La gestione a lungo termine della HAART

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Emergence of Non-AIDS Comorbidities

AGING

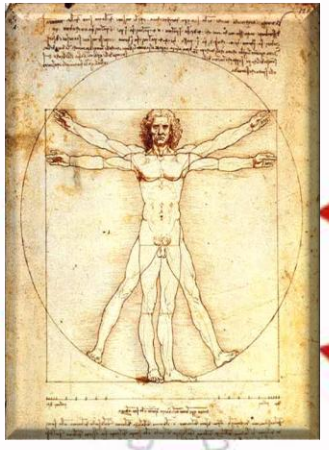
Genetics

Obesity, Exercise, Diet, Smoking

Chronic HIV Infection

ART Toxicity

HCV and other Co-infections



Decreased Physical Functioning

Inflammation & Fibrosis

Dyslipidemia

Insulin Resistance

END ORGAN DISEASE

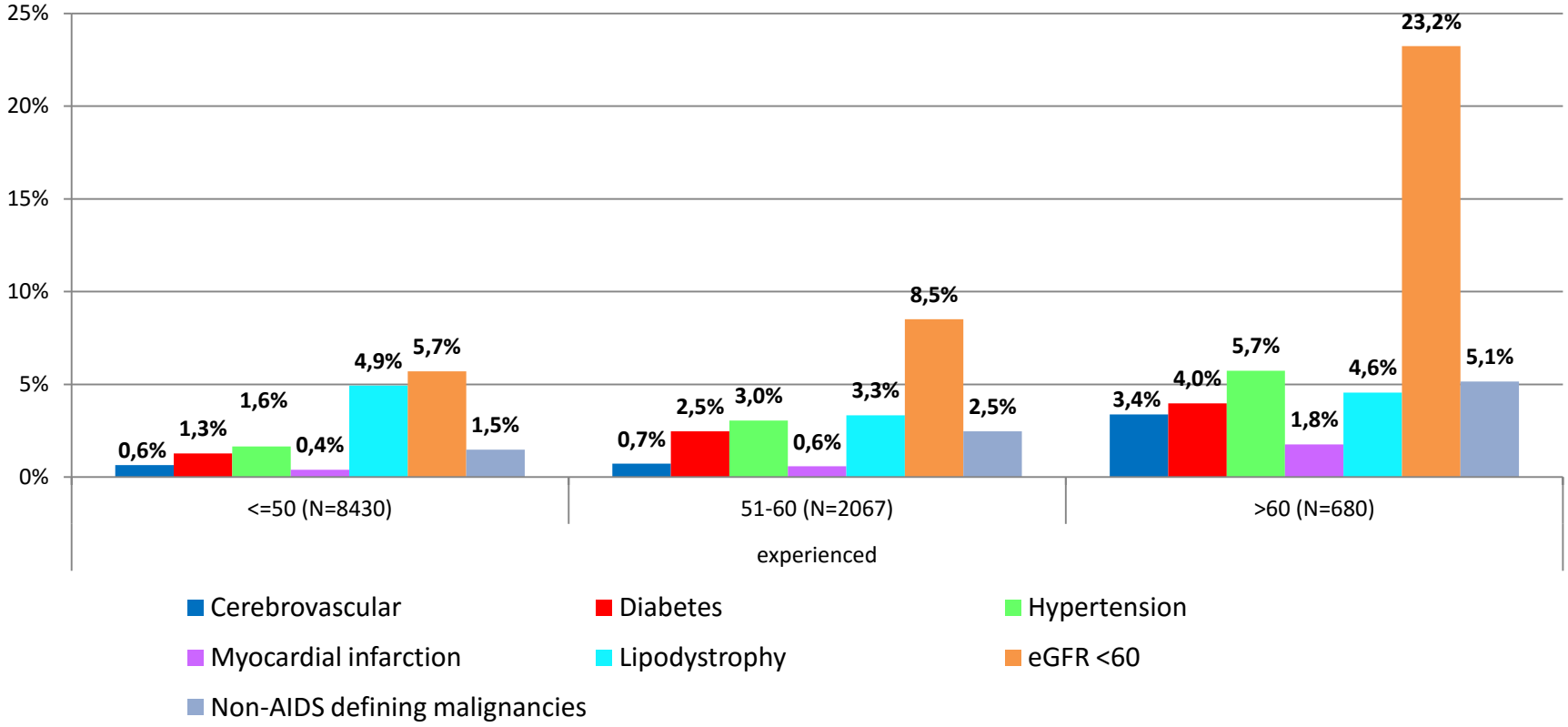




Warriner AH et al.
ID Clin N Am. 2014

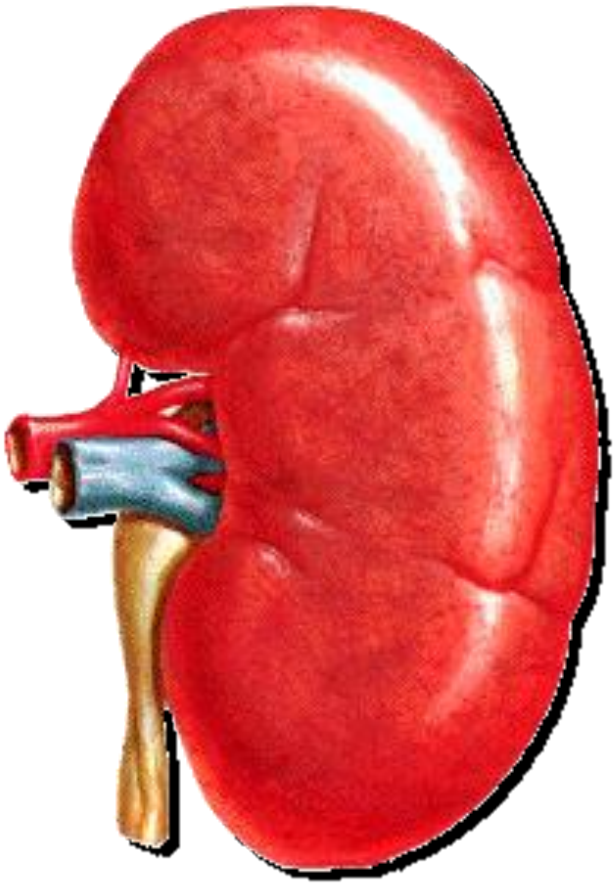
Fondazione Icona
ITALIAN COHORT NAIVE ANTIRETROVIRALS

Prevalence of different non-AIDS related co-morbidities at different age strata in ART-treated patients



