

Tenofovir-diphosphate in PBMC following increasing TAF vs. TDF dosing under directly observed therapy

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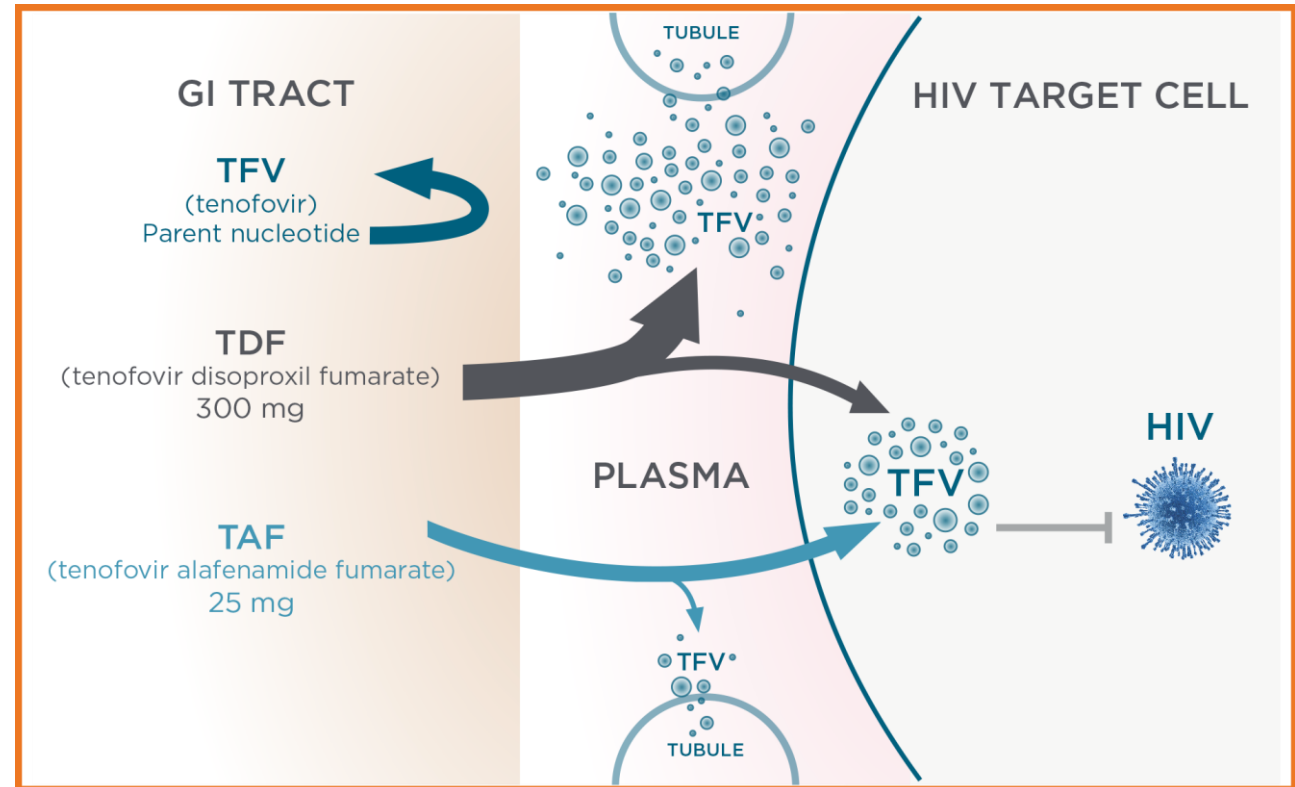
Disclosures – Jenna Yager

No conflicts of interest to disclose

Background

TAF vs. TDF:

