VIH: Inflamación, el enemigo invisible

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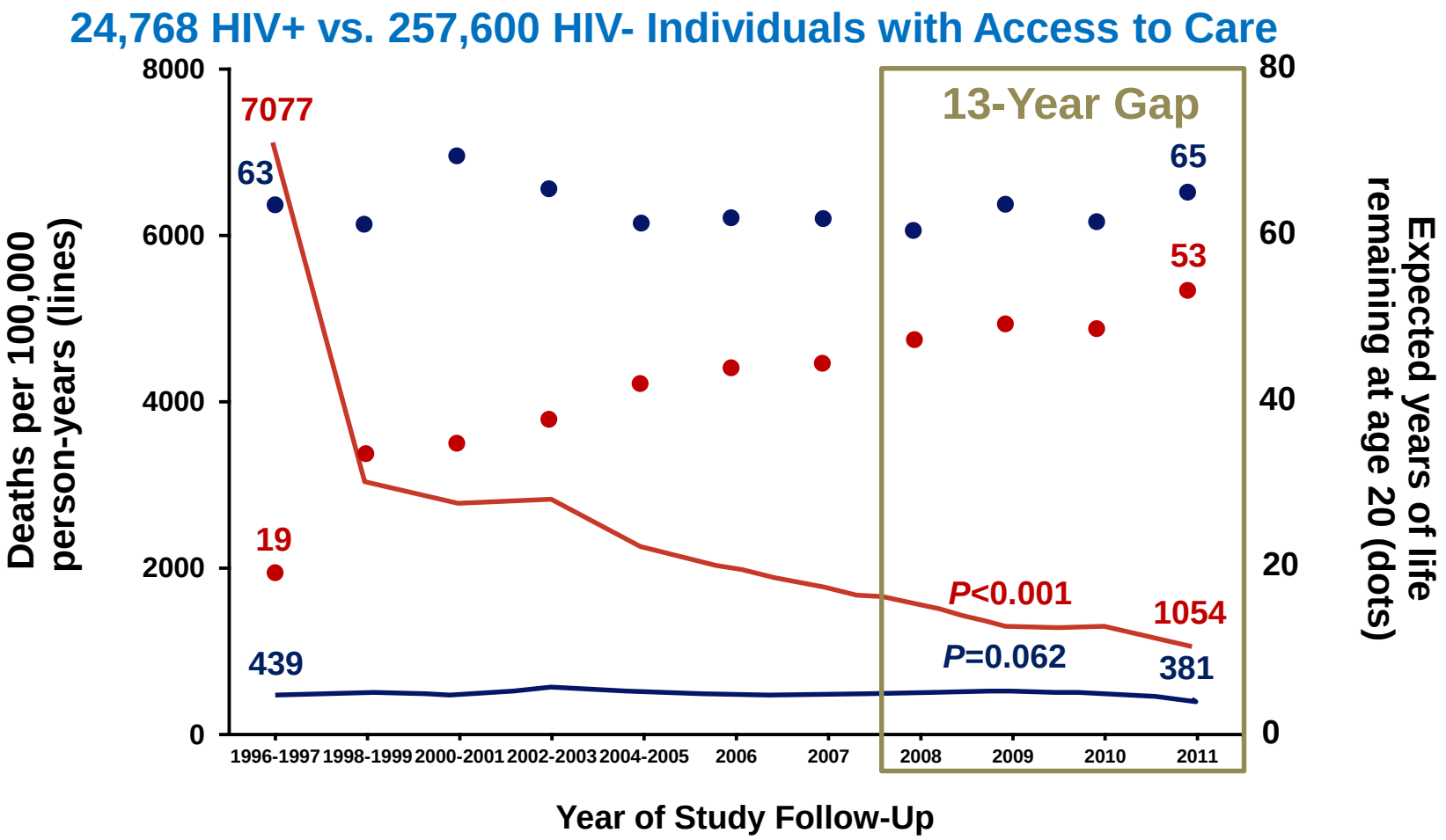
Kaiser Permanente HIV Cohort: Narrowing the Gap in Life Expectancy

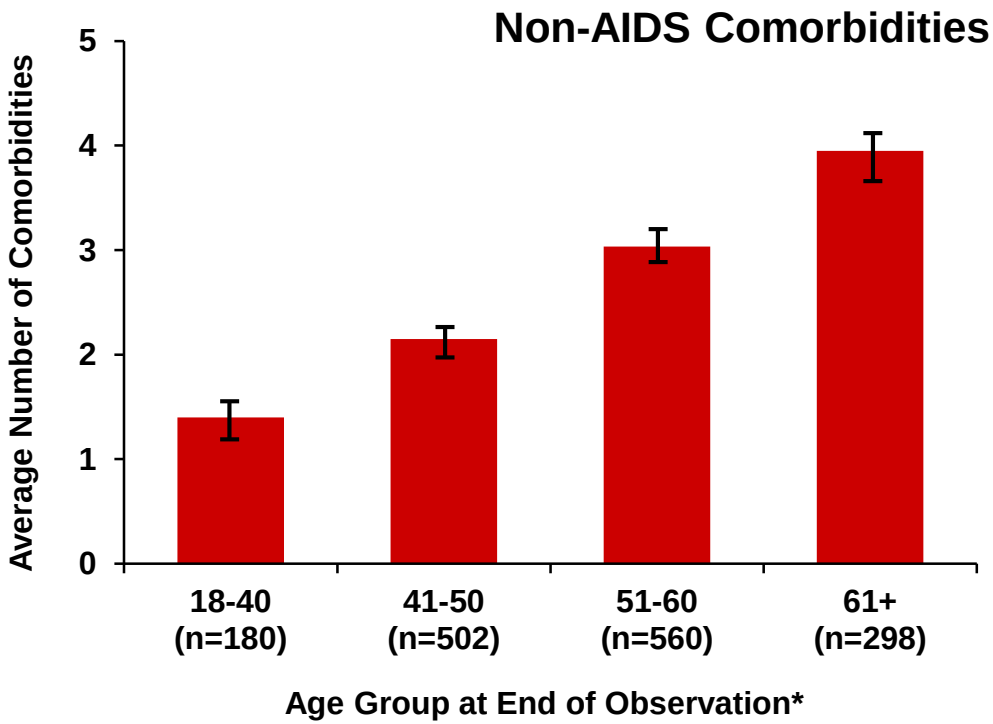


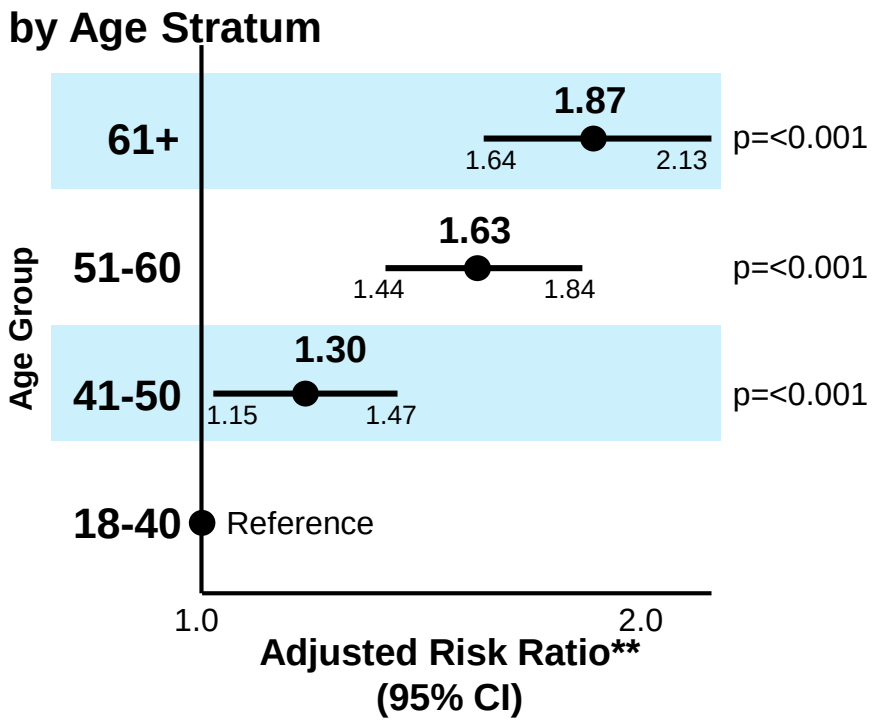
8-year gap with ART initiation at CD4 ≥ 500. Life expectancy ↓ Blacks, IVDU, Hispanics
Gap narrowed if no hepatitis B or C, drug/alcohol abuse, or smoking

Marcus J, et al. JAIDS 2016:1:39-46.

Non-AIDS Illness Burden in Aging HIV+ Adults (HOPS Cohort)

1. **Non-AIDS chronic co-morbidities among 1,540 aging HIV+ adults**
2. **On ARV (≥75% observation time with VL <200 copies/mL)**
3. **Seen for a minimum of 5 years at 8 US HIV clinics (1997–2015)**





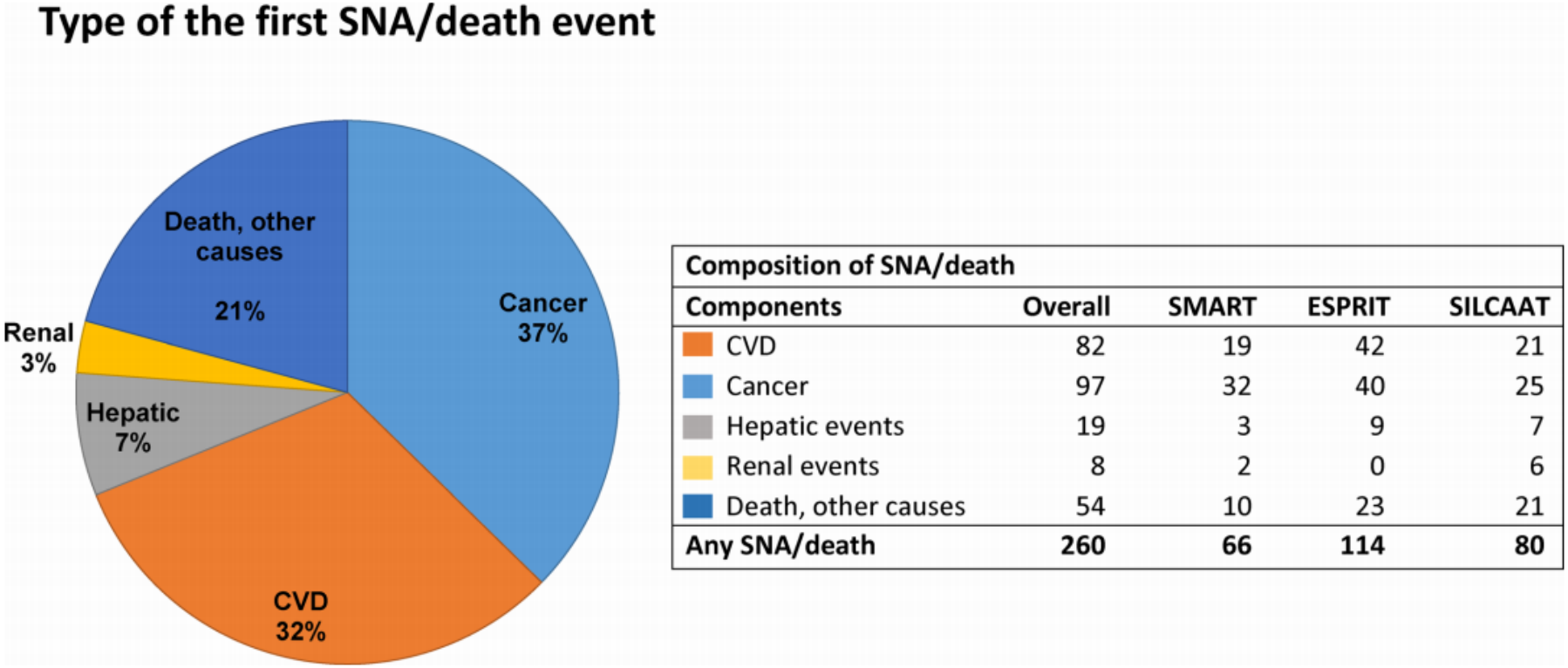
Age-related increases in prevalence of multiple chronic co-morbidities and observed as early as 4th decade

* Bars represent 95% confidence intervals for the average number of comorbidities; p-value for trend across all groups <0.001

** Included CVD, cancer, HTN, **DM**, dyslipidemia, degenerative joint disease/fracture, chronic HBV or **HCV** infection, CKD, **anemia**, and psychiatric illness

Serious Non-AIDS Conditions are the Primary Cause of Severe Morbidity and Mortality in HIV-Infected People on Effective ART

3766 SMART/ESPRIT/SILCAAT participants on ARV therapy with HIV RNA levels ≤ 500 copies/mL followed by 5 year

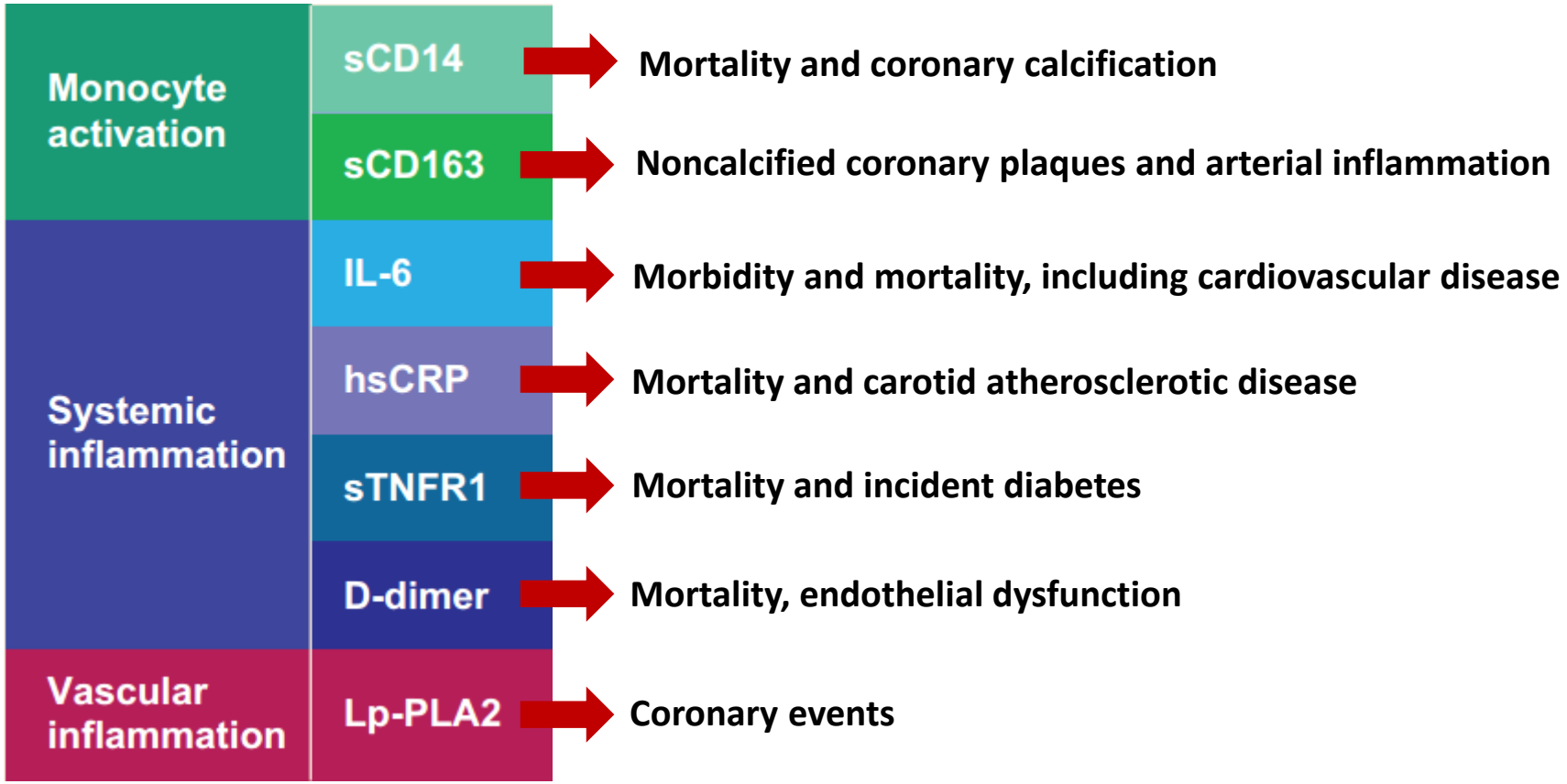


Composition of SNA/death				
Components	**Overall**	**SMART**	**ESPRIT**	**SILCAAT**
CVD	82	19	42	21
Cancer	97	32	40	25
Hepatic events	19	3	9	7
Renal events	8	2	0	6
Death, other causes	54	10	23	21
Any SNA/death	**260**	**66**	**114**	**80**

Grund B et al. PLOSone 2016;11:e0155100.

Plasma Markers of Innate Immune Activation and Inflammation

Stronger predictors of non-AIDS-defining morbidity and mortality than cellular markers of T-call activation



Lp-PLAA2: Lipoprotein-associated phospholipase A2

McComsey G et al. 23rd CROI; Boston, MA; February 22-25, 2016. Abst. 717.

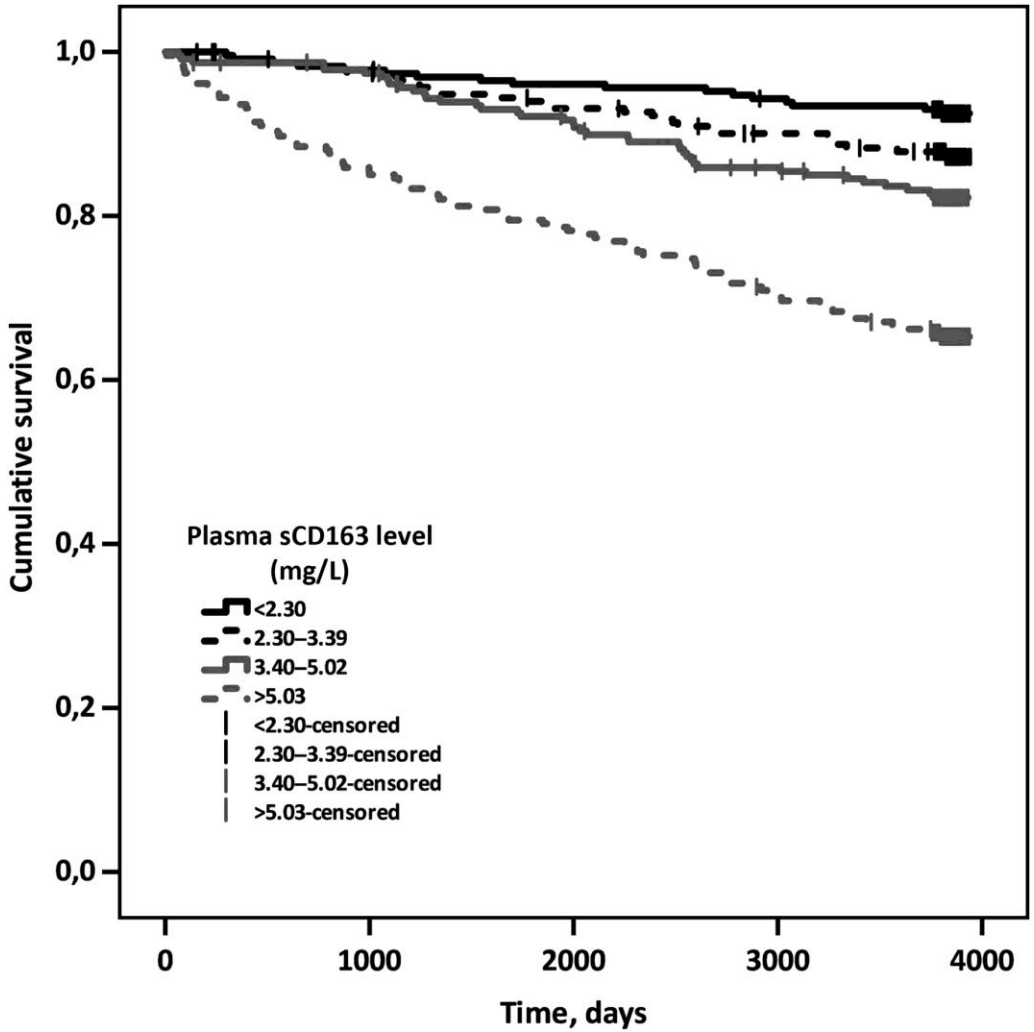
Increased Mortality in HIV–Infected Subjects with High Baseline sCD14 Levels (SMART)

Biomarker	<25th Percentile(Reference)	25th – 49th Percentile OR (95% CI)	*P*	50th – 74th Percentile OR (95% CI)	*P*	≥74th Percentile OR (95% CI)	*P*
sCD14 ($\times 10^6$ pg/mL)							
N (case patients/control subjects)	10/46	16/39		21/35		27/28	
Univariate	1.0	2.1 (0.8–5.7)	.12	3.3 (1.3– 8.6)	.01	6.0 (2.2–16.1)	<.001
Adjusted—risk factors[a]	1.0	2.8 (0.8–10.0)	.10	2.7 (.8–9.0)	.11	8.0 (2.0–31.9)	.003
Adjusted—inflammation[b]	1.0	2.3 (0.7–8.1)	.18	2.9 (.9–9.4)	.07	4.1 (1.2–13.9)	.02
LPS, pg/mL							
N (case patients/control subjects)	0	20/35		22/34		15/40	
Univariate	1.0	1.5 (0.6–3.5)	.39	1.6 (.7–3.7)	.25	0.9 (0.4–1.9)	.76
Adjusted—risk factors[a]	1.0	1.1 (0.4–3.1)	.82	1.3 (.5–3.5)	.63	0.4 (0.2–1.2)	.11
Adjusted—inflammation[b]	1.0	1.5 (0.5–4.7)	.45	1.4 (.5–4.4)	.55	1.2 (0.4–3.2)	.78
I-FABP, pg/mL							
N (case patients/control subjects)	23/59	9/20		19/36		23/32	
Univariate	1.0	1.1 (0.5–2.7)	.79	1.4 (.6–2.9)	.42	1.8 (0.9–3.7)	.10
Adjusted—risk factors[a]	1.0	1.2 (0.4–3.6)	.80	2.2 (.8–5.9)	.12	1.8 (0.7–4.4)	.20
Adjusted—inflammation[b]	1.0	1.5 (0.5–4.5)	.44	1.7 (.6–4.7)	.29	1.5 (0.6–3.9)	.38

Sandler N et al. JID 2011; 203: 780–790.

