The Relationship Between Plasma Oxylipins and INSTI-Associated Weight Gain in Women Living with HIV

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Introduction

- Starting or switching to integrase strand-transfer inhibitors (INSTIs) for HIV is linked to weight gain, especially in women, with unclear mechanisms.
- Omega-6 polyunsaturated fatty acids (PUFAs) are linked to increased adiposity in HIV-negative individuals.
- The purpose of this study was to explore the association between INSTI-related weight gain and plasma oxylipin concentrations in women living with HIV (WLH) using targeted lipidomics.

Methods

- Sixty virologically suppressed WLH (CD4 <200 cells/mL) from the Atlanta Women's Interagency HIV Study (WIHS), on antiretroviral therapy, were categorized by INSTI use and weight change (gain, as ≥5% from baseline, maintenance, as <5% change).
- Plasma was obtained at three time points: 6-12 months before switching to or adding INSTI (baseline), 1-6 months post switch/add, and 1-2 years post switch/add, with corresponding times in the non-INSTI WLH group.
- Targeted lipidomics assessed 40 plasma oxylipins via liquid chromatography-mass spectrometry (LC-MS).
- Group differences analyzed with linear mixed-effect models, controlling for age and tenofovir (TAF) usage at baseline.

Results

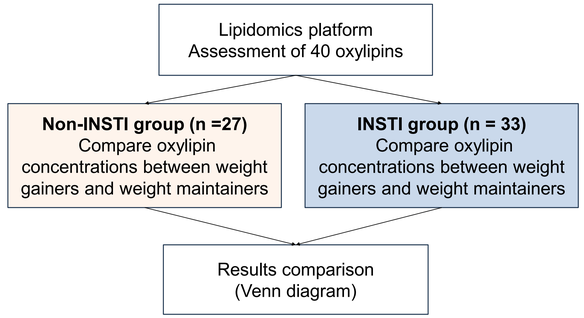

Figure 1. The analytical workflow

Table 1. Baseline demographic and clinical characteristics for WLH in WIHS

	INSTI Group			Non-INSTI Group		
Mean (SD), or n (%)	Weight gainer N= 18	Weight maintainer N= 15	*p*-value	Weight gainer N= 9	Weight maintainer N= 18	*p*-value
Age, years	52.8 (7.2)	47.5 (7.9)	0.0561	45.9 (8.1)	49.8 (9.3)	0.2692
BMI, kg/m²	34.9 (9.5)	36.6 (9.5)	0.6161	40.2 (8.0)	32.5 (8.1)	0.0284
TAF use	4 (22.2)	3 (20.0)	>0.999	6 (66.7)	9 (50.0)	0.6828
Race **NH Black** **NH White** **Hispanic**	17 (94.4) 0 (0.0) 1 (5.6)	14 (93.3) 1 (6.7) 0 (0.0)	0.7102	9 (100.0) 0 (0.0) 0 (0.0)	16 (88.9) 2 (11.1) 0 (0.0)	0.539
<high school education	8 (44.4)	8 (53.3)	0.6109	4 (44.4)	7 (38.9)	>0.999
Annual income < $12,000	12 (66.7)	11 (73.3)	0.7220	6 (66.7)	12 (66.7)	>0.999
CD4, cells/mm³	796.9 (231.4)	802.9 (355.6)	0.9540	829.8 (168.6)	779.7 (327.0)	0.6715

- Baseline demographics and clinical characteristics, except for BMI, were similar between weight gainers and maintainers in both groups.

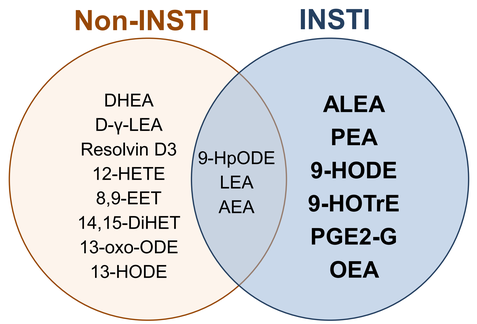

Figure 2. The Venn diagram shows the oxylipins that differ between weight change groups within the INSTI group (blue) and non-INSTI group (brown).

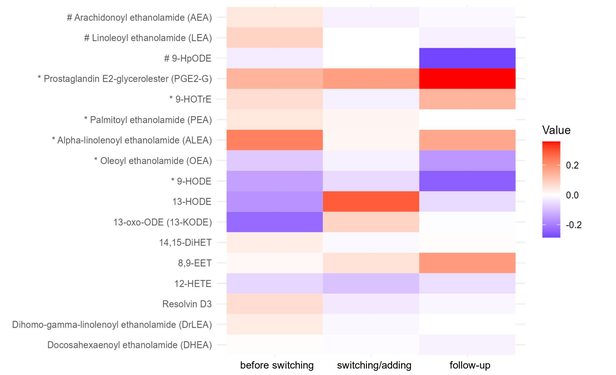

Figure 3: Heatmap displays Estimated Marginal Mean (EMM) differences in oxylipin concentrations in the INSTI group over time. *Significant oxylipins observed uniquely in the INSTI group. #Significant oxylipins in both INSTI group and non-INSTI group.

- Six oxylipins were specifically associated with INSTI-associated weight gain.

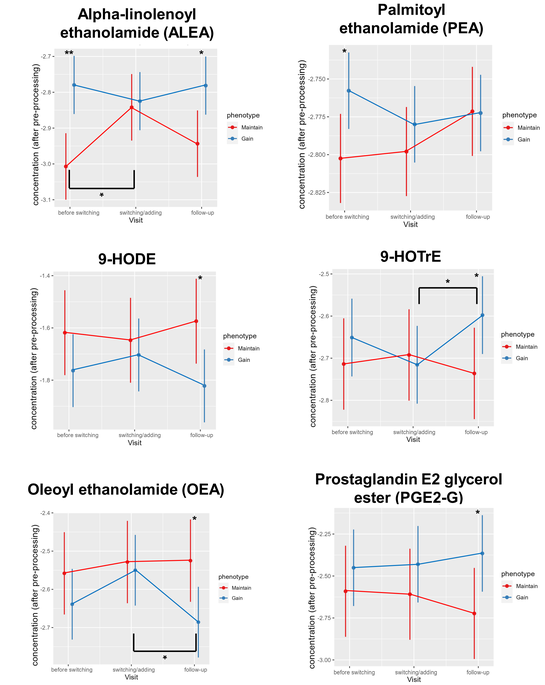

Figure 4. Temporal concentration patterns of six oxylipins which were specifically associated with INSTI-associated weight gain in INSTI group. *p-value < 0.05

- Plasma levels of ALEA, 9-HOTrE, and PGE2-G were higher in weight gainers over time, especially after 1-2 years post-switch, while plasma 9-HODE and OEA levels were lower.
- Initially, PEA levels were higher in weight gainers, but after 1-2 years were similar to weight maintainers.

Summary and Conclusions

- Using targeted lipidomics, we identified six plasma oxylipins linked to INSTI-associated weight gain in WLH, including ALEA and OEA, previously implicated in healthy adult weight gain, and 9-HODE and 9-HOTrE, linked to weight gain in mouse models.
- Further research is needed to identify oxylipin profiles unique to INSTI usage and to determine the potential role of oxylipins in the underlying biological mechanisms for INSTI-associated weight gain.