Dec 2014 Report

1. Il rene

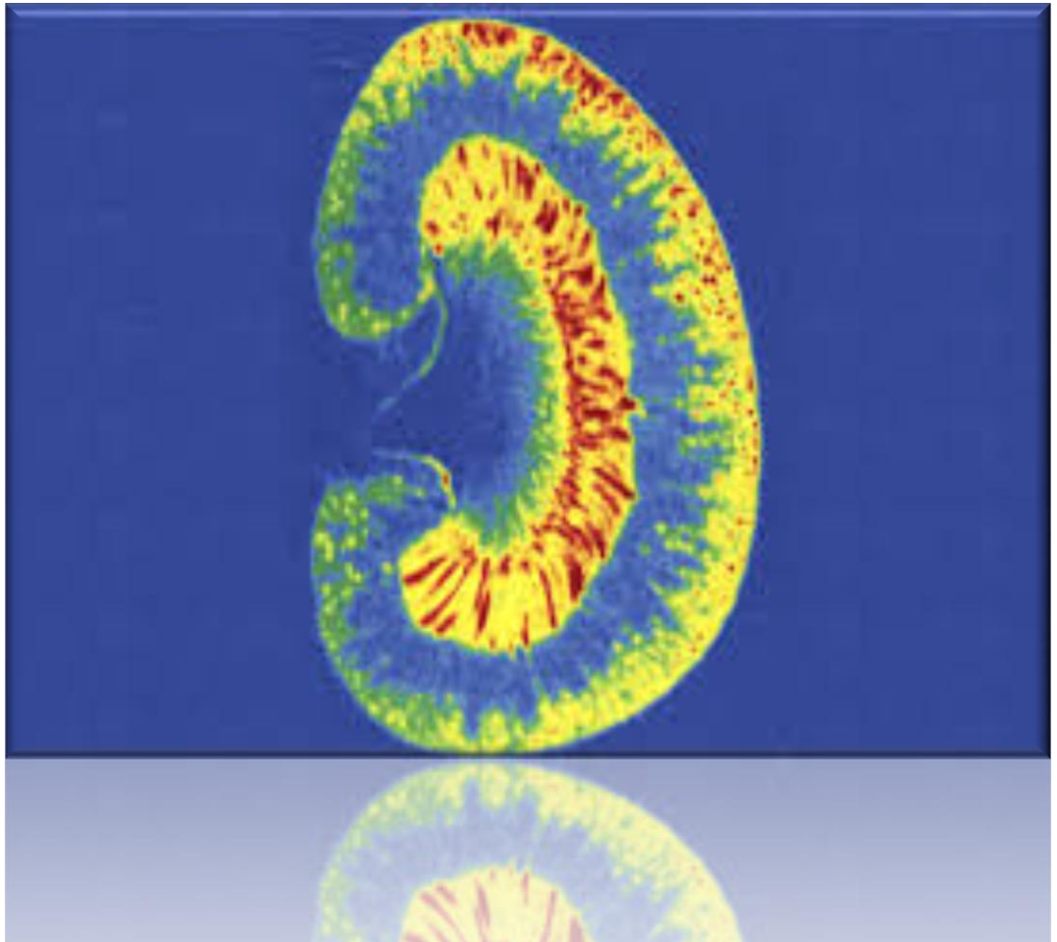


Giandomenico Tiepolo (1727-1804): Il mondo nuovo

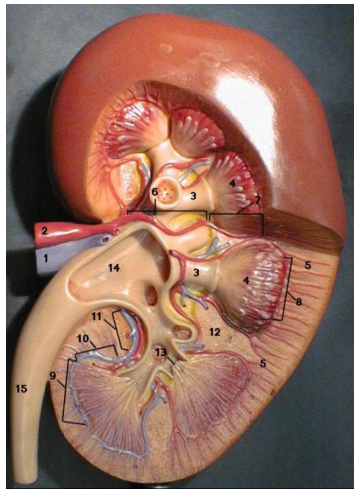

NEPHROLOGIST

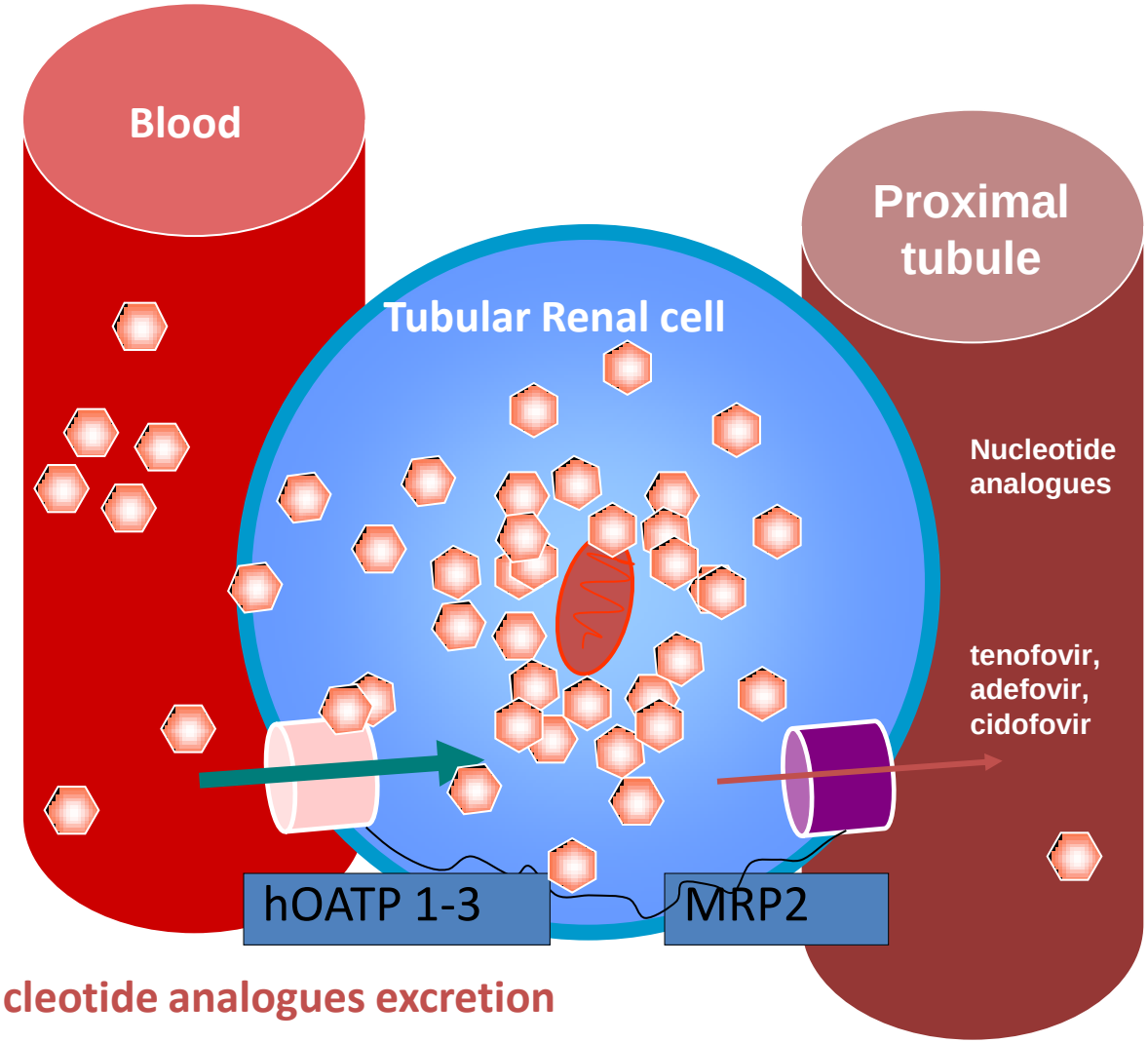
Rene 1 / 2:

- Waiting for TAF



Proposed mechanism of TDF excretion





Nucleotide analogues excretion

Animation based on Izzedine H et al., Nat Rev Nephrol. 2009;5:563-73

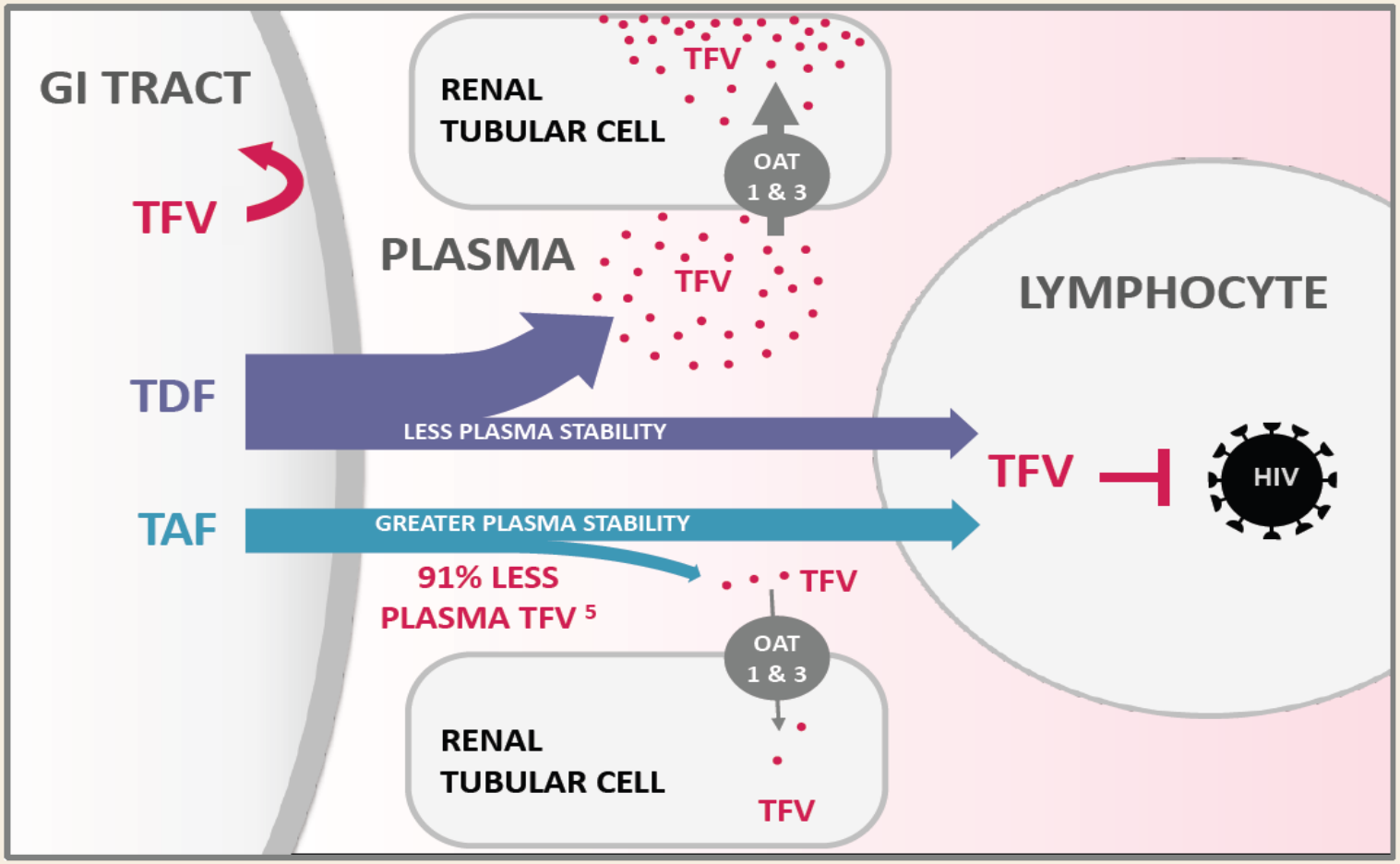
CROI 2015 BOSTON

Renal Safety of Tenofovir Alafenamide in Patients at High Risk of Kidney Disease

David Wohl[1], Anders Thalme[2], Robert Finlayson[3], Shinichi Oka[4], Thai Nguyen[5], Susan Guo[5], Andrew Cheng[5], Moupali Das[5], Marshall Fordyce[5]

[1]University of North Carolina at Chapel Hill, USA; [2]Karolinska University Hospital, Stockholm, Sweden; [3]Taylor Square Private Clinic, NSW, Australia; [4]National Center for Global Health and Medicine Hospital, Tokyo, Japan; [5]Gilead Sciences, Inc., Foster City, CA, USA

Mechanism of Action
Tenofovir Disoproxil Fumarate and Tenofovir Alafenamide



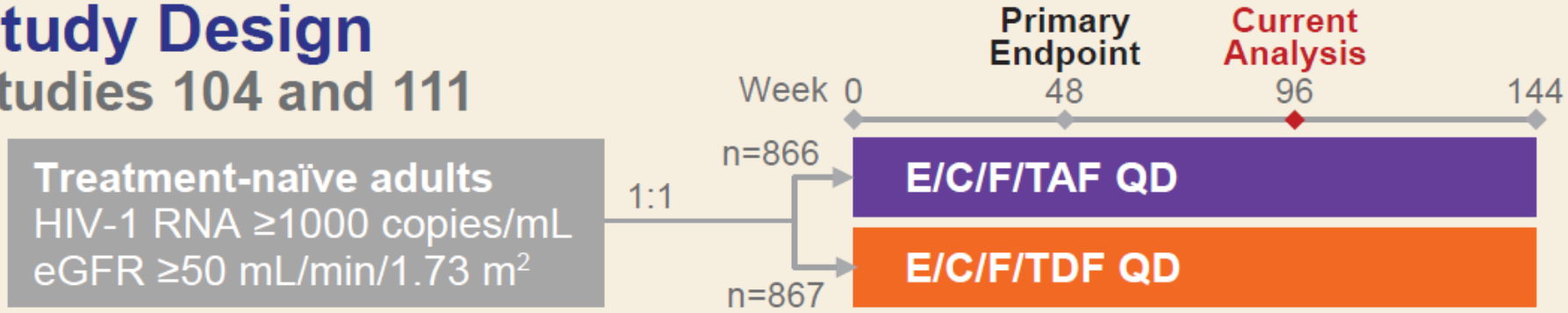
OAT, organic anion transporter; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; TFV, tenofovir.

