Tenofovir-Diphosphate in Dried Blood Spots and HIV-1 RNA Suppression Among PWH on TAF (ACT Study)

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BACKGROUND

- ACT (NCT05335590) is an ongoing observational study that aims to evaluate tenofovir-diphosphate (TFV-DP) concentrations in dried blood spots (DBS) among persons with HIV (PWH) receiving tenofovir alafenamide (TAF)-based antiretroviral therapy (ART) with suppressed compared with detectable HIV-1 RNA.
- Previously, QUANTI-TAF (NCT04065347) reported a pharmacokinetic (PK)-based TFV-DP in DBS benchmark of ≥1800 fmol/punches for PWH with ≥85% adherence using digital pills to objectively quantify adherence[1].

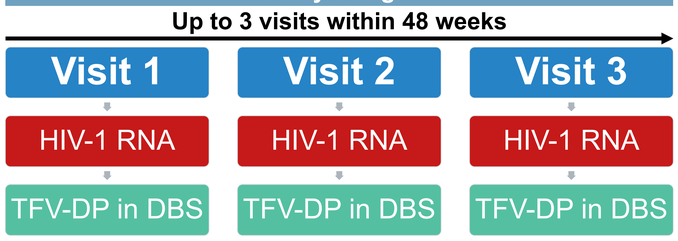
OBJECTIVE

- We investigated the relationship between this TFV-DP concentration threshold (≥1800 fmol/punches) and HIV-1 RNA suppression (<200 c/mL) in the ACT Study.

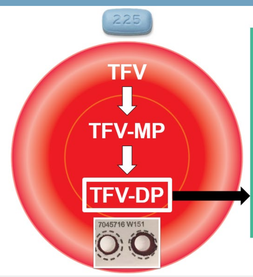
METHODS

- PWH prescribed TAF-based ART (25mg ± booster or 10mg + booster) for ≥3 months were prospectively enrolled.
- Participants who completed three convenience-based visits within 48 weeks during which HIV-1 RNA and DBS were collected were included in analysis (*N*=69 [207 visits]).
- 205/207 (99%) visits had results for HIV-1 RNA and DBS.
- We reported TFV-DP in DBS mixed model estimates as geometric mean (GM [95% CI]) according to HIV-1 RNA category (<20, 20-199, or ≥200 c/mL).
- We used generalized linear mixed effects models with a logit link to estimate the odds ratio (OR [95% CI]) for HIV-1 RNA suppression (<200 c/mL) according to dichotomized TFV-DP in DBS category (<1800 or ≥1800 fmol/punches).

Study design[2]



TFV-DP in DBS for TAF[3,4]



TFV-DP in DBS:
- Phosphorylated anabolite of tenofovir (TFV)
- 21-day half-life
- Cumulative adherence (previous 6-12 weeks)
- LC-MS/MS: fmol/2x7mm punches

- Among PWH on TAF, an individual's odds for HIV-1 RNA suppression (<200 c/mL) were 39.2 times higher if their TFV-DP in DBS was ≥1800 compared with <1800.
- TFV-DP in DBS was similar among those with HIV-1 RNA <20 and 20-199 c/mL.

Figure 1. Observed and modeled GM (95% CI) TFV-DP in DBS by HIV-1 RNA category and visit

