Destination zero new acquisitions: Hailing a CAB to PrEP success

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Evaluating CAB-LA concentration and breastmilk transfer in postpartum PrEP: results from the Tshireletso PK Substudy

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Summary

What is your main question?

Among women who initiate CAB-LA PrEP immediately after delivery in Botswana, what are the CAB concentrations among post-partum women and their breastfed infants?

What did you find?

Maternal plasma CAB levels were >4x PA-IC90 within 1 week after the second dose in nearly all breastfeeding mothers. Breastmilk concentrations of CAB were low, with the estimated relative infant dose from breastmilk below 10% of the adult oral dose.

Why is it important? Adequate maternal plasma, and low breastmilk and infant plasma CAB concentrations suggest that maternal CAB-LA during breastfeeding may be safe and effective.

Background

HIV prevalence and gravida in Botswana 2015-2019 (Tsepamo Study)

Initiating long-acting PrEP on the maternity ward after delivery is a potentially efficient strategy to prevent incident HIV in young women and breastfeeding infants

- The post-partum period is a time when
  - HIV acquisition risk is increased
  - Women are engaged in healthcare
  - Adherence to a daily pill can be particularly difficult
- There is a paucity of data on the pharmacokinetics (PK) of CAB-LA started immediately post-partum and infant exposure to CAB through breastmilk

Tshireletso Study Overview

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'Tshireletso' is a single-arm implementation and safety study of CAB-LA PrEP initiated on the post-natal ward in a predominantly breastfeeding population in Botswana

- N=500 mother and infant pairs are being followed for 24 months
- The first CAB injection (600mg IM) is given on the post-natal ward within 14 days of delivery (no oral lead-in)
- Follow-up CAB injections (at 1 month then every 2 months) are usually given at the participant's maternal child health (MCH) clinic

PK substudy: Methods

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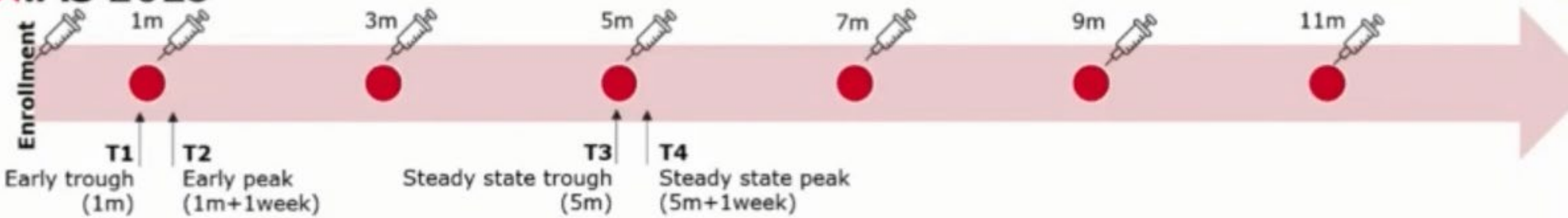

- We enrolled a subset of 27 women from Tshireletso who intended to exclusively breastfeed (and who had singleton birth) in a PK Substudy

- Paired maternal and infant blood and breastmilk samples were collected at 4 time points:
  - just before the 1 month injection (**T1**, early trough) and 1 week later (**T2**, early peak)
  - just before the 5 month injection (**T3**, steady state trough) and 1 week later (**T4**, steady state peak)

- Plasma and whole breast milk concentrations of CAB were measured using a liquid chromatography-tandem mass spectrometry (LC -MS/MS) assay in the Capparelli lab at UCSD

PK substudy: Results

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	Median (IQR)
Maternal age (yrs)	23 (20,26)
Maternal BMI enrollment **Maternal BMI at T1 (1m)** **Maternal BMI at T3 (5m)**	23.5 (21.8,29.9) 23.7 (20.6, 28.7) 25.6 (19.8, 29.3)
# days from delivery to 1st CAB injection **# days from 1st CAB injection to T1 (1m)** **# days from 2nd CAB injection to T2 (1m+1wk)** **# days from 3rd injection (3m) to T3 (5m)** **# days from 4th injection to to T4(5m+1wk)**	1 (1,2.5) 30 (29,30.5) 7 (7,7) 58 (56,63) 7 (7,7)
Infant gestational age at birth (wks)	38 (37,39)
Infant weight (kg) at T1 (1m) **Infant weight (kg) at T3 (5m)**	4.4 (4.0,4.6) 7.5 (6.8,8.0)
Proportion exclusively breastfeeding at **T1, T2 (1m, 1m+1wk)** **T3, T4 (5m, 5m+1wk)**	 100% 81.5% (4 stopped BF, 1 BF+solids)

This analysis includes 27 participants with specimens collected at ≥ two time points