- ↓ Plasma TFV
- ↓ TFV-DP in DBS
- ↑ TFV-DP in PBMC



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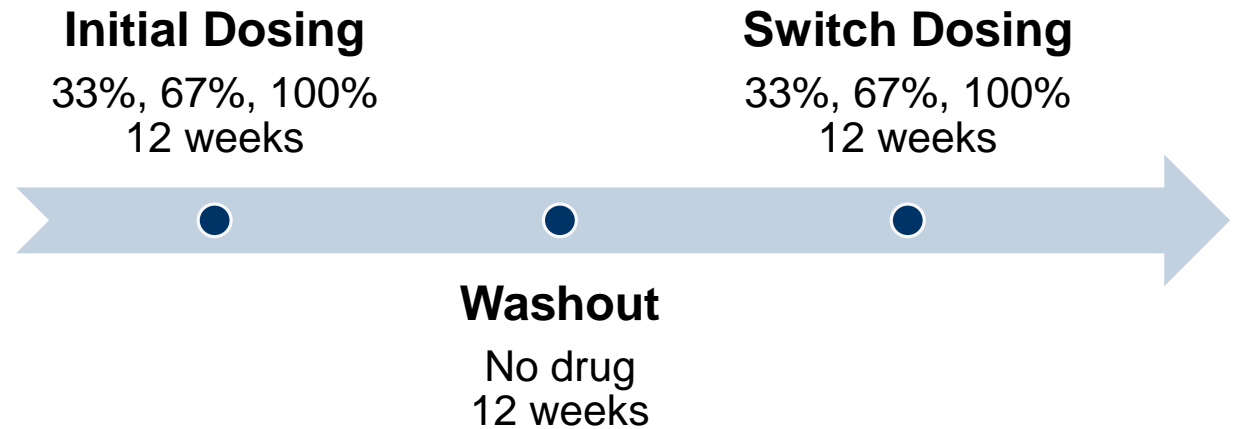
Objective

- TAF vs. TDF not directly compared in:
 - DOT studies
 - Less than daily dosing

To compare TFV-DP concentrations in target cells (PBMC) following increasing TDF/FTC vs. TAF/FTC dosing under DOT




Study Design

- Two randomized studies
 - DOT-DBS (NCT02022657): TDF/FTC
 - TAF-DBS (NCT02962739): TAF/FTC
- Adults without HIV at low risk for infection
- Randomized to two DOT doses
 - Doses observed in person or by video








Dosing Randomization








33%

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
						

67%

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
						

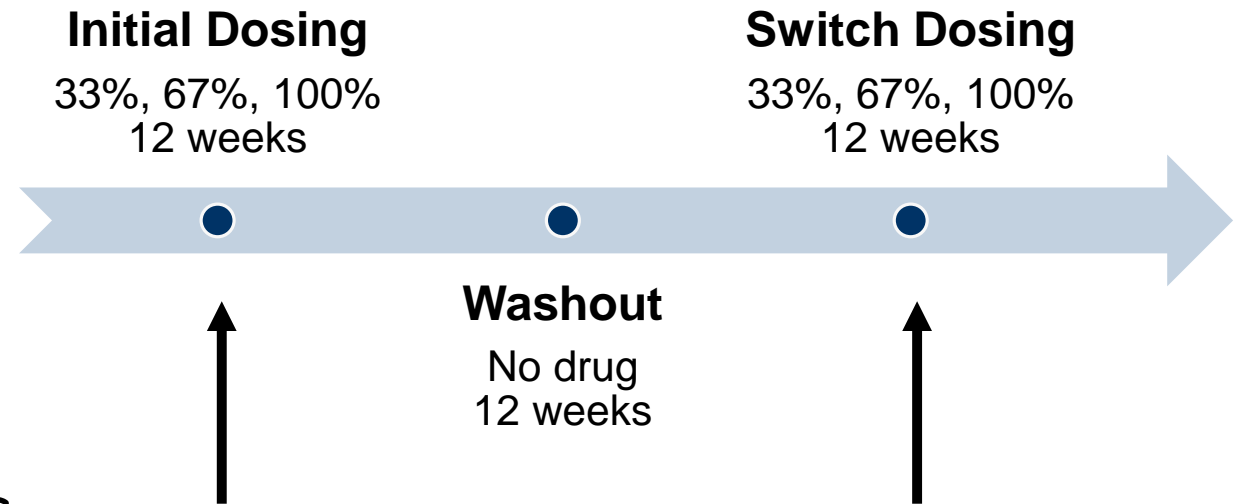
100%

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
						



Methods

- Convenience sampling
- Samples from last dosing visit pooled and analyzed
 - Weeks 12 and 36
- TFV-DP concentrations in PBMC determined using a validated LC-MS/MS assay