Longer-Term Renal Safety of Tenofovir Alafenamide vs Tenofovir Disoproxil Fumarate

Bart Rijnders,[1] Frank Post,[2] Armin Rieger,[3] Eugenio Teofilo,[4] David Wohl,[5] Paul Sax,[6] Susan Guo,[7] Andrew Cheng,[7] Moupali Das,[7] Marshall Fordyce[7]

[1]Erasmus MC, Rotterdam, The Netherlands; [2]King's College London, UK; [3]Medical University of Vienna, Austria; [4]Centro Hospitalar de Lisboa Central, EPE, Lisbon, Portugal; [5]The University of North Carolina at Chapel Hill, NC; [6]Brigham and Women's Hospital, Boston, MA; [7]Gilead Sciences, Inc., Foster City, CA

Study Design
Studies 104 and 111

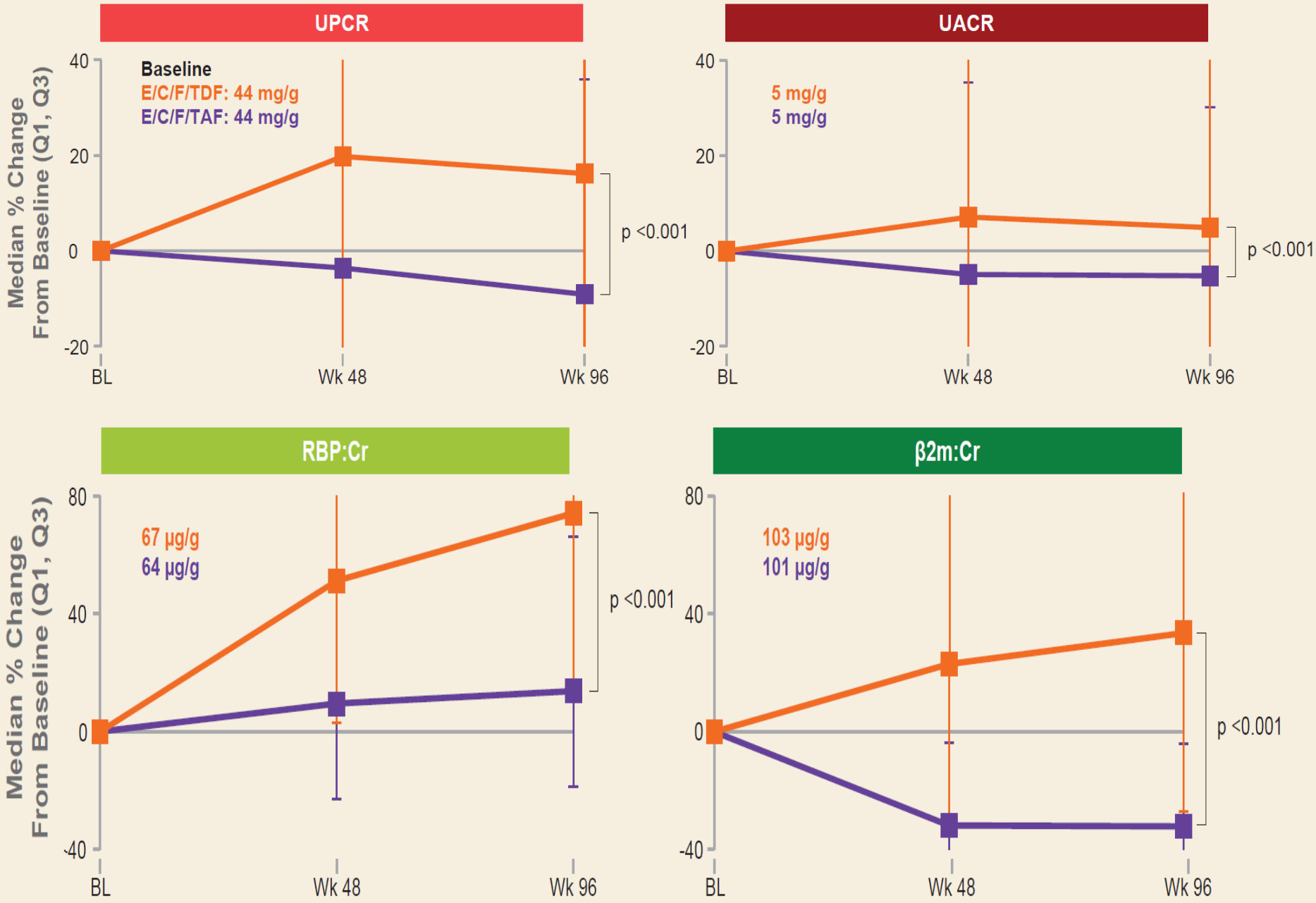


eGFR, estimated glomerular filtration rate.

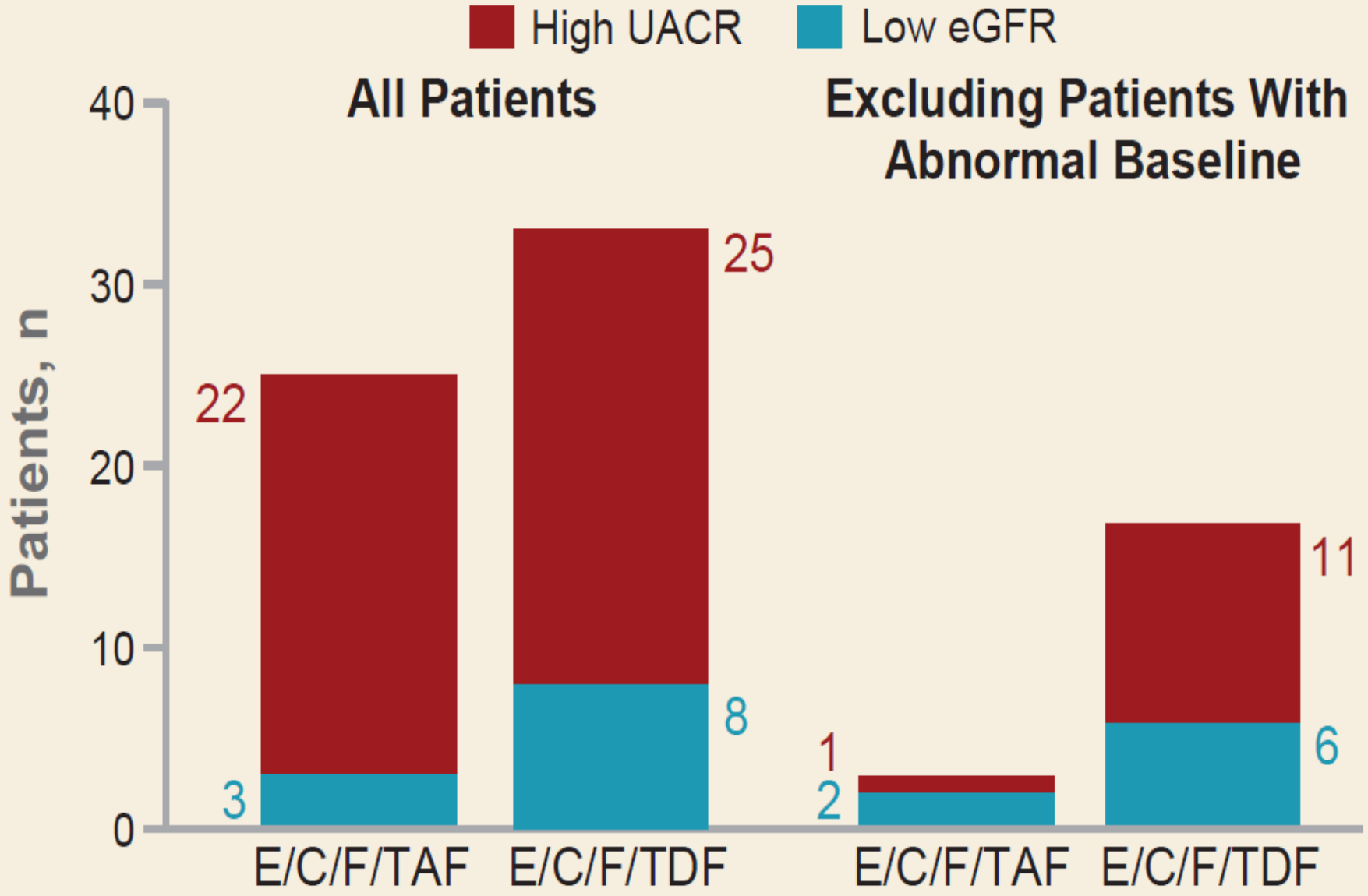
- Two Phase 3 randomized, double-blind, double-dummy, active-controlled studies
  - Study 104 (North America, European Union, Asia; NCT01780506)
  - Study 111 (North America, European Union, Latin America; NCT01797445)
  - Patients stratified by HIV-1 RNA, CD4 cell count, and geographic region
- Treatment-naïve HIV-1–infected adults with eGFR ≥50 mL/min/1.73 m² were randomized 1:1 to a single-tablet regimen of E/C/F/TAF or E/C/F/TDF
- Renal function assessments included serum creatinine (SCr) and eGFR by Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI)
- Measures of proteinuria were assessed at baseline and throughout the study

Quantitative Proteinuria	Urine albumin:creatinine ratio (UACR)
	Urine protein:creatinine ratio (UPCR)
Tubular Proteinuria	Urine retinol-binding protein:creatinine ratio (RBP:Cr)
	Urine β2-microglobulin:creatinine ratio (β2m:Cr)

