Factors Affecting TFV-DP Concentrations in PBMC and Relationships With DBS in PWH on TAF-Based ART

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BACKGROUND

- Tenofovir alafenamide (TAF) undergoes cellular conversion to its active anabolite, tenofovir-diphosphate (TFV-DP), within cells (Figure 1).[1-4]
- TFV-DP concentrations in PBMC confer important clinical implications for HIV treatment and prophylaxis. However, PBMC require specialized and lengthy processing.[6-8]
- TFV-DP in red blood cells, as measured in dried blood spots (DBS), have demonstrated strong relationships with adherence and clinical outcomes in persons with and without HIV.[9]
- Relationships between steady-state TFV-DP concentrations (Css) in PBMC, adherence, and DBS have not been well-described in people with HIV (PWH) on TAF-containing antiretroviral therapy (ART).

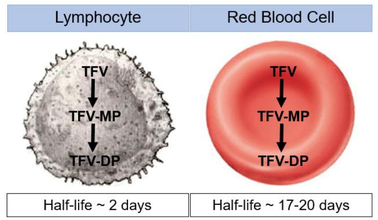


Figure 1. Cellular TFV-DP half-lives[5]

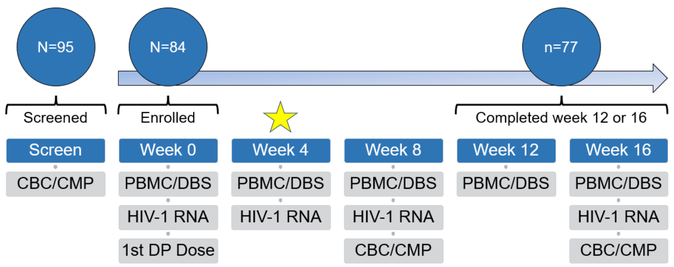
OBJECTIVES

- To assess the influence of adherence and other factors on TFV-DP Css in PBMC, and examine relationships with TFV-DP Css in DBS.

METHODS

- QUANTI-TAF was a 16-week observational study that enrolled PWH on TAF-based ART for >6 months (Figure 2). Adherence was measured using TAF-based ART co-encapsulated with an ingestible biosensor (ID-CAP System).

Figure 2. Enrollment flow and study design



- TFV-DP was quantified using validated LC/MS-MS and reported as fmol/10^6 cells (PBMC) or fmol/2x7mm punches (DBS).[10,11]
- A linear mixed-effects model with backward selection was used to evaluate factors associated with TFV-DP Css in PBMC, which included adherence, age, sex at birth, weight, BMI, race, eGFR, CD4 count, hematocrit, and NNRTI or INSTI.
- Pearson correlation was performed to evaluate the relationship between week 4 TFV-DP Css in DBS and PBMC for 79 PWH on unboosted ART.

TFV-DP concentrations in PBMC in PWH on TAF-based ART are affected by adherence and were moderately correlated with DBS

