Differences in Virologic Suppression by TFV-DP in DBS and TAF Regimen: Results from ACTG A5359

Stefanie K. Schwab[1], Mary Morrow[1], Samantha MaWhinney[1], Raphael J. Landovitz[2], Chanelle Wimbish[3], Lu Zheng[4], Sara Sieczkarski[5], Pablo F. Belaunzaran-Zamudio[6], Paul Wannamaker[7], Jose R. Castillo-Mancilla[1,7], Jennifer J. Kiser[1,8], Peter L. Anderson[1], Aadia I. Rana[9], Kristina M. Brooks[1] for the ACTG A5359 team

[1]University of Colorado Anschutz Medical Campus, Aurora, CO, USA, [2]University of California Los Angeles, Los Angeles, CA, USA, [3]DLH, ACTG Network Coordinating Center, Bethesda, MD, USA, [4]Harvard TH Chan School of Public Health, Boston, MA, USA, [5]ACTG Data Management Center, Frontier Science and Technology Research Foundation, Inc., Amherst, NY, USA, [6]Division of AIDS, NIAID, NIH, Rockville, MD, USA, [7]ViiV Healthcare, Durham, NC, USA, [8]Merck, Rahway, NJ, USA, [9]University of Alabama at Birmingham Heersink School of Medicine, Birmingham, AL, USA

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University of Colorado Anschutz Medical Campus

BACKGROUND

- ACTG A5359/LATITUDE demonstrated superiority of long-acting cabotegravir/rilpivirine (LA-CAB/RPV) when compared to oral ART in PWH with prior adherence challenges.[1]
- Evaluating relationships between virologic suppression (VS) and objective adherence measures (i.e., tenofovir-diphosphate [TFV-DP] concentrations in dried blood spots [DBS]) is essential to understanding the findings among those on oral ART (Fig. 1).
- Newer second-generation INSTIs may also have improved adherence-forgiveness than first-generation INSTIs and PIs, and boosted tenofovir alafenamide (TAF) can increase TFV-DP in DBS by ~2.5-fold,[2,3] necessitating evaluations by regimen.

Figure 1. Framework linking TAF-Based ART, TFV-DP in DBS, and VS[4]

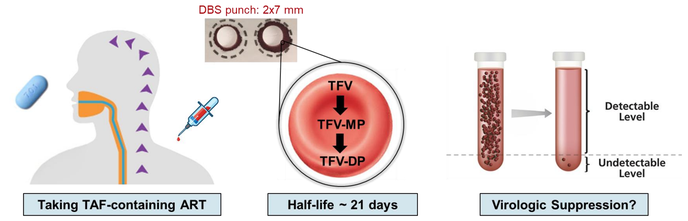


Image in right panel adapted from "HIV/AIDS Glossary" on clinicalinfo.hiv.gov

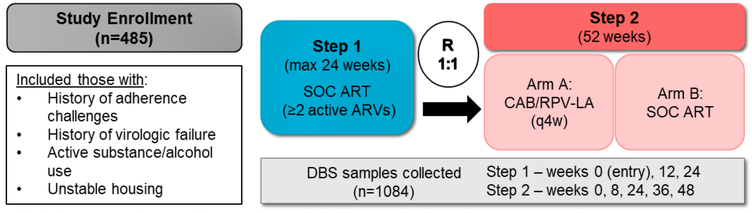
OBJECTIVES

- To examine associations between TFV-DP in DBS, VS and other clinical/demographic factors among PWH on TAF-based ART enrolled in ACTG A5359/LATITUDE.

METHODS

- LATITUDE (NCT03635788) is a phase III, prospective, randomized, open-label study that enrolled ART-experienced PWH with a history of adherence challenges (Fig. 2).[1]
- TFV-DP in DBS (2x7mm punches) were quantified using validated LC-MS/MS methods (LLOQ 31.3 fmol/punches).[5,6]
- Generalized estimating equations with a logit link were used to estimate the adjusted odds ratio (aOR) of VS (<200 c/mL) by:
  - TFV-DP adherence categories (based on historical data)[7,8]
  - ART regimen (unboosted TAF 25mg, boosted TAF [b/TAF] 10mg, b/TAF 25mg)
  - Other factors: sex, age, weight, race, eGFR, CD4 category