Plasma sCD163 Independently Predicts All-Cause Mortality in HIV–Infected Individuals

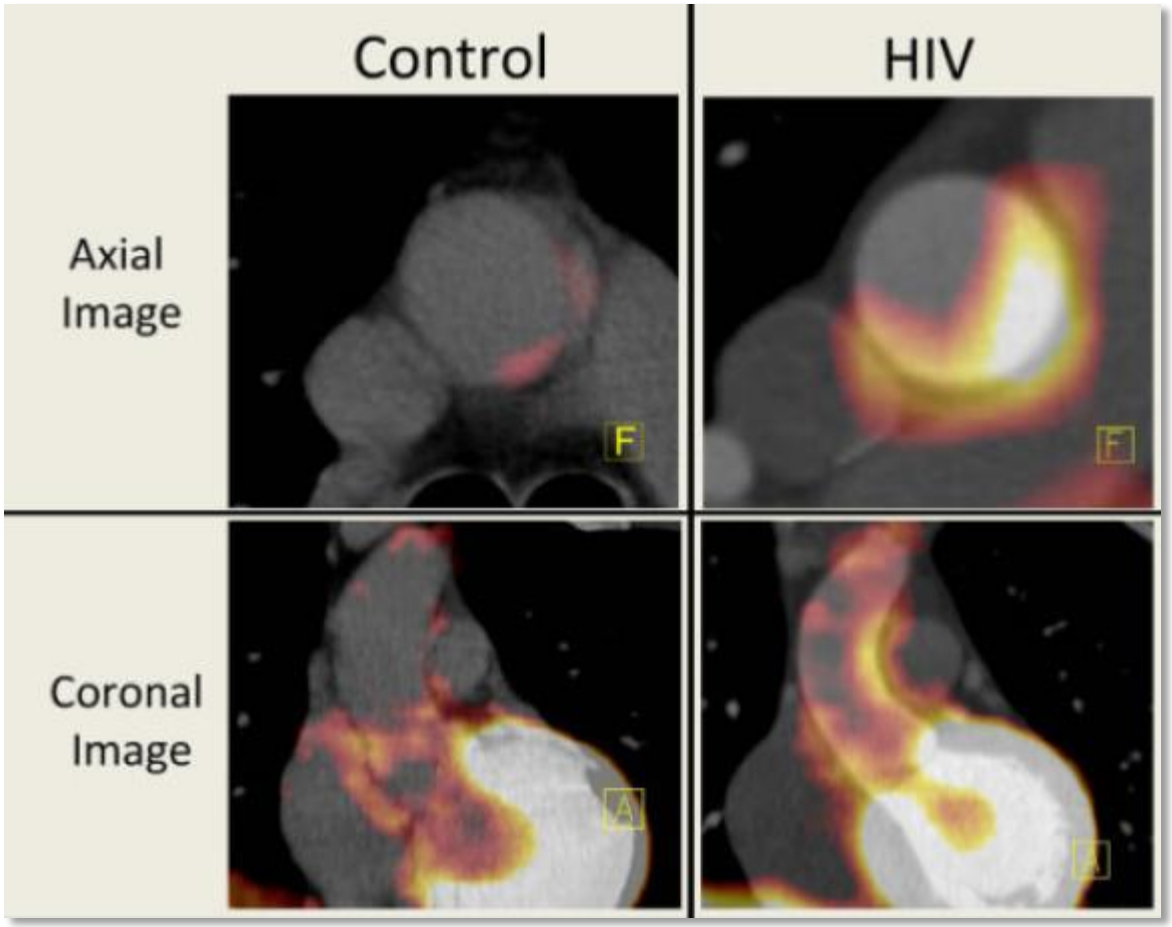
933 HIV–Infected Individuals on ART



Knudsen TB et al. J Infect Dis. 2016;214:1198-1204

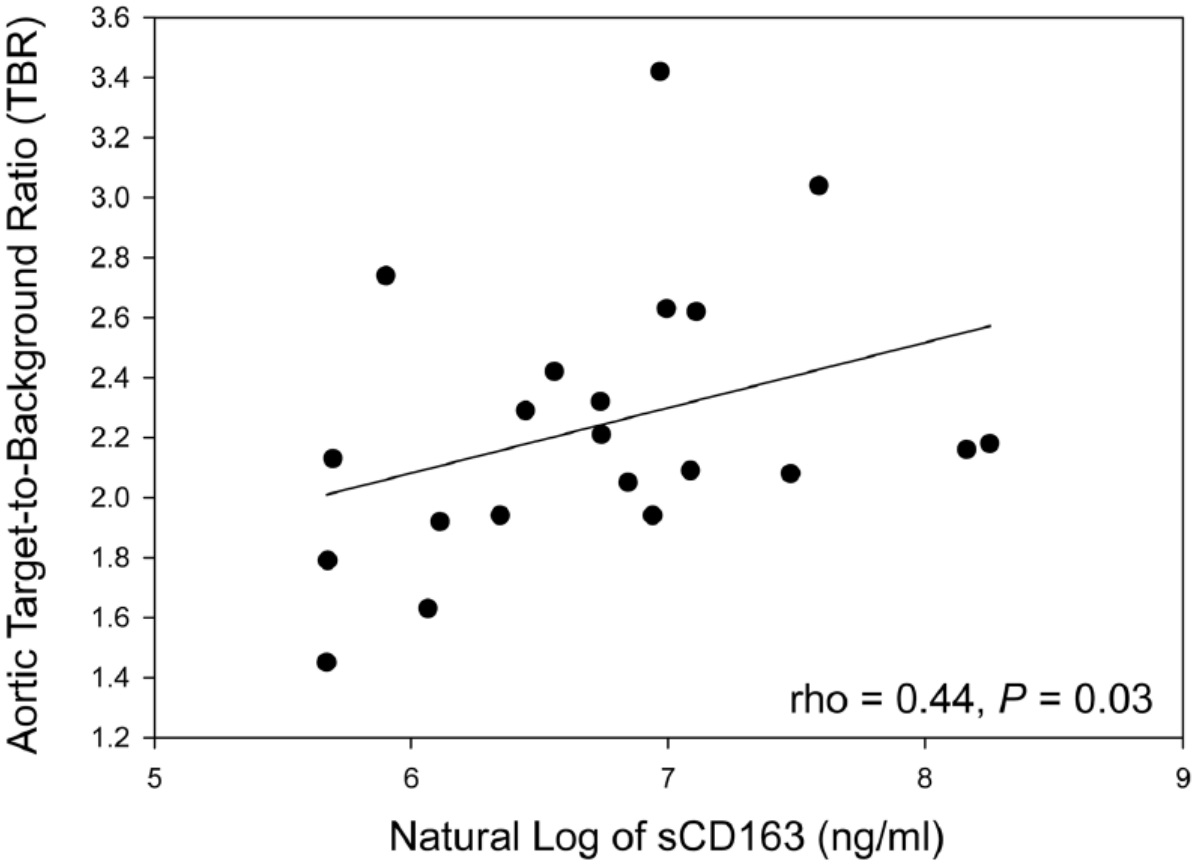
Axial and Coronal Images of the Aorta on FDG-PET

Increased aortic PET-FDG uptake (red coloration) in an HIV-infected subject (42 years old) compared with a non-HIV FRS-matched control subject (43 years old)



Subramanian S et al. JAMA. 2012;308:379–386.

Linear regression of Aortic Target-to-Background Ratio versus the natural log of sCD163 among HIV-infected patients with undetectable Viral Load (n=21)



Subramanian S et al. JAMA. 2012;308:379–386.

Circulating CD16+ Monocytes Associated with Greater Likelihood of 2-Year CAC Progression

	Multivariate Model (n=436)		Restrict Cohort to Suppressed VL (n=314)		Restrict Outcome to CAC increase (n=436)		Restrict Outcome to CAC Incidence (n=436)	
Monocytes (%)	**OR***	**(95% CI)**	**OR***	**(95% CI)**	**OR***	**(95% CI)**	**OR***	**(95% CI)**
CD14+/CD16−	0.64	(0.32, 1.25)	0.65	(0.32, 1.31)	0.04	(0.00, 0.79)	1.53	(0.31, 7.42)
CD14+/CD16+	1.66	(1.09, 2.55)	2.02	(1.21, 3.38)	2.87	(1.21, 6.77)	1.13	(0.67, 1.89)
$CD14^{dim}$/CD16+	1.36	(0.98, 1.88)	1.48	(1.01, 2.17)	1.81	(1.01, 3.25)	1.10	(0.73, 1.67)
$CD14^{var}$/CD16+	1.69	(1.13, 2.55)	1.96	(1.21, 3.18)	3.13	(1.35, 7.28)	1.16	(0.71, 1.89)
T-cells (%)								
CD4+/HLADR+/CD38+	1.17	(0.87, 1.58)	1.10	(0.78, 1.55)	1.16	(0.58, 2.31)	1.10	(0.74, 1.63)
CD4+/CD57+/CD38+	1.09	(0.83, 1.41)	1.26	(0.93, 1.70)	1.60	(0.98, 2.60)	0.83	(0.58, 1.19)
CD4+/CD57+	1.03	(0.80, 1.31)	1.02	(0.76, 1.35)	1.43	(0.93, 2.21)	0.84	(0.61, 1.14)

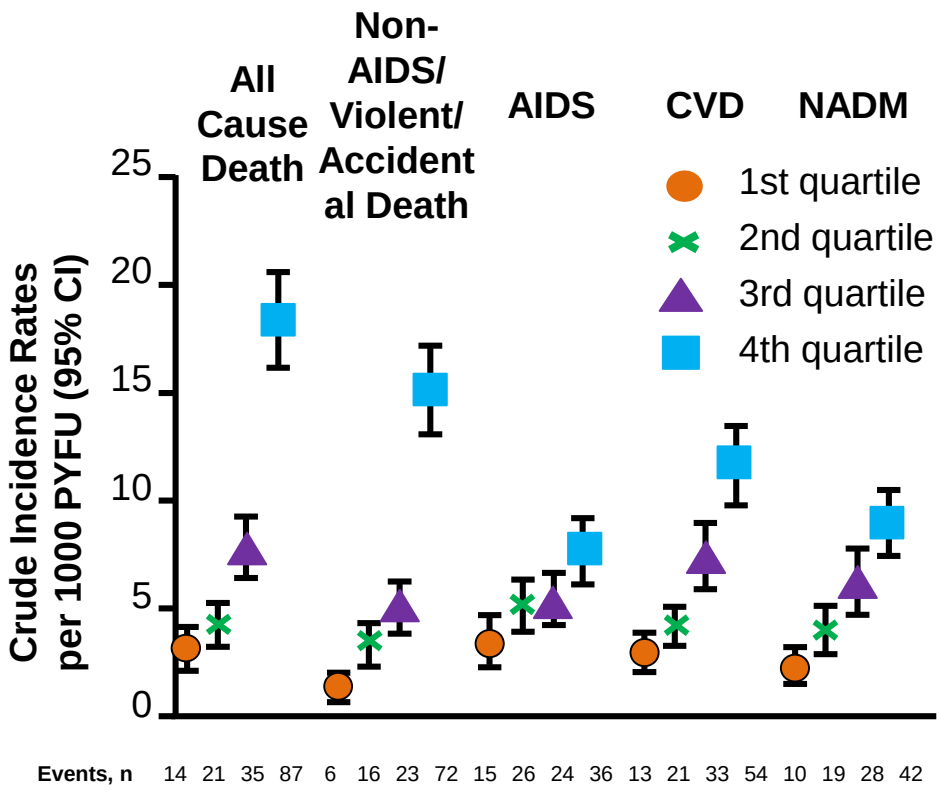
CD14 and CD16 phenotypes:
classical (CD14+/CD16−)
intermediate (CD14+/CD16+)
nonclassical (CD14dim/CD16+)

Baker J et al. AIDS 2014;28:831–840.

Plasma IL-6 Levels Correlated With Incidence of Mortality

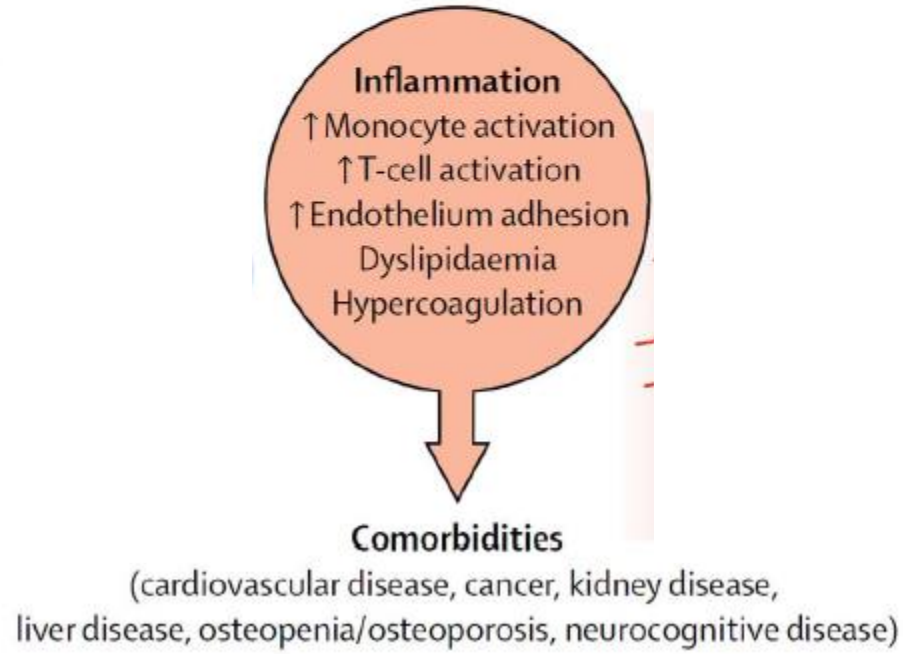
- SMART and ESPRIT trials (control arms)
- 19,000 person-yrs of follow-up among 4304 patients (median age: 42 yrs; median CD4+ cell count: 526; 77% men)
  - –157 all-cause deaths
  - –117 non-AIDS deaths
  - –101 AIDS
  - –121 CVD
  - –99 NADM (non-AIDS defining Malignancies)
- **Baseline plasma IL-6 was a stronger predictor of all cause mortality and many fatal non-AIDS events than D-dimer and hsCRP**

Crude Incidence of Clinical Outcomes by Plasma IL-6



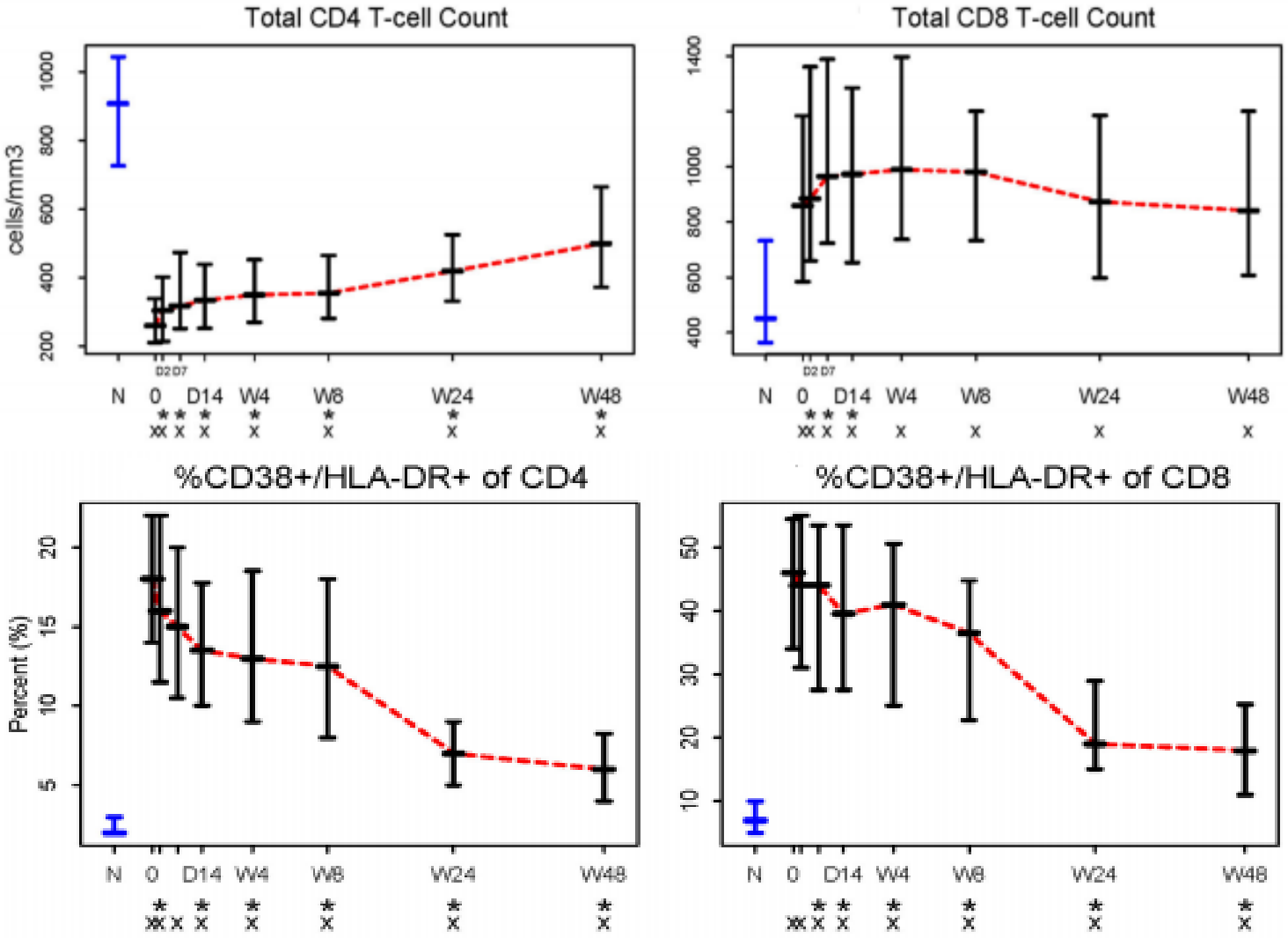
Borges A, et al. CROI 2015. Abstract 761. Borges et al. JID 2016;214:408-416.

Causes of Immune Activation/Chronic inflammation in HIV-Infection



Deeks S et al. Lancet 2013;382:1525.

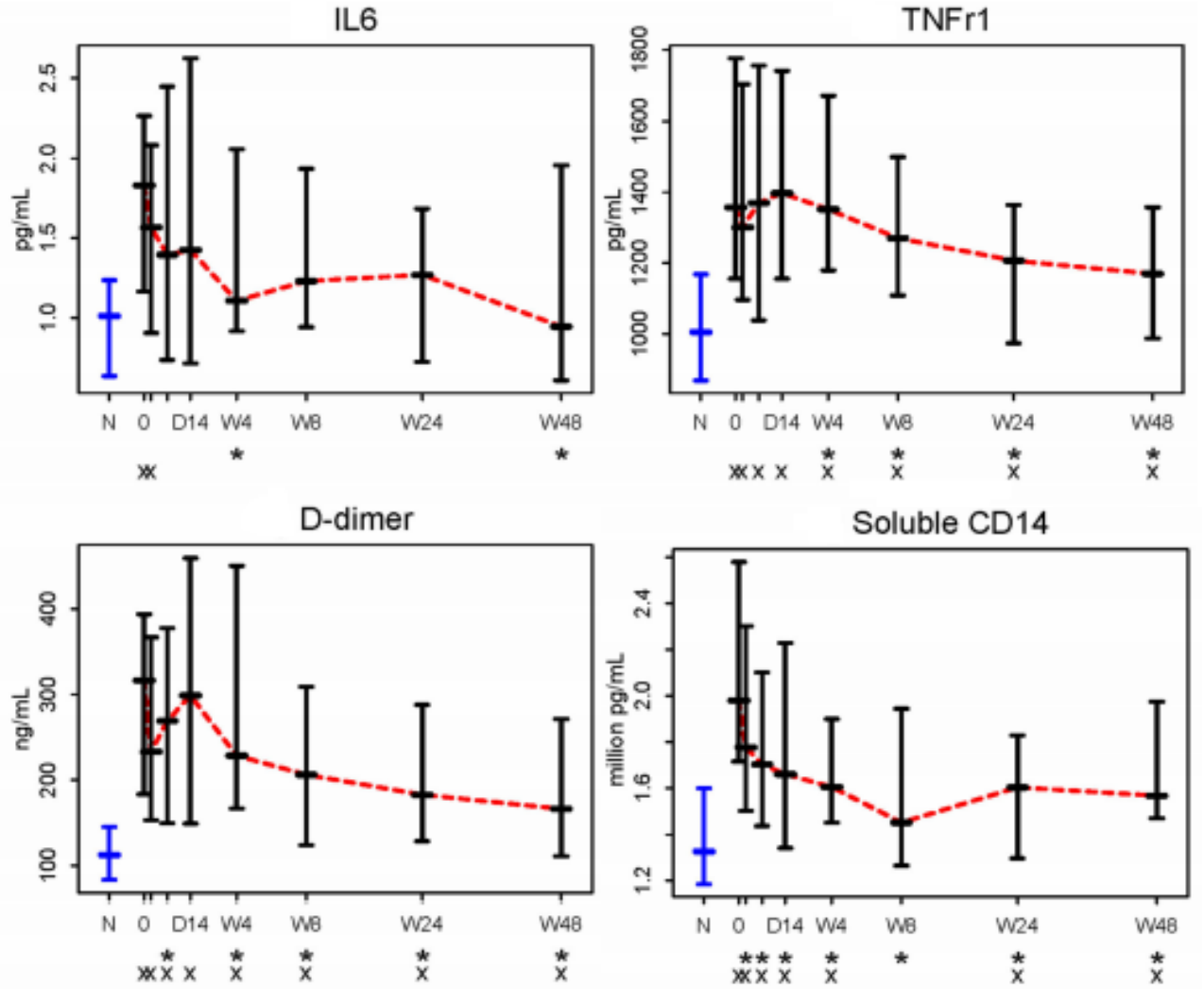
Immune Reconstitution and Activation Markers in 39 Treatment-Naïve HIV-Infected Patients Treated with RAL/TDF/FTC



Funderburg NT et al. PLoS ONE 2013;8:e83514.

