnancy (74%)
- N=5 women switched of CAB/RPV during pregnancy (at median 7 weeks)

Results:

- 90% maintained HIV RNA <200 copies/mL
- No cases of vertical transmission
- Small sample size; unable to analyze pregnancy outcomes (Table)
- **More research needed with larger cohorts to determine long-term safety**

Table 5: Delivery and neonatal outcomes

	N=23
Birth outcome, n (%)	
Live birth	21 (92)
Miscarriage	1 (4)
Stillbirth	1 (4)
Gestational age at delivery, weeks, median (IQR)	37 (36, 39)
Birth weight, grams, median (IQR)	2588 (2241, 2816)
Neonatal HIV status, n (%)	
Negative	20 (95)
Unknown	1 (5)

DOLPHIN-3: a postpartum switch study (PI Malaba & Orrell, UCT/SAMRC)

Temporary switch to CAB/RPV long-acting ART after delivery - not initiation of LA ART during pregnancy

Question

Can a temporary switch to long-acting cabotegravir/rilpivirine (CAB/RPV LA) in early postpartum maintain viral suppression & improve retention in HIV care compared with continuing daily oral ART?

Who & where?

- 309 women living with HIV
- ≥16 years; initiating and continuing ART in pregnancy
- Enrolled antenatally
- Randomised only after delivery, when VL <50 cps/mL
- South Africa & Uganda
- 1:2 allocation:
  103 LA ART / 206 oral ART

What happens?

LA ART arm: CAB 600 mg + RPV 900 mg IM

Optional 4wk oral CAB/RPV lead-in, followed by a second injection 4wks later, then four further injections every 8wks

Final injection at week 40 → switch back to oral ART at week 48 → follow to week 96

PARTICIPANT PATHWAY

Pregnancy	Delivery	0–6 wk	0–48 wk	48–96 wk
A1 enrolment	P0 ≤14 days	VL <50 → randomise	LA vs oral ART	All oral ART

DOLPHIN-3 Protocol v2.1 (July 2026); DOLPHIN-3 study presentation, 2026

DOLPHIN-3: what the study will tell us? (PI Malaba & Orrell)

The protocol combines virologic efficacy, retention, maternal/infant PK, safety, acceptability and implementation evidence

Primary endpoint

% of participants with VL <50 copies/mL at 48 wks postpartum.

Comparing temporary CAB/RPV LA versus continued daily oral ART during the 48-wk switch phase.

Secondary outcomes

- VL suppression at 96w & during the post-switch period
- VL >400 and >1000 copies/mL and treatment-emergent resistance
- Retention in HIV care and missed visits
- Safety and acceptability
- Safe re-establishment of oral ART after CAB/RPV LA

PK, lactation & implementation

- Maternal CAB/RPV PK, incl elimination after last injection
- CAB/RPV concentrations in breastmilk and infant plasma
- Milk-to-plasma and infant-to-maternal concentration ratios
- Infant drug elimination
- Nested qualitative & implementation research with women, providers & stakeholders

Safety is monitored throughout the study. Infant clinical care is provided through routine local services; dedicated infant study procedures are PK sampling rather than systematic infant clinical safety assessment.

DOLPHIN-3 Protocol v2.1 (July 2026); DOLPHIN-3 study presentation, 2026

Safety-first clinical workflow

A practical pathway for ANC, PNC and lactation care.

Before start

- Confirm HIV-negative status; assess acute symptoms
- Ask pregnancy/lactation status and intention
- Review interactions and clinical eligibility
- Discuss available choices and values

→

During use

- HIV testing at routine follow-up
- Adverse event and injection-site assessment
- Pregnancy exposure documentation
- Infant growth and outcome follow-up

→

Stop/switch/miss

- Missed-injection plan before the first dose
- Oral bridge when indicated
- Manage pharmacologic tail
- Return pathway without blame

Document: product, gestational/postpartum timing, exposure window, infant outcomes, and adverse events.

Sources: HHS Perinatal HIV Guidelines 2026; WHO Workshop on harmonized pregnancy/infant outcome data; CDC injectable PrEP guidance.

HIV testing, resistance and the pharmacologic tail

Long-acting prevention adds a new safety domain: infection diagnosis must stay ahead of long drug exposure.

Before injection

Use sensitive HIV testing strategy; evaluate acute retroviral symptoms; avoid initiating during undiagnosed acute infection.

During follow-up

Test at follow-up; act quickly on symptoms, late injections, or ambiguous tests; consider RNA where clinically indicated/available.

After stopping

Tail management matters: residual drug can persist while protection wanes; provide oral PrEP/ART coverage when indicated.

For LA CAB/RPV treatment, if switching to oral ART in pregnancy, avoid gaps:
Current guidance advises a fully suppressive alternative no later than 1 month after the final injection.

Sources: HHS Perinatal HIV Guidelines 2026; WHO LEN/testing guidance 2025; NIH CAB/RPV pregnancy guidance.

Implementation in ANC/PNC: make safety easy to deliver

Long-acting products will succeed only if delivery systems are designed around maternal care pathways.

1 → 2 → 3 → 4

Risk & preference

HIV risk, partner context, pregnancy/lactation timing, method values

Same-day option

Offer available PrEP choices without making women return repeatedly

Aligned visits

Sync injections/refills with ANC, postnatal, EPI or infant visits

Support loop

SMS reminders, peer support, discreet documentation, return after missed visits

Measure implementation safety: missed injections, HIV testing completion, adverse events, pregnancy/infant outcomes, and method switching.

Sources: Joseph Davey et al. Curr Opin HIV AIDS 2024; Chen-Charles et al. AIDS Behav 2025; de Vos et al. AIDS Behav 2025.

Research and pharmacovigilance agenda

The next evidence frontier is not whether pregnant and lactating people should be included - it is how fast we can learn responsibly.

PK/PD

Pregnancy trimester, postpartum, lactation, high BMI, interacting ART

Infant outcomes

Growth, congenital anomalies, neurodevelopment, HIV testing and drug exposure

Early pregnancy

Periconception and first-trimester data, including early losses

Equity

Adolescents, transgender and gender-diverse PLP, rural access, disability

Implementation

Differentiated delivery, privacy, integration with STI/FP services

Resistance/cost

Delayed detection, tail management, affordability and procurement

Minimum dataset for every rollout: maternal exposure timing + HIV outcomes + pregnancy outcomes + infant outcomes + adverse events.

Sources: Sullivan et al. AIDS 2026; WHO pregnancy/infant outcome data harmonization; HHS Perinatal HIV Guidelines 2026.

Take-home messages

Right product, right person, right time - without waiting for women to exit pregnancy or lactation.

1. Normalize prevention

Pregnancy and breastfeeding are periods for proactive HIV prevention counseling, not automatic exclusion.

2. Separate prevention from treatment

PrEP data for TDF/FTC, LEN and CAB-LA are increasingly reassuring; LA CAB/RPV treatment requires specialist caution.

3. Make choice safe

Safety means shared decision-making, reliable HIV testing, missed-dose plans, pregnancy registries, and infant follow-up.

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