Pharmacokinetics of Switching to B/F/TAF in PWH Post-Renal Transplant: BIC-Switch Study

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BACKGROUND

- Clinical trials and real-world data have demonstrated bictegravir (BIC), emtricitabine (FTC), tenofovir alafenamide (TAF) (B/F/TAF) is safe and efficacious with low risk for renal toxicity
- Antiretroviral therapy (ART) is critical for persons with HIV (PWH) post-renal transplant for virologic control and graft preservation
- There is little known about the pharmacokinetics (PK) in PWH post-renal transplant when using B/F/TAF
- We hypothesized that switching participants from their current ART to B/F/TAF will continue to be safe and efficacious with predictable changes in PK

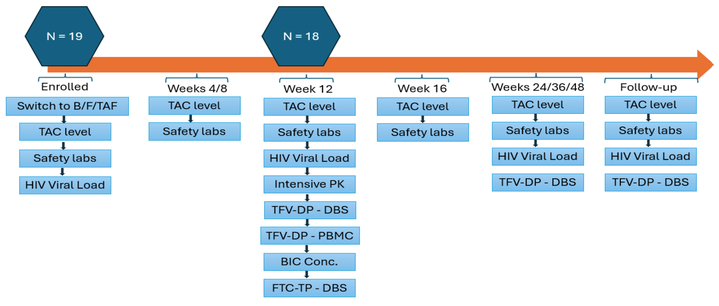
OBJECTIVES

To assess the PK of B/F/TAF in PWH post-renal transplant when compared to historical controls with similar renal function.

METHODS

- Single arm, open-label, switch study among virally suppressed (HIV VL <50 c/mL) PWH post-renal transplant switched from baseline ART to B/F/TAF and followed for 72 weeks. (Figure 1)
- Baseline renal function (CrCl), viral efficacy (HIV VL) and tacrolimus trough concentrations were collected
- At week 12, an intensive plasma PK visit was conducted with sampling at hours 0, 0.5, 1, 2, 4, and 24 post-dose; TVF-DP and FTC-TP were analyzed in the samples at 0 (pre-dose), 4, and 24 hrs post-dose in PBMC and pre-dose for DBS
- Plasma PK values for BIC, TAF, FTC, and TFV were then compared with PWH with normal (≥90 ml/min) and similar renal function (30-59 ml/min) from package inserts
- Tenofovir diphosphate (TFV-DP) and emtricitabine triphosphate (FTC-TP) were compared using geometric mean ratio with values from QUANTI-TAF assuming a significance level of α=0.05 (NCT04065347; controls) (Table 1)
- QUANTI-TAF controls were matched with BIC-Switch participants by age, BMI, sex, race, ethnicity, and CrCl (as close as possible)

Fig 1. Study design



B/F/TAF was effective and safe in PWH post-renal transplant and plasma AUC for BIC, FTC, TAF and TFV were in the range of historical controls with similar renal function

RESULTS

Table 2 . Plasma PK mean (range) in BIC-Switch compared with package insert controls mean (CV%)

Analyte	BIC-Switch AUC (ng*h per mL) (N=18)	Package insert CrCl 30-59 AUC[b]	Package insert normal renal function AUC[c]	BIC-Switch C_{max} ng/mL (N=18)	BIC-Switch C_{trough} ng/mL (N=18)
BIC	74627 [22222-144395]	NA	102000 (27%)	5045 [1432-9027]	1855 [404-3852]
FTC	22758 [13796-32844]	23000 (23.6%)	12300 (29%)	2505 [1448-5512]	355 [110-1385]
TAF	389.5 [45.8-1406.9]	260 (58.8%)	142 (17%)	287.3 [11-891]	NA[a]
TFV	613 [211-1140]	610 (28.4%)	290 (27%)[b]	32.1 [10.5-58.8]	23.5 [8.7-44.5]

[a]TAF C_{trough} not quantifiable; [b]F/TAF package insert; [c]B/F/TAF package insert

Table 3. Drug concentrations in BIC-Switch (test) compared with controls from QUANTI-TAF (ref.)

Drug	Matrix (units)	Group	GM	GM 95% CI	GMR (Test/Ref.)	GMR 95% CI	P-value
TFV-DP	DBS (fmol/punches) (N=19)	BIC-SWITCH (Test)	5408	4391, 6662	1.45	1.11, 1.89	0.0083
		QUANTI-TAF (Ref.)	3738	3110, 4491			
	PBMC (fmol/10^6 cells) (N=19)	BIC-SWITCH (Test)	1475	1055, 2064	2.38	1.61, 3.51	<0.0001
		QUANTI-TAF (Ref.)	621	497, 776			
FTC-TP	DBS (pmol/punches) (N=19)	BIC-SWITCH (Test)	6.34	5.27, 7.62	1.09	0.82, 1.44	0.54
		QUANTI-TAF (Ref.)	5.82	4.64, 7.30			
	PBMC (pmol/10^6 cells) (N=19)	BIC-SWITCH (Test)	14.98	11.00, 20.40	2.67	1.89, 3.78	<0.0001
		QUANTI-TAF (Ref.)	5.60	4.69, 6.68			

GM, geometric mean. GMR, geometric mean ratio, CI confidence interval. PBMC Css average for BIC-SWITCH compared with single convenience time point in QUANTI-TAF.

Results

Table. 1 Baseline demographics and clinical characteristics

Variable	Study Cohort: BIC-SWITCH (n=19)	Study Cohort: QUANTI-TAF (n=19)
Age (years), median (IQR)	57 (48, 63)	58 (47, 61)
Gender; Male n (%)	13 (68%)	15 (79%)
Race, n (%)		
Black	17 (89%)	8 (42%)
Non-Black	2 (11%)	11 (58%)
Ethnicity, n (%)		
Hispanic or Latino	4 (21%)	2 (11%)
Non-Hispanic or Latino	15 (79%)	17 (89%)
CrCl (mL/min), median (IQR)*	52 (45, 67)	75 (61, 102)
BMI (kg/m^2), median (IQR)	26 (22, 29)	27 (22, 33)

*CrCl was calculated using Cockroft-Gault and actual body weight; CrCl was significantly higher in QUANTI-TAF controls P=0.0004 Mann-Whitney

- BIC-Switch CrCl remained stable (mean of 54.9 to 60.9 mL/min, p=0.11) by end of study
- Tacrolimus doses and trough concentrations remained stable without need to change dosing
- HIV VL remained suppressed (<50 c/mL) in all BIC-Switch participants
- Plasma AUCs of TAF, FTC, and TFV were similar with package insert controls who had CrCl 30-59 ml/min (Table 2)
- Plasma AUC for BIC was in the same range as controls from the package insert with normal renal function (Table 2)
- Concentrations of intracellular TFV-DP in both DBS and PBMC, and FTC-TP in PBMC were significantly higher when compared with QUANTI-TAF participants (Table 3)

CONCLUSIONS

- B/F/TAF was safe and efficacious, and tacrolimus doses were stable in PWH post-renal transplant
- Plasma B/F/TAF PK in BIC-Switch was similar to package insert controls with CrCl of 30-59 ml/min
- Intracellular TFV-DP and FTC-TP were higher in BIC-Switch than QUANTI-TAF controls; a limitation was that QUANTI-TAF controls had better renal function
- B/F/TAF is an appropriate option for post-renal transplant with CrCl > 30 ml/min

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