A5248

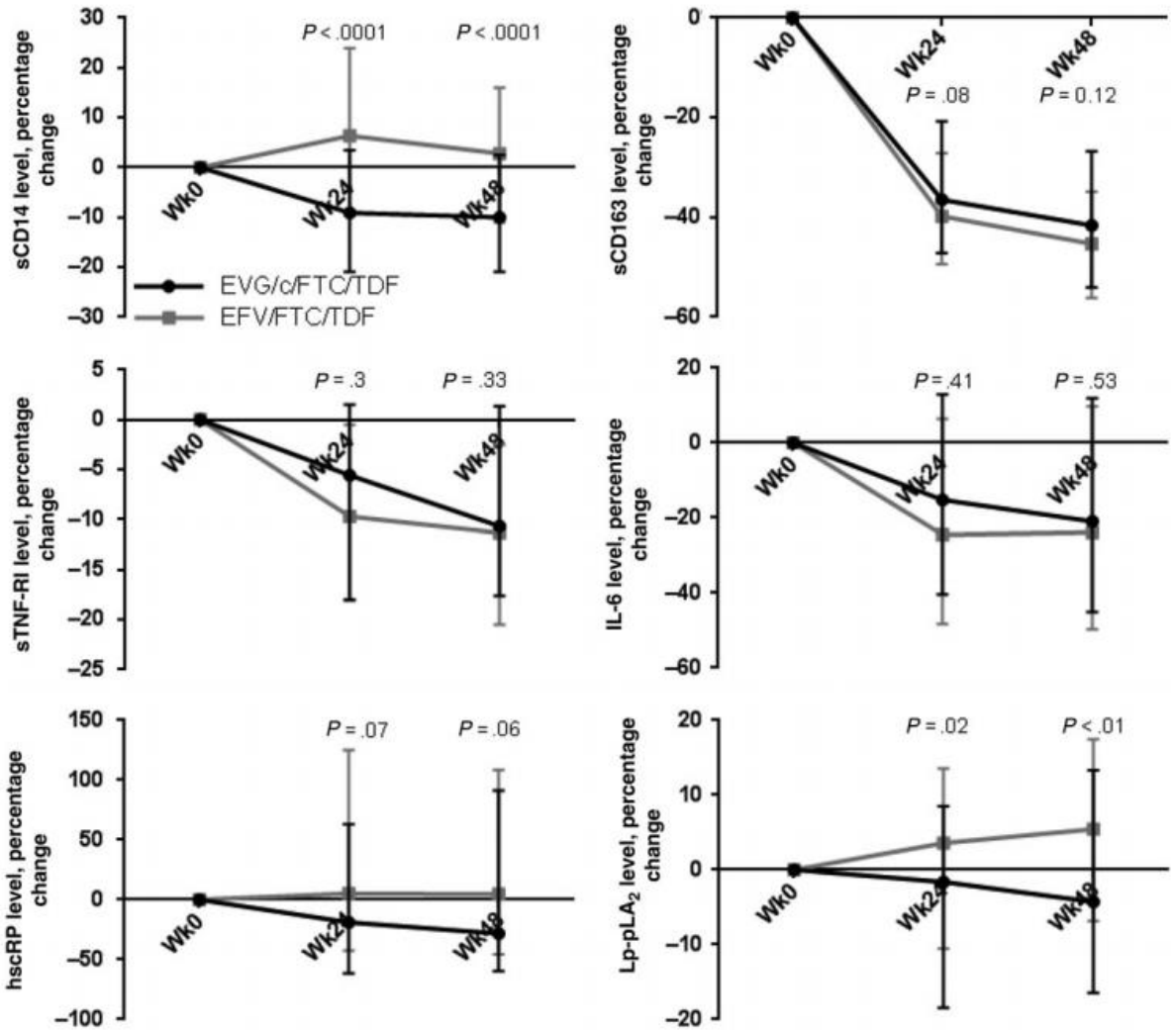
Immune Reconstitution and Activation Markers in HIV+ Treatment-Naïve Patients Treated with RAL/TDF/FTC



Funderburg NT et al. PLoS ONE 8:e83514.

A5248

Greater Decreases in sCD14, hsCRP, and Lp-PLA2 with EVG/c/FTC/TDF than EFV/FTC/TDF

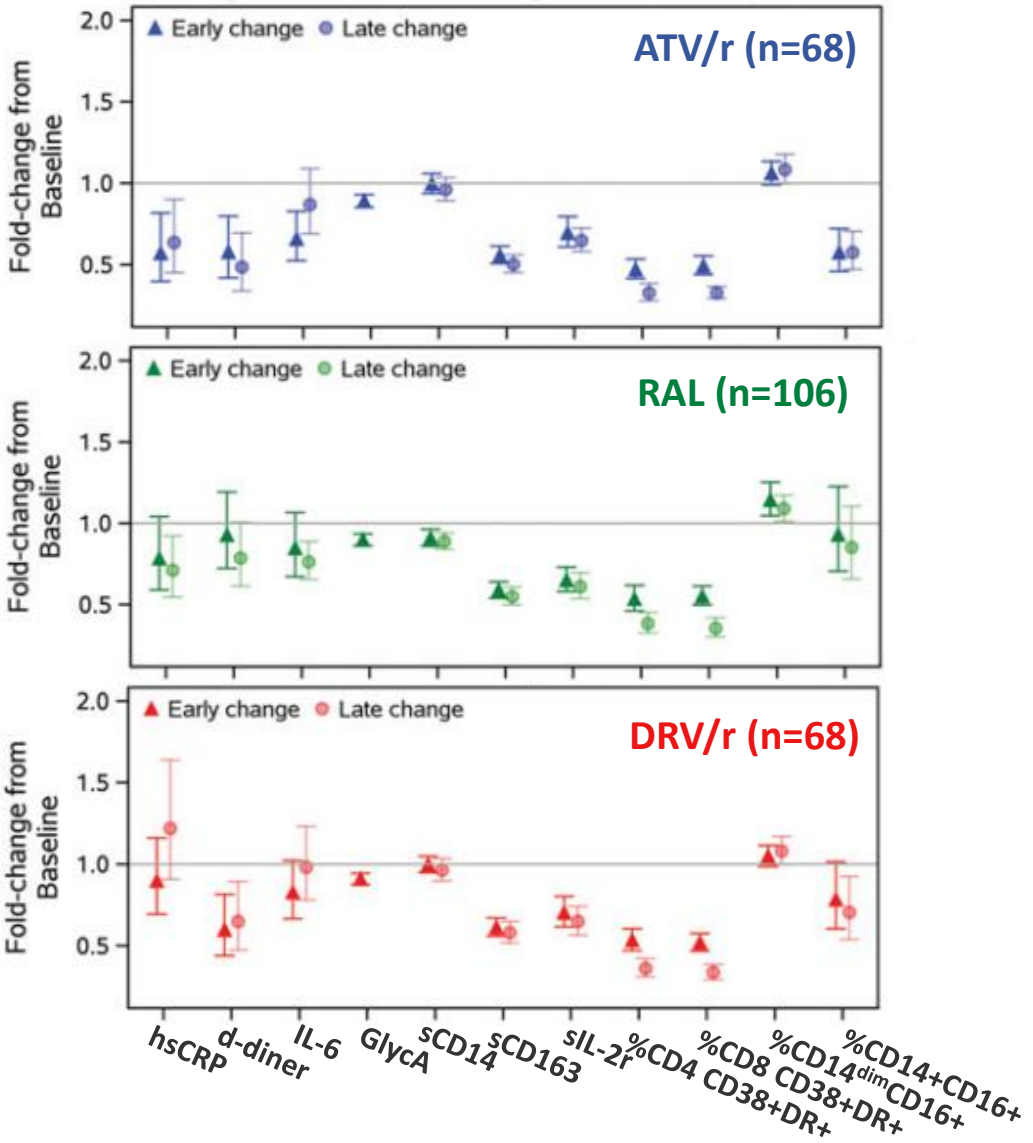


Hileman CO et al. J Infect Dis 2015;212:345-54.

No Consistent Pattern in Reduction of IA and Inflammation Between RAL and bPI Regimens

A5260s

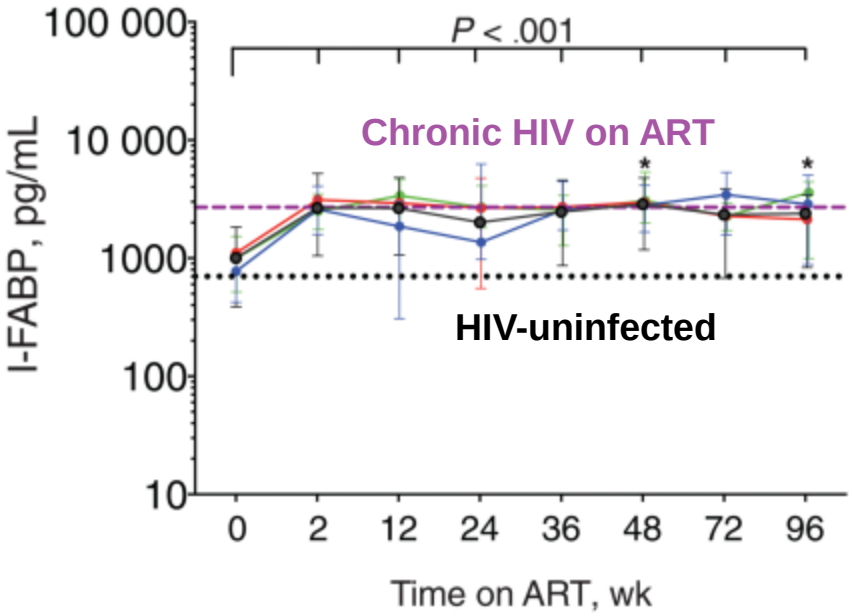
Early Change: from BSL to W24 or W48
Late Change: from BSL to W96



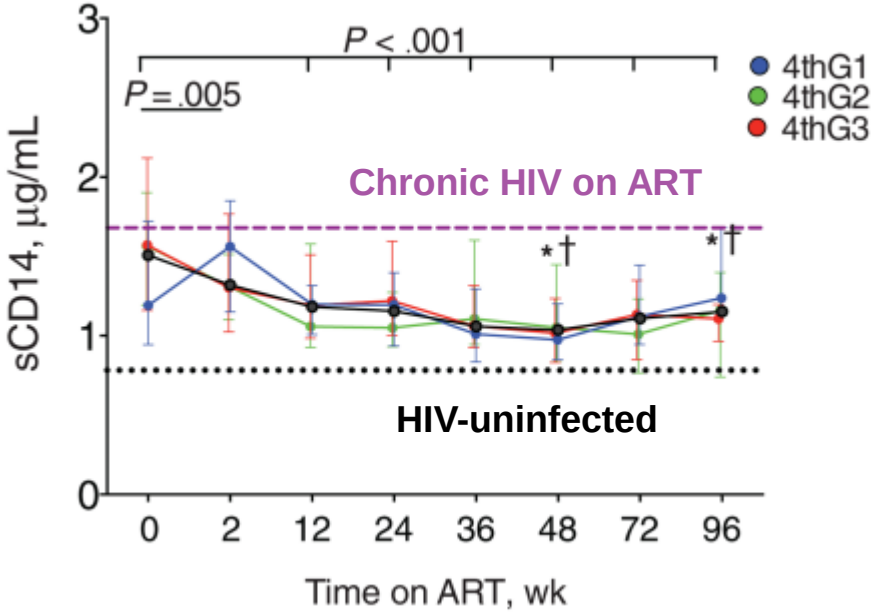
Kelesidis T et al. CID 2015;61:651-60.

Inflammation Persists Despite Early Initiation of ART in Acute HIV Infection

Enterocyte turnover

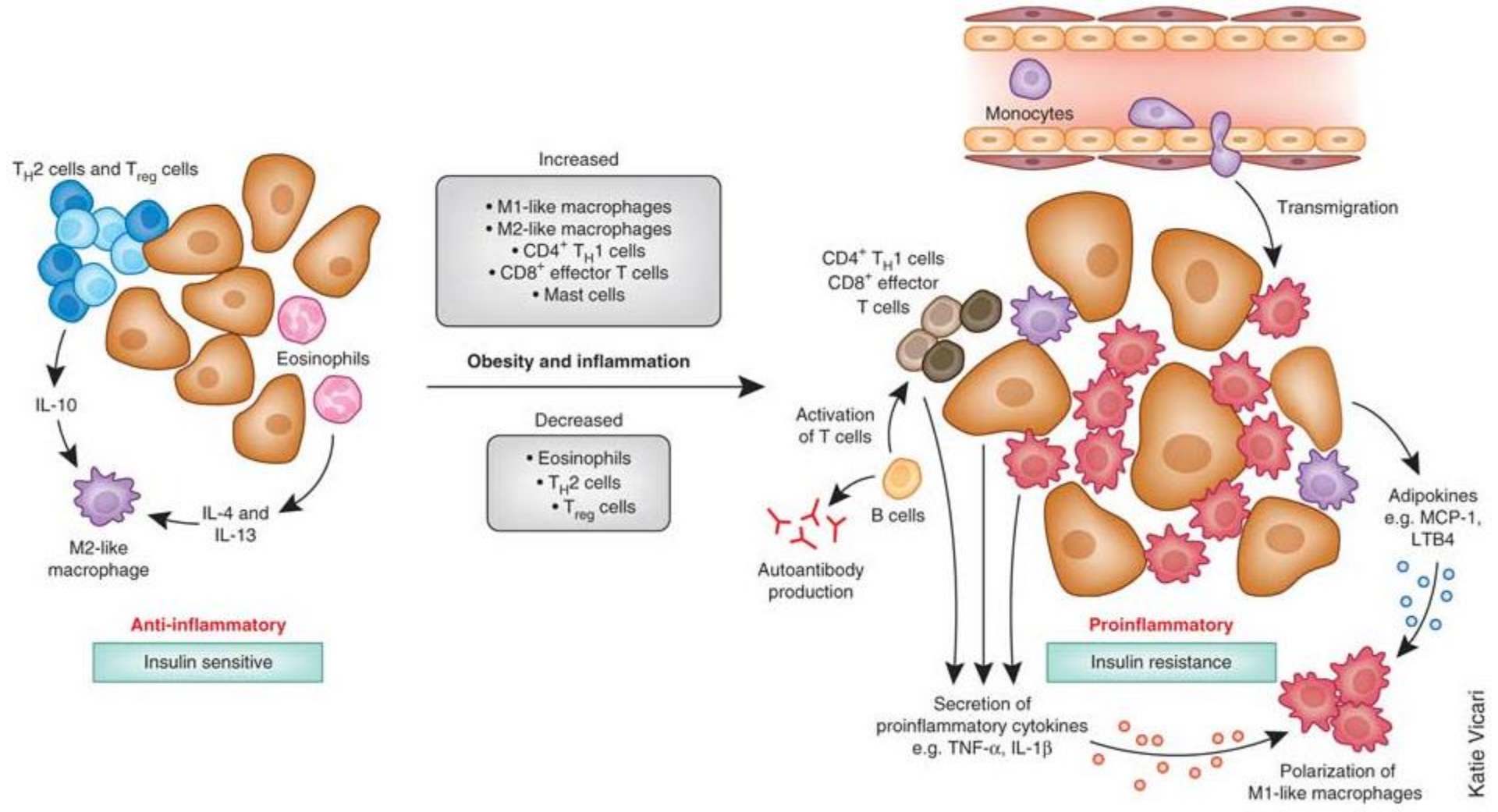


LPS-induced monocyte activation



Sereti I et al. Clin Inf Dis 2017;64:124.

Immune Cells Mediate Inflammation in Adipose Tissue



Osborn O and Olefsky J. Nature Medicine 2012;18:363–374.

Obesity of Associated with Increased Serum Inflammatory Markers in HIV-Infected Persons

AIDS RESEARCH AND HUMAN RETROVIRUSES
Volume 32, Number 1, 2016

DOI: 10.1089/aid.2015.0147

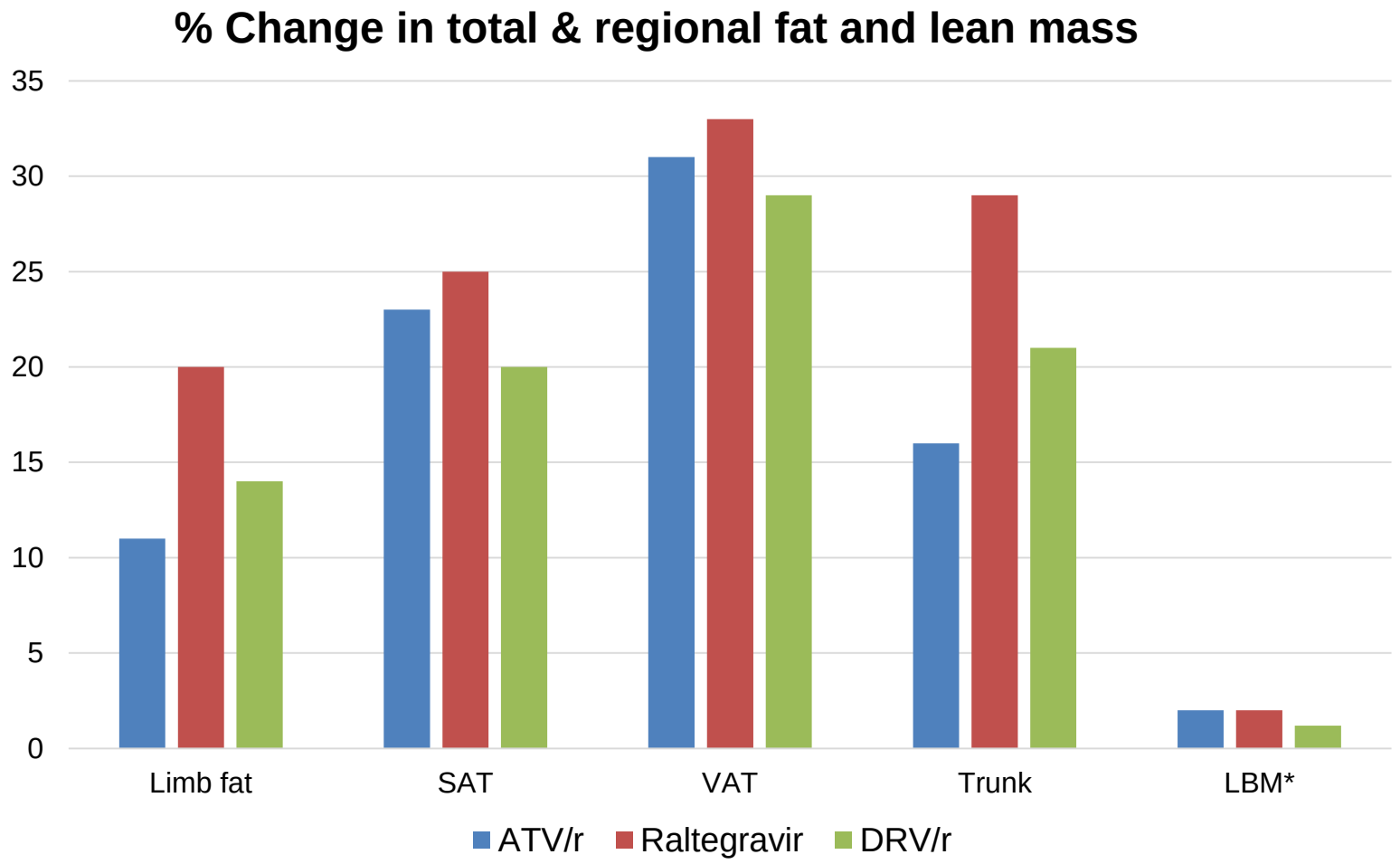
OUTCOMES RESEARCH

Rising Obesity Prevalence and Weight Gain Among Adults Starting Antiretroviral Therapy in the United States and Canada

John R. Koethe,[1] Cathy A. Jenkins,[1] Bryan Lau,[2] Bryan E. Shepherd,[1] Amy C. Justice,[3,4] Janet P. Tate,[3,4] Kate Buchacz,[5] Sonia Napravnik,[6] Angel M. Mayor,[7] Michael A. Horberg,[8] Aaron J. Blashill,[9] Amanda Willig,[10] C. William Wester,[1] Michael J. Silverberg,[11] John Gill,[12] Jennifer E. Thorne,[2] Marina Klein,[13] Joseph J. Eron,[6] Mari M. Kitahata,[14] Timothy R. Sterling,[1] and Richard D. Moore,[2] for the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD)

A total of 14,084 patients from 17 cohorts contributed data; 83% were male, 57% were nonwhite, and the median age was 40 years. Median BMI at ART initiation increased from 23.8 to 24.8 kg/m^2 between 1998 and 2010 in NA-ACCORD, but the percentage of those obese (BMI ≥30 kg/m^2) at ART initiation increased from 9% to 18%. After 3 years of ART, 22% of individuals with a normal BMI (18.5–24.9 kg/m^2) at baseline had become overweight (BMI 25.0–29.9 kg/m^2), and 18% of those overweight at baseline had become obese. HIV-

ACTG 5260s: Body Composition over 96 weeks

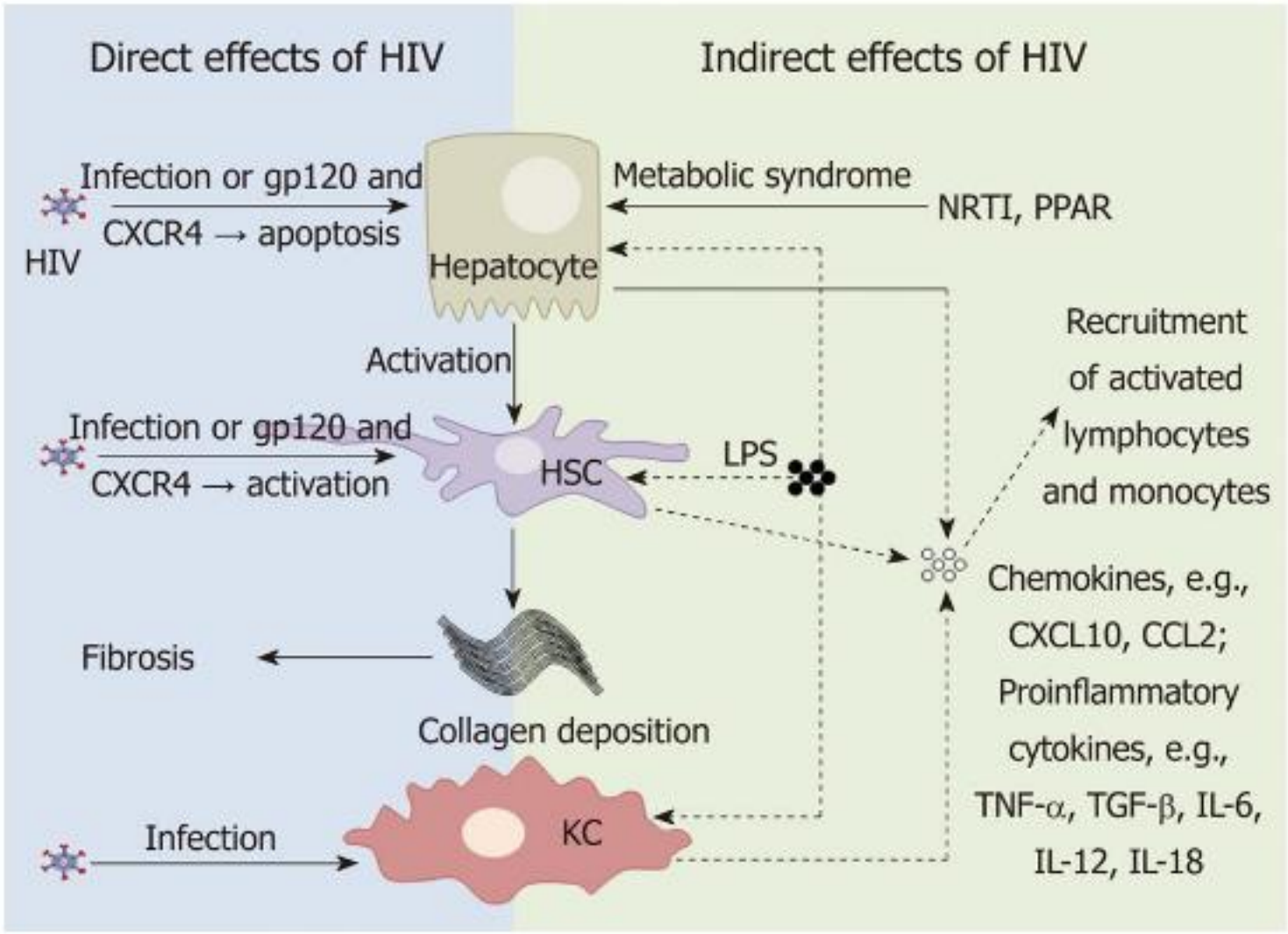


*p=0.05 ATV/r vs DRV/r

n=328

McComsey G, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 140.

