University of Colorado Anschutz Medical Campus

Higher cumulative ART exposure with boosted single and multiple-tablet regimens in persons with HIV taking tenofovir disoproxil fumarate

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Background

Undetectable=Untransmittable (U=U)

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Adherence to antiretroviral therapy (ART) is required for Undetectable HIV viral load

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ART regimen complexity affects adherence

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Once Daily ART

Single-Tablet Regimens (STR) | **Multiple-Tablet Regimens (MTR)**

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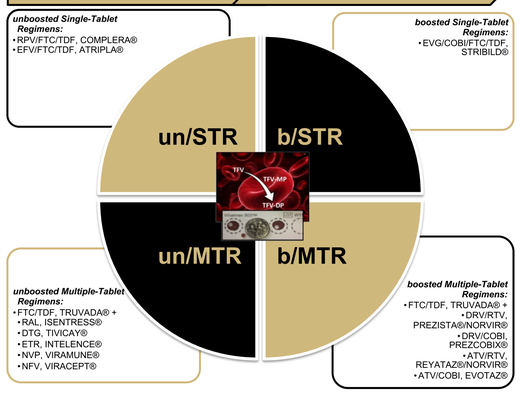
Is drug exposure different in people with HIV (PWH) on STR vs MTR?

Can be compared using an objective biomarker with a long half-life: Tenofovir diphosphate (TFV-DP) in dried blood spots (DBS)

Methods

Prospective clinical cohort (UCH-IDGP) → **Study Period: 2014-2017**



Results

Table 1. Baseline demographic and clinical characteristics of the study population.

Variable: *n* (%) or mean (±SD)	HIV VL: Suppressed at all visits: *n*=303 (57%)	*P*-Value	Viremic at ≥ 1 visit: *n*=229 (43%)	Overall: *N*=532 (100%)
Race				
Black	55 (18%)	0.90	46 (20%)	101 (19%)
White	178 (59%)		127 (55%)	305 (57%)
Hispanic	56 (18%)		45 (20%)	101 (19%)
Other	14 (5%)		11 (5%)	25 (5%)
Gender				
Male	252 (83%)	0.054	204 (89%)	456 (86%)
Female	51 (17%)		25 (11%)	76 (14%)
Age (years)	46 (±10)	0.03	44 (±11)	45 (±11)
BMI (Kg/m^2)	27 (±6)	0.15	26 (±5)	26 (±5)
HCT (%)	45 (±4)	0.09	44 (±5)	44 (±4)
eGFR (mL/min/1.73 m^2)	88 (±22)	0.09	91 (±22)	89 (±22)
CD4$^+$ T-cells (cells/mm^3)	680 (±334)	<0.0001	515 (±342)	609 (±347)
3-month self-reported adherence (%)	95 (±9)	<0.0001	87 (±19)	92 (±14)
Current ART duration				
<1 month	4 (1%)	<0.0001	17 (7%)	21 (4%)
1-3 months	18 (6%)		26 (11%)	44 (8%)
3-6 months	13 (4%)		18 (8%)	31 (6%)
≥6 months	268 (88%)		168 (73%)	436 (82%)
Current ART type				
Unboosted MTR	80 (26%)	<0.0001	51 (22%)	131 (25%)
Unboosted STR	94 (31%)		33 (14%)	127 (24%)
Boosted MTR	89 (29%)		89 (39%)	178 (33%)
Boosted STR	40 (13%)		56 (24%)	96 (18%)
pMRCI disease score	4.3 (±2.4)	0.052	4.8 (±2.8)	4.5 (±2.5)

Table 2. TFV-DP percent difference or change (95% CI) for each adjustment variable in the full (2A) and virologically-suppressed (2B) models.

Table 2A

Variable	TFV-DP % Difference (95%CI)	*P*-Value
Race		
Black	REF	REF
White	8% (-6–24%)	0.28
Hispanic	18% (0–39%)	0.047
Other	37% (5–78%)	0.02
Gender		
Male	REF	REF
Female	19% (2–39%)	0.03
Age (every 1 year)	1% (0–1%)	0.04
BMI (every 1 Kg/m^2)	-2% (-3–-1%)	<0.0001
HCT (every 1%)	3% (1–4%)	<0.0001
eGFR (every 10 mL/min/1.73 m^2)	-6% (-8–-4%)	<0.0001
CD4$^+$ T-cells (every 50 cells/mm^3)	1% (0–2%)	0.11
3-month self-reported adherence (every 10%)	28% (24–31%)	<0.0001
Current ART duration		
<1 month	REF	REF
1-3 months	5% (-21–69%)	0.83
3-6 months	29% (-17–102%)	0.26
≥6 months	18% (-24–82%)	0.46
Current ART type		
Unboosted MTR	REF	REF
Unboosted STR	7% (-7–24%)	0.34
Boosted MTR	37% (17–59%)	<0.0001
Boosted STR	25% (7–47%)	0.005
pMRCI disease score (every 1 unit)	-1% (-4–2%)	0.53

