Pharmacokinetic Study Comparing TAF and TDF as PrEP in Pregnant and Postpartum Women in South Africa

#00900

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BACKGROUND

- Pregnant women receiving tenofovir disoproxil fumarate and emtricitabine (TDF/FTC) may experience lower plasma tenofovir (TFV) and intracellular tenofovir-diphosphate (TFV-DP) concentrations in red blood cells and PBMC when compared to postpartum periods.
- No studies have been conducted to establish concentrations of TFV-DP after administration of tenofovir alafenamide (TAF) in pregnancy and postpartum.

- High concentrations of TFV-DP in PBMC in pregnancy & postpartum among women receiving TAF above TDF levels, **suggesting PrEP efficacy is retained.**
- **Efficacy and safety studies are warranted to evaluate TAF** for PrEP in pregnant and postpartum women.

CONCLUSIONS

- High concentrations of TFV-DP in PBMC in pregnancy and postpartum among women receiving TAF well above TDF levels, **suggesting PrEP efficacy is retained.**
- DBS adherence benchmarks for daily dosing were established for TAF in pregnant and postpartum African women.
- **Efficacy and safety studies are warranted to evaluate TAF for PrEP in pregnant and postpartum women.**

METHODS

- Between June, 2022 to March 2023, we recruited eligible, consenting pregnant women in antenatal care in Cape Town.
- We randomized participants in the 2nd trimester 1:1 to daily dosing of tenofovir alafenamide-emtricitabine (TAF/FTC) or TDF/FTC.
- Participants had 8 weekly study visits and bloods drawn (plasma, PBMC, DBS) during pregnancy and again postpartum.
- Adherence was monitored using video directly observed therapy. **(see Poster #901)**
- We compared TFV-DP concentrations for TDF and TAF arms between pregnancy vs. postpartum in both DBS and PBMCs using geometric mean ratios (GMR) for log concentrations and 95% CIs.



RESULTS

- 34 paired pregnancy and postpartum women who recorded daily video DOTS were evaluated: 18 in the TAF arm and 16 in the TDF arm (excluded n=5 who did not adhere to the protocol).
- Median age was 28 years (IQR=23-32); median gestation age at PrEP start was 24 weeks (IQR=21-24 weeks; range: 20-30 weeks pregnant)
- **Comparing postpartum to pregnancy in TDF/FTC arm (Table 1):**
  - GMR for TFV-DP in DBS was 1.34 (1.30-1.39) for DBS at 4w and 1.16 (1.14-1.18) at 8w
  - GMR for TFV-DP in PBMC was slightly higher in pregnancy at 4w (GMR=1.04, 95% CI: 1.03, 1.05) but did not differ at 8w
- **Comparing postpartum to pregnancy in TAF/FTC arm:**
  - GMR for TFV-DP in DBS was 1.63 (1.54-1.73) for DBS at 4w; 1.44 (1.24-1.68) at 8w
  - GMR for TFV-DP in PBMC was 1.40 (1.32-1.48) at 4w and 1.15 (1.14-1.16) at 8w
- **No safety related adverse events were found.**

Table 1. Median levels of TFV-DP and FTC-TP in TAF and TDF arms in pregnant vs. postpartum periods with log transformed GMR in Cape Town, South Africa (PrEP-PP PK Study, June 2022 – June 2023)

	Pregnancy (4-week follow-up) GM (95% CI)	Pregnancy (8-week follow-up) GM (95% CI)	Postpartum (4-week follow-up) GM (95% CI)	Postpartum (8-week follow-up) GM (95% CI)	Mean (SE) [1]	GMR (95% CI) comparing log transformed Postpartum vs. Pregnant concentrations (4 weeks)	GMR (95% CI) comparing log transformed Postpartum vs. Pregnant concentrations (8 weeks)
TDF/FTC	**n = 13**	**n = 16**	**n = 13**	**n = 16**			
GA (median, IQR) weeks	28 (27-30)	32 (31-34)	4.1 (3.5-4.6)	8.43 (7.5-9.0)			
TFV-DP PBMC (fmol/10^6cells)	67 (47-94)	71 (44-112)	69 (98-48)	73 (50-108)	89 (5.7)	1.04 (1.03-1.05)	1.04 (0.96-1.12)
FTC-TP in PBMC (pmol/10^6 cell)	7 (5-10)	8 (5-13)	5.1 (3.3-7.9)	4.9 (2.9-8.2)	8 (0.9)	0.76 (0.72-0.80)	0.60 (0.58-0.62)
TFV-DP DBS (fmol/3mm punch)	431 (358-517)	583 (471-722)	579 (465-721)	675 (537-849)	619 (34)	1.34 (1.30-1.39)	1.16 (1.14-1.18)
TAF/FTC	**n = 18**	**n = 18**	**n = 18**	**n = 18**			
GA (median, IQR) weeks	28 (25-31)	31 (29-35)	4.1 (4 -6)	8.7 (8- 10)			
TFV-DP PBMC (fmol/10^6 cells)	712 (537-944)	580 (341-985)	996 (797-1 245)	666 (396-1123)	933 (62)	1.40 (1.32-1.48)	1.15 (1.14-1.16)
FTC-TP in PBMC (pmol/10^6 cells)	8 (6-11)	7 (4-13)	12 (10-14)	9 (6-12)	10 (0.7)	1.49 (1.29-1.73)	1.25 (0.91-1.72)
TFV-DP DBS (fmol/7mm punches)	632 (575-694)	832 (751-922)	1032 (887-1202)	1199 (929-1549)	981 (51)	1.63 (1.54-1.73)	1.44 (1.24-1.68)

Table 2. Fitted percentiles (25th, 50th and 75th) for TFV-DP at steady state during pregnancy and postpartum.

	Pregnancy (8 weeks follow-up)		Postpartum (8 weeks follow-up)	
	Observed 50th percentile	Fitted 25th, 50th and 75th percentiles	Observed 50th percentile	Fitted 25th, 50th and 75th percentiles
TDF/FTC TFV-DP DBS (fmol/3mm punch)	**n = 14**		**n = 14**	
Css	**753**	750 (707 – 797)	**833**	834 (789 – 867)
Half-life (per week)	2.36	-	1.35	-
TAF/FTC TFV-DP DBS (fmol/7mm punches)	**n = 18**		**n = 18**	
Css	**882**	883 (851 – 915)	**1254**	1258 (1199 – 1320)
Half-life (per week)	1.93	-	1.31	-

Css, concentration at steady state

Table 2 compares fitted percentiles of TFV-DP in DBS at steady state in pregnancy (at 8 weeks) and postpartum (at 8 weeks) in women taking TDF/FTC and TAF/FTC:

TDF/FTC:
- Pregnancy: 750 (95% CI: 707-797)
- Postpartum: 834 (95% CI: 789-867)

TAF/FTC:
- Pregnancy: 883 (95% CI: 851-915)
- Postpartum: 1258 (95% CI: 1199-1320)

ADDITIONAL KEY INFORMATION

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