TFV-DP is Associated with Baseline Virologic Suppression in PWH on TAF: Results from ACTG A5359

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BACKGROUND

- Tenofovir (TFV)-diphosphate (TFV-DP) concentrations in dried blood spots (DBS) demonstrate strong associations with adherence, virologic suppression (VS), future viremia and mental health engagement in persons with HIV (PWH).[1-4]
- Data are limited to tenofovir disoproxil fumarate (TDF) or adherent (>85%) populations with VS on tenofovir alafenamide (TAF).[5]
- Evaluating TFV-DP relationships with clinical outcomes in diverse populations on TAF-containing regimens is needed to enhance HIV viral load interpretation, predict future viremia, and enable timely, tailored interventions (Figure 1).[6]

Figure 1. Proposed clinical interpretations using linked HIV viral load and TFV-DP concentrations in DBS.

		Pharmacologic Adherence Measure	
		High	Low
HIV Viral Load	Suppression	Expected outcome POSITIVE FEEDBACK	Impending Problem COUNSEL
	Viremia	Concern for Resistance PERFORM GENOTYPE	Adherence Challenge IDENTIFY BARRIER

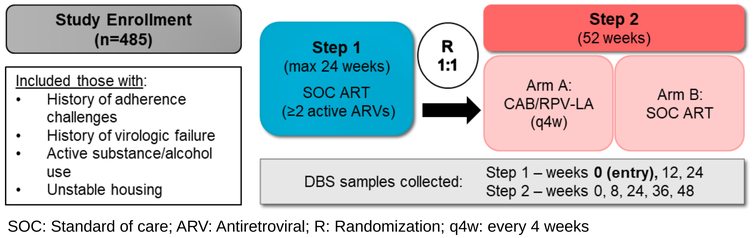
OBJECTIVES

- To examine TFV-DP in DBS and its association with VS at baseline among PWH on TAF enrolled in ACTG A5359/LATITUDE.

METHODS

- LATITUDE (NCT03635788) is a phase III, prospective, randomized, open-label study that demonstrated superiority of long-acting cabotegravir/rilpivirine (CAB/RPV-LA) when compared to oral ART in PWH with a history of adherence challenges (Figure 2).[7]
- TFV-DP in DBS (2x7mm punches) were quantified using validated LC-MS/MS methods (LLOQ 31.3 fmol/punches).[8,9]
- Logistic regression was used to model the probability (95% CI) of VS (<200 copies/mL) by ln(TFV-DP) and boosted PI use (increases TFV-DP concentrations by ~ 2.5-fold)
- Probabilities at select values from very low to very high adherence based on historical TFV-DP data were estimated.[5,9]

Figure 2. Study enrollment and design



SOC: Standard of care; ARV: Antiretroviral; R: Randomization; q4w: every 4 weeks

Higher baseline TFV-DP in DBS increased the likelihood of virologic suppression at entry, with differential adherence-forgiveness patterns observed between INSTI/NNRTI- and PI-containing regimens