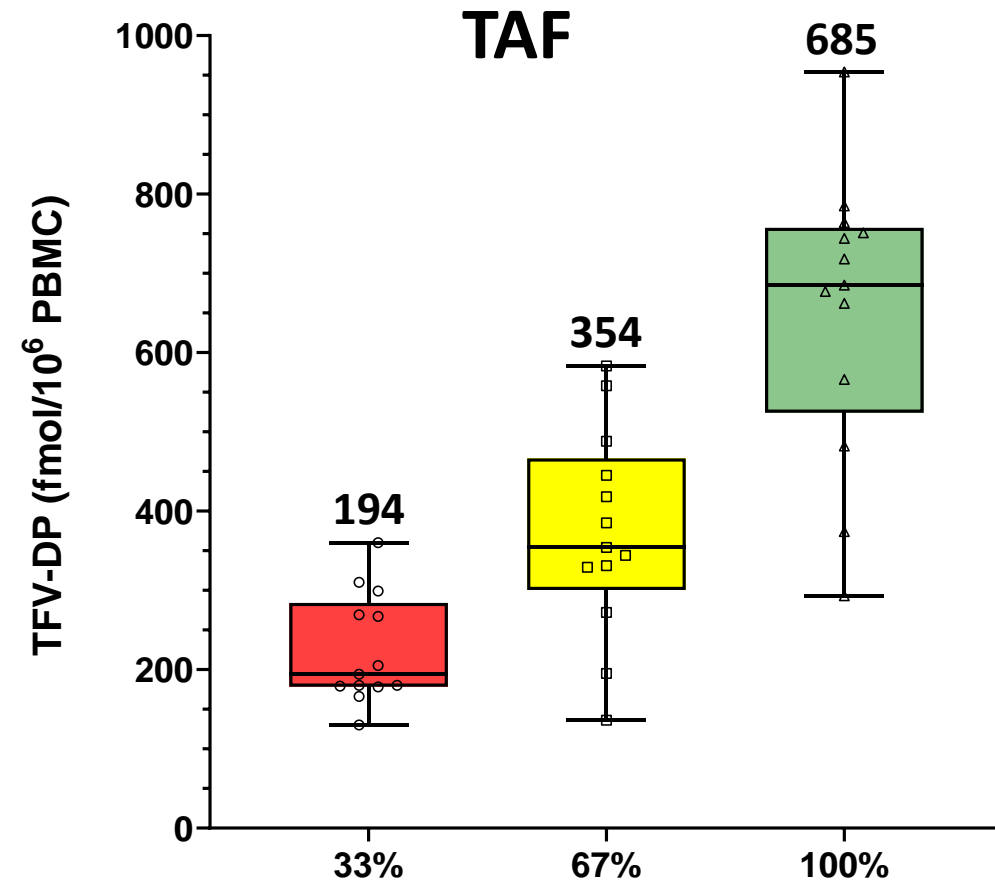
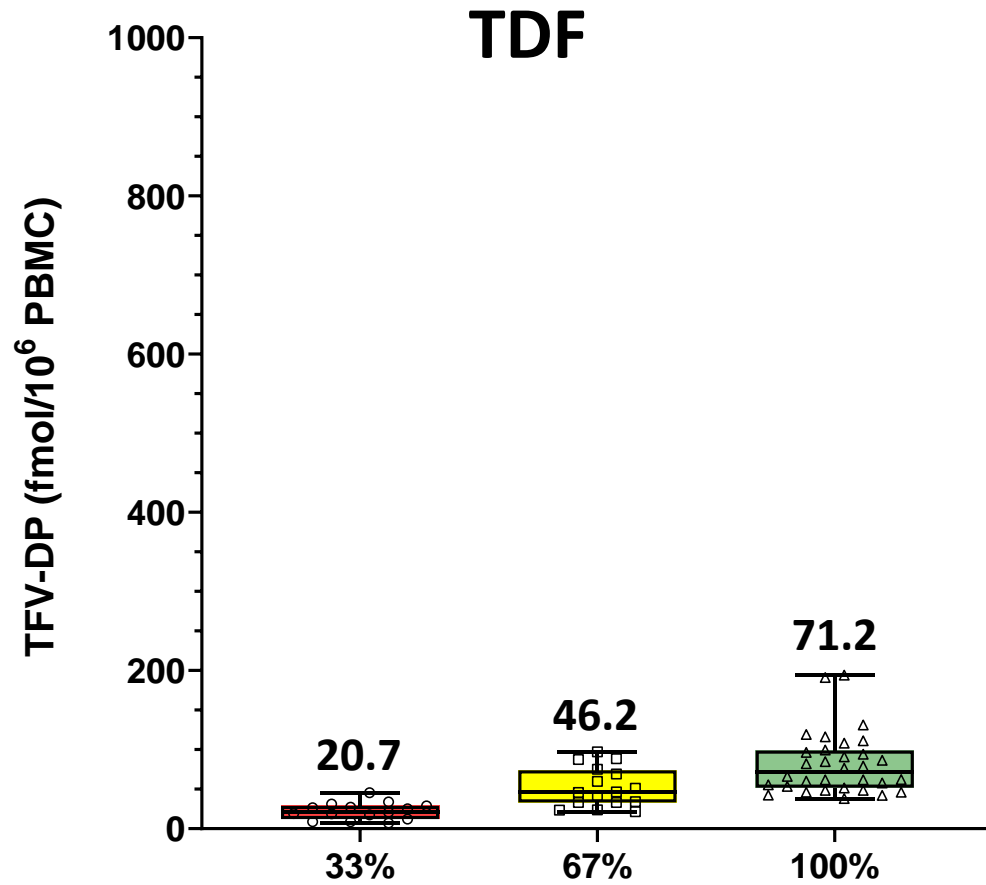
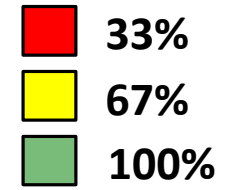
Participant Characteristics

