HIV-INFECTED, ART-SUPPRESSED PLWH RECEIVING NALTREXONE HAVE LOWER IMMUNE ACTIVATION COMPARED TO SIMILAR PATIENTS RECEIVING METHADONE.

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BACKGROUND

Opioid use results in systemic immune activation (partly through increased microbial translocation) and may accelerate the progression of untreated HIV infection. Medication-assisted treatment of opioid use disorder (MOUD) is based on μ opioid receptor (MOR) agonists (e.g.: methadone - MET or buprenorphine) or antagonists (e.g: extended-release Naltrexone - NTX). The effect of MOUDs on microbial translocation, immune reconstitution and HIV persistence in PLWH receiving suppressive antiretroviral treatment (ART) remains unclear.

STUDY GROUPS

Group	Treatment	Sex	AA	C/W	Other	Tot
MET	Methadone	F	1	4		13
		M	3	4	**1**	
NTX	XR-Naltrexone	F	2	1		14
		M	6	3	2	
Ctrl	Non-OUD	F		4		12
		M	5	2	1	

DEMOGRAPHICS AND CLINICAL CHARACTERISTICS

Variable	Group	Mean	S.D.	Min	Max
Age	MET	49.85	11.92	25	62
	NTX	48.17	10.21	24	60
	CTRL	46.14	9.429	26	60
OST (Months)	MET	39.37	21.35	10.75	69
	NTX	18.88	9.656	8	37.3
	CTRL	n/a	n/a	n/a	n/a
ART (Years)	MET	12.52	9.359	0.75	29
	NTX	9.583	5.9	2	23
	CTRL	9.964	5.58	2	19
Nadir CD4	MET	186.2	151.2	7	588
	NTX	257.2	166.3	24	651
	CTRL	221.5	209.3	10	713
Current CD4	MET	605.8	430.1	132	1629
	NTX	550.8	278.6	252	1309
	CTRL	608	280.8	158	1240

METHODS

Study groups (all receiving suppressive ART (VL < 50 copies/ml):

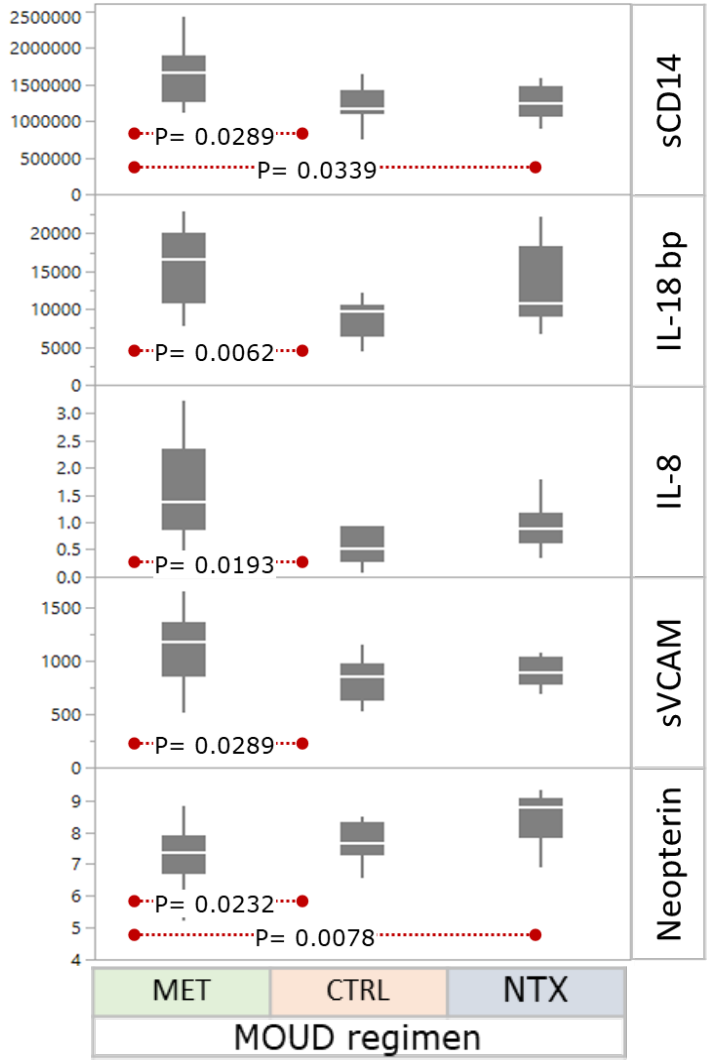
1. individuals with OUD receiving MET-based MAT (group 1, N= 10);
2. NTX-based MAT (group B, N=6)
3. non-OUD individuals (no MAT; group C, N=10).

All subjects were recruited at the Jonathan Lax Clinic/Philadelphia FIGHT (Philadelphia, PA) under the supervision of the Philadelphia FIGHT and Wistar Institute IRBs.

Assessments:

- Plasma levels of sCD14 (an indicator of myeloid activation and microbial translocation) and other markers of inflammation, immune activation and enteric mucosa integrity using ELISA, Luminex and digital ELISA (SIMOA)
- CD4+ and CD8+ T-cell and myeloid activation using multicolor flow cytometry on fresh blood specimens
- Cell associated HIV DNA and RNA using ddPCR

Analysis: differences between groups were assessed performing ANOVA (Dunn post run tests) and linear models using JASP



Differential expression of immune activation and inflammation markers

VARIABLE	KW ANOVA	CTR vs MET [1]	NTX vs MET [1]	NTX vs CTR [1]
Neopterin	**0.0114**	0.2815	**0.0078**	**0.0232**
IL-18bp	**0.0182**	**0.0062**	0.2633	0.1485
sCD14 *(Luminex)*	**0.0248**	0.0694	**0.0228**	0.1266
IL-8	**0.0297**	**0.0193**	0.0895	0.2153
sCD14 *(ELISA QC)*	**0.0344**	**0.0289**	**0.0339**	0.9014
sVCAM1	**0.0479**	**0.0289**	0.0972	0.3423
sTNFR-II	0.0513	**0.0247**	0.0826	0.7102
CD169 MFI *(on CD169⁺ monocytes)*	0.0765	0.3416	**0.0446**	0.0786
% CD69⁺ CD25⁻ of CD4⁺	0.0923	0.3418	0.2548	**0.0307**
sICAM1	0.0983	0.0694	0.0826	0.9014

*P values are reported for all tests; **α = 0.05**; p values are not adjusted for multiple comparison.*

[1] Post-run comparisons were performed using the Wilcoxon rank sum test.

Independent associations with sCD14

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	470679	151135.6	3.11	0.0047
sTNFR-II	106.0066	21.68247	4.89	**<.0001**
CD69⁺ CD25⁺ of CD4⁺	126284.9	33937.22	3.72	**0.0011**

Summary of Fit: R^2 = 0.6562; adj. R^2= 0.6276; n=27

OBSERVATIONS. PLWH receiving ART + methadone have higher expression of chronic inflammation and immune activation markers than PLWH receiving either ART + naltrexone or ART alone

CONCLUSIONS. Treatment with MOR agonists may reduce the benefits of ART by sustaining immune activation. This hypothesis will be tested in the AMOHI study.

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