Human Immunodeficiency Infection and the Liver

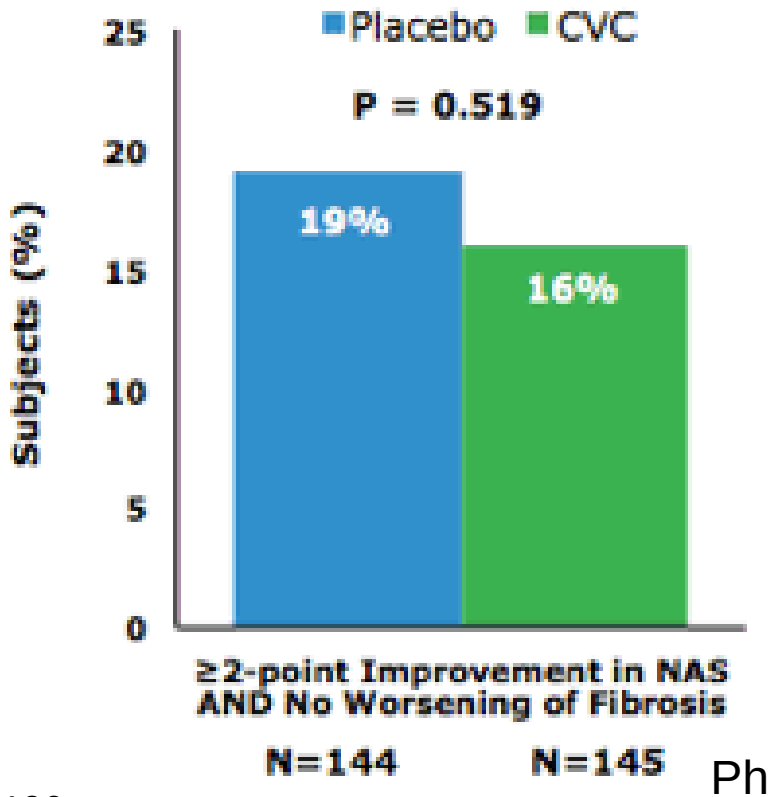


Crane M et al. World J Hepatol 2012;4:91-98.

Cenicriviroc Vs Placebo for the Treatment of Nonalcoholic Steatohepatitis with Liver Fibrosis

Cenicriviroc: Dual CCR2 and CCR5 Antagonist

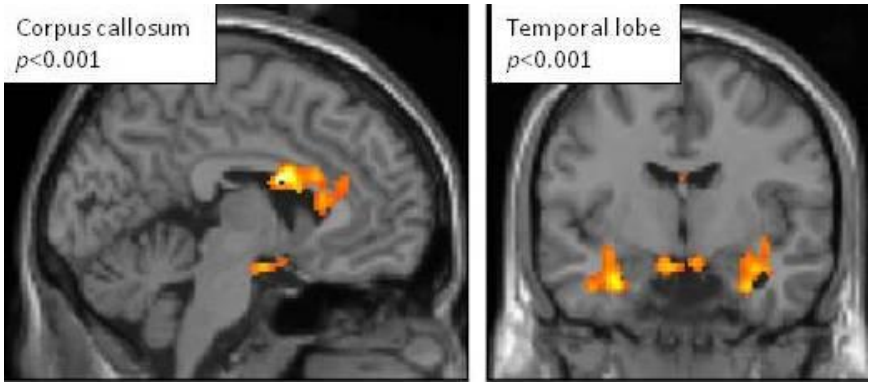
Primary endpoint: proportion of subjects with improvement in NAS by ≥2 points with at least a 1-point reduction in either lobular inflammation or hepatocellular ballooning AND with no concurrent worsening of fibrosis stage at Year 1



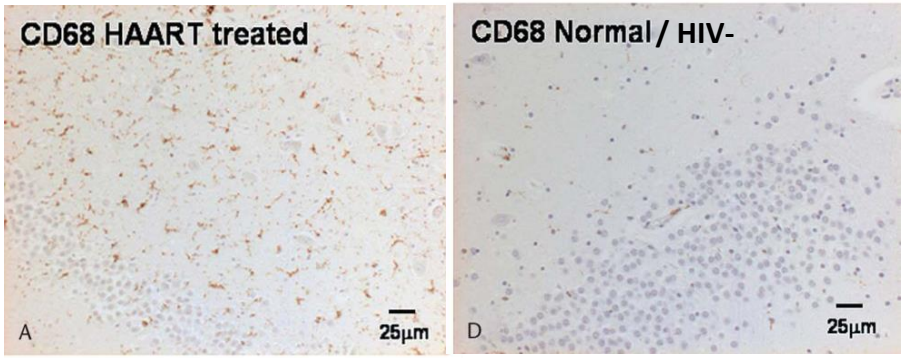
Phase 2b CENTAUR Study

Sanyal A et al. AASLD Nov 11-15, 2106.

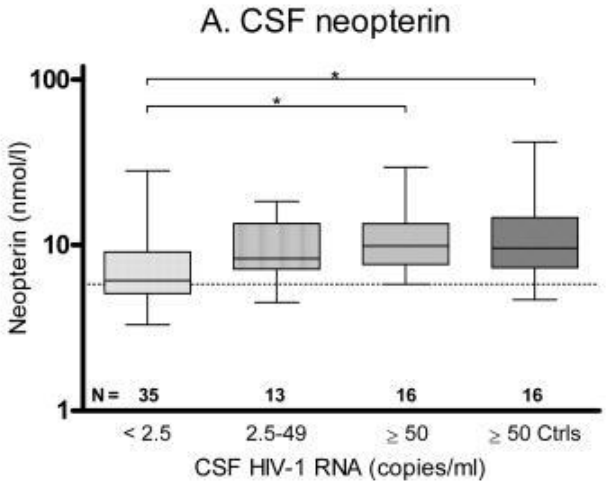
Persistent CNS Immune Activation on ART



Positron emission tomography (PET): Increased brain PK11195 uptake (specific for activated microglia) in 7 HIV subjects on 3.6 years suppressive ART.



Brain pathology: Excess activated microglia (CD68+ cells) in HIV-infected individuals on > 1.5 years suppressive ART.



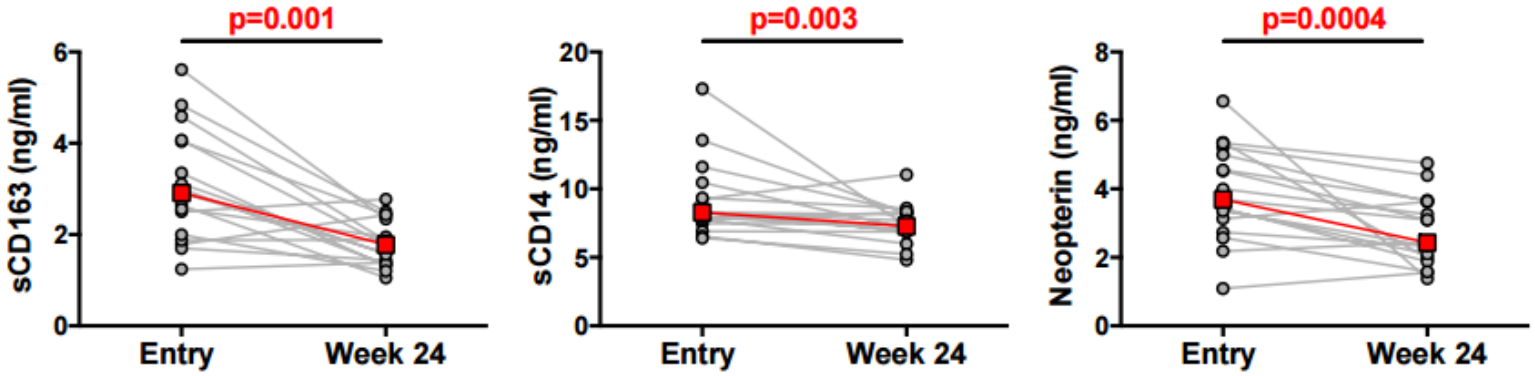
CSF: Elevated CSF neopterin associates with detectable CSF HIV RNA on ART.

Slide courtesy of Serena Spudich MD

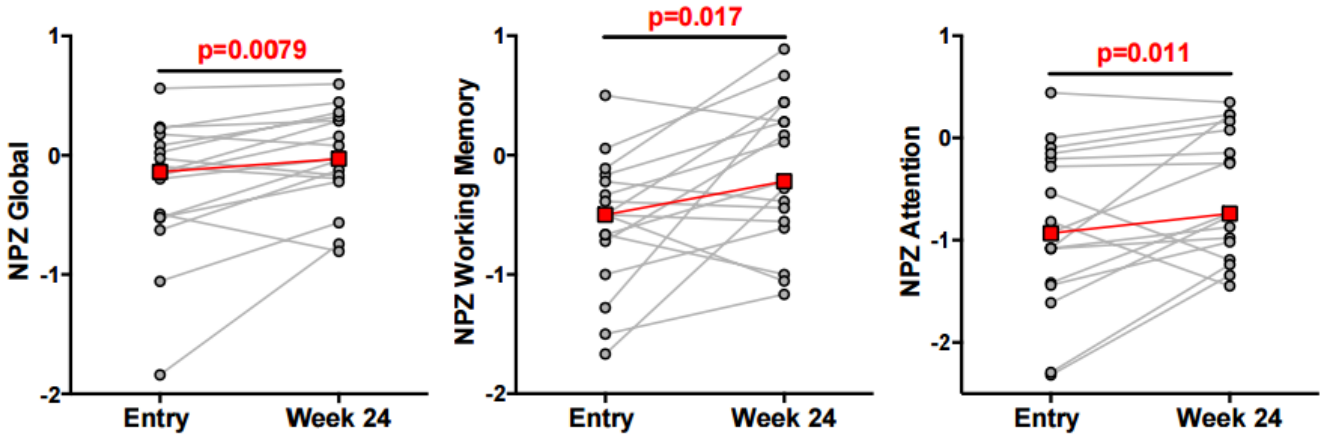
Garvey et al, AIDS, 2014; Anthony et al, J Neuropathol Exp Neurol, 2005; Yilmaz et al., J Acquir Immune Defic Syndr, 2008.

Intensification with Cenicriviroc, a Dual CCR2 and CCR5 Antagonist, Improves Neurocognition

CVC decreased soluble markers of monocyte/macrophage activation (sCD163, sCD14 and neopterin)

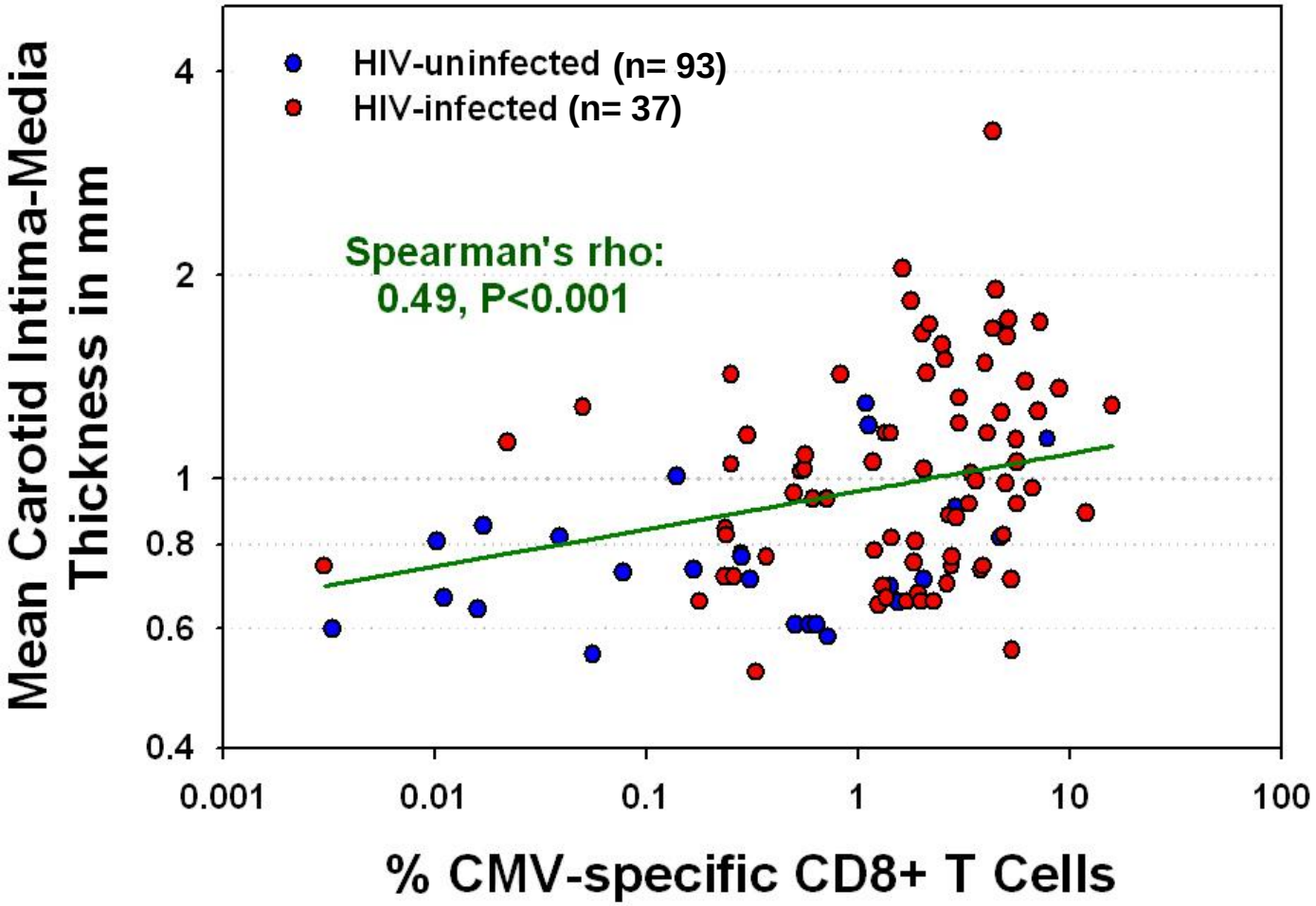


CVC improved cognitive performance in global and domains of working memory and attention



Ndhlovu LC et al. CROI 2017. Abs 381.

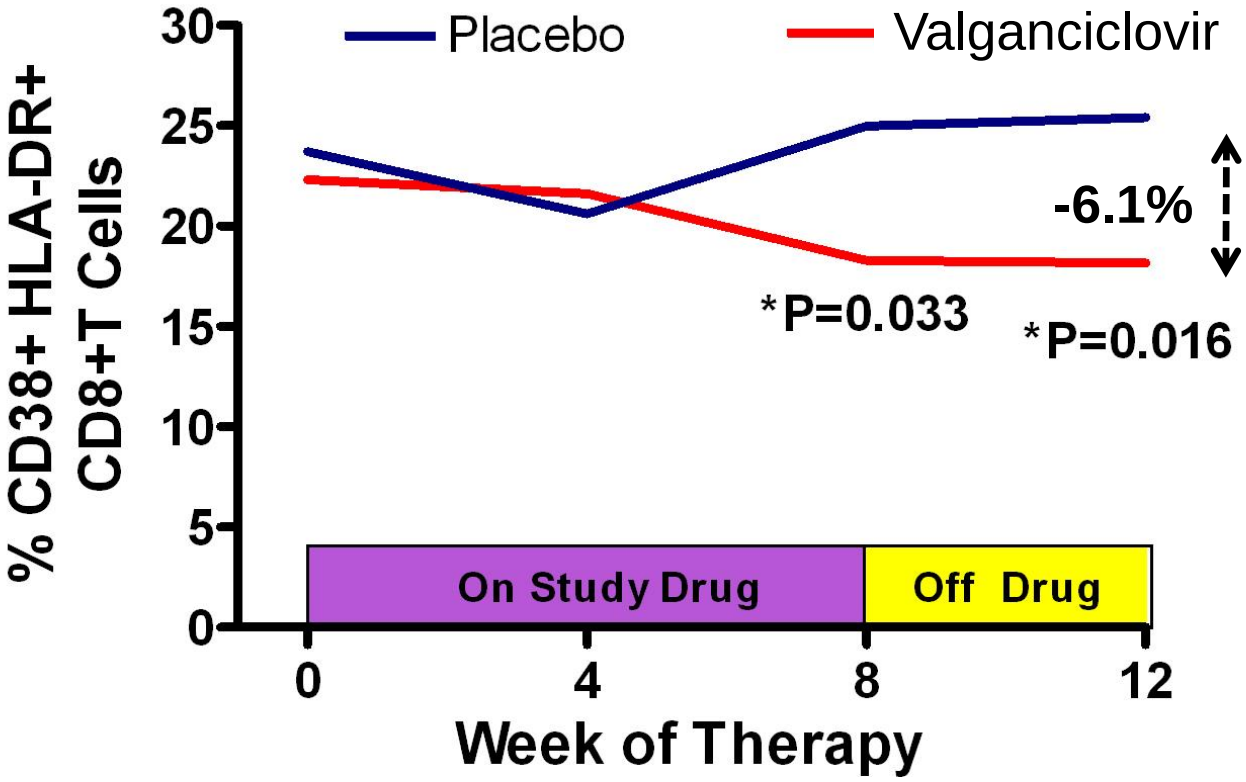
Higher CMV-specific CD8 IFN-γ Production Associated with More Atherosclerosis



Hsue PY et al. AIDS 2006;20:2275.