PK substudy: Maternal Results

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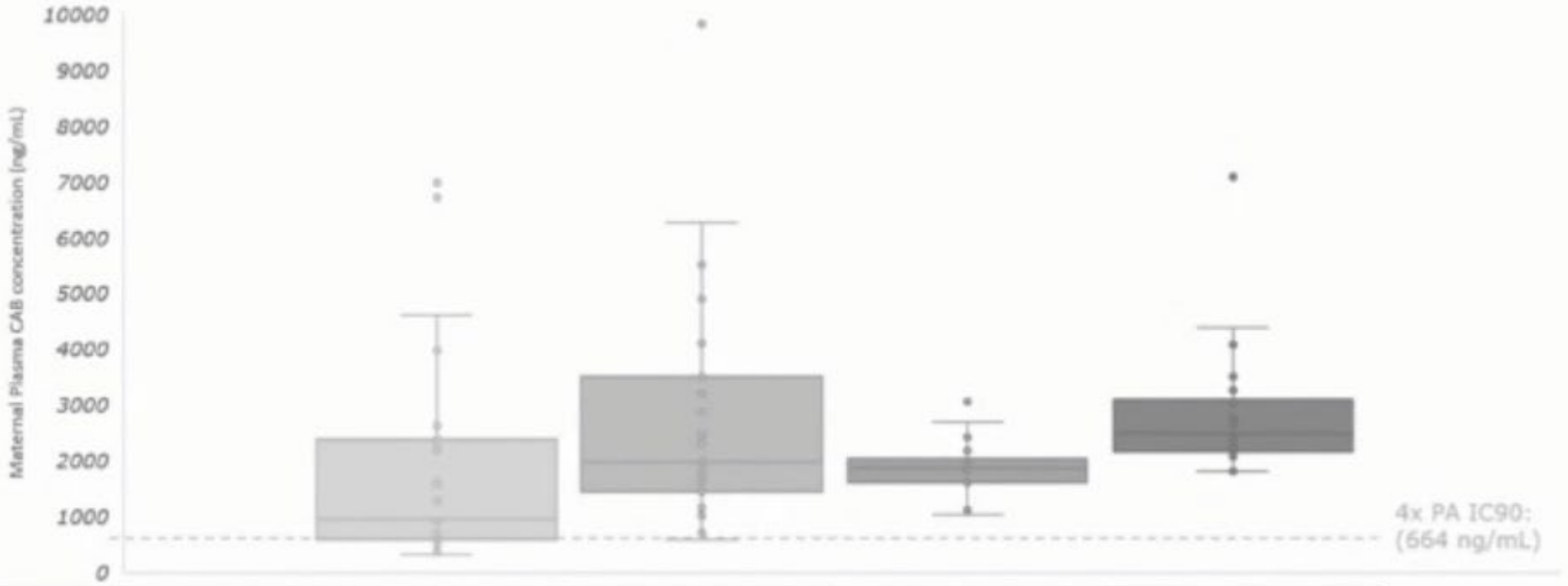
74% of maternal CAB concentrations were >4x PA-IC90 (664ng/mL) at T1: 1m (trough)

- All but 1 (from 1m+1wk) exceeded this threshold at all other timepoints

No incident HIV infection occurred in the PK participants

Maternal plasma CAB concentrations (ng/mL)



Time since initial CAB injection	T1: 1m (trough)	T2:1m+1w (peak)	T3:5m (trough)	T4:5m+1wk (peak)
Maternal Plasma CAB concentration (ng/mL) median (range)	941 (322,6980)	1980 (580,9820)	1875 (1030,3050)	2480 (1800,7080)

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PK substudy: Breastmilk Results

Time since initial CAB injection	T1: 1m (trough)	T2:1m+1w (peak)	T3:5m (trough)	T4:5m+1wk (peak)
Maternal Plasma CAB concentration (ng/mL) median (range)	941 (322,6980)	1980 (580,9820)	1875 (1030,3050)	2480 (1800,7080)
Breastmilk CAB concentration (ng/mL) median (range)	14.6 (2.5,89)	29.8 (6.7,143)	27.4 (10.8,129)	36.1 (17.2,108)
Breastmilk to plasma ratio of CAB median (range)	1.5% (0.8%,2.6%)	1.5% (0.8%, 2.6%)	1.3% (0.7%,7.5%)	1.4% (0.8%, 2.6%)

The overall median (IQR) breastmilk to plasma ratio of CAB was 1.4% (1.1%, 1.9%)