Changes in Proteinuria Through Week 96

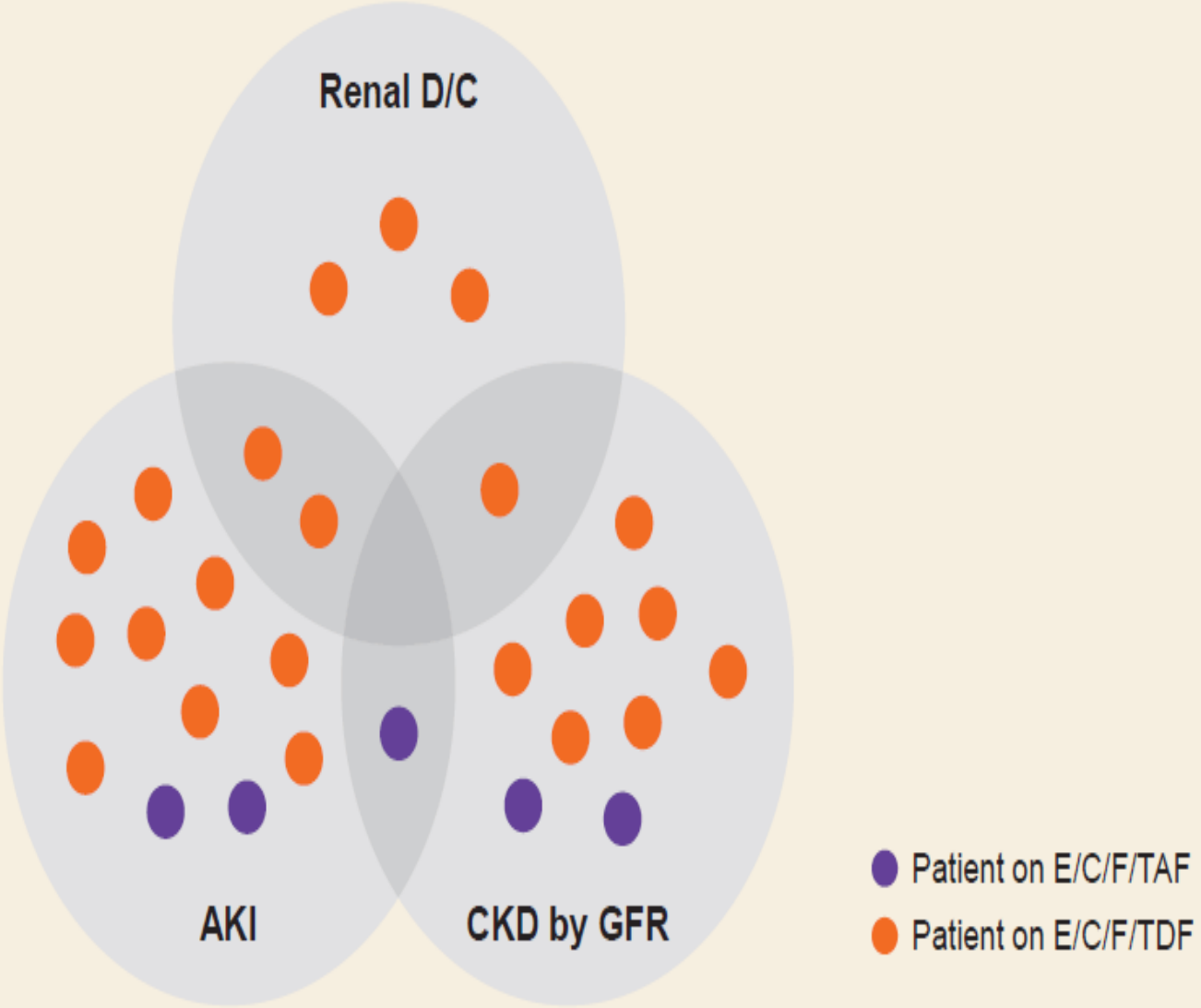


New-Onset Chronic Kidney Disease*



*UACR >30 mg/g or eGFR <60 mL/min/1.73 m^2 for ≥90 days.

Patients With Renal Events



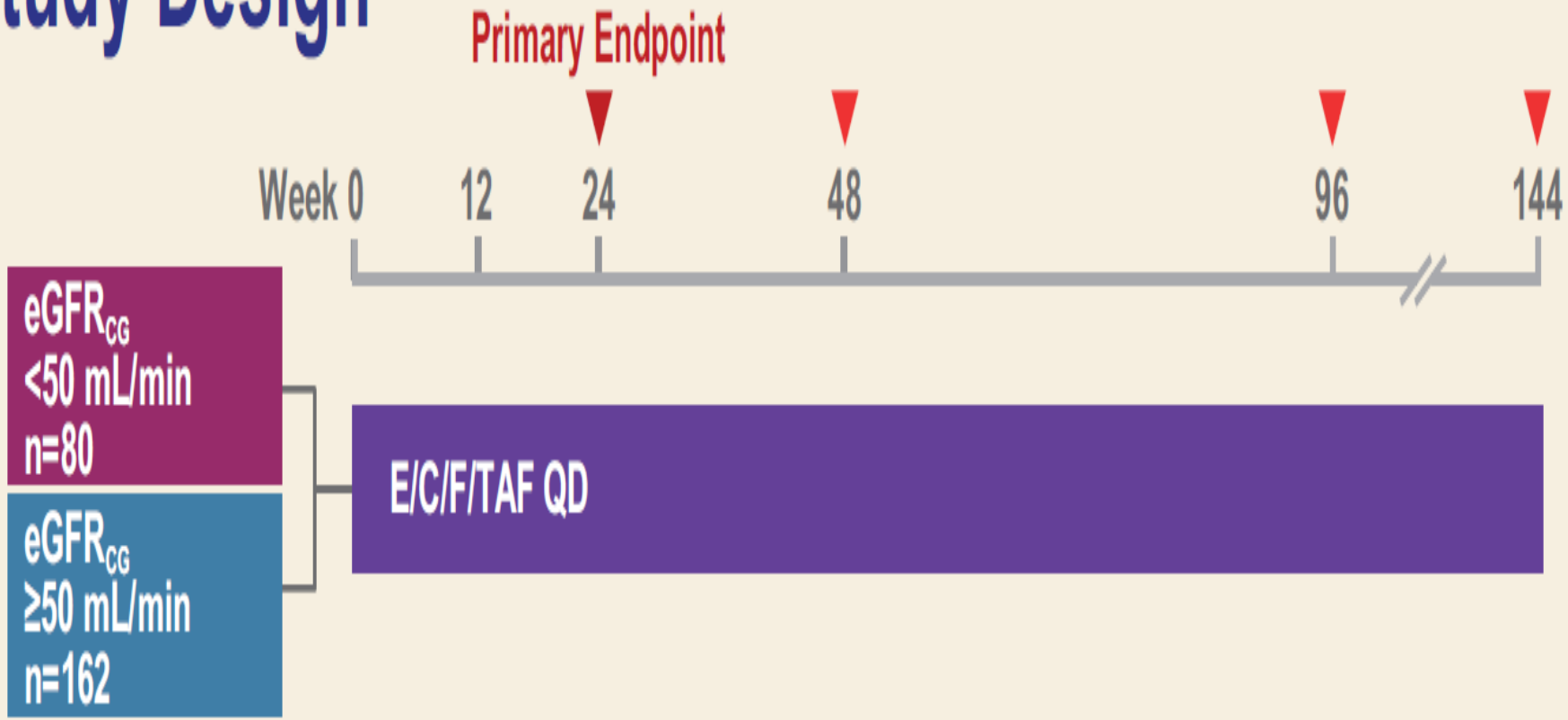
AKI, acute kidney injury; CKD, chronic kidney disease; D/C, discontinuation.

Longer-Term Safety of Tenofovir Alafenamide in Renal Impairment

Frank A. Post,[1] Pablo Tebas,[2] Amanda Clarke,[3] Laurent Cotte,[4] William Short,[2] Michael E. Abram,[5] Shuping Jiang,[5] Andrew Cheng,[5] Moupali Das,[5] Marshall W. Fordyce[5]

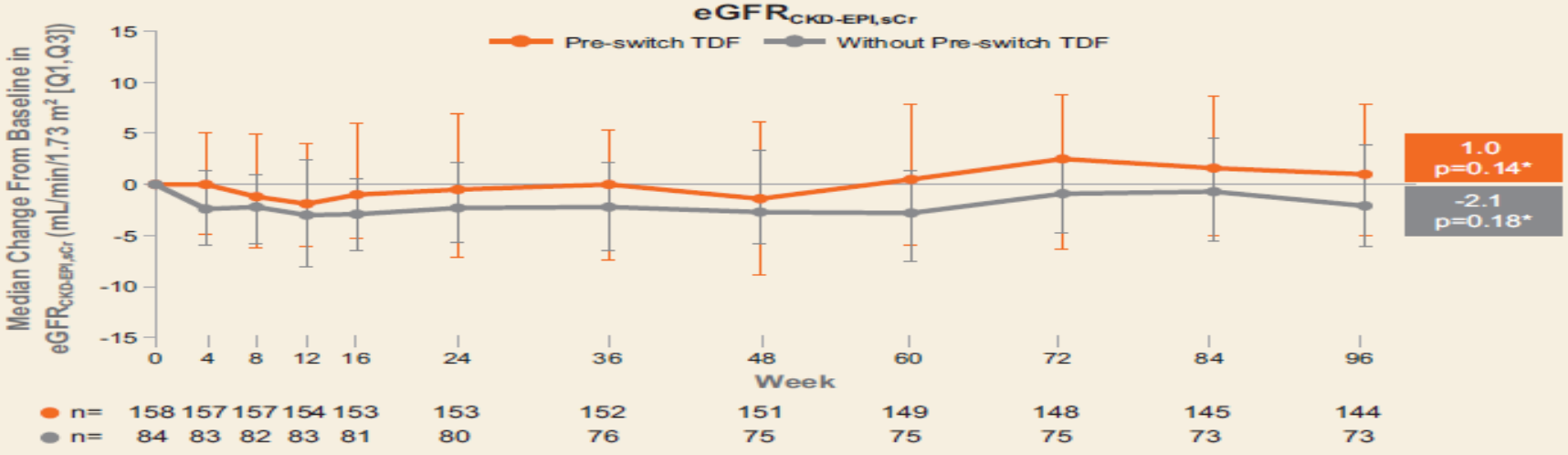
[1]King's College Hospital NHS Foundation Trust, London, UK; [2]University of Pennsylvania, Philadelphia, PA; [3]Brighton and Sussex University Hospitals NHS Trust, Brighton, UK; [4]Croix-Rousse Hospital, Hospices Civils de Lyon, France; [5]Gilead Sciences, Inc., Foster City, CA

Study Design

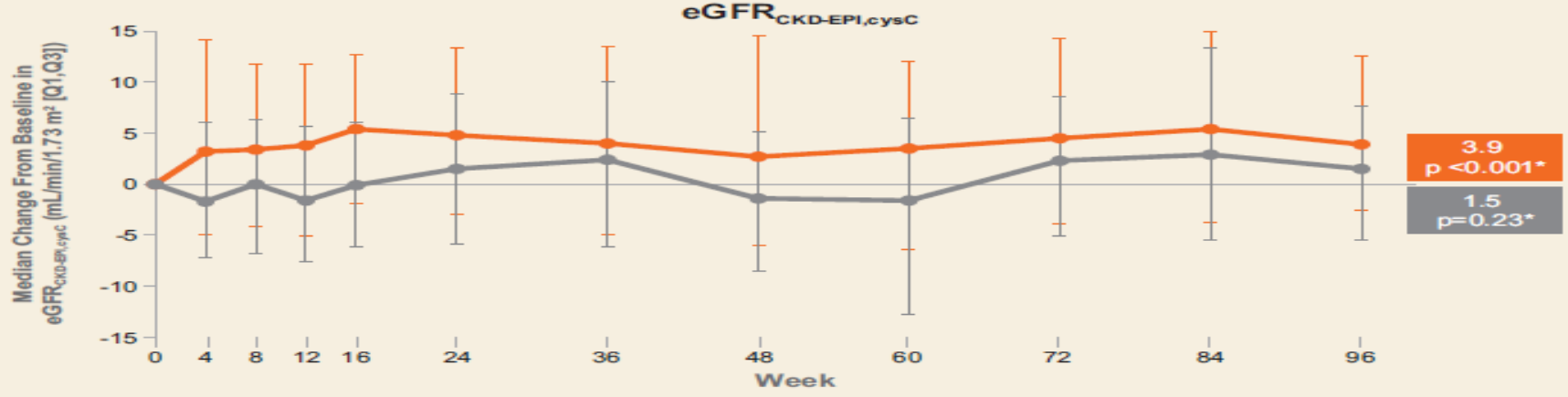


QD, once daily.