Decreasing Asymptomatic CMV Replication with Valganciclovir Decreases Immune Activation

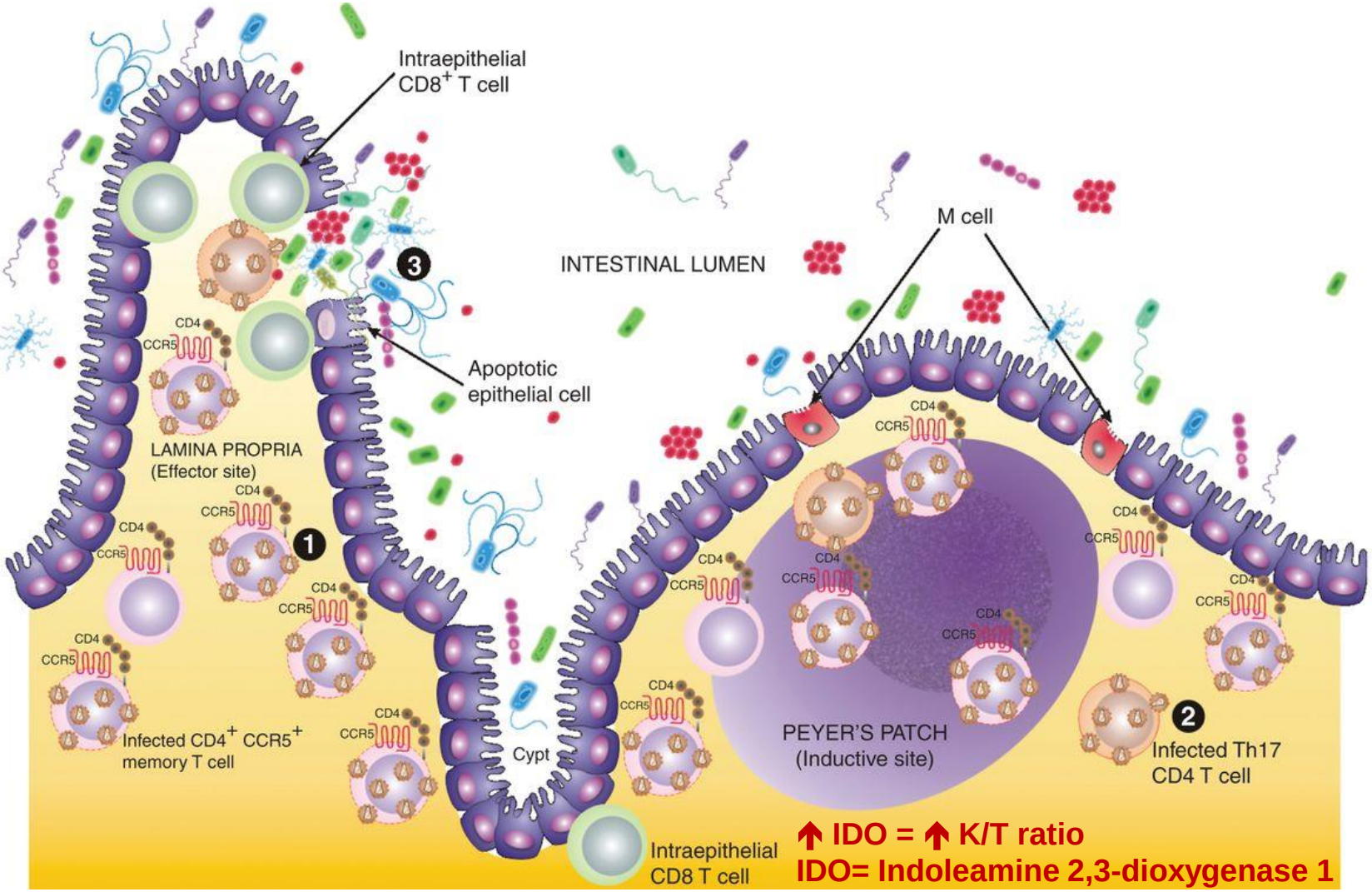
30 ARV-treated HIV-infected Patients with CD4<350



Valacyclovir did not decrease systemic immune activation or inflammatory biomarkers in HIV-1/HSV-2–co-infected adults on suppressive ART (Yi et al. CID 2013)

Hunt P et al, JID 2011;203:1474.

The Effects of HIV Infection in the Gastrointestinal Tract



Lackner A et al. Cold Spring Harb Perspect Med 2012;2:a007005

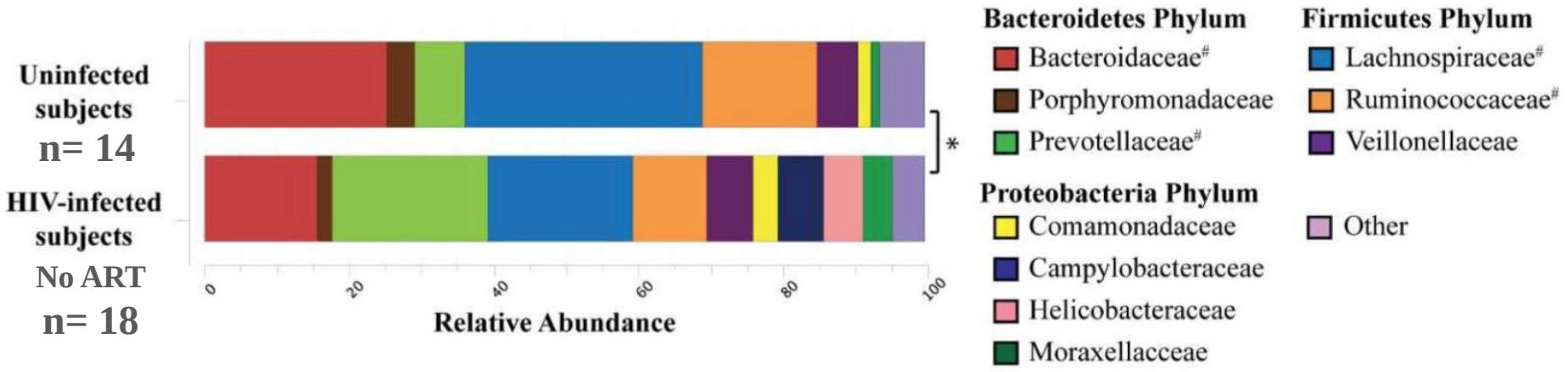
Microbiome: Definitions

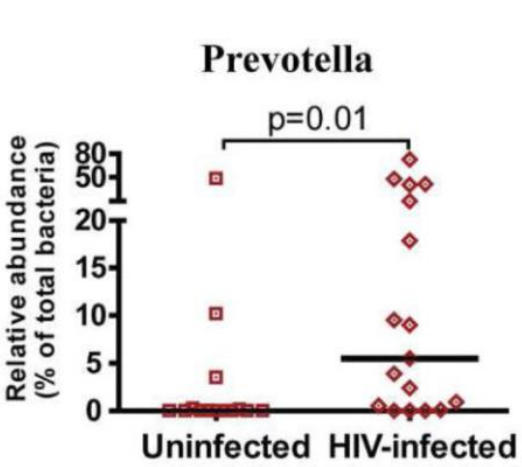
- **Microbiota:** Ecological communities of microorganisms comprising bacteria, archaea, protists, fungi and viruses found in and on all multicellular organisms
- **Microbiome:** The entirety of microorganisms, including their genes, functional gene products and metabolites, found in a given habitat, e.g., the human host, at a given point in time
- **Dysbiosis:** An imbalanced intestinal microbial community characterized by quantitative and qualitative changes in the composition of the microbiota itself, in its modified metabolic activities or in the local distribution of its members

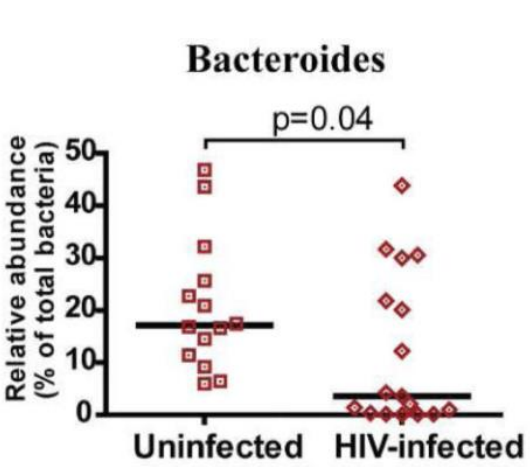
Gut Commensal Bacteria

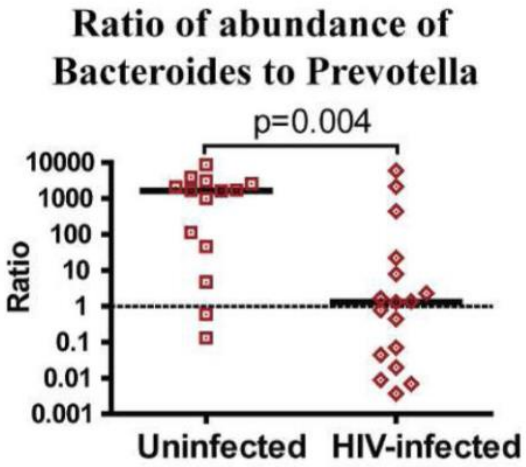
- Gut colonized by 10^{14} of microorganisms, >500 different species: bacteria, virus and fungi
- Microbiome interindividual variation at the genus and species level
- Phylum level is relatively consistent among individuals:
  - **High abundance of:**
    - Bacteroidetes (*Bacteroides*, *Prevotella*, *Porphyromonas*)
    - Firmicutes (*Lactobacillus*)
  - **Lower abundance of:**
    - Proterobaceria (*E. coli*, *Salmonella*, *Vibrio*, *Helicobacter*)
    - Tenericutes (*Mycoplasma*)
    - Fusobacteria (*Fusobacterium*)

Altered Intestinal Mucosal Microbiome in HIV-1 Infection



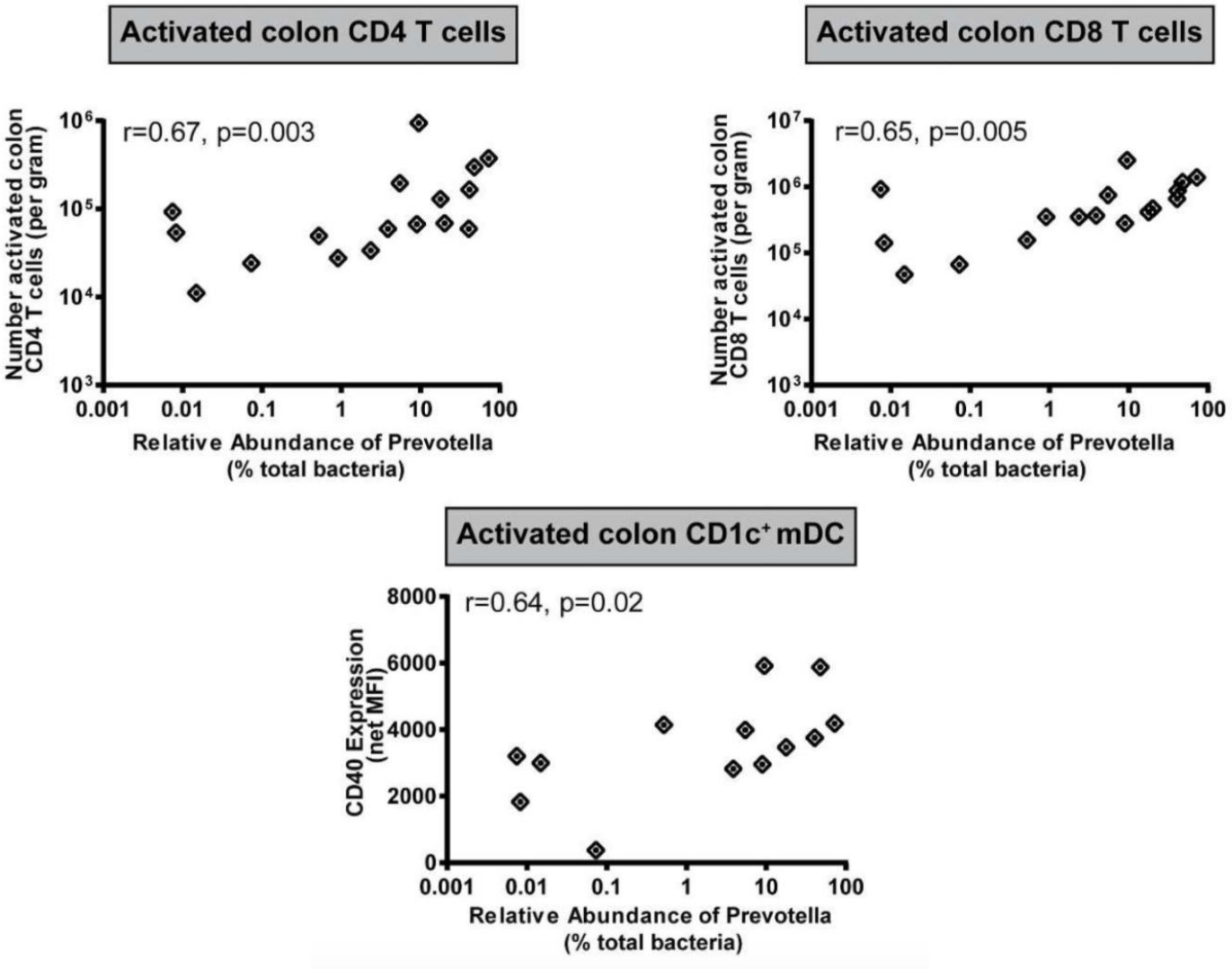






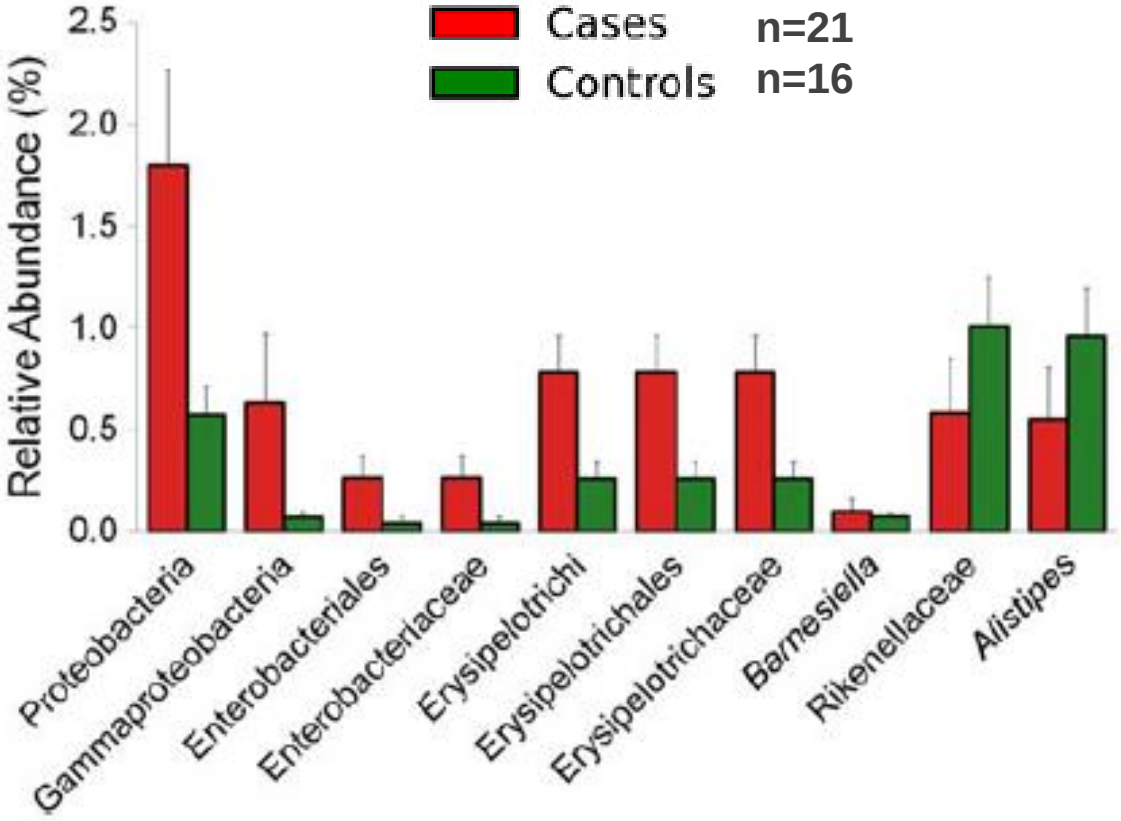
Dillon SM, et al. Mucosal Immunol 2014;7:983-94.

HIV-1 Associated Increase in the Relative Abundance of *Prevotella* is Associated with Colonic T cell and mDC Activation

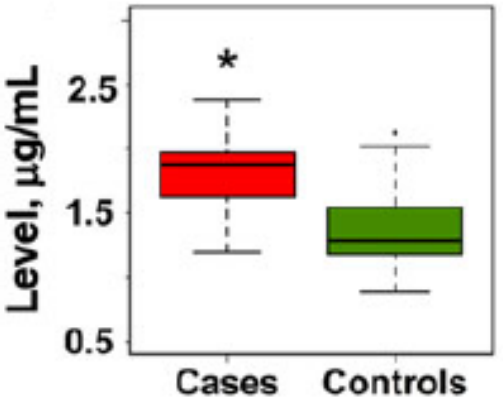


Dillon SM, et al. Mucosal Immunol 2014;7:983-94.

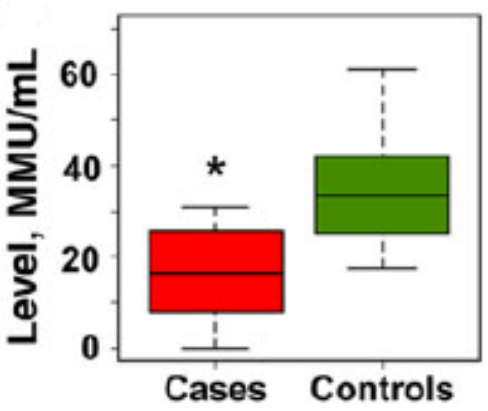
HIV-Infected People on Suppressive ART Display Intestinal Dysbiosis Associated with Inflammation



Soluble CD14 [sCD14]



Endotoxin core antibody [EndoCAb]

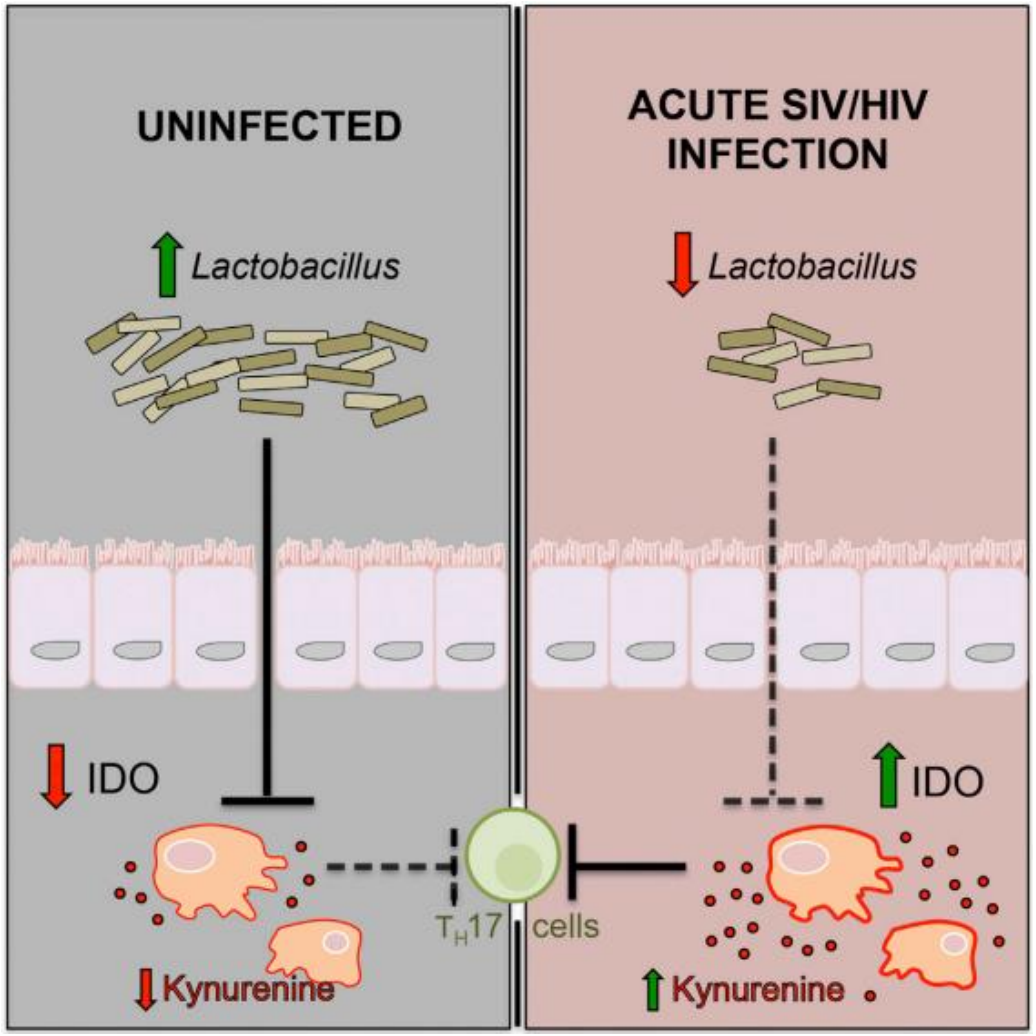


Dinh DM et al. JID 2015;211:19–27.

Lactobacillus Abundance Associates with IDO-1 Inhibition of Th17 in SIV-Infected Macaques

- IDO-1 activity correlates with loss of barrier-promoting Th17 cells in SIV infection
- Abundance of gut-resident *Lactobacillus* correlates with IDO-1 activity and Th17 cells
- Probiotics containing Lactobacillus reduce IDO1 activity in SIV-infected macaques

IDO: indoleamine 2,3-dioxygenase



Vujkovic-Cvijin I et al. Cell Reports 2015;13:1589-97.

Gut Microbiota and Tryptophan Catabolism Associated to Atherosclerosis in HIV Infection

Associations of tryptophan, metabolites and carotid artery plaque

	All		HIV+	HIV-	$P_{interaction}$
	RR (95% CI)	P	RR (95% CI)	RR (95% CI)	
Tryptophan					
Model 1*	0.75 (0.64-0.88)	<0.001	0.75 (0.63-0.89)	0.78 (0.53-1.13)	0.78
Model 2†	0.81 (0.69-0.94)	0.005	0.83 (0.70-0.98)	0.67 (0.45-0.99)	0.34
Kynurenic acid					
Model 1*	1.34 (1.08-1.65)	0.007	1.30 (1.03-1.64)	1.51 (0.98-2.31)	0.53
Model 2†	1.26 (1.02-1.54)	0.03	1.25 (1.01-1.55)	1.30 (0.83-2.04)	0.85
Kyn/Trp ratio					
Model 1*	1.41 (1.22-1.64)	<0.001	1.38 (1.18-1.62)	1.65 (1.06-2.57)	0.44
Model 2†	1.30 (1.11-1.53)	0.002	1.28 (1.08-1.51)	1.47 (0.93-2.31)	0.55

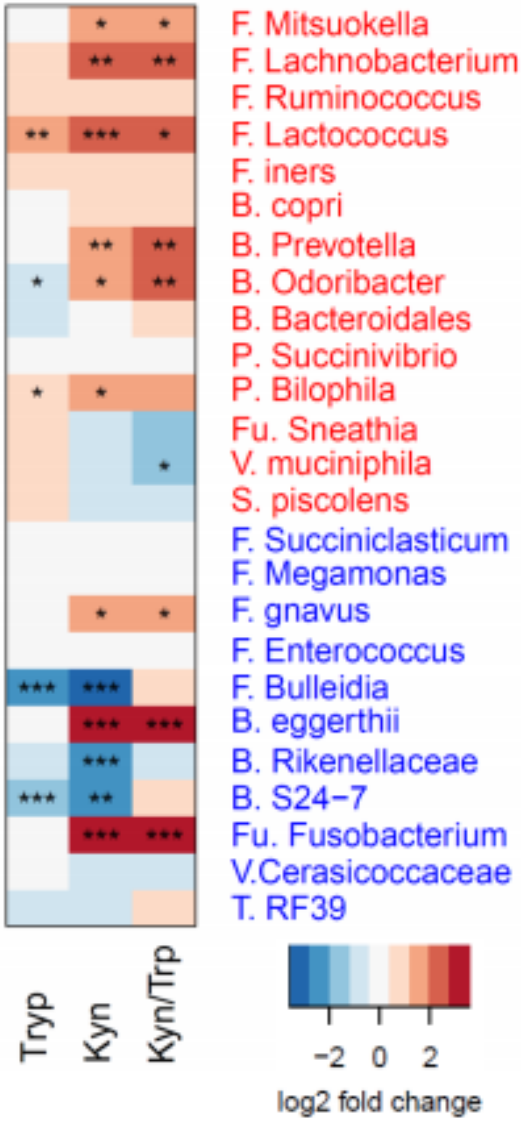
Data are risk ratio (95% CI) of focal plaque formation per SD increase in metabolites.
*Model 1 adjusted for demographic, behavioral, and HIV infection related factors.
†Model 2 further adjusted for traditional CVD risk factors.

