TFV-DP concentrations in PBMCs and safety of daily directly observed F/TDF PrEP during pregnancy

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BACKGROUND

- Data on tenofovir diphosphate (TFV-DP) levels in peripheral blood mononuclear cells (PBMCs) during pregnancy are limited.
- We evaluated the effect of pregnancy on TFV-DP levels in PBMCs and pregnancy outcomes and infant growth in cisgender women under directly observed therapy (DOT) of F/TDF.

METHODS

- **Study Design:** Directly observed daily F/TDF PrEP was administered to healthy 18 pregnant and 18 non-pregnant Kenyan women for 8 weeks (clinicaltrials.gov: NCT05057858)
- **Outcomes**:
  - Weekly steady-state PBMC TFV-DP levels from weeks 2 to 8 quantified using LC-MS/MS assays
  - Pregnancy outcomes: pregnancy loss, preterm birth, and birth defect
  - Infant growth: age- and sex-adjusted Z-scores for weight, length, and head circumference (HC) at 12 months of age
- **Statistical analysis:**
  - Linear mixed model compared log transformed TFV-DP levels between groups
  - Pregnancy outcomes and infant growth compared to historical controls from the placebo arm (no F/TDF PrEP exposure) of the Partners PrEP Study (NCT00557245)

RESULTS

- Between May to December 2023, 18 non-pregnant and 18 pregnant women were enrolled
  - One pregnant woman was excluded from the analysis due to non-adherence
- Directly observed doses: 1922/1925 (99.8%)

PBMCs TFV-DP concentrations from directly observed therapy of daily oral F/TDF PrEP were comparable in pregnant and non-pregnant African women

Table 1 Baseline characteristics for pregnant and non-pregnant women at baseline

# or median(IQR)	Non-pregnant women	Pregnant women
N	18	18
Maternal age (years)	23 (20, 25)	23 (20, 27)
Gestational age (weeks)	--	16 (14, 20)
Weight (kg)	58 (53, 63)	55 (52, 62)
Hematocrit (%)	41 (39, 44)	36 (34, 38)
Hemoglobin(g/dL)	14 (13, 15)	12 (12, 13)
Creatinine(mL/min)	131 (113, 145)	176 (154, 196)

Table 2 Summary of the steady-state PBMC TFV-DP levels (fmol/10^6)

	Non-pregnant women	Pregnant women
# of participants	18	17
# of steady-state samples	121	68
Range	12–152.3	24–88
Median (IQR)	60 (45, 74)	50 (38, 60)
Geometric mean (95%CI)	56 (48, 66)	48 (40, 57)
Geometric mean ratio (95%CI; p-value)	Ref	0.85 (0.68, 1.06; p=0.151)

Figure 1 Observed and modeled steady-state PBMC TFV-DP levels

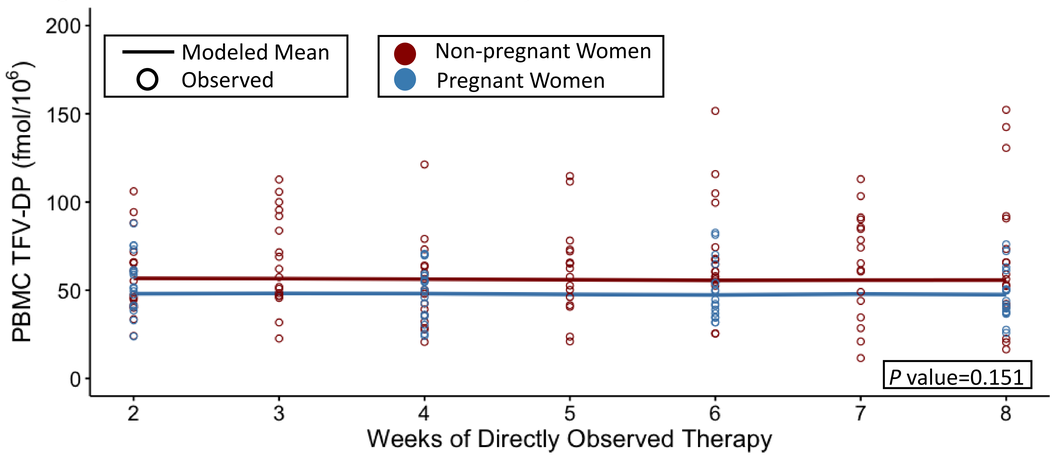


Table 3 Pregnancy outcomes among women exposed and unexposed to F/TDF PrEP

	PrEP unexposed	PrEP exposed
# of pregnancies	71	18
# of women	70	18
Live births	65 (92%)	17 (94%)
Pregnancy loss	6 (8%)	1 (6%)
Preterm delivery	5 (8%)	0 (0%)
Birth defect	5 (8%)	0 (0%)

Table 4 Z-scores for infant growth among women exposed and unexposed to F/TDF PrEP at 12 months of age

Z-scores for	PrEP unexposed	PrEP exposed	P-value[2]
HC[1]	0.3 ± 1.3	0.4 ± 1.0	0.791
Weight	-0.5 ± 1.2	-0.4 ± 1.6	0.857
Length	-1.1 ± 1.7	-0.6 ± 1.3	0.243

[1]HC: head circumference; [2]Two Sample t-Test

CONCLUSIONS

- Steady state TFV-DP levels in PBMCs from DOT of daily oral F/TDF PrEP were reassuringly comparable in pregnant and non-pregnant African women.
- Consistent with previous non-DOT studies, pregnant and infant growth outcomes up to one year were also comparable between DOT of F/TDF PrEP-exposed and unexposed pregnancies.

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