Estimated GFR: Changes Over Time



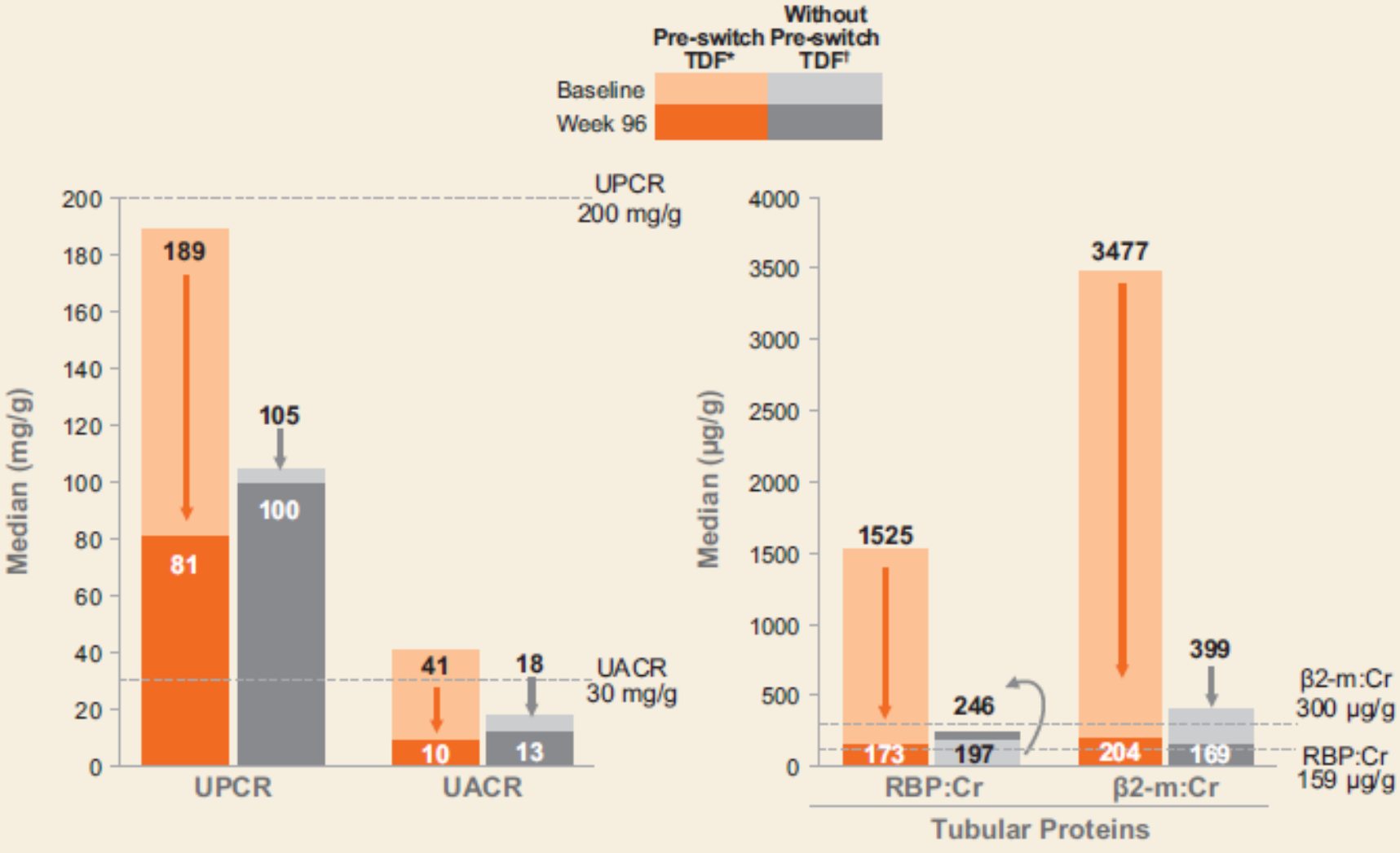
Median, mL/min/1.73 m² (Q1, Q3)	Baseline	Week 96
Pre-switch TDF	55.8 (48.9, 64.6)	58.3 (51.6, 67.5)
Without Pre-switch TDF	50.2 (39.9, 55.8)	49.7 (40.9, 55.5)



Median, mL/min/1.73 m² (Q1, Q3)	Baseline	Week 96
Pre-switch TDF	75.4 (60.9, 86.2)	80.1 (65.8, 95.7)
Without Pre-switch TDF	60.4 (47.7, 75.0)	62.3 (50.4, 77.9)

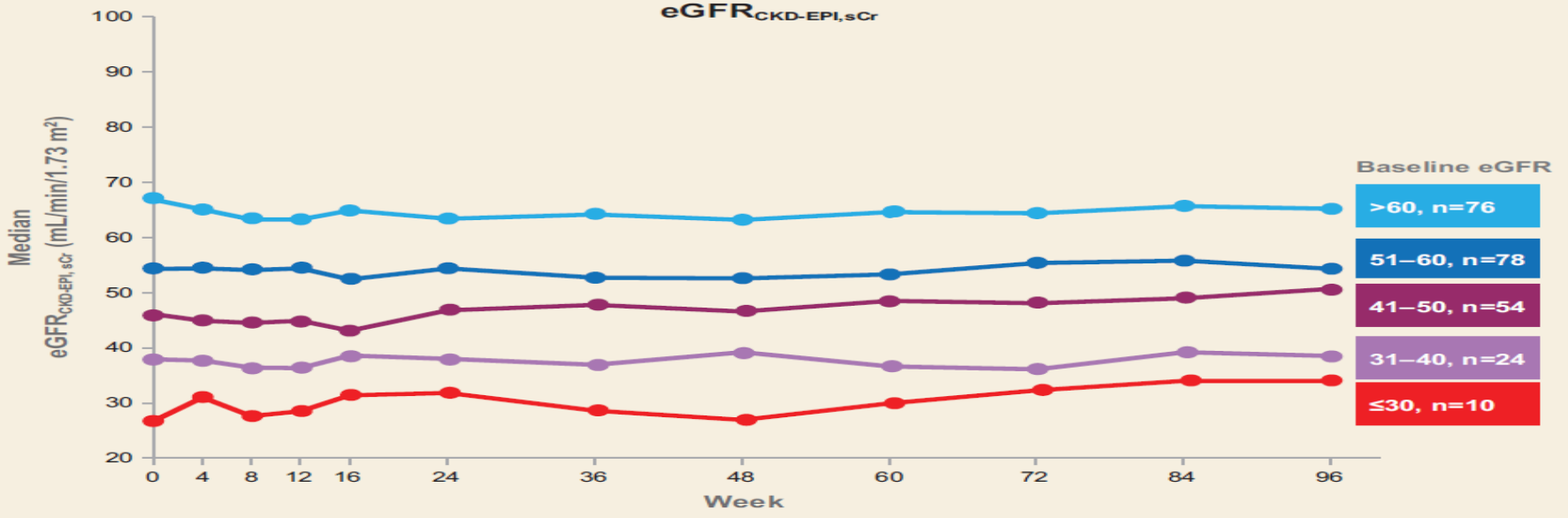
*P-values for differences between baseline and Week 96 based on the two-sided Wilcoxon signed-rank test.

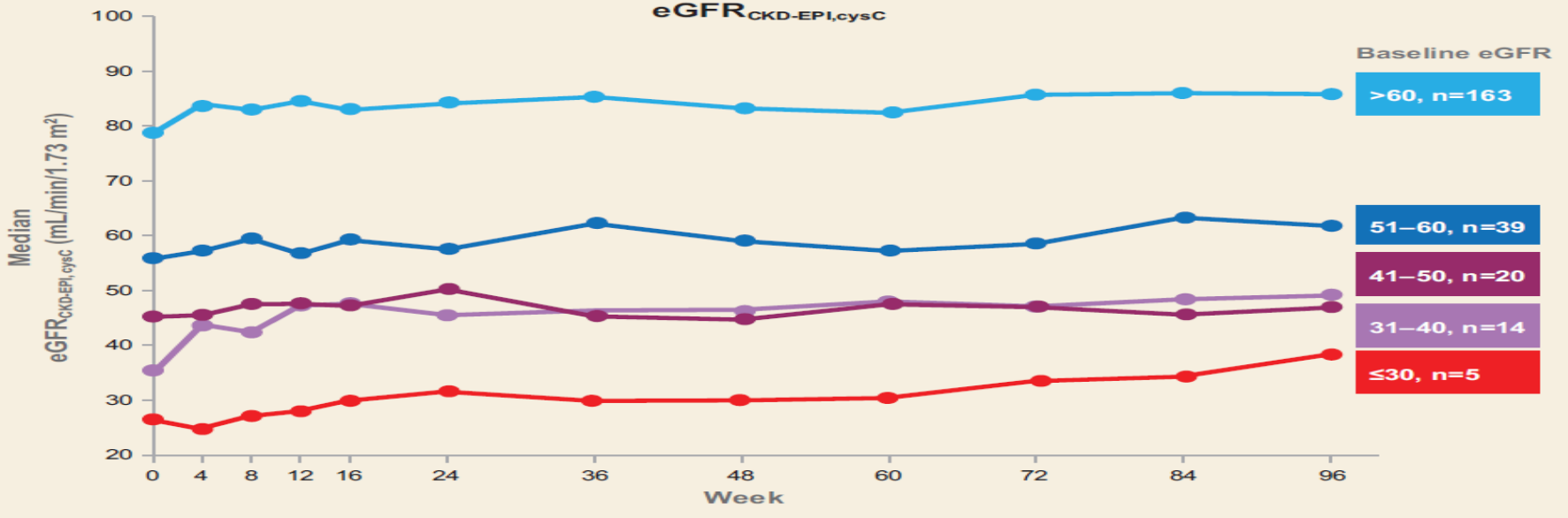
Renal Biomarkers: Changes From Baseline to Week 96



*All changes statistically significant; †all changes not statistically significant with exception of β2-microglobulin (β2-m):Cr. RBP, retinol-binding protein.