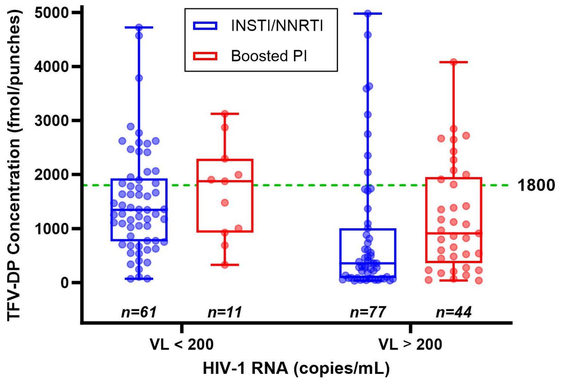
RESULTS

Table 1. Baseline Demographics for Participants on TAF at Entry

Characteristic	Total (n=193)	Characteristic	Total (n=193)
Age (years), median (IQR)	39 (31, 52)	CD4⁺ T-cells (cells/μL), median (IQR)	287 (126, 540)
Sex at birth, male (%)	137 (71%)	Time since HIV diagnosis (years), median (IQR)	13 (7, 21)
Ethnicity, Hispanic/Latino (%)	39 (20%)	AUDIT-C score ≥4 (males) or ≥3 (females), n (%)	64 (33%)
Race, n (%)		DUDIT score, n (%)	
Black	123 (64%)	Drug-use problems (females ≥2, males ≥6)	82 (43%)
White	55 (28%)	Drug dependence (≥25)	8 (4%)
Other/multiple/unknown	15 (8%)		
BMI (kg/m^2), median (IQR)	25 (22, 30)	History of IV Drug Use, Currently + Previous (%)	19 (10)
ART anchor prior to entry*, n (%)		PHQ-9 Depression Category, n (%)	
INSTI-based	153 (79%)	None/Minimal (0-4)	92 (48%)
NNRTI-based	7 (4%)	Mild (5-9)	57 (30%)
Boosted PI-based	55 (28%)	Moderate (10-14)	22 (11%)
		Moderate-Severe (15-19)	16 (8%)
		Severe (20-27)	6 (3%)
HIV-1 RNA (copies/mL), n (%)		GAD-7 Anxiety Category, n (%)	
<200	72 (37%)	Minimal (0-4)	89 (46%)
200 – 9999	56 (29%)	Mild (5-9)	52 (27%)
10,000 – 99,999	46 (24%)	Moderate (10-14)	30 (16%)
≥100,000	19 (10%)	Severe (15-21)	22 (11%)

*May be on multiple anchor ARTs; AUDIT-C: Alcohol Use Disorders Identification Test – Consumption; DUDIT: Drug Use Disorders Identification Test; PHQ-9: Patient Health Questionnaire – 9 items; GAD-7: Generalized Anxiety Disorder – 7 items

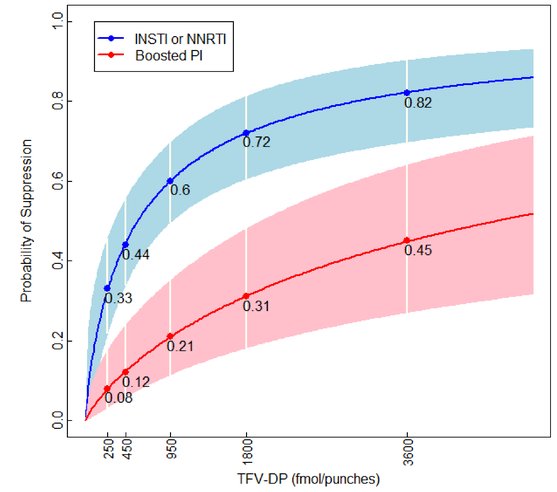
Figure 3. Baseline TFV-DP Concentrations by Virologic Suppression (VL <200 vs. VL ≥200) in Participants on INSTI/NNRTI or Boosted PI Regimens.



	Median (IQR)	
	VL < 200	VL ≥200
INSTI/NNRTI	1347 (764-1926)	358 (83.9-1007)
Boosted PI	1876 (924-2293)	909 (360-1954)

Green dashed line corresponds with TFV-DP concentration for ≥ 85% adherence

Figure 4. Probability of VS at Baseline by TFV-DP Concentrations and INSTI/NNRTI or Boosted PI Use



Shaded area represents 95% CI; TFV-DP concentrations (fmol/punches): ≥1800: ≥6 doses/week; 950-1799: 4-5 doses/week; 450-949: 2-3 doses/week, <450: <2 doses/week; <31.3 = no doses/week.

TFV-DP (fmol/punches)	Adherence Interpretation	Probability of Suppression (95% CI)	
		INSTI/NNRTI	Boosted PI
BLQ	-	0 (0, 0.17)	0 (0, 0.34)
250	Very low	0.33 (0.22, 0.46)	0.08 (0.03, 0.18)
450	Low	0.44 (0.34, 0.55)	0.12 (0.06, 0.24)
950	Moderate	0.60 (0.50, 0.70)	0.21 (0.11, 0.35)
1800	High	0.72 (0.61, 0.81)	0.31 (0.18, 0.48)
3600	Very high	0.82 (0.70, 0.90)	0.45 (0.27, 0.64)

- The odds of VS were 5.7 (2.4, 13.2) times higher for regimens containing INSTIs/NNRTIs vs boosted PIs (p<0.001)

CONCLUSIONS

- VS occurred from very low to very high adherence on TAF-containing regimens, with increased probabilities of VS as TFV-DP concentrations increased.
- Differential adherence-forgiveness is suggested between INSTI/NNRTI- and PI-containing ART among PWH.
- Analyses of longitudinal TFV-DP trends, virologic suppression, and their interplay with psychosocial factors are ongoing.

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