Qin Q et al. CROI 2017. Abs 636LB.

Gut Microbiota and Tryptophan Catabolism Associated to Atherosclerosis in HIV Infection

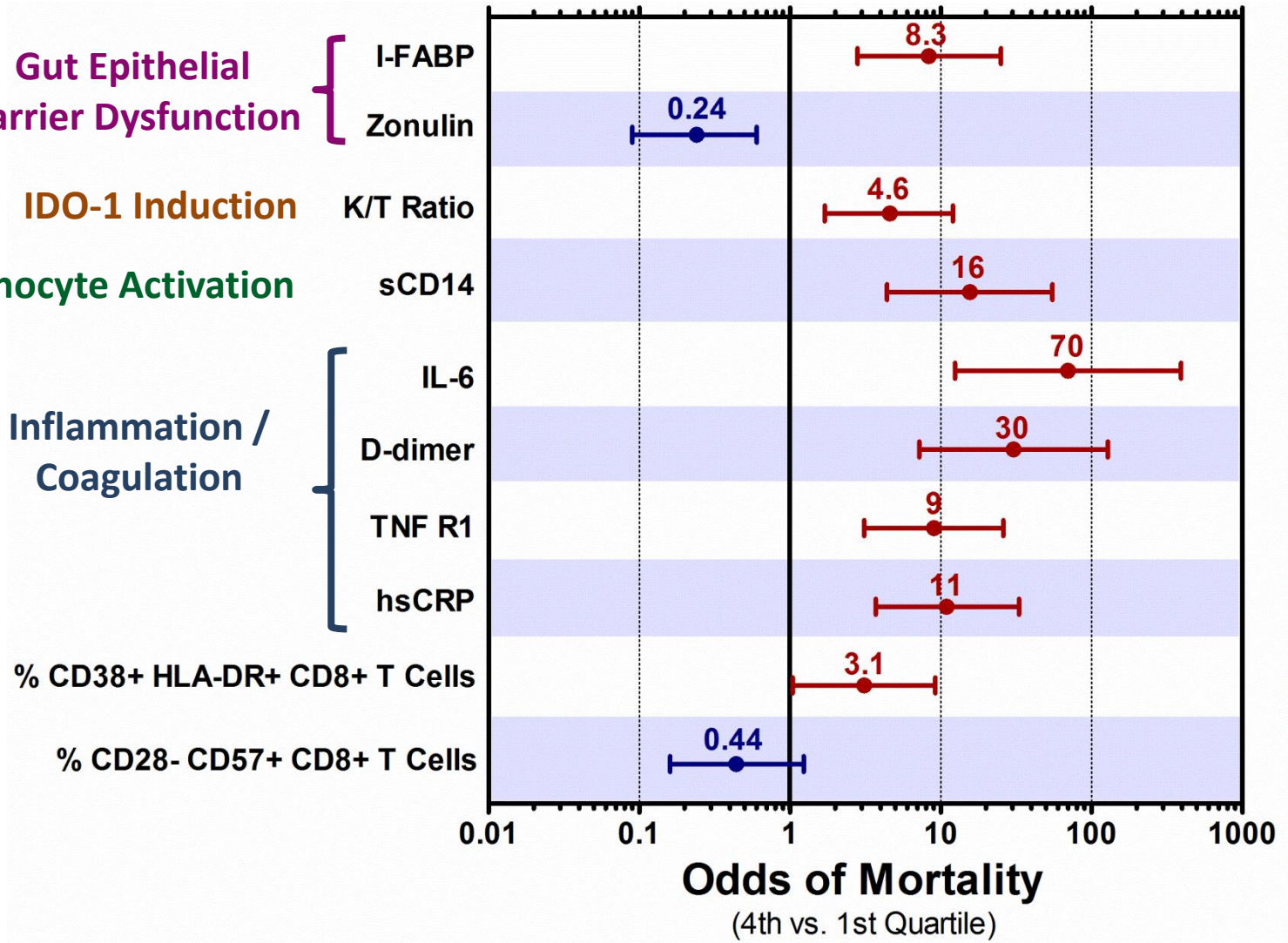
GMB and Tryptophan Metabolites

- Taxa increased in HIV+ (in red) showed positive associations with kynurenic acid and Kyn/Trp ratio
- Taxa decreased in HIV+ (in blue) showed inverse associations with tryptophan and kynurenic acid, but not with Kyn/Trp ratio



Qin Q et al. CROI 2017. Abs 636LB.

Markers of Inflammation and Gastrointestinal Dysfunction Predict Mortality in HIV Infection

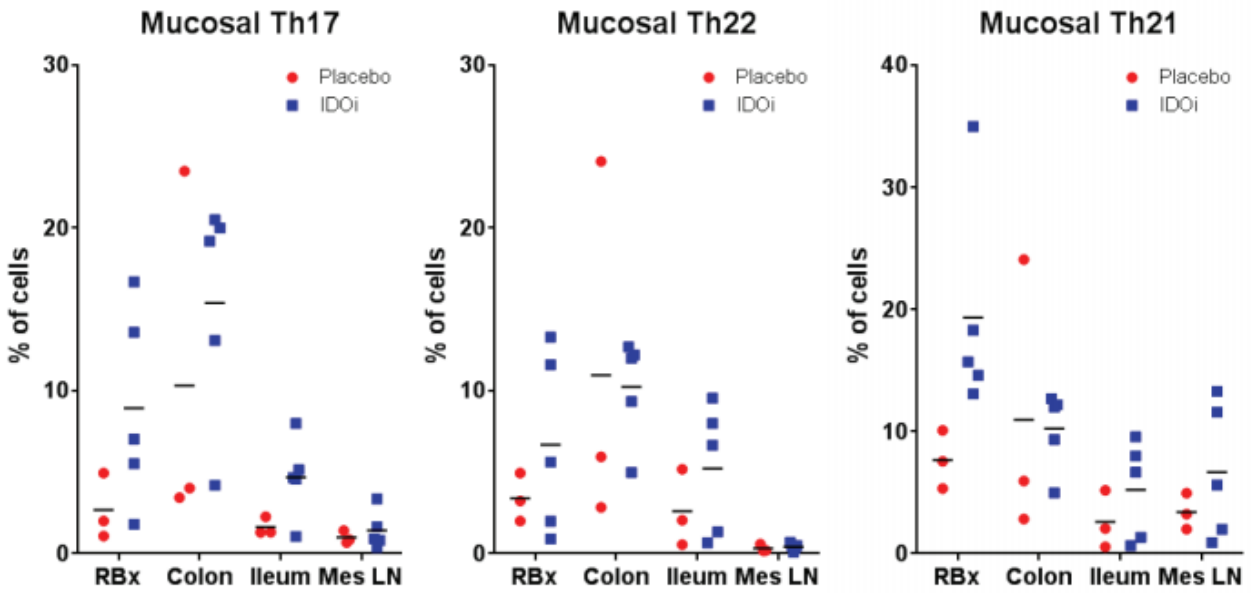


Hunt P et al. 19th CROI. March 5-8, 2012; Seattle, Washington. Abs 278.

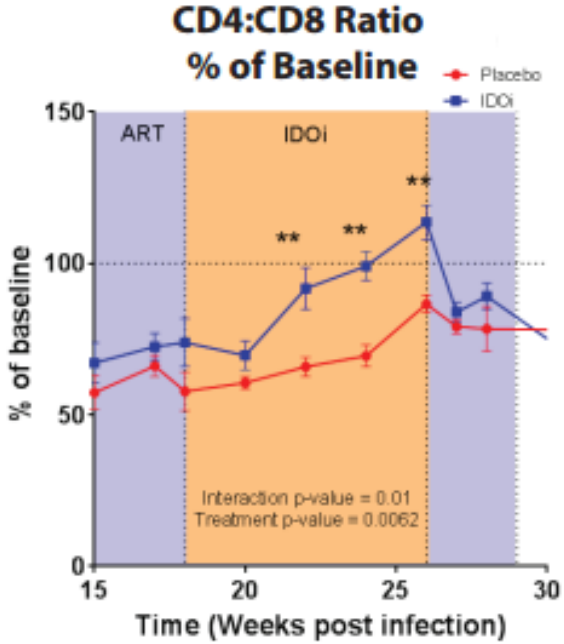
Pharmacologic Inhibition of IDO1 Blunts Features of SIV-Related Chronic Inflammation

12 rhesus macaques infected with SIVmac251, treated with cART, and divided into two groups after virologic suppression to receive either placebo or IDOi (INCB024360) for 8 weeks while continuing ART.

Trend to increase in mucosal Th17, Th22, Th21 with IDOi

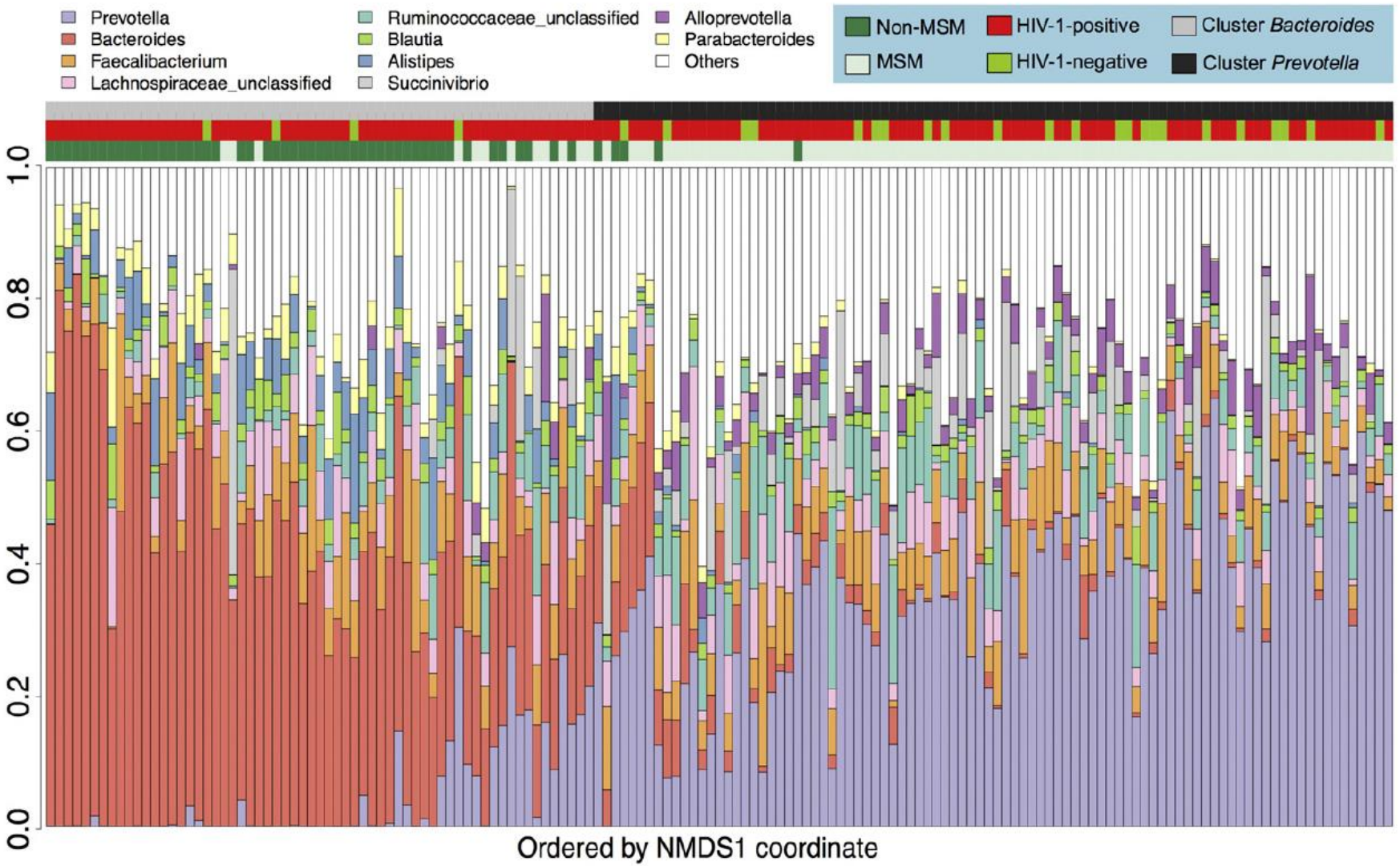


Increased CD4:CD8 ratio in peripheral blood



Durnham RM et al. CROI 2017. Abs 252.

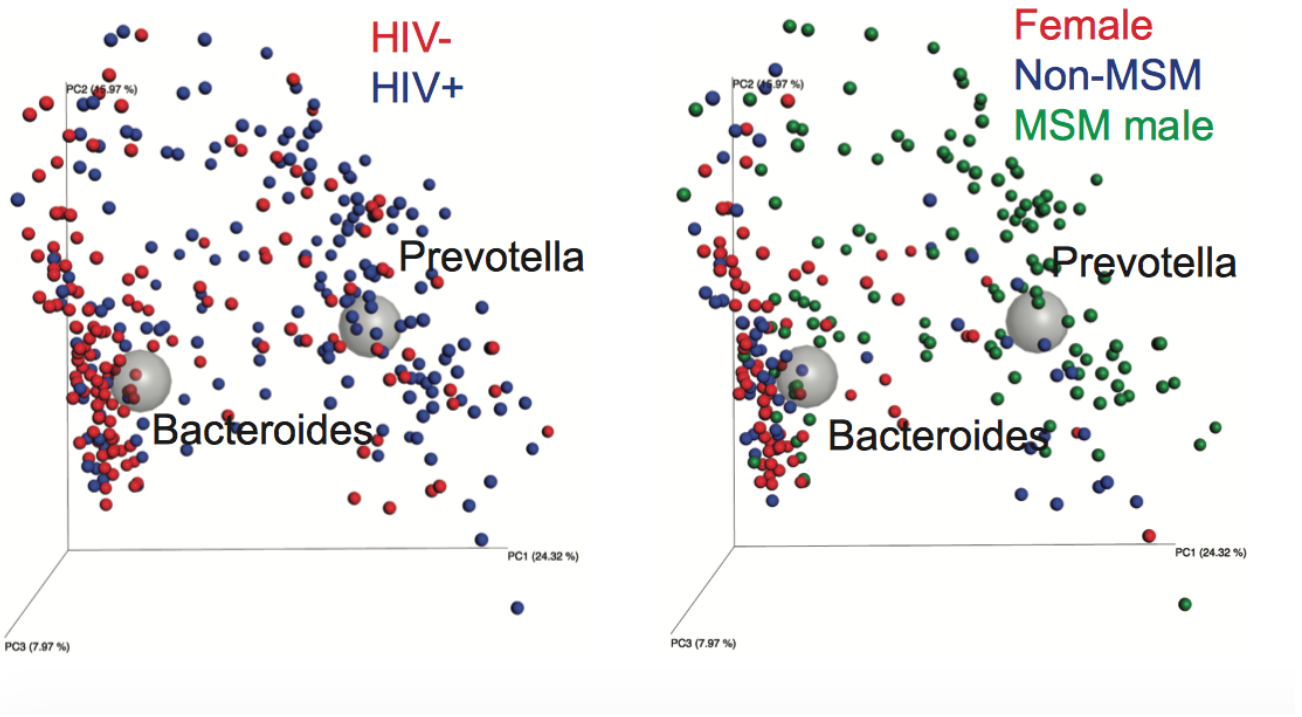
Distinct Fecal Microbiota Composition (increased *Prevotella*, reduced *Bacteroides*) is Associated with MSM but not HIV Status in European Gay Men



Noguera-Julian M, et al. EBioMedicine 2016; 5:135–146

Impact of MSM-Associated Microbiota on Immune Activation and in vitro HIV Infection

- HIV infection associated with Prevotella rich/Bacteroides poor gut microbiome
- Confounded by MSM, who are Pervotella rich regardless of HIV status

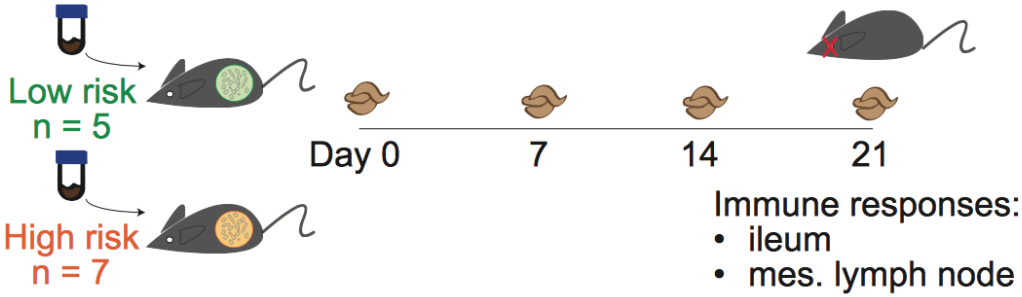


Li S, et al. CROI 2017. Abst. 207.

Do MSM-associated microbiota impact immune activation?

Methods

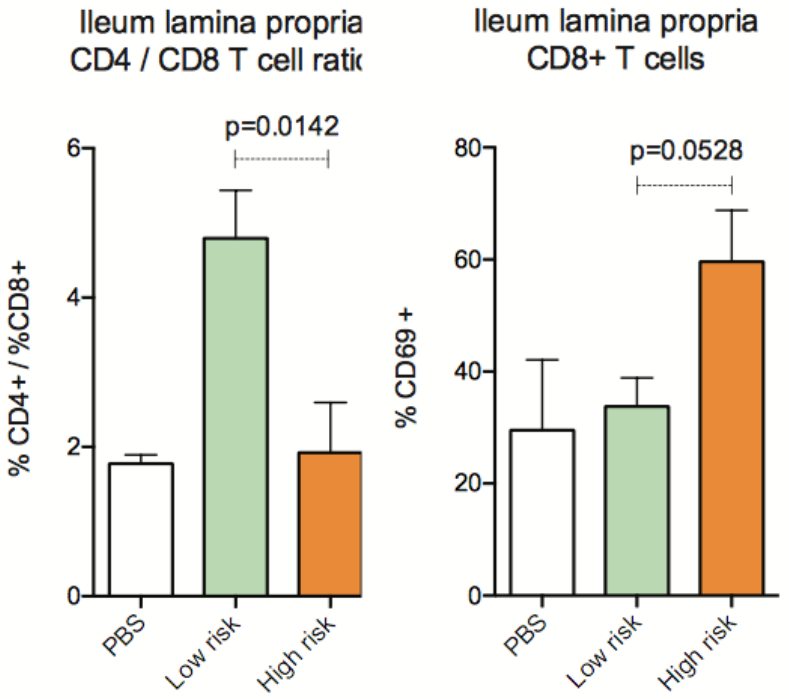
Stools from HIV-low risk heterosexual men and high risk MSM →gavage germ free mice, colonized 21 days



Results

MSM mice had:

- Increased CD8 T cell frequency and activation
- increased IFN-γ production in the gut
- increased CD4+ T cell activation in the mesenteric lymph node (CD69)



Li S, et al. CROI 2017. Abst. 207.

Do MSM-associated microbiota impact immune activation?

