Estradiol concentrations in trans women on INSTIs compared to those without HIV

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Introduction

- Accessing feminizing hormone therapy (FHT) is essential to trans women. Concern of negative drug interactions between their FHT and antiretroviral therapy (ART) can be a barrier to acceptance of ART in trans women with HIV.
- In this study, we measured serum estradiol concentrations in trans women with HIV taking FHT and integrase strand transfer inhibitor (INSTI)-based ART versus trans women without HIV taking FHT.

Methodology

- This was a single-center, parallel group, clinical cross-sectional study of trans women with and without HIV, 18 years or older, and taking at least 2 mg/day of oral 17-beta estradiol plus a form of anti-androgen therapy, with no medication changes for at least one month prior to inclusion. Women with HIV were to be on suppressive ART (HIV viral load < 50 copies/mL on 2 occasions at least 3 months apart); the ART regimen could include any INSTI.
- ART and oral estradiol were co-administered with a standardized meal under observed conditions.
- Blood was collected prior to ART and estradiol dosing and then at 2, 4, 6, and 8 hours post-dose and estradiol concentrations were measured from serum using CMIA (LifeLabs®).
- Median estradiol concentrations at each time point, estradiol C_{max},, T_{max} and area under the curve (AUC) were compared between groups using Wilcoxon rank-sum tests; AUC was calculated using the linear trapezoidal rule in R version 3.6.1 (Vienna, Austria).

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Results

	Median (Q1, Q3)			
	Overall sample (n=15)	HIV positive (n=8)	HIV negative (n=7)	P value
C_{0h} (pmol/L)	230 (166,333)	226 (102,391)	230 (206,256)	0.78
C_{2h} (pmol/L)	331 (215,568)	476 (298,805)	225 (215,300)	0.19
C_{4h} (pmol/L)	268 (212,503)	421 (216,581)	265 (210,319)	0.34
C_{6h} (pmol/L)	256 (168,345)	267 (131,379)	233 (199,310)	0.96
C_{8h} (pmol/L)	240 (179,365)	235 (141,435)	240 (198,303)	0.96
C_{max} (pmol/L)	369 (224,666)	560 (343,806)	265 (224,319)	0.19
T_{max} (hours)	4 (4, 4)	4 (4, 4)	4 (4, 4)	0.73
Area Under Curve (pmol×h/L)	2447 (1629,3857)	2839 (2177,5027)	1950 (1629, 2380)	0.34

Table 1. Summary of median oral estradiol concentrations overall and by HIV status

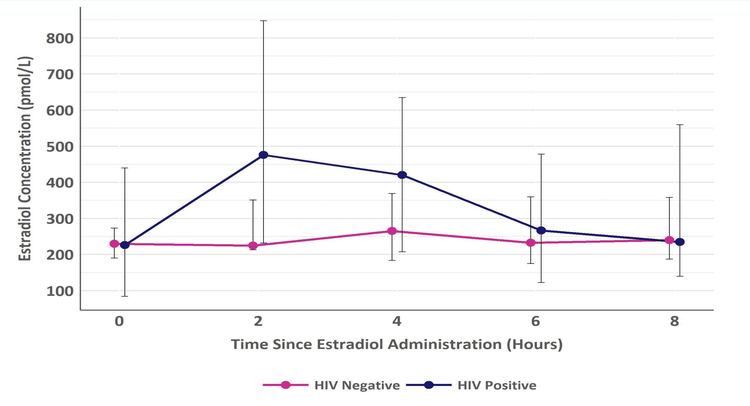


Figure 1. The time dependent estradiol concentrations curves among the full study samples and differentiated by HIV status

Summary of Results

- Participants (n=15) were enrolled March to August 2022 and had a median age of 32 (IQR: 28, 39).
- Among trans women with HIV, the median duration of HIV was 9.5 years (IQR: 5.0, 23.0); 6 were taking bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) and 2 were taking dolutegravir/abacavir/lamivudine (DTG/ABC/3TC).
- Participants had been taking FHT for a median of 4 years (IQR: 2, 8).
- Among all participants (n=15), the median oral estradiol dose was 4 mg (range 2-6 mg). Anti-androgen therapy (some on multiple) included spironolactone (n=8), orchidectomy (n=6), central hypogonadism (n=1), and cyproterone (n=1). Three participants were taking progesterone.
- Eleven (73%) participants had target estradiol concentrations of 200 to 735 pmol/L (54-200 pg/mL) at C4h (75% among women with HIV and 71% among those without HIV).
- Table 1 and Figure 1 summarize oral estradiol concentrations overall and by HIV status.

No statistically significant differences in estradiol concentrations were identified between trans women with HIV on the INSTI-based regimens of BIC/FTC/TAF and DTG/ABC/3TC and trans women without HIV.

Conclusion

- In trans women on FHT, estradiol concentrations were similar between trans women on unboosted INSTI-based ART regimens and trans women without HIV with a slightly higher C_{max} (statistically non-significant) among those with HIV.
- This suggests a low probability of clinically relevant drug-drug interactions between FHT and INSTI-based ART.