	TDF/FTC	TAF/FTC
N	44 (63 data points)	28 (39 data points)
Age (years), mean (SD)	31 (7.07)	29 (5.64)
Male sex at birth, n (%)	21 (47.7%)	13 (46.4%)
Transgender, n (%)	1 (2.3%)	0 (0.0%)
BMI (kg/m ²), mean (SD)	27.9 (7.8)	25.6 (5.4)
Race/Ethnicity, n (%)		
White	21 (47.7%)	21 (75.0%)
Black/African American	8 (18.2%)	5 (17.9%)
Hispanic	12 (27.3%)	4 (14.3%)
Asian	3 (6.8%)	0 (0.0%)
CrCl ¹ (mL/min), mean (SD)	106.4 (23.4)	111.2 (19.9)
eGFR ² (mL/min/1.73 m ²), mean (SD)	97.7 (17.3)	100.2 (14.0)

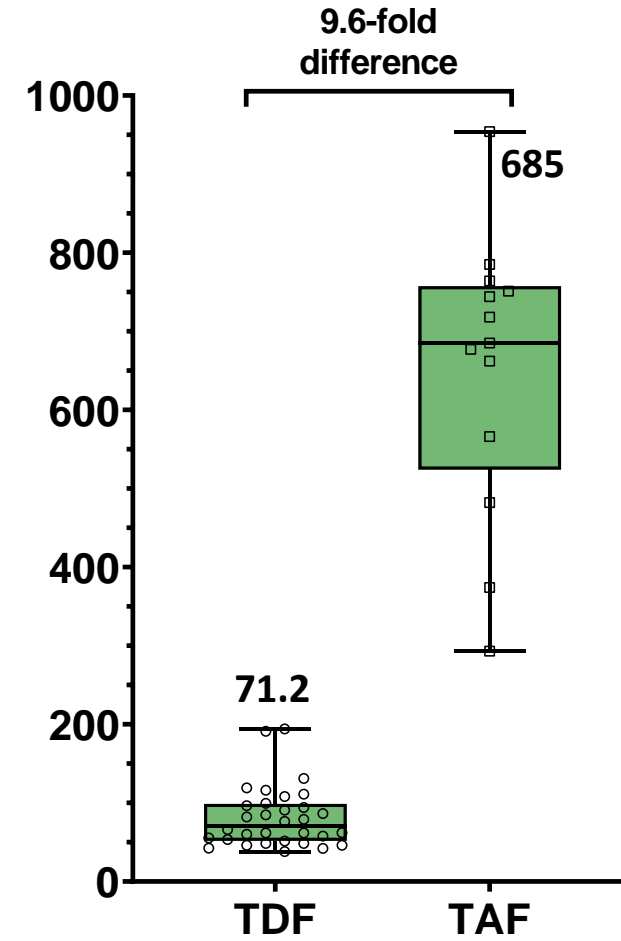
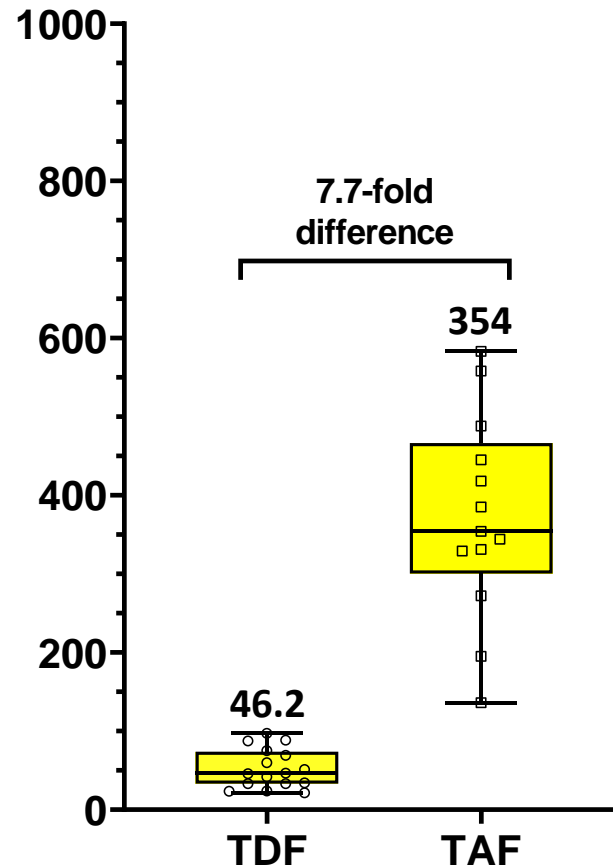
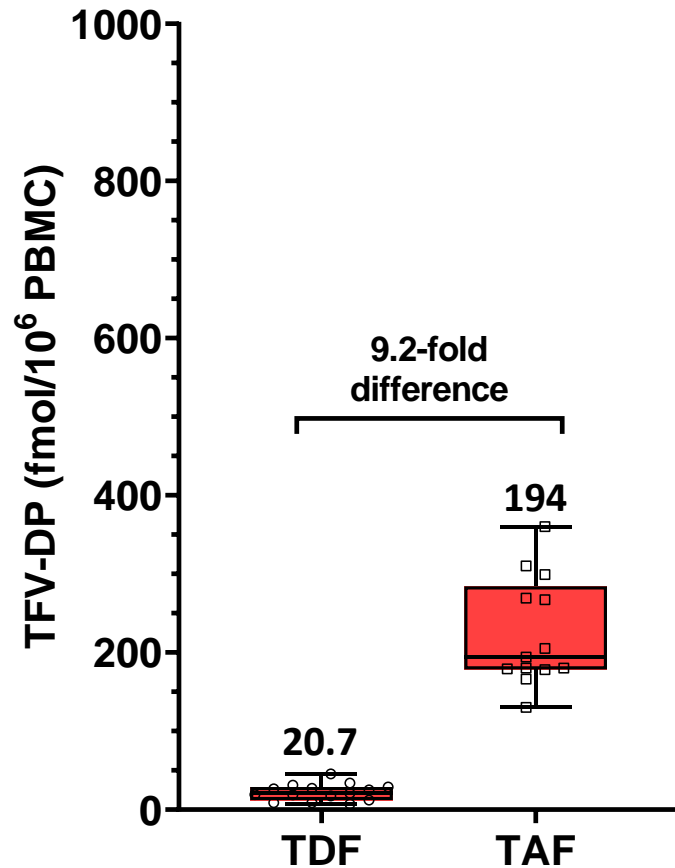
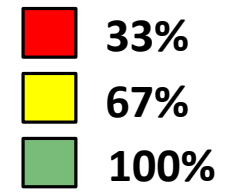
¹ CrCl determined using ideal body weight and Cockcroft-Gault Equation

² eGFR determined using MDRD equation.