Methods

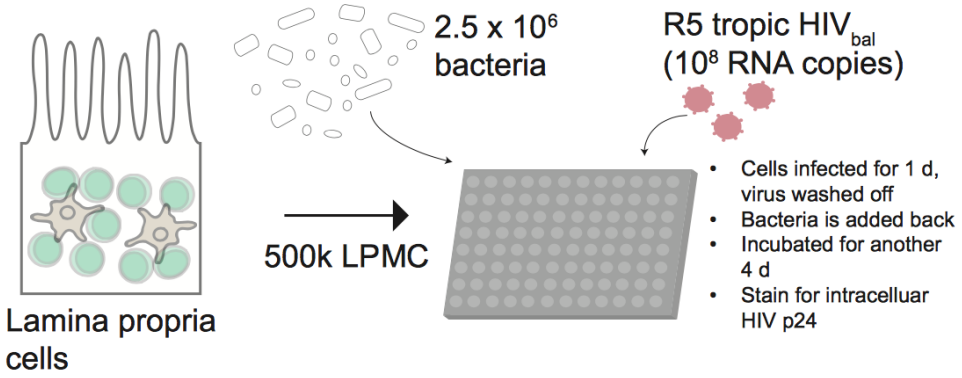
- Bacteria isolated from stools of HIV-low risk heterosexual men and high risk MSM →stimulate lamina propria cells, then infect

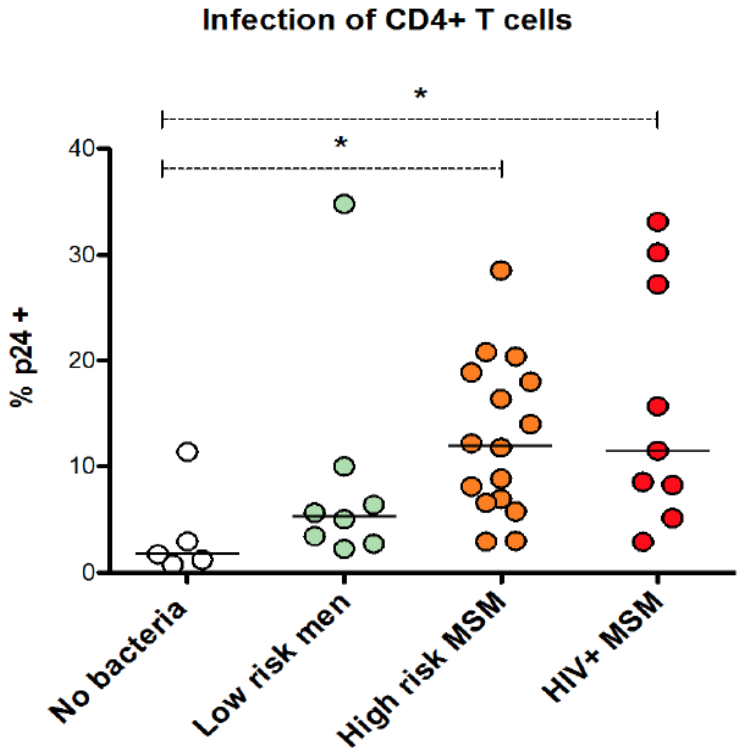
Results

- MSM bacteria stimulated higher HIV infection levels
- Higher infection levels associated with higher T cell activation (CD38)

Conclusions

- MSM-associated microbiota stimulate
  - increased immune activation
  - increased HIV infection of human lamina propria cells in vitro
- Suggest gut microbiome may impact transmission in MSM

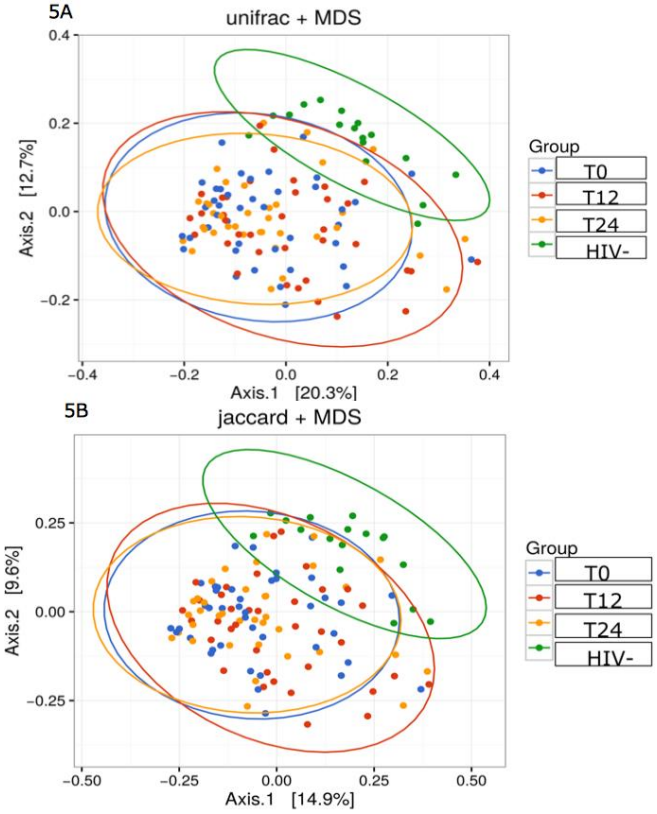




Li S, et al. CROI 2017. Abst. 207.

Differences in Gut Microbiome pre and post ART?

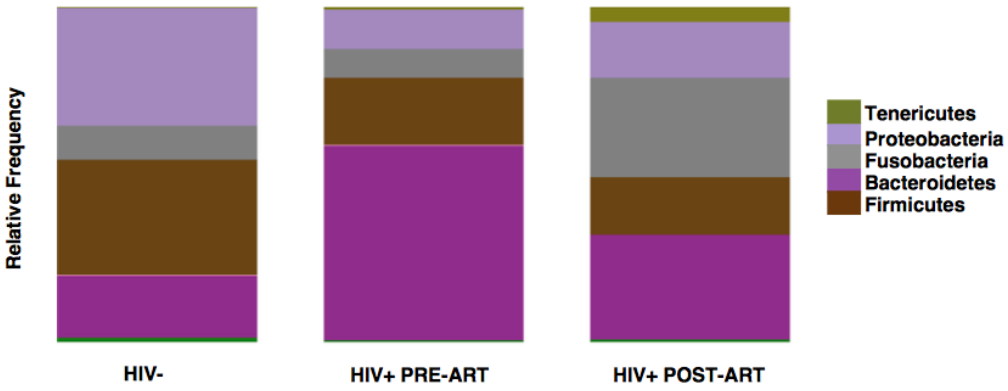
- 41 ART naive HIV+ patient - T0, 12, 24 mos after ART
- 15 HIV-controls; stool samples used
- Changes in gut microbiome persisted in HIV+



Tincati C, et al. CROI 2017. Abst. 215.

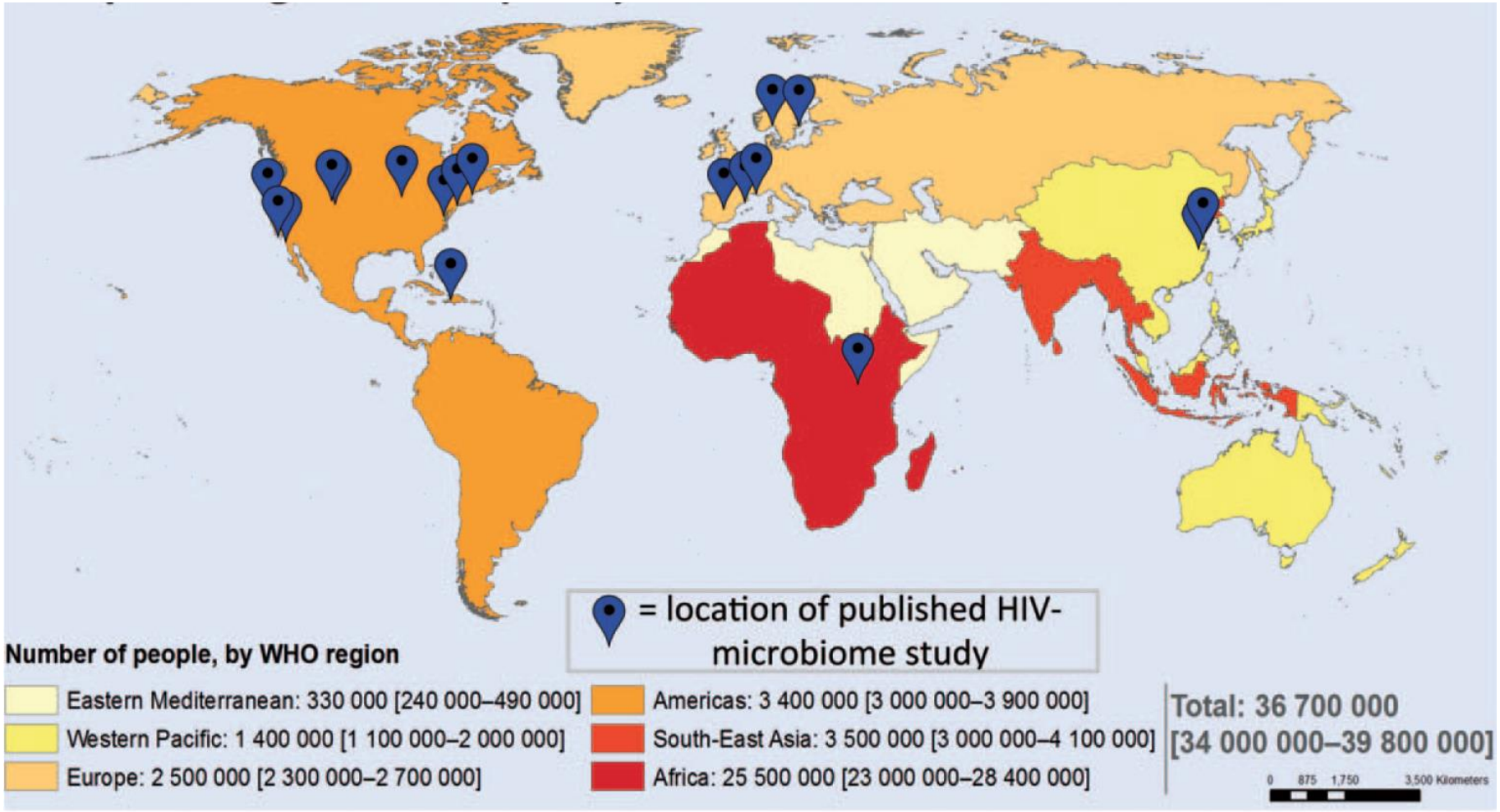
- 59 cutely HIV infected Thai subjects
- Pre and 6 months post ART
- 4 HIV-controls; anal swabs used
- Increase in Fusobacteria, Tenericutes

Abundance of bacterial phyla in cases pre and post-ART and controls



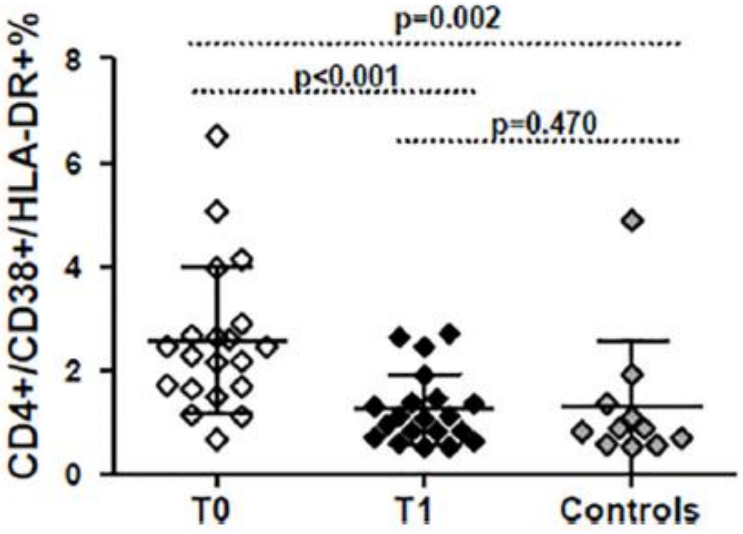
Sortino O, et al. CROI 2017. Abst. 214.

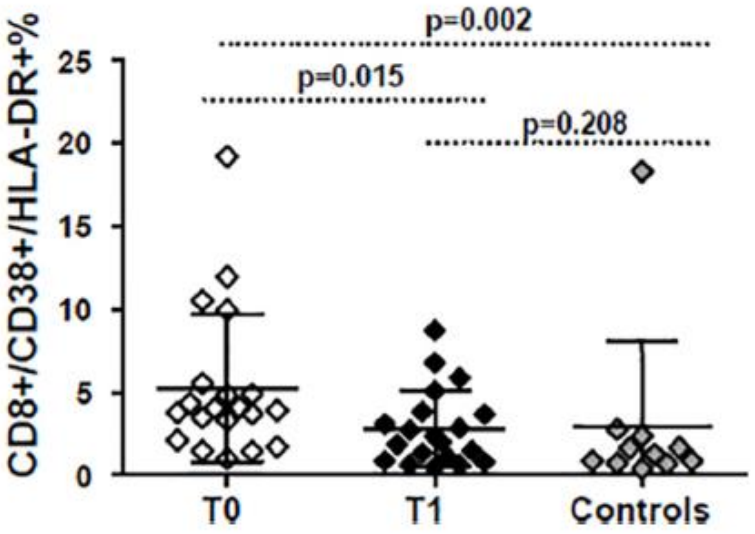
People living with HIV (2015) and Locations of HIV-Microbiome Studies

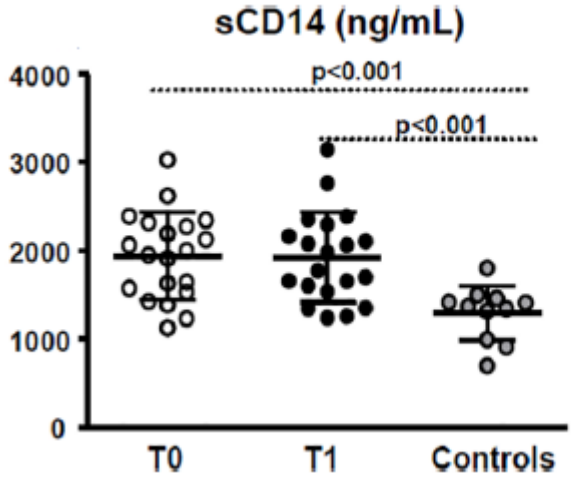


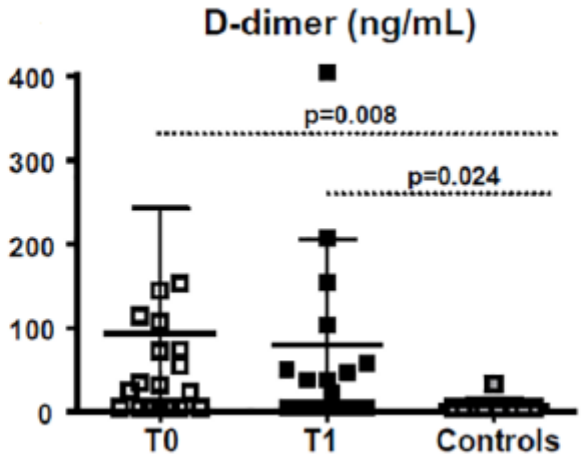
Gootenberg DB et al. Curr Opin Infect Dis 2017, 30:31–43

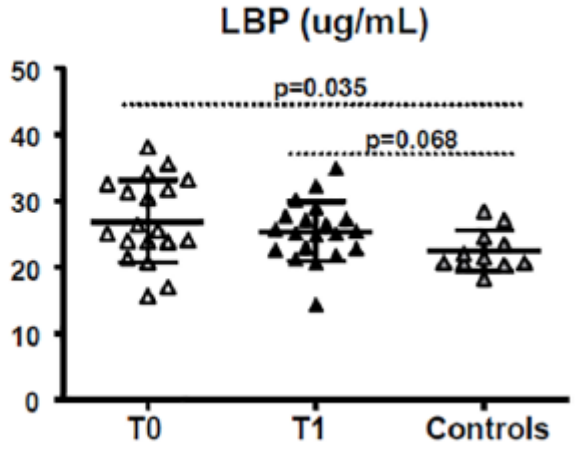
Probiotics Reduce Inflammation in ARV Treated HIV-Infected Individuals











d'Ettore G et al, PLoS ONE 2015;10:e0137200.

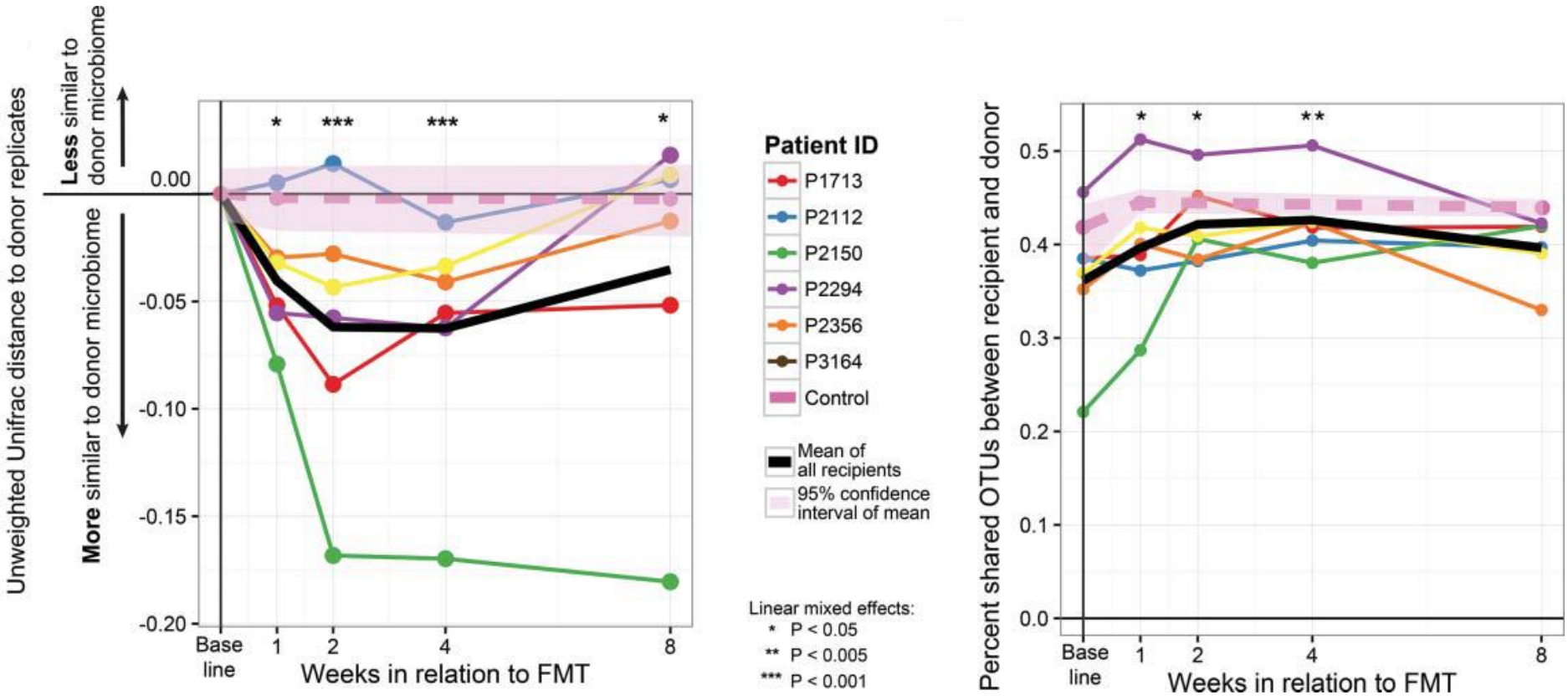
Limited Engraftment of Donor Microbiome Via One-Time FMT in Treated HIV-Infected Individuals

Table 1. Characteristics of the study participants.

FMT	ID	Age	Gender	Race	CD4 count (cells/μL)	CD8 count (cells/μL)	CD4/8 ratio
Yes	1713	31	Male	White	463	1393	0.34
Yes	2112	61	Male	White	835	613	1.34
Yes	2150	53	Male	White	431	532	0.79
Yes	2294	70	Male	White	357	819	0.44
Yes	2356	72	Male	White	401	1027	0.39
Yes	3164	69	Male	White	622	1122	0.56
No	2447	57	Female	White	815	927	0.88
No	2558	71	Male	Black	257	301	0.85

Vujkovic-Cvijin I et al. Gut Microbes 2017;0:1–11.

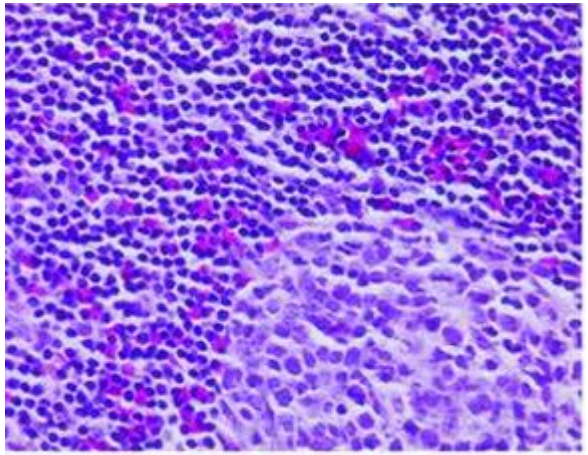
Limited Engraftment of Donor Microbiome Via One-Time FMT in Treated HIV-Infected Individuals



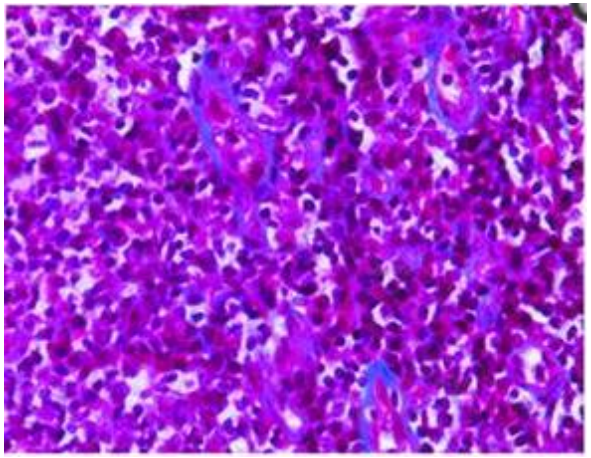
Vujkovic-Cvijin I et al. Gut Microbes 2017;0:1–11.

Immune Activation Causes Lymphoid Tissue Fibrosis

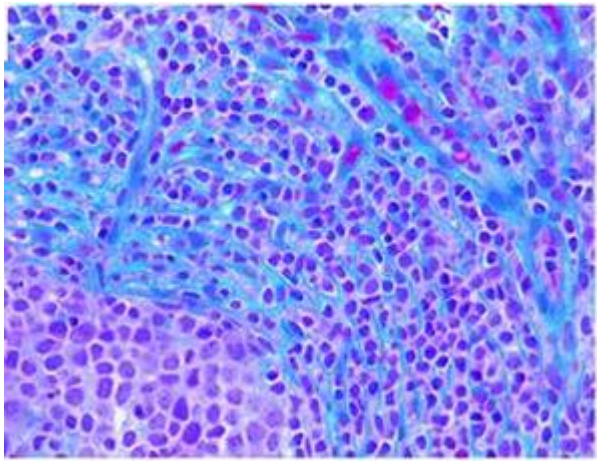
HIV negative



HIV positive



AIDS

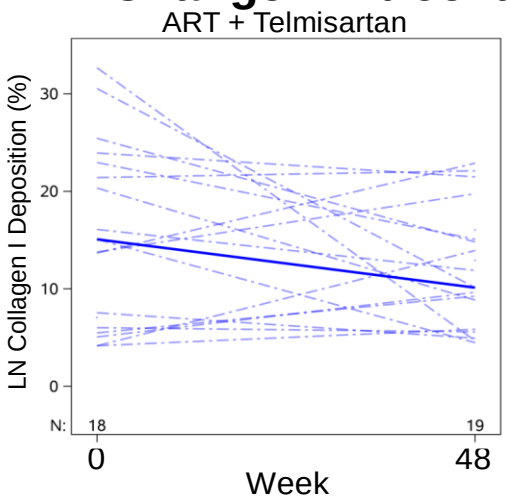


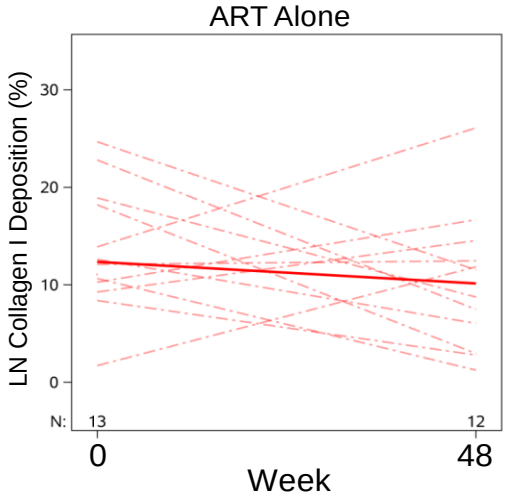
Schacker T et al. JCI 2002;110:1133.