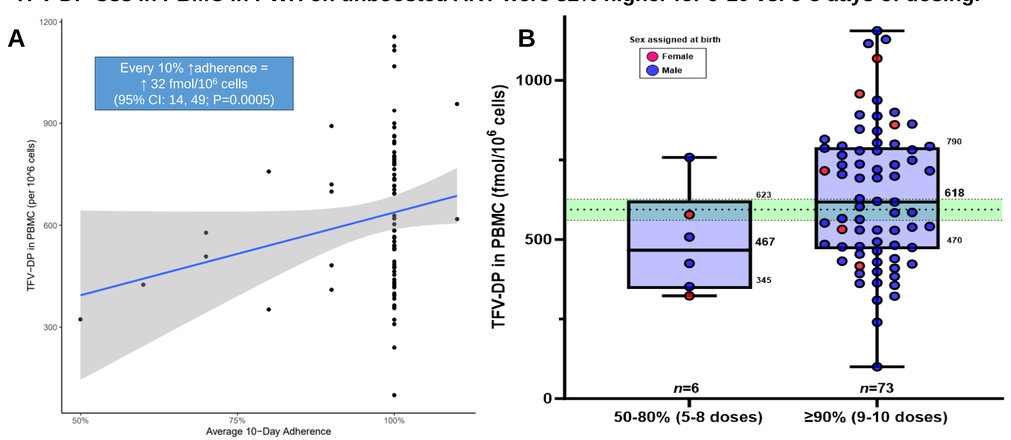
RESULTS

Table 1. Baseline Demographics

Baseline characteristics, n (%) or median (IQR)	ART anchor class, n (%)			
	INSTI 74 (88%)	NNRTI 5 (6%)	PI 5 (6%)	Overall 84 (100%)
Sex assigned at birth				
Female	7 (9%)	1 (20%)	1 (20%)	9 (11%)
Male	67 (91%)	4 (80%)	4 (80%)	75 (89%)
Gender identity				
Female	7 (9%)	1 (20%)	1 (20%)	9 (11%)
Male	65 (88%)	4 (80%)	3 (60%)	72 (86%)
Transgender	2 (3%)	0 (0%)	1 (20%)	3 (4%)
Race/ethnicity				
Black	15 (20%)	2 (40%)	3 (60%)	20 (24%)
Hispanic/Latino	16 (22%)	1 (20%)	1 (20%)	18 (21%)
White	43 (58%)	2 (40%)	1 (20%)	46 (55%)
HIV-1 RNA, copies/mL				
<20	62 (84%)	5 (100%)	4 (80%)	71 (85%)
≥20-<200	12 (16%)	0 (0%)	1 (20%)	13 (15%)
Age, years	52 (40-59)	57 (54-58)	57 (54-58)	54 (43-59)
Weight, kg	84 (70-98)	90 (72-100)	75 (72-96)	84 (71-98)
BMI, kg/m^2	28 (23-32)	31 (25-36)	26 (26-31)	28 (23-32)
eGFR, mL/minute/1.73 m^2	84 (69-99)	80 (62-88)	81 (76-93)	83 (69-97)
$CD4^+$ T-cells, cells/mm^3	717 (540-972)	806 (612-836)	476 (418-504)	700 (534-907)
Hematocrit, %	45 (44-48)	45 (43-46)	43 (42-48)	45 (43-48)
Mean corpuscular volume, fL	92 (88-96)	91 (90-95)	92 (92-93)	92 (88-95)
TAF/FTC-based ART duration, months	51 (33-62)	43 (42-44)	62 (57-62)	51 (35-62)

*TAF dose was 25 mg/dose for all regimens

Figure 3. A) 10-day adherence was the only significant predictor of TFV-DP in PBMC; B) Median TFV-DP Css in PBMC in PWH on unboosted ART were 32% higher for 9-10 vs. 5-8 days of dosing.

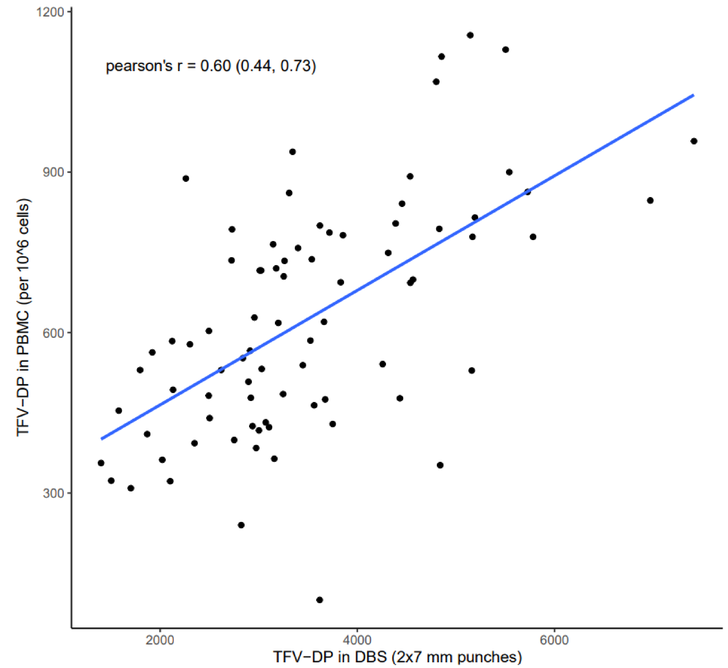


Green line: Mean (95% CI) in people without HIV and 100% F/TAF Adherence (NCT02962739).

RESULTS CONTINUED

- Median TFV-DP Css for boosted ART was 72% higher than unboosted ART (1007 [IQR: 868, 1297] vs. 585 [IQR: 459, 780] fmol/10^6 cells, respectively).

Figure 4. Week 4 TFV-DP Css in PBMC in PWH on unboosted TAF-based ART was moderately correlated with TFV-DP in DBS.



CONCLUSIONS

- 10-day adherence was the only significant predictor identified for TFV-DP Css in PBMC in PWH on unboosted TAF-containing regimens.
- TFV-DP was higher in PWH on boosted ART, which may enhance virologic effect, dose forgiveness, and/or side effects.
- TFV-DP in DBS and PBMC were moderately correlated, which may be due in part to TFV-DP in PBMC being more susceptible to recent non-adherence given the shorter half-life in PBMC vs. DBS (2 vs. 17 days).
- Further investigation of other factors contributing to variability in TFV-DP in PBMCs is warranted.

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