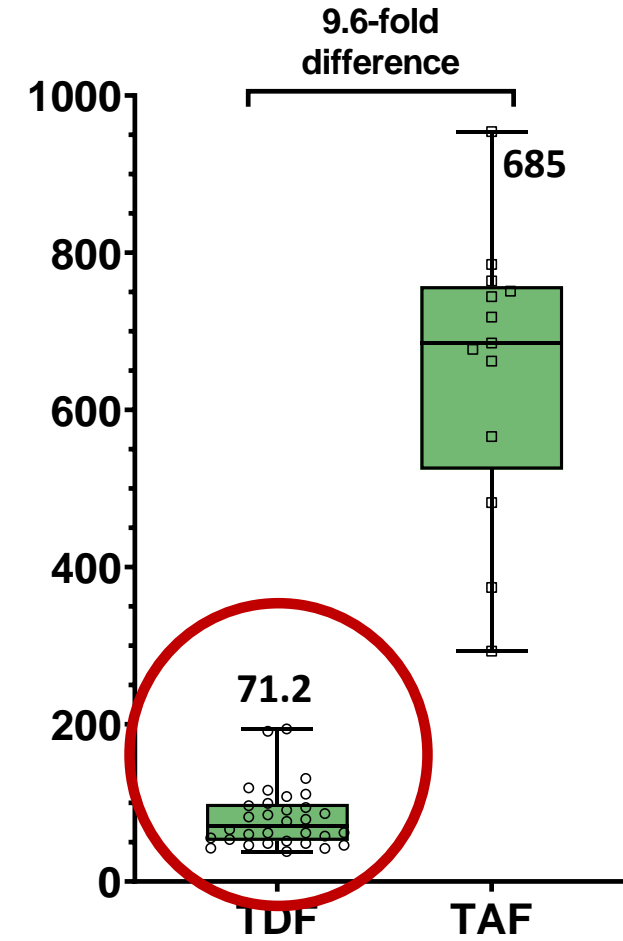
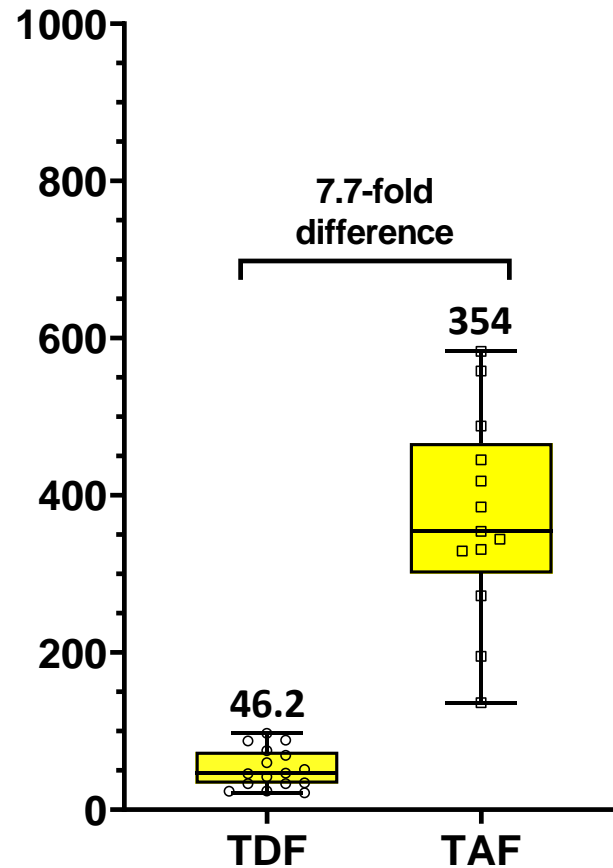
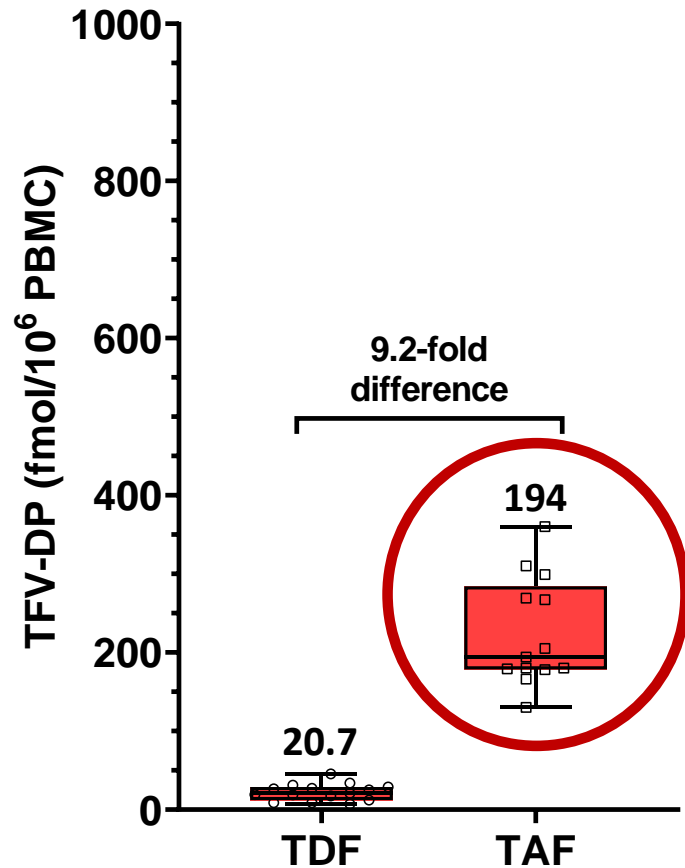
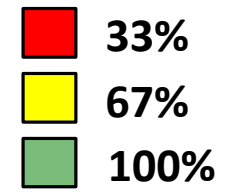
TFV-DP by Dosing