PK substudy: Infant Results

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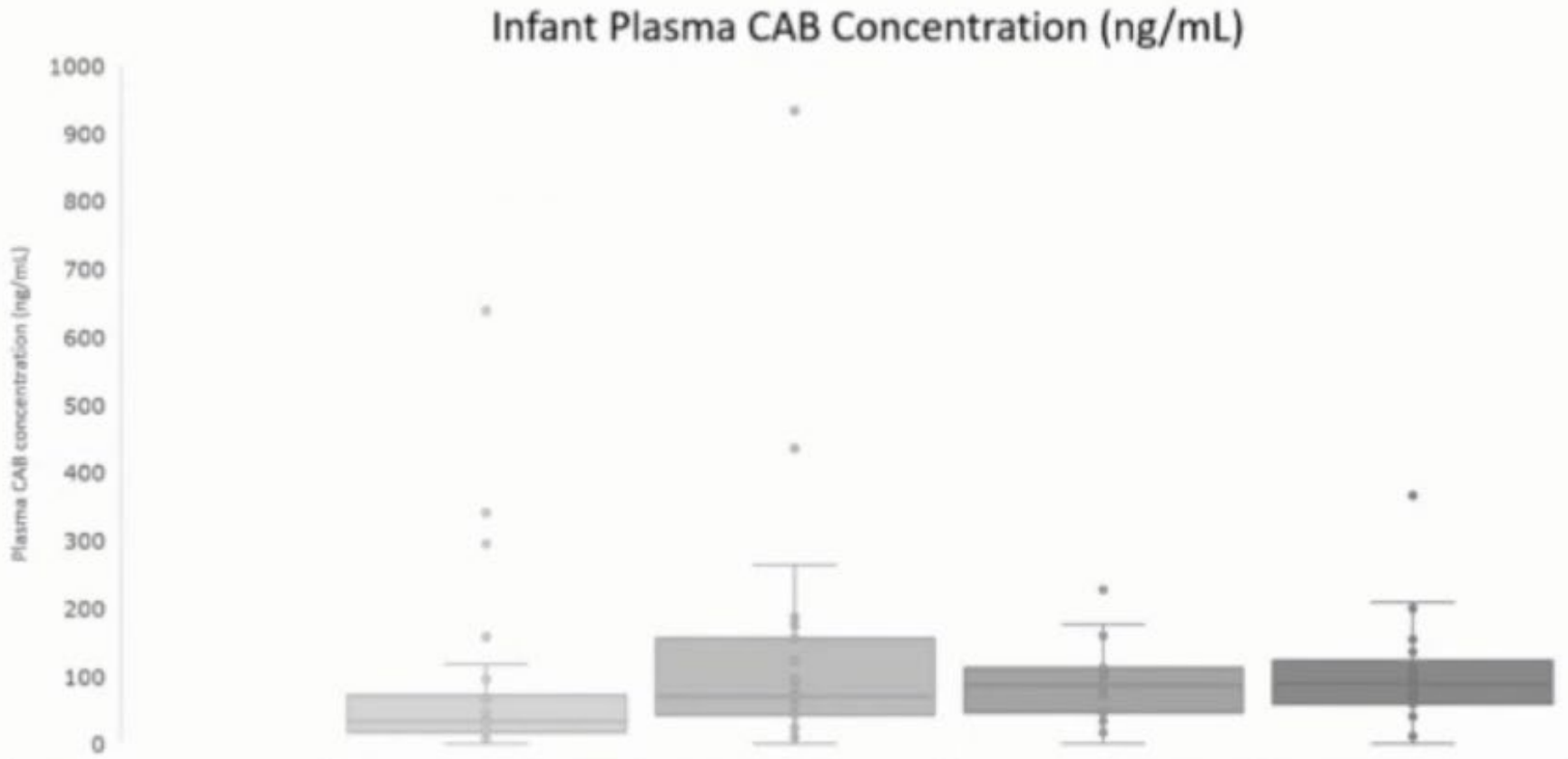
All infant CAB levels were <1000 ng/mL



Time since initial CAB injection	T1: 1m (trough)	T2:1m+1w (peak)	T3:5m (trough)	T4:5m+1wk (peak)
Infant Plasma CAB concentration (ng/mL) BQL=<39ng/mL median (range)	33.2 (16 BQL, 638)	69.2 (5 BQL, 933)	85.3 (5 BQL, 226)	92.1 (1 BQL, 365)

PK substudy: Infant Results

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Relative infant dose (%)	2.1%	4.6%	6.7%	8.9%

- **Relative infant dose (RID)** is an estimate of the % of an adult oral dose (30mg/d) that the infant gets through ingesting breastmilk
  - We assumed an average milk intake of 150 mL/kg/day and used observed breastmilk concentrations in the maternal sample

The overall median (IQR) RID was 4.9% (3.1%, 9.2%)

PK Substudy: Summary

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- The proportion of maternal post-partum plasma samples with CAB levels >4x PA-IC90 at the first trough (74%) and subsequent time points (97%) is generally similar to non-pregnant/post-partum female populations[1]
  - Future analysis will model post-partum PK from our data and compare it to the general population

- CAB-LA gets into breastmilk in low amounts (median 1.4% of plasma)

- Estimated relative infant transfer of CAB-LA via breastmilk is <10% of the adult oral dose (which is considered low exposure), and infant CAB levels were all <1000ng/mL

1. Han K, Patel P, McCallister S, Rinehart AR, Gandhi Y, Spreen W, Landovitz RJ, Delany-Moretlwe S, Marzinke MA, McKeon T, Budnik P, van Wyk J, Ford SL. 2024.Long-acting cabotegravir pharmacokinetics with and without oral lead-in for HIV Prep. Antimicrob Agents Chemother 68: e01475-23.https://doi.org/10.1128/aac.01475-23

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Conclusions

These findings support the call from UNAIDS (2022) to expand HIV prevention options for breastfeeding women, demonstrating that CAB-LA may be a safe and effective strategy in the postpartum period.

THANK YOU, KEALEBOGA/URAKOZE CYANE/ ASANTE

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- Study Participants

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