Poster 673

The Impact of Weight Gain and Sex on Immune Activation Following Initiation of ART

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Background

- Immune activation persists despite suppressive antiretroviral therapy (ART) and may also differ by sex or body composition.
- We hypothesized that weight gain, sex and BMI would be associated with changes in immune activation following ART initiation and explored these relationships in a selected subset of women and men who had initiated ART in two large randomized ACTG trials (A5202 and A5257).

Objectives

- To test if baseline biomarker levels differ by sex, baseline BMI category or whether person later gained weight or had stable weight over time, if these differences vary by levels of the other 2 factors, and whether these differences persist after adjustment by age, or pre-ART CD4 and viral load.
- To test if changes from baseline levels in selected inflammatory markers differ by whether person later gained weight or had stable weight over time, and explore if these differences persist after adjustment for sex, age, pre-ART BMI category, CD4 and viral load.

Methods

- A purposeful sampling design selected participants who achieved virologic suppression on ART and either maintained weight within +/- 0.5 kg/m2 ("maintainers") or gained 2.6-6.4 kg/m2 ("gainers") from baseline to 96 weeks.
- From stored plasma samples, we measured IL-6, sTNF-RI and II, IP-10, hsCRP, sCD14 and sCD163 at weeks 0 and 96.
- Multivariable linear regression explored associations of weight gain (gainers vs maintainers), sex, and pre-ART BMI with outcomes of pre-ART biomarker concentrations and changes from baseline to week 96, adjusting for baseline age, race/ethnicity, ART regimen, CD4 count and HIV-1 RNA.

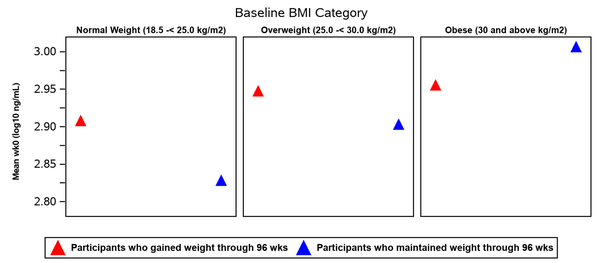
Results

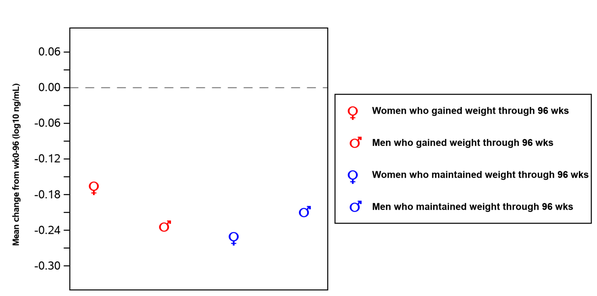
	Women and men who gained weight (2.6-6.4 kg/m²) (n=196)	Women and men who maintained weight (+/- 0.5 kg/m²) (n=144)	P-Value (weight gain)	Women (n=166)			Men (n=174)		
				Gained weight (n=96)	Maintained weight (n=70)	P-Value (weight gain within women)	Gained weight (n=100)	Maintained weight (n=74)	P-value (weight gain within men)
Clinical Trial, n (%)									
A5202	82 (42%)	55 (38%)	NA†	42 (44%)	25 (36%)	NA†	40 (40%)	30 (41%)	NA†
A5257	114 (58%)	89 (62%)		54 (56%)	45 (64%)		60 (60%)	44 (59%)	
ART Regimen, n (%)									
ATVr + NUCs*	74 (38%)	58 (40%)	NA†	34 (35%)	23 (33%)	NA†	40 (40%)	35 (47%)	NA†
DRVr + NUCs*	37 (19%)	29 (20%)		20 (21%)	17 (24%)		17 (17%)	12 (16%)	
EFV + NUCs*	43 (22%)	26 (18%)		26 (27%)	13 (19%)		17 (17%)	13 (18%)	
RAL + NUCs*	42 (21%)	31 (22%)		16 (17%)	17 (24%)		26 (26%)	14 (19%)	
Age (years), median (Q1, Q3)	42 (34, 49)	42 (33, 49)	NA†	43 (35, 49)	42 (34, 49)	NA†	42 (33, 49)	42 (31, 49)	NA†
Race/Ethnicity, n (%)									
White Non-Hispanic	56 (29%)	55 (38%)	0.26	13 (14%)	16 (23%)	0.46	43 (43%)	39 (53%)	0.55
Black Non-Hispanic	89 (45%)	53 (37%)		56 (58%)	35 (50%)		33 (33%)	18 (24%)	
Hispanic	48 (24%)	33 (23%)		26 (27%)	18 (26%)		22 (22%)	15 (20%)	
Other	3 (2%)	3 (2%)		1 (1%)	1 (1%)		2 (2%)	2 (3%)	
Pre-ART BMI (kg/m²), median (Q1, Q3)	25.4 (22.4, 29.5)	25.9 (22.4, 29.0)	0.70	27.1 (23.3, 32.8)	27.7 (23.6, 32.3)	0.69	24.1 (21.7, 27.6)	24.2 (22.4, 27.1)	0.74
Pre-ART CD4 (cells/mm³), median (Q1, Q3)	195 (47, 337)	344 (232, 460)	<.01	219 (56, 363)	328 (231, 441)	<.01	174 (45, 299)	361 (242, 465)	<.01

