INTERACTION BETWEEN TAF-BASED PrEP AND HORMONE THERAPY IN TRANSGENDER WOMEN: iFACT 3

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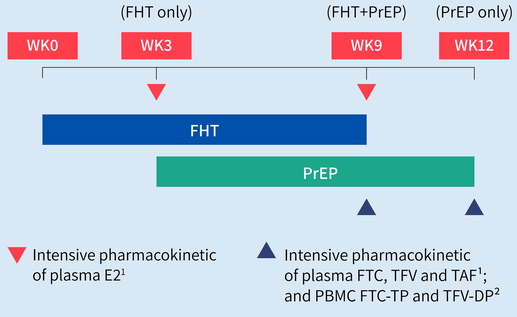
Background

- Feminizing hormone therapy (FHT) is common among transgender women (TGW) receiving PrEP.
- To evaluate the potential drug-drug interactions (DDI) between FHT and emtricitabine (FTC)/tenofovir alafenamide (TAF)-based PrEP, we assessed the pharmacokinetics (PK) of FTC, TAF, tenofovir (TFV) and estradiol (E2) among TGW receiving FHT in Thailand.

Methods

- Twenty TGW who had not undergone orchiectomy and had not received injectable FHT within 3 months were enrolled between January and February 2022.
- FHT (estradiol valerate 2 mg and cyproterone acetate 25 mg) was prescribed to participants at baseline until week 9, while PrEP (FTC 200 mg/TAF 25 mg) was initiated at week 3 until week 12.
- Intensive PK sampling was performed at weeks 3 (FHT only) and 9 (PrEP and FHT) for E2; and weeks 9 (PrEP and FHT) and 12 (PrEP only) for plasma FTC, TAF, and TFV **(Figure 1)**.
- Blood bioavailable testosterone, FSH, and LH were also measured.

Figure 1 iFACT study scheme



[1] Plasma will be collected at t=0 (pre-dose), 0.5, 1, 2, 4, 6, 8, 10, 12, and 24 hours after directly observed medication ingestion with a standardized meal (a total of 10 samples)

[2] PBMC will be collected at t=2 and 24 hours after directly observed medication ingestion with a standardized meal (a total of 2 samples)

The AUC and Cmax GMRs of FTC and TFV were within the bioequivalence range, indicating no clinically significant DDI from FHT towards FTC/TAF-based PrEP

Results

- 18/20 participants completed the PK visits and were included in this analysis.
- Median (interquartile range [IQR]) age and body mass index were 28 (23-32) years and 20.8 (19.9-21.9) kg/m^2, respectively.
- The area under the curve (AUC) and maximum concentration (C_{max}) geometric mean ratios (GMRs) (90%CI) at week 3 (reference) and week 9 for E2 were 0.80 (0.72-0.90, *p*=0.002) and 1.11 (0.96-1.27, *p*=0.23), respectively **(Table 1 and Figure 2)**.

Table 1 Summary of E2 pharmacokinetic parameters; data are presented in geometric mean (%CV)

E2 PK parameter	Week 3 (without PrEP)	Week 9 (with PrEP)	GMR (90%CI)	*p*
AUC_{0-24} (pg*h/mL)	799.41 (35.63)	642.65 (50.29)	0.80 (0.72 – 0.90)	0.002
C_{max} (pg/mL)	60.13 (36.46)	66.59 (39.78)	1.11 (0.96 – 1.27)	0.23

- The AUC and C_{max} GMRs at week 9 and week 12 (reference) were as follows: FTC, 0.92 (0.88-0.97, *p*=0.009) and 0.93 (0.84-1.03, *p*=0.24); TAF, 1.05 (0.83-1.33, *p*=0.73) and 1.14 (0.85-1.52, *p*=0.46); and TFV, 0.92 (0.88-0.97, *p*=0.01) and 0.97 (0.89-1.05, *p*=0.50) **(Figure 3 and Table 2)**.
- No significant changes in bioavailable testosterone, FSH, and LH between weeks 3 and 9 were observed (bioavailable testosterone, median [IQR] 0.031 [0.025-0.120] vs 0.024 [0.006-0.122], *p*=0.17; FSH, 0.75 [0.6-1.3] vs 0.85 [0.4-1.6], *p*=0.24; and LH, 0.52 [0.21-0.86] vs 0.44 [0.25-0.79], *p*=0.95.
- No participants discontinued the study due to a reported adverse event.
- There were no significant changes in creatinine clearance and alanine aminotransferase levels over the study period.

Conclusion

- Plasma E2, FTC and TFV exposures trended lower when FTC/TAF was administered with FHT; however, the AUC and C_{max} GMRs of FTC and TFV were within the bioequivalence range, indicating no clinically significant DDI from FHT towards FTC/TAF-based PrEP.
- Intracellular and tissues rectal measurements of TFV-DP and FTC-TP levels are ongoing.

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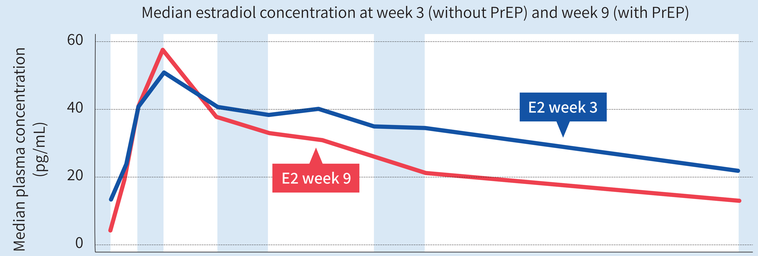
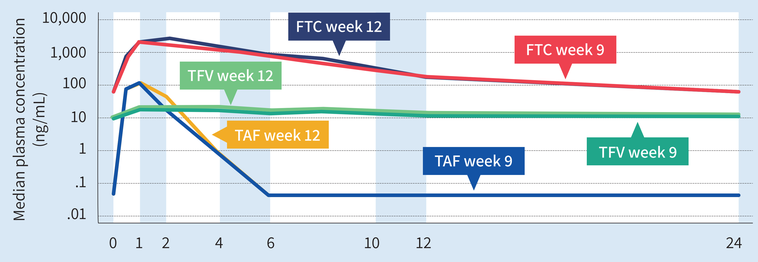
Figure 2 Median E2 concentration-time curves



Undetectable E2 (<5 pg/mL) imputed as 2.5 pg/mL

Figure 3 Median ARV concentration-time curves



Undetectable TAF imputed as o.o5ng/mL

Table 2 Summary of ARV pharmacokinetic parameters; data are presented in geometric mean (%CV)

ARV	PK parameter	Week 9 (with FHT)	Week 12 (without FHT)	GMR (90%CI)	*p*
TAF	AUC_{0-24} (ng*h/mL)	208.09 (65.5)	197.88 (50.04)	1.05 (0.83 – 1.33)	0.73
	C_{max} (ng/mL)	166.78 (90.76)	146.65 (56.84)	1.14 (0.85 – 1.52)	0.46
TFV	AUC_{0-24} (ng*h/mL)	295.01 (18.43)	319.75 (16.25)	0.92 (0.88 – 0.97)	0.01
	C_{max} (ng/mL)	19.47 (24.37)	20.17 (16.79)	0.97 (0.89 – 1.05)	0.50
FTC	AUC_{0-24} (ng*h/mL)	9,944.74 (15.66)	10,791.14 (13.56)	0.92 (0.88 – 0.97)	0.009
	C_{max} (ng/mL)	2,197.23 (33.0)	2,366.24 (23.17)	0.93 (0.84 – 1.03)	0.24