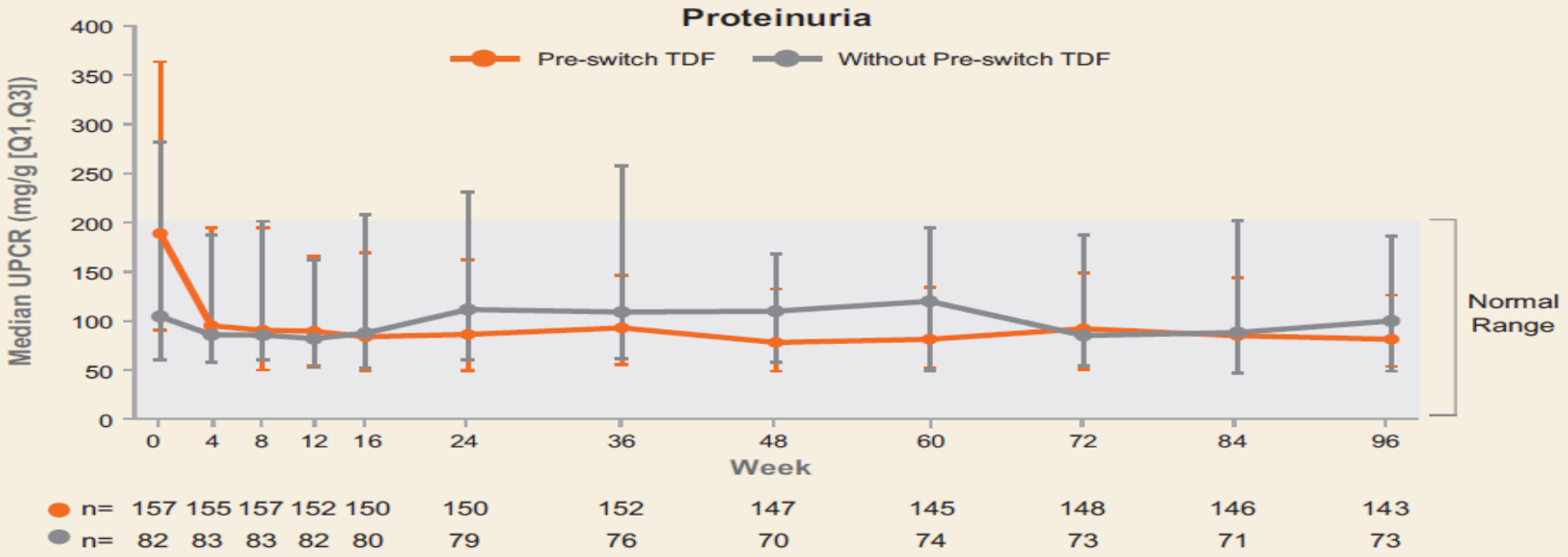
Changes in eGFR by Baseline eGFR Strata

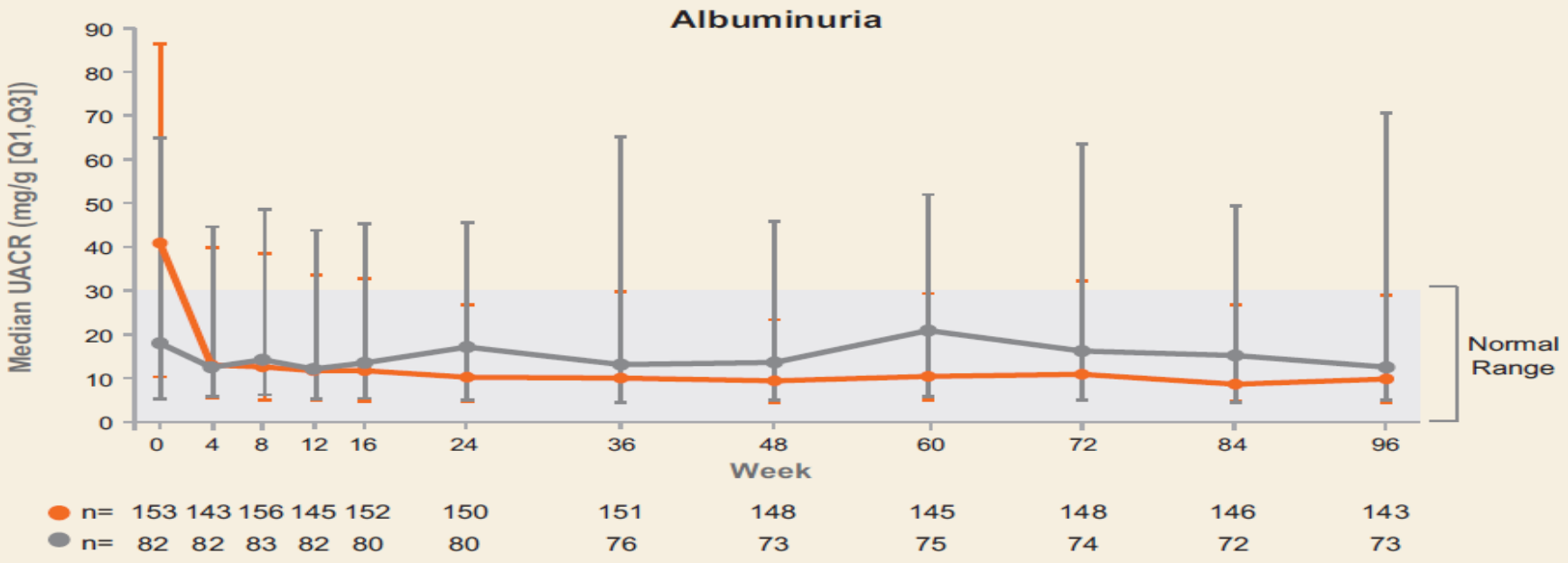




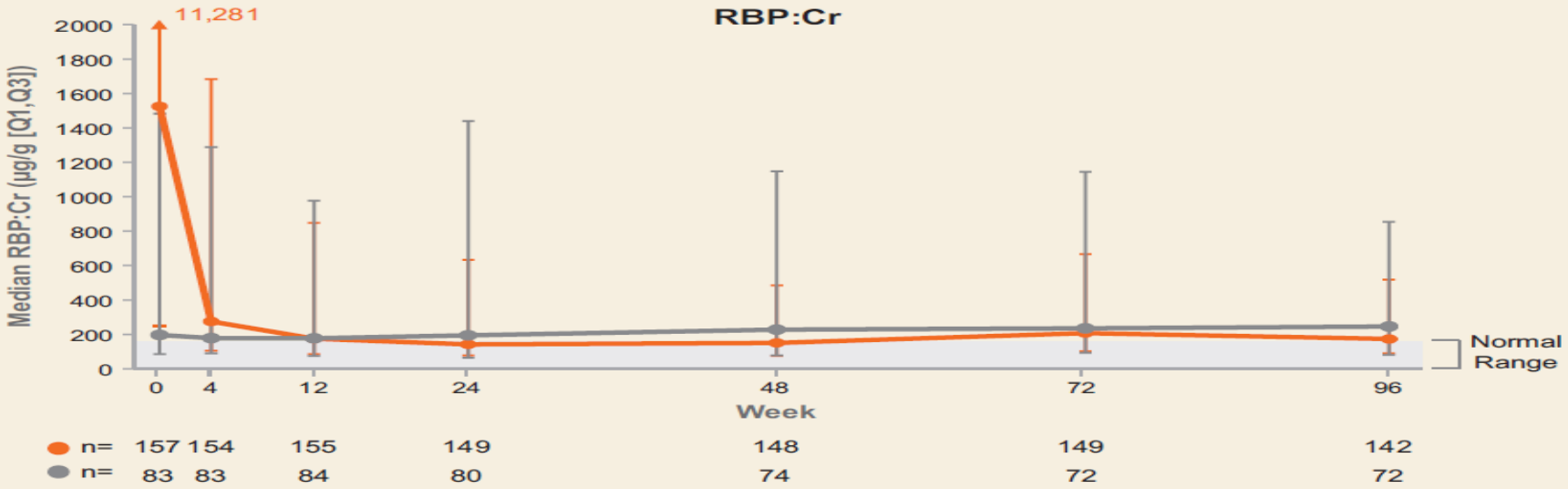
One patient was excluded due to missing cysC data at baseline.

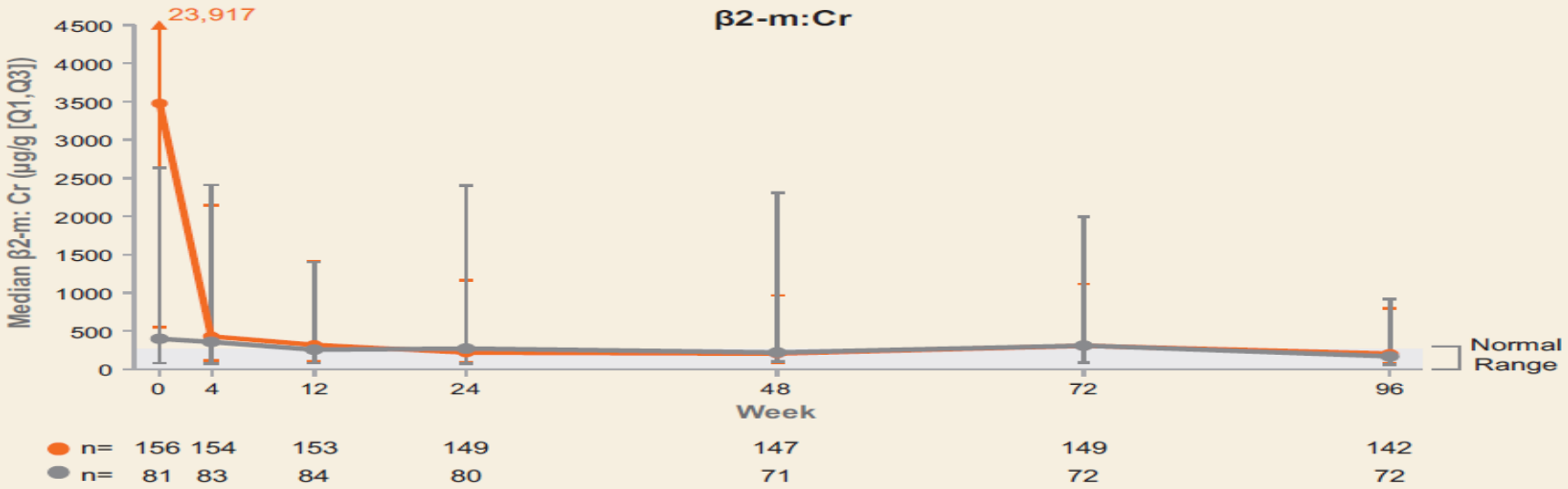
Renal Biomarkers: Changes Over Time





Renal Biomarkers: Changes Over Time





Classic risk factors:

Genetic

age

high blood pressure

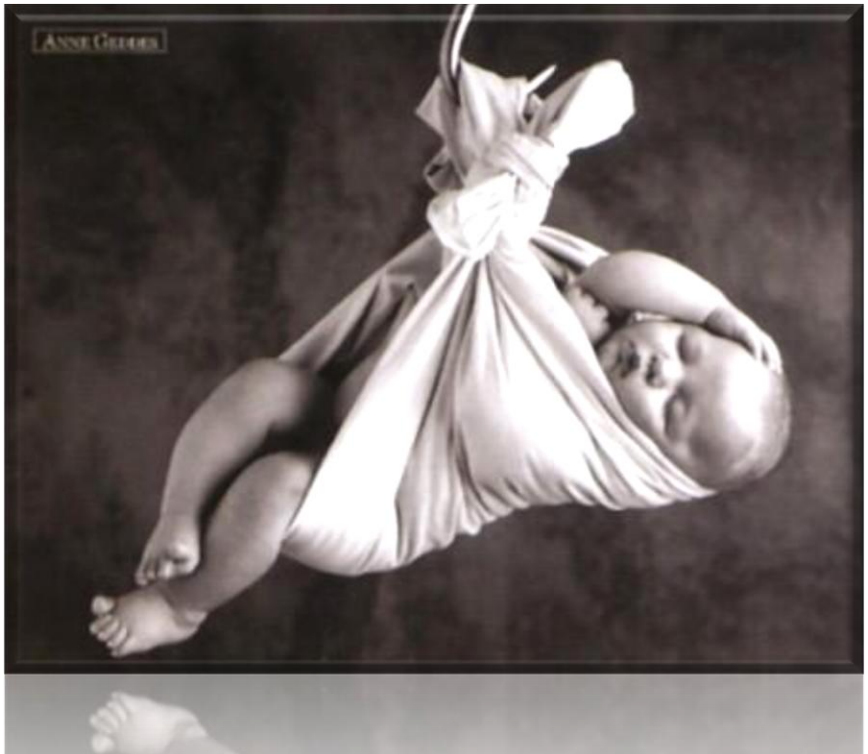
diabetes

Virus

Drugs

Rene 2 / 2:

- I nuovi nati (dolutegravir, cobicistat, rilpivirina)

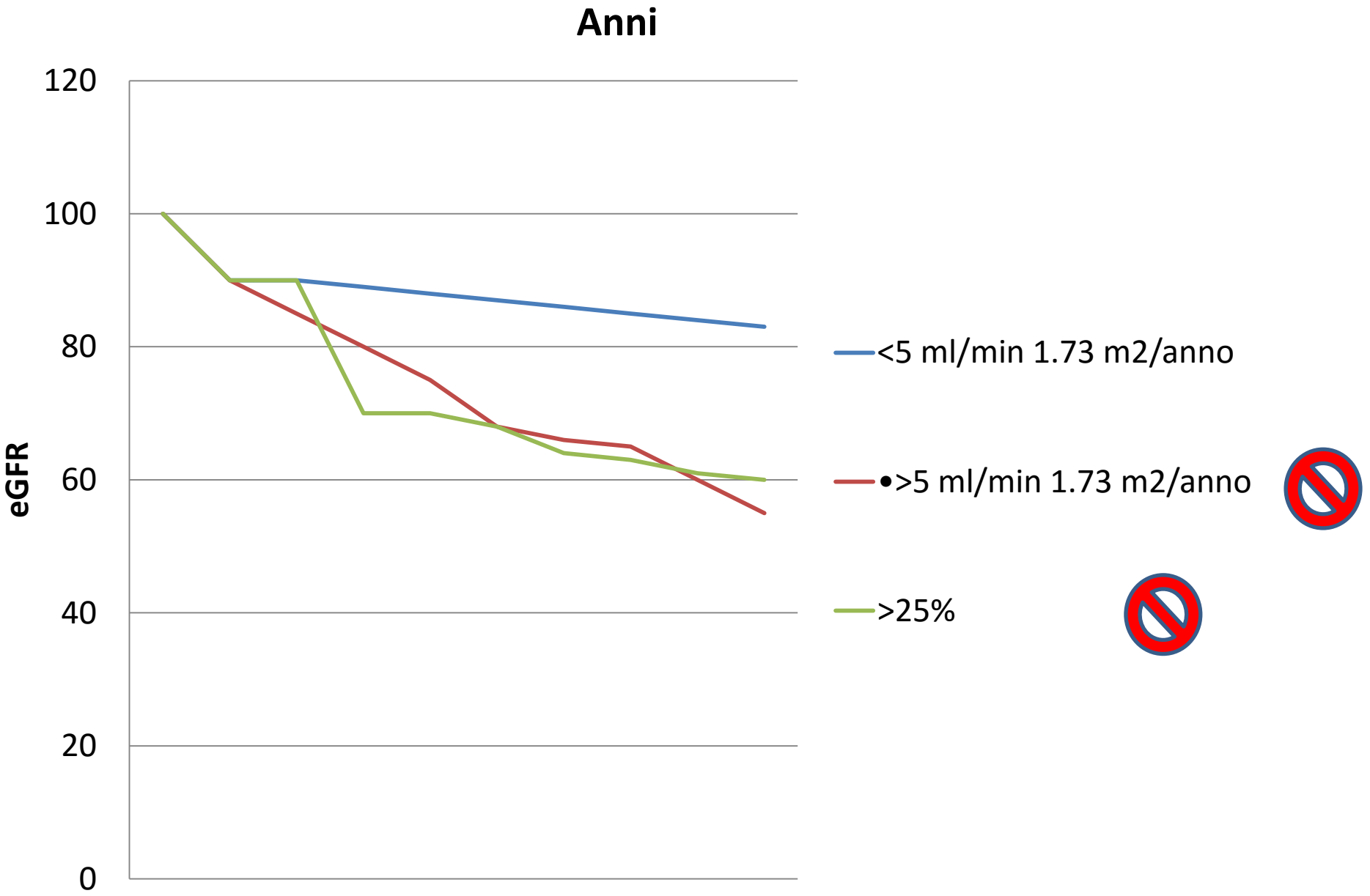


COBI Inhibits Active Tubular Secretion of Creatinine, Resulting in Increased SCr[1,2]

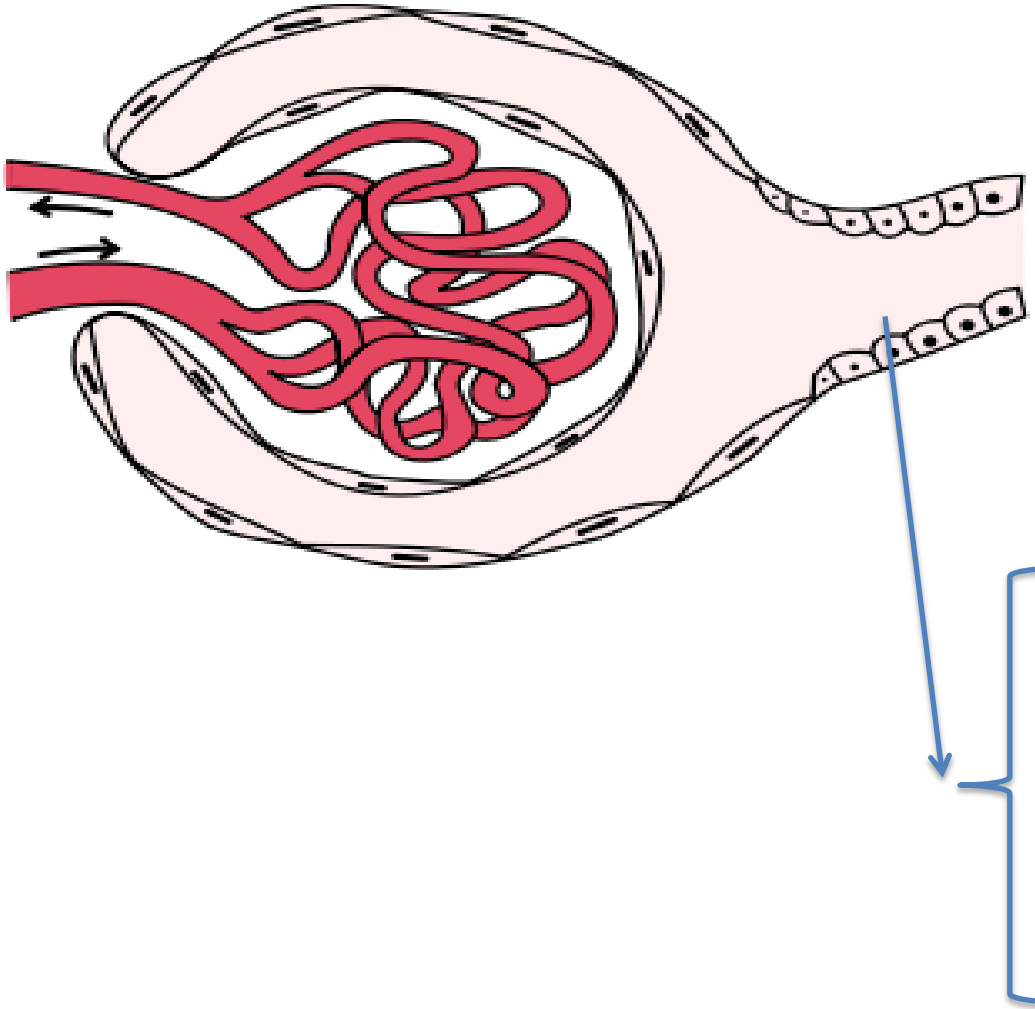
- Preclinical studies indicate that COBI blocks a transport pathway used for creatinine secretion from the proximal tubule by inhibiting a transport protein called MATE1 that is responsible for transporting creatinine into the proximal tubule[1-3]
- Other drugs have been reported to block tubular secretion of creatinine, such as ritonavir, cimetidine, and trimethoprim[4-6]

For illustrative purposes only.

[1] Lepist EI, et al. ICAAC 2011. Abstract A1-1724; [2] German P, et al. J Acquir Immune Defic Syndr. 2012;61:32-40; [3] Lepist EI, Ray AS. Expert Opin Drug Metab Toxicol. 2012;8:433-448; [4] Cohen C, et al. CROI 2010. San Francisco, CA. 58LB; [5] Andreev E, et al. J Intern Med. 1999;246:247-252; [6] Naderer O, et al. Antimicrob Agents Chemother. 1997;41:2466-2470.