† Clinical trial, ART regimen, and Age used in sampling design to enforce balance by these factors; therefore, no hypothesis testing performed.
*NUCS included TDF/FTC, or ABC/3TC (only with EFV or ATV/r)

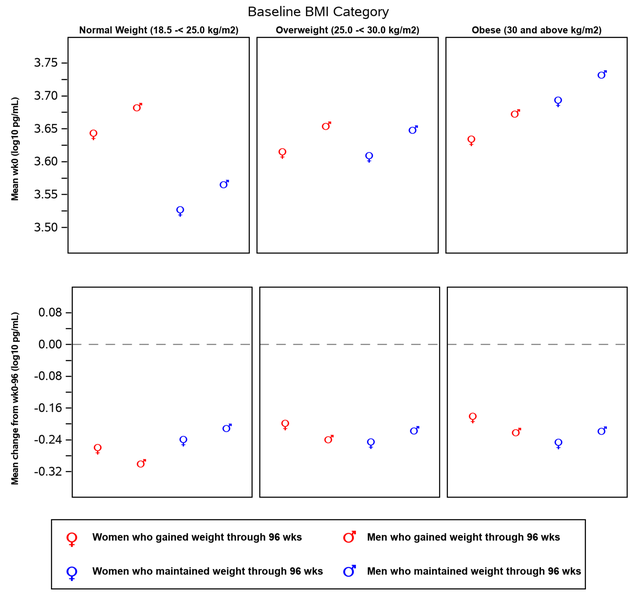
Results

sCD163 Model-Based Estimates by Various Factors





STNF-RII Model-Based Estimates by Various Factors



Results

- While pre-ART BMI was similar between gainers and maintainers (overall and within sex), gainers had significantly lower pre-ART CD4 vs maintainers.
- In adjusted models among those with normal pre-ART BMI, pre-ART IL-6, sTNF-RII, IP-10, and sCD163 were higher for gainers versus maintainers.
- Association of weight gain on week 96 changes of these 4 biomarkers differed by sex; women who gained weight had smaller declines in biomarkers compared to men who gained.
- For sTNF-RII and IL-6, the association between weight gain and changes in these biomarkers also varied by pre-ART BMI.

- NOTE: Similar changes were noted for the other biomarkers

	Pre-ART concentrations Adjusted differences (95% CI)	Women (n=166)		Men (n=174)		Sex by weight gain interaction p-values
		Gained weight (n=96)	Maintained weight (n=70)	Gained weight (n=100)	Maintained weight (n=74)	
		Changes from baseline by sex [model based means]				
IL-6 (log_{10} pg/mL)	0.26 (0.17, 0.35)	-0.11 normal 0.02 overwt 0.08 obese	-0.16 -0.03 0.03	-0.25 -0.13 -0.07	-0.12 0.01 0.07	.004[β]
sCD163 (log_{10} ng/mL)	0.08 (0.02, 0.14)	-0.17	-0.25	-0.23	-0.21	<.001
sTNF-RII (log_{10} pg/mL)	0.12 (0.07, 0.16)	-0.26 normal -0.20 overwt -0.18 obese	-0.24 -0.25 -0.25	-0.30 -0.24 -0.22	-0.21 -0.22 -0.22	.021
IP-10 (log_{10} pg/mL)	0.19 (0.11, 0.27)	-0.47	-0.50	-0.53	-0.41	.004

*Pre-ART concentrations for subgroup of participants with normal pre-ART BMI

Conclusions

- Among non-obese persons, higher pre-treatment immune activation markers are significantly associated with weight gain following ART initiation, even after controlling for pre-ART CD4 cell count.
- Weight gain attenuates the decline in several immune activation markers following ART initiation among women; thus, women may be at increased risk for complications of weight gain.
- Identifying individuals at risk of weight gain may allow for targeted investigation of preventive interventions.

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