Figure 2. Study enrollment and design

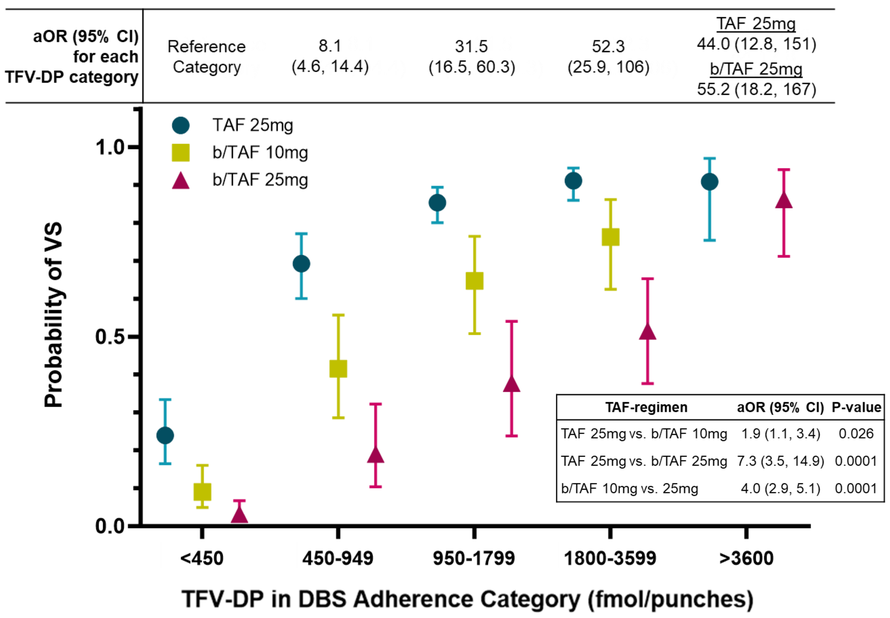


SOC: Standard of care; ARV: Antiretroviral; R: Randomization; q4w: every 4 weeks

Using TFV-DP in DBS, odds of VS were higher by adherence category, but differential adherence-forgiveness patterns were observed across TAF regimens as follows: TAF 25mg + 2nd generation INSTI > boosted TAF 10mg > boosted TAF 25mg

RESULTS

Figure 3. aOR of VS by TFV-DP in DBS adherence category. aORs were significantly higher for all adherence categories ≥450 vs. <450 fmol/punches. Within categories, aORs were higher with TAF 25mg vs. b/TAF 10mg and b/TAF 25mg for <3600, but did not differ for ≥3600 fmol/punches.



	<450 (n=184)	450–949 (n=160)	950–1799 (n=298)	1800–3599 (n=343)	≥3600 (n=99)
Adherence Interpretation	Very Low	Low	Moderate	High	Very High
Doses per week	<2	2-3	4-5	6-7	6-7
Step 1	142 (77)	114 (71)	193 (65)	209 (61)	58 (59)
Step 2	42 (23)	46 (29)	105 (35)	134 (39)	41 (41)
TAF 25 mg	132 (72)	112 (70)	241 (81)	267 (78)	51 (52)
b/TAF 10 mg	36 (20)	38 (24)	34 (11)	24 (7)	0 (0)
b/TAF 25 mg	16 (9)	10 (6)	23 (8)	52 (15)	48 (49)

Step and TAF regimens reported as n (%)

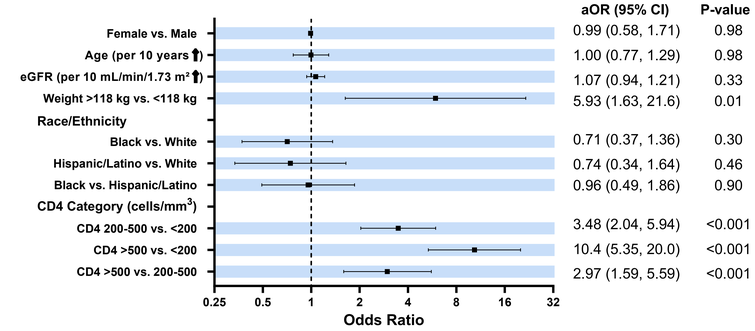
RESULTS

Table 1. Baseline Characteristics in Step 1 (n=292)

Variable		Variable	
Age (years), median (IQR)	40 (32, 52)	Weight (kg), median (IQR)	74.8 (65.4, 87.1)
Sex at birth, male (%)	204 (70)	eGFR (mL/min/1.73 m²), median (IQR)	99.5 (83.2, 114)
Race/Ethnicity, n (%)		CD4+ category (cells/mm³), n (%)	
Black	174 (60)	<200	104 (36)
White	55 (19)	200–500	109 (37)
Hispanic/Latino	62 (21)	>500	79 (27)

- A total of 1084 DBS samples were analyzed across Steps 1 and 2:
  - TAF 25 mg (n=806 visits): BIC (52%) or DTG (48%)
  - b/TAF 10 mg (n=130 visits): DRV (79%) or EVG (21%)
  - b/TAF 25 mg (n=148 visits): DRV (59%) ± BIC or DTG (39%)

Figure 4. CD4 count and weight were the only other factors associated with VS after accounting for TFV-DP in DBS



**aORs in Fig. 3 originate from the same overall multivariable model.*

CONCLUSIONS

- TFV-DP in DBS was associated with higher odds of VS by adherence category. Patient characteristics (i.e., weight and CD4 count) were also associated with VS after controlling for TFV-DP.
- When comparing within TFV-DP adherence categories <3600 fmol/punches, the odds of VS were higher in those on TAF 25mg regimens in comparison to b/TAF 10mg or b/TAF 25mg.
- These findings support differences in adherence-forgiveness patterns between TAF regimens, which may be driven in part by second generation INSTI vs. PI use.

Plain Language Summary: TFV-DP in DBS can be used to measure adherence in PWH. Higher rates of VS were seen as people took more doses of their medications containing TAF, but some combinations might be more forgiving to missed doses than others.

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References: (1) Rana et al. N Eng J Med 2026. (2) Schwab et al. CROI 2025 [Abstract #653]. (3) Brooks et al. 2020, J Antimicrob Chemother. (4) Castillo-Mancilla et al. 2013, IDS Res Hum Retroviruses. (5) Bushman et al. 2011, J Pharm Biomed Anal. (6) Zheng et al. 2016, J Pharm Biomed Anal. (7) Coyle et al. 2024, Clin Infect Dis. (8) Yager et al. 2020, J Acquir Immune Defic Syndr.