Telmisartan Does Not Improve Lymph Node or Fat Fibrosis in Treated HIV Infection

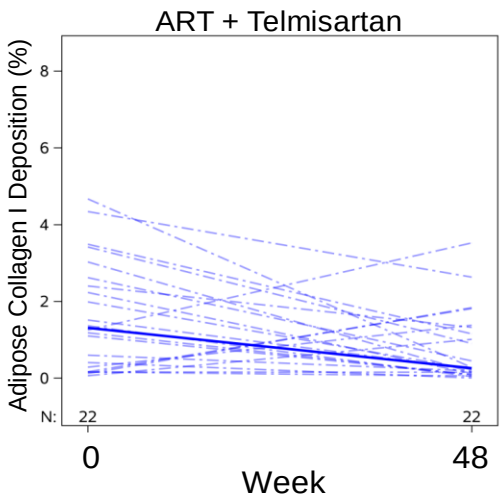
Telmisartan is an angiotensin receptor blocker and PPAR-γ agonist with anti-inflammatory and anti-fibrotic properties

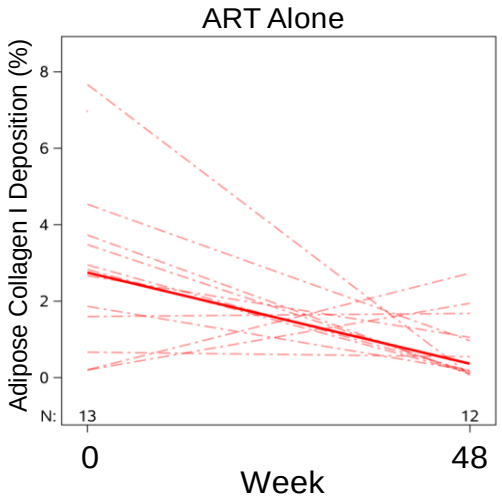
Change in % collagen I in LN over 48 weeks





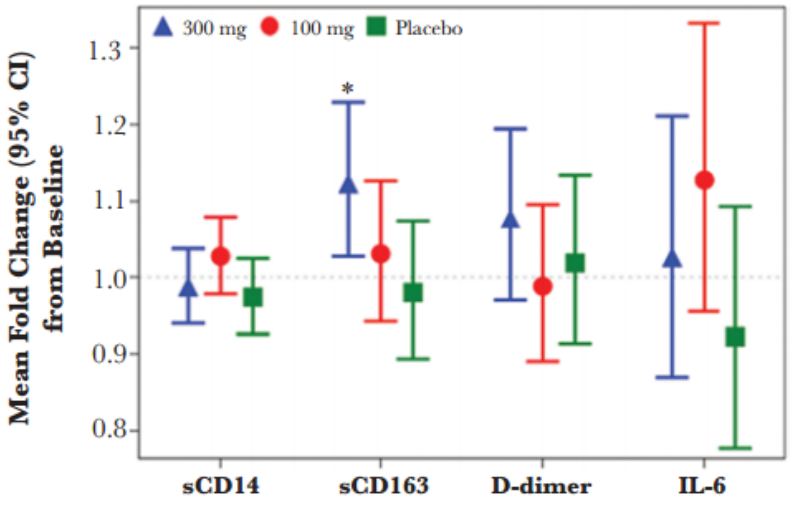
Change in % collagen I in adipose tissue over 48 weeks

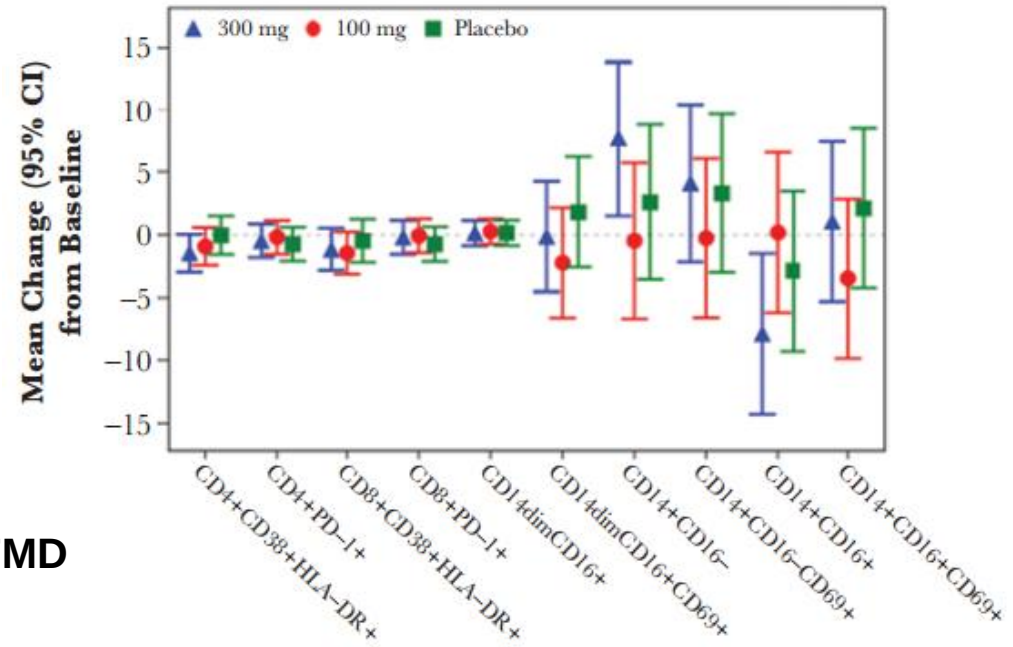




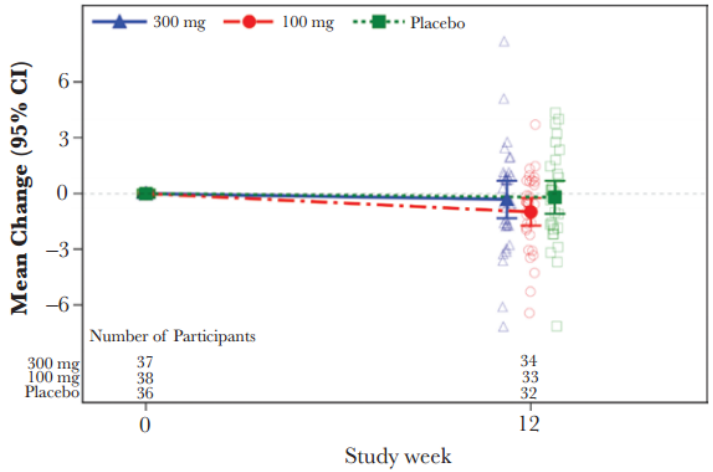
Utay NS, et al. CROI 2017. Abst. 251.

Aspirin Fails to Impact Immune Activation or Endothelial Function in Treated HIV





No evidence for an effect of aspirin on FMD

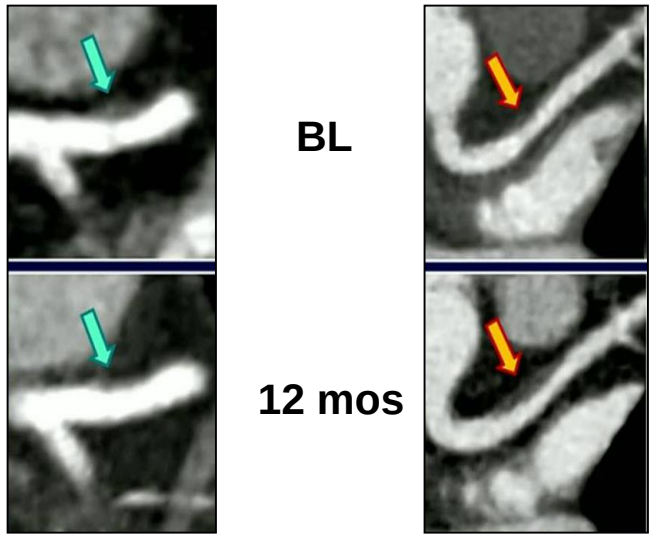


O'Brien M, et al. Open Forum Infect Dis 2017;4:ofw278.

Randomized Trial of Statin Therapy and Coronary Plaque Progression

- Randomized 12-month trial in 40 HIV+ patients on stable ART with LDL < 130 and ≥ 1 coronary plaque
  - Atorvastatin 20 mg (↑ to 40 mg at 3 months) (n = 19) vs
  - Placebo (n = 21)
- Statin therapy reduced progression of coronary plaques
  - Reduced non-calcified plaque volume
  - Reduced high-risk morphology plaques
- Statin therapy safe and well tolerated

Plaque Progression in Proximal Left Anterior Descending Coronary Artery With Atorvastatin or Placebo



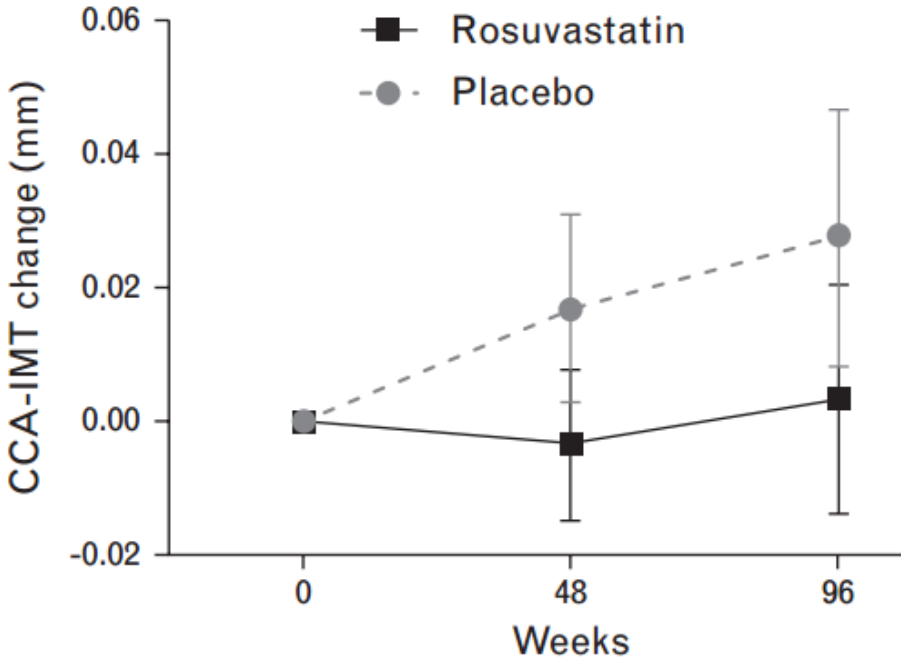
Median change **-19.4%** (IQR: -39.2%, 9.3%) versus **+20.4%** (-7.1%, 94.4%; p=0.009, n=37)

Lo J, et al. Lancet HIV 2015;2:e52-63.

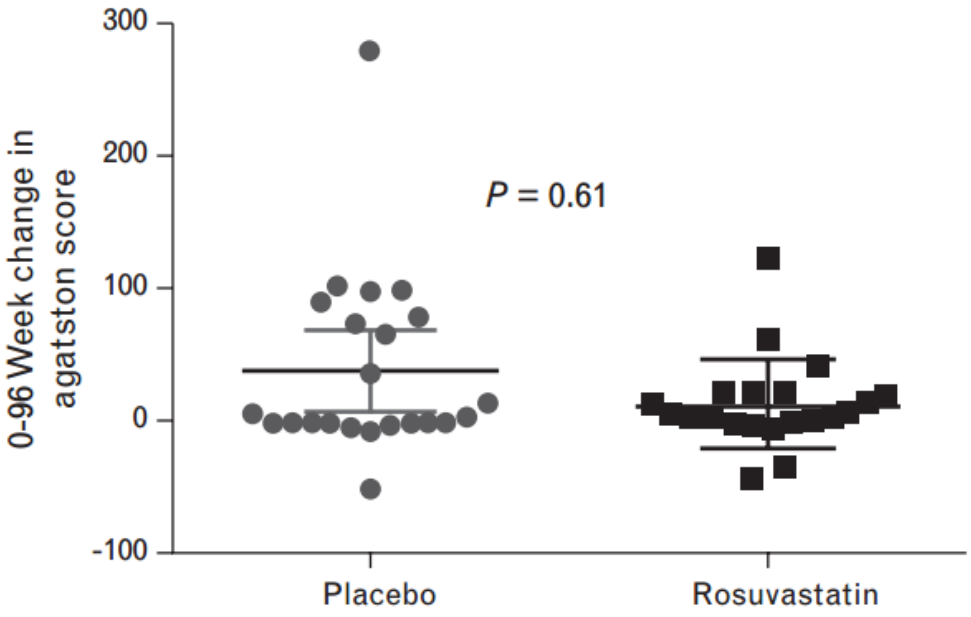
Rosuvastatin Effects on Carotid Intimal Thickness and Coronary Calcium Score

SATURN-HIV: double-blind, randomized, placebo-controlled trial of rosuvastatin 10 mg daily in HIV-positive patients (N = 147) on stable ART and LDL <130 mg/dL

0–96-week change in carotid intima–media thickness



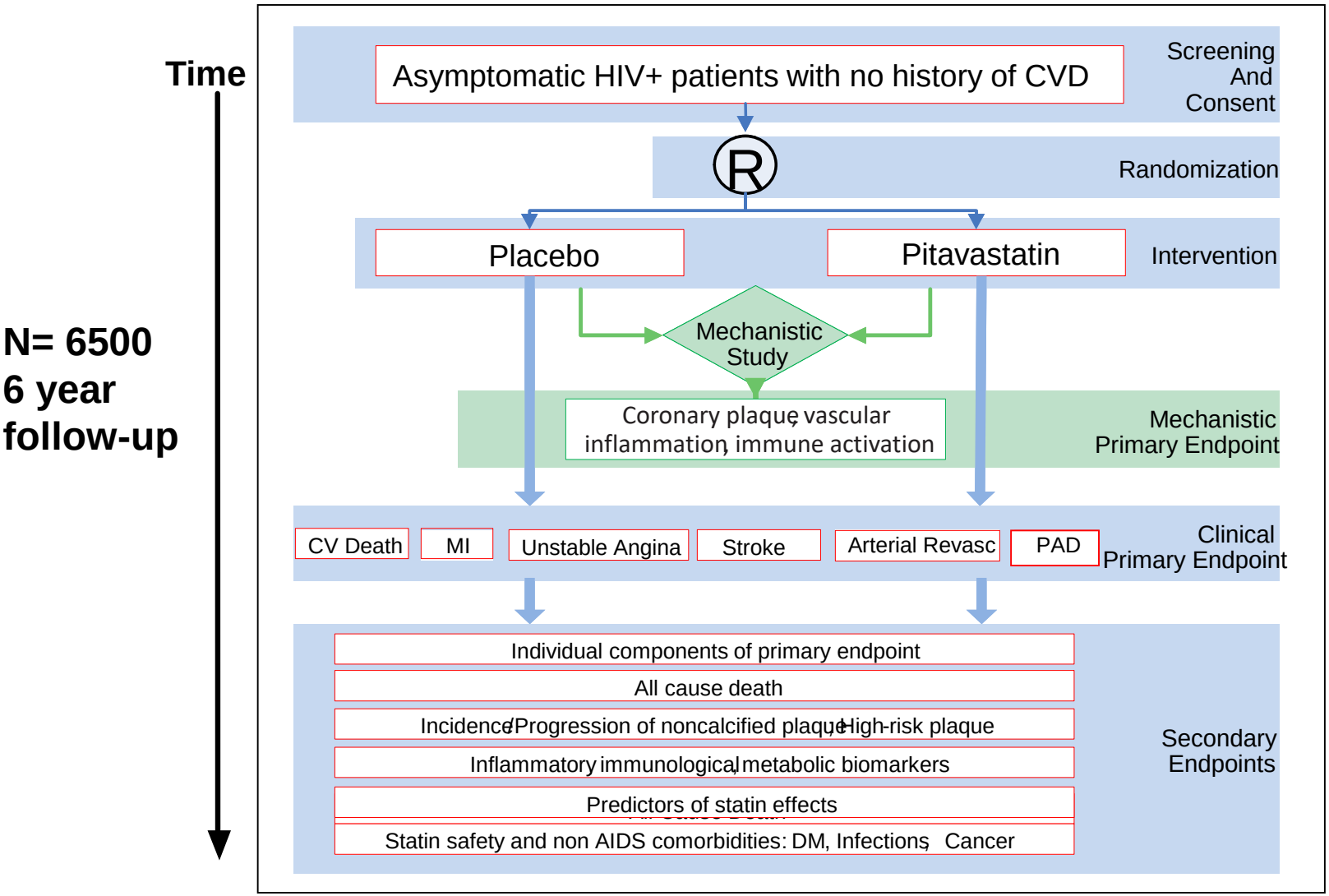
Prevalence of coronary artery calcium score



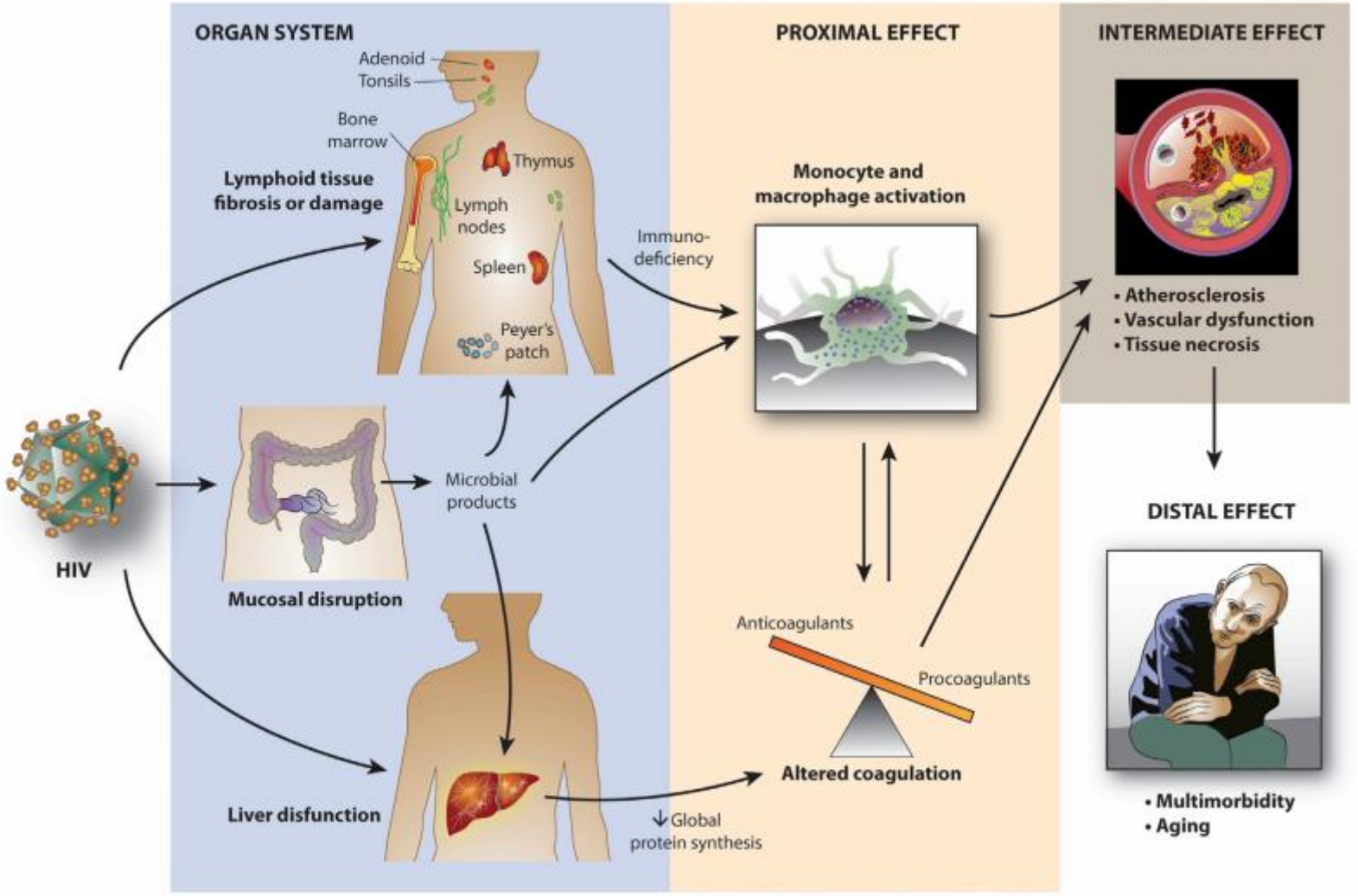
Longenecker T, et al. AIDS 2016;30:2195-2203.

Stopping **A**therosclerosis and **T**reating **U**nhealthy bone with **R**osuvastati**N** in HIV infection

REPRIEVE (A5332) Design



Pathogenesis of Inflammation-Associated Disease in HIV-Infected Adults



Deeks SG et al. Immunity 2013;39:633–45.