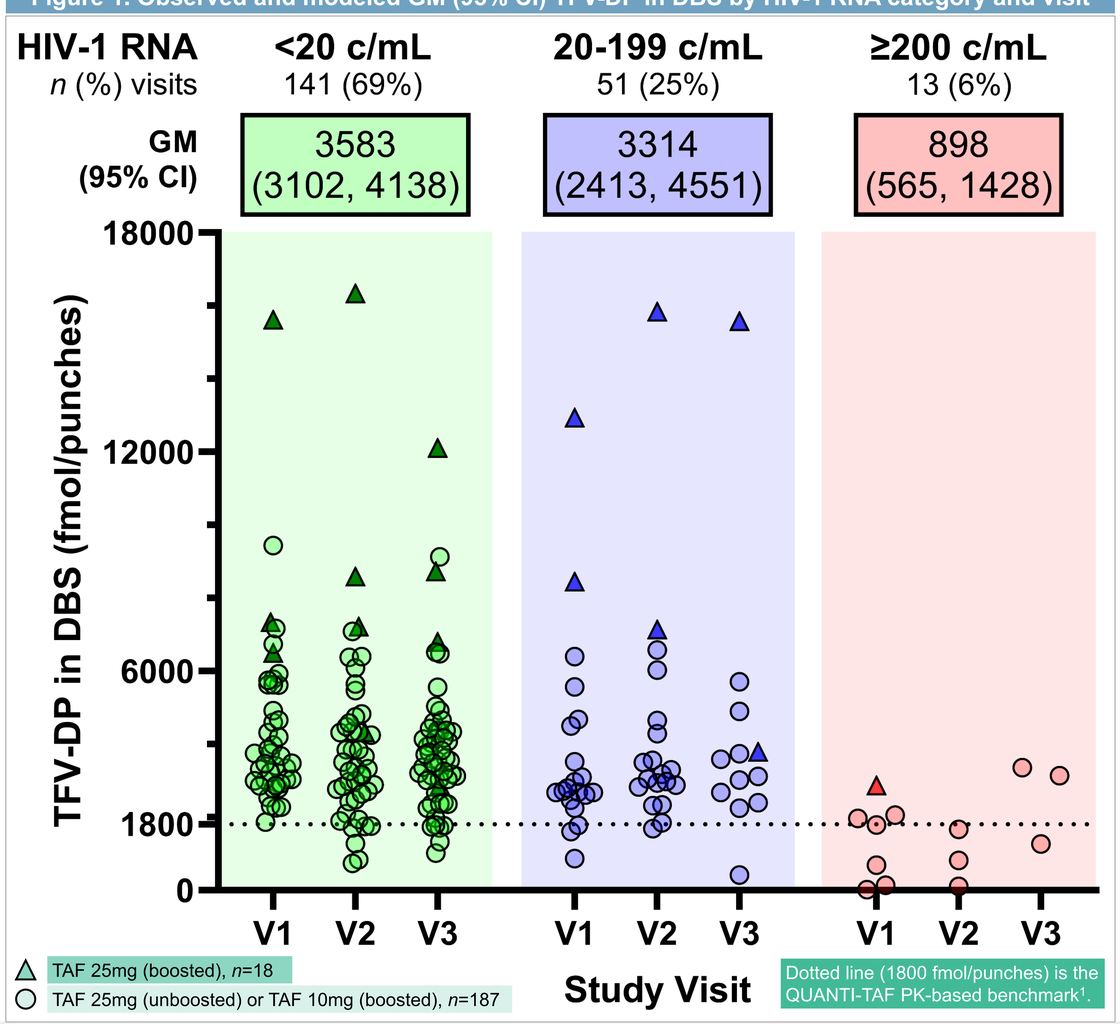
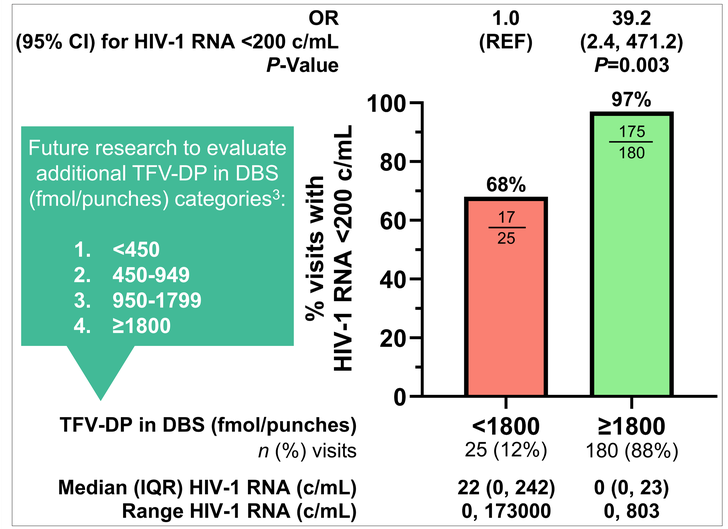


Table 1. Baseline characteristics (*N*=69)

Variable		Variable	
Gender, *N* (%)		**eGFR (mL/minute/1.73 m^2), median (IQR)**	84 (69, 103)
Female	6 (9%)	**CD4$^+$ T-cells (cells/μL), median (IQR)**	674 (442, 866)
Male	61 (88%)	**TAF dose, *N* (%)**	
Transgender	2 (3%)	25mg (unboosted) or 10mg (boosted)	63 (91%)
Race/ethnicity, *N* (%)		25mg (boosted)	6 (9%)
Black	15 (22%)	**ART anchor class, *N* (%)**	
Hispanic/Latino	15 (22%)	INSTI	46 (67%)
White	34 (49%)	NNRTI	3 (4%)
Other/Unknown	5 (7%)	PI/b	4 (6%)
Age (years), median (IQR)	55 (42, 61)	Multiclass	16 (23%)
BMI (kg/m^2), median (IQR)	26 (24, 30)	**BIC/FTC/TAF alone, *N* (%)**	33 (48%)

BMI=body mass index; eGFR=estimated glomerular filtration rate (2021 CKD-EPI equation); INSTI=integrase strand transfer inhibitor; NNRTI=non-nucleos(t)ide reverse transcriptase inhibitor; PI/b=boosted protease inhibitor; BIC/FTC/TAF=bictegravir/emtricitabine/tenofovir alafenamide.

Figure 2. OR (95% CI) for HIV-1 RNA suppression (<200 c/mL) by TFV-DP in DBS category



CONCLUSIONS AND FUTURE RESEARCH

- Our previously established PK-based TFV-DP in DBS benchmark of ≥1800 fmol/punches was associated with HIV-1 RNA suppression (<200 c/mL) among PWH receiving TAF-based ART.
- TFV-DP in DBS was similar among those with HIV-1 RNA <20 c/mL and 20-199 c/mL[1].
- Given the small number of visits with HIV-1 RNA ≥200 c/mL, additional data will confirm the additional benchmark(s) to predict viral breakthrough (e.g., <450, 450-949, 950-1799, and ≥1800 fmol/punches[3]).
- Multivariate models will assess the impact of biological and clinical characteristics on TFV-DP in DBS for PWH on TAF[1,2,5].
- Logistic prediction models to identify TFV-DP cut points will be used to estimate the OR for future viremia in PWH on TAF, similar to our previous work with PWH on tenofovir DF (TDF)[6].

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