Table 2B

Variable	TFV-DP % Difference (95%CI)	*P*-Value
Race		
Black	REF	REF
White	12% (-2–27%)	0.09
Hispanic	19% (2–38%)	0.02
Other	20% (-5–53%)	0.13
Gender		
Male	REF	REF
Female	31% (15–50%)	<0.0001
Age (every 1 year)	0% (0–1%)	0.06
BMI (every 1 Kg/m^2)	-3% (-3–-2%)	<0.0001
HCT (every 1%)	1% (0–2%)	0.02
eGFR (every 10 mL/min/1.73 m^2)	-2% (-4–0%)	0.01
CD4$^+$ T-cells (every 50 cells/mm^3)	0% (-1–1%)	0.67
3-month self-reported adherence (every 10%)	8% (5–13%)	<0.0001
Current ART duration		
<1 month	REF	REF
1-3 months	43% (-8–121%)	0.11
3-6 months	46% (-3–120%)	0.07
≥6 months	55% (4–132%)	0.03
Current ART type		
Unboosted MTR	REF	REF
Unboosted STR	-4% (-15–8%)	0.50
Boosted MTR	12% (-2–27%)	0.09
Boosted STR	34% (16–55%)	<0.0001
pMRCI disease score (every 1 unit)	2% (-1–5%)	0.15

Figure 1. Percent differences and estimated TFV-DP in DBS by ART regimen type in the full cohort.

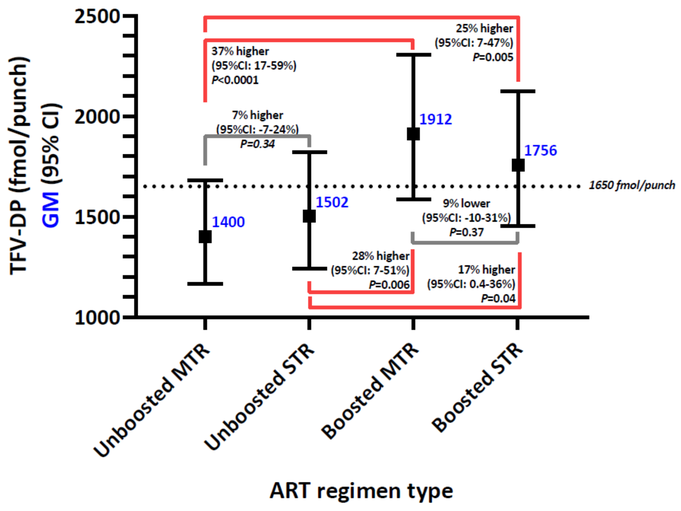
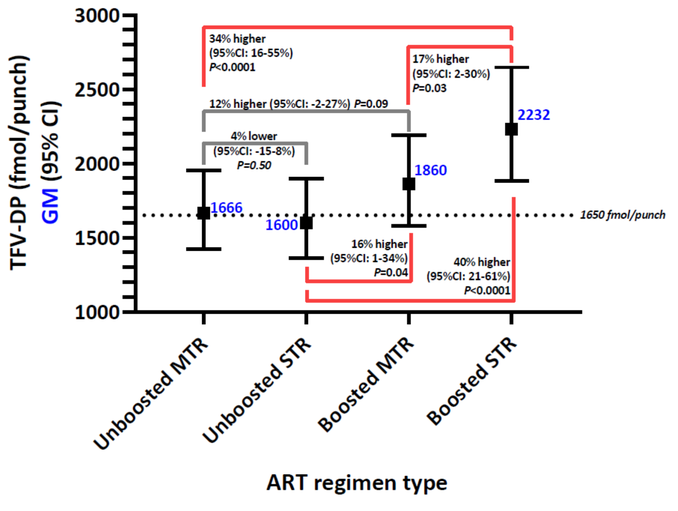


Figure 2. Percent differences and estimated TFV-DP in DBS by ART regimen type in the virologically-suppressed cohort.



Conclusions

This association is likely driven by pharmacokinetic (PK) boosters (RTV or COBI) in certain ART regimens

In virologically suppressed PWH, b/STR are associated with the highest drug exposure

Boosted ART regimens are associated with higher drug exposure than unboosted ART regimens, regardless of STR/MTR

Implications

Boosted ART regimens could be beneficial to PWH that would benefit from more drug forgiveness to missed doses

Could aid in initial ART regimen selection that is more patient-tailored/specific

The PK boosters used in certain ART regimens affect common concomitant medications, requiring careful evaluation

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