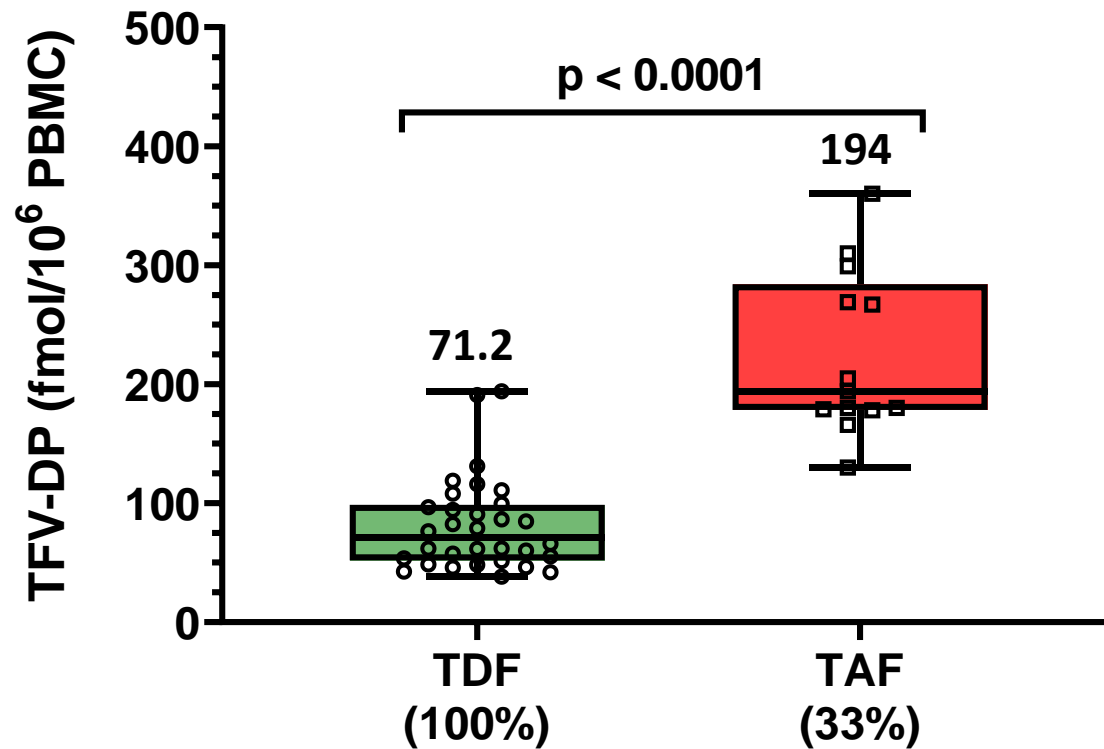
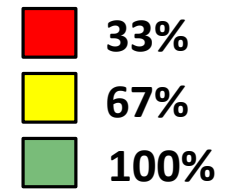
TFV-DP: TDF vs. TAF



TFV-DP: TDF vs. TAF



TFV-DP: TDF vs. TAF



- 2-fold difference
- All TFV-DP following 33% TAF dosing above median for 100% TDF dosing

Conclusion

- TFV-DP in PBMC increases with increasing dose frequency
- 8- to 10-fold higher TFV-DP in PBMC with TAF vs. TDF
- These observations would support increased systemic potency and pharmacologic forgiveness for TAF

Limitations

- Ongoing analyses
- Did not measure mucosal or lymph node tissue concentrations
- Efficacy outcomes not included

Acknowledgements

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