Anni
120
100
80
60
40
20
0
eGFR
<5 ml/min 1.73 m2/anno
•>5 ml/min 1.73 m2/anno
>25%

Solo due parole sull'osso…



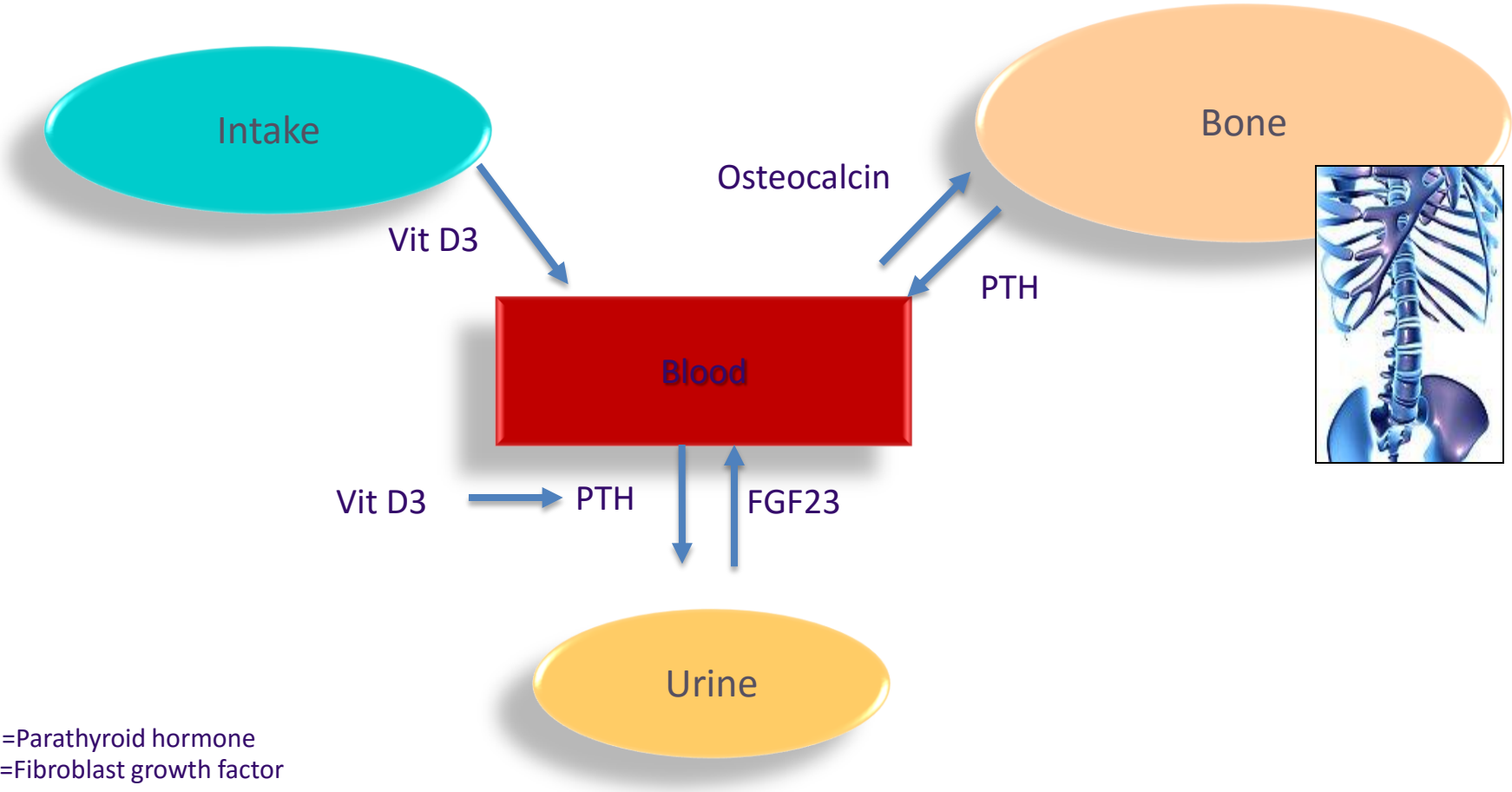
proteine a basso pm

fosforo

glucosio

acido urico

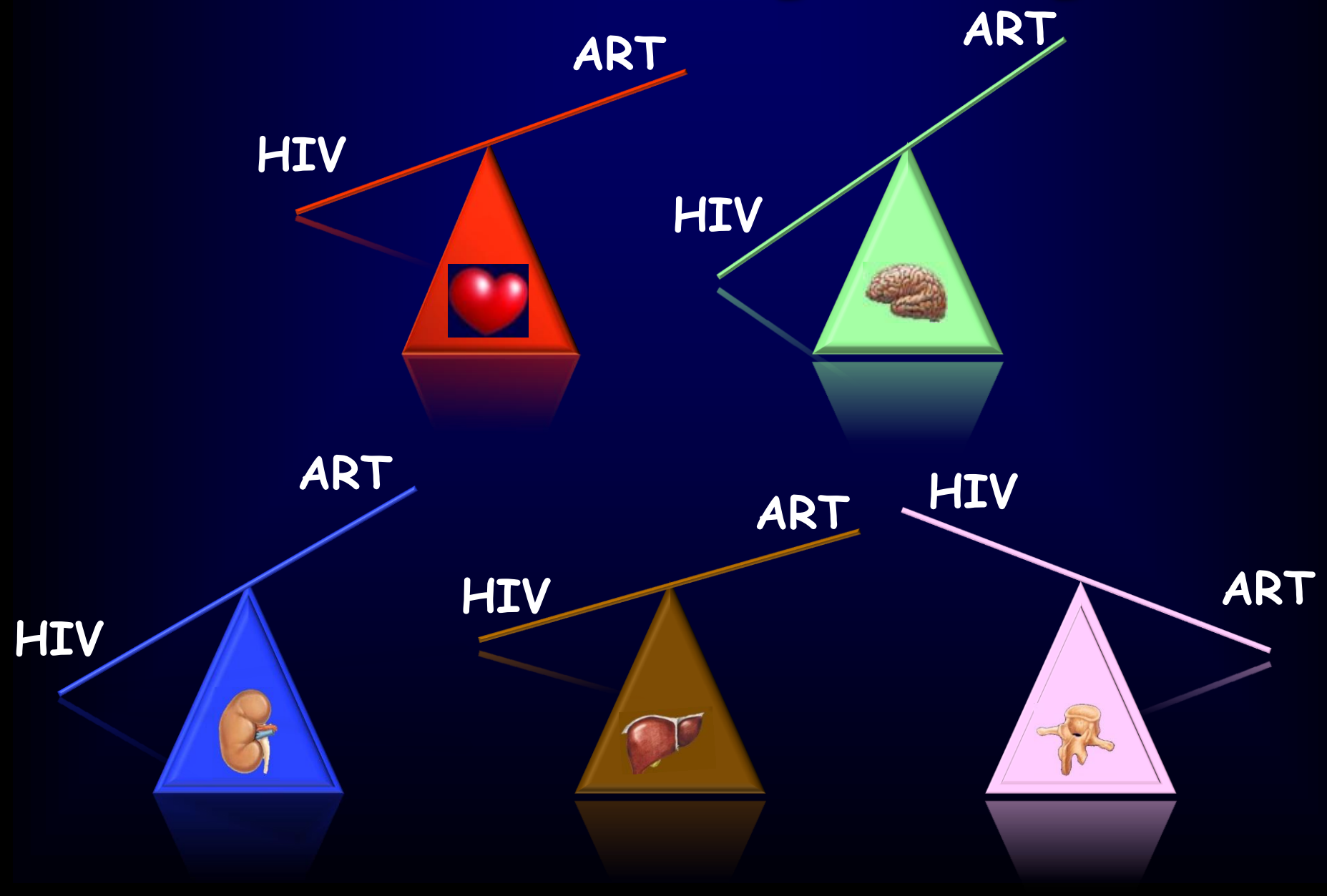
Tubular lesions can be associated with Phosphaturia



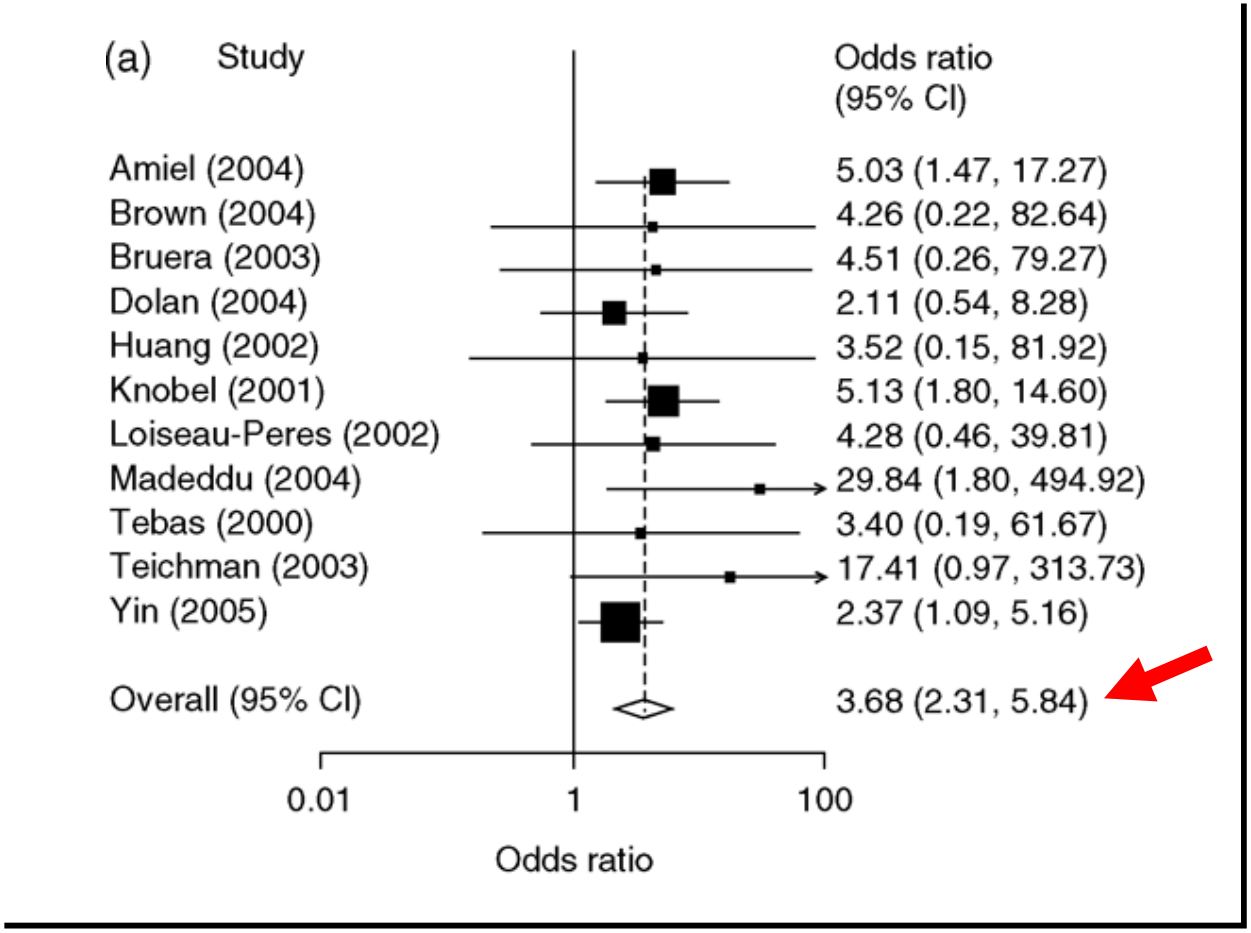
PTH=Parathyroid hormone
FGF=Fibroblast growth factor

Essig M, et al. *J Acquir Immune Defi Syndr.* 2007;46:256–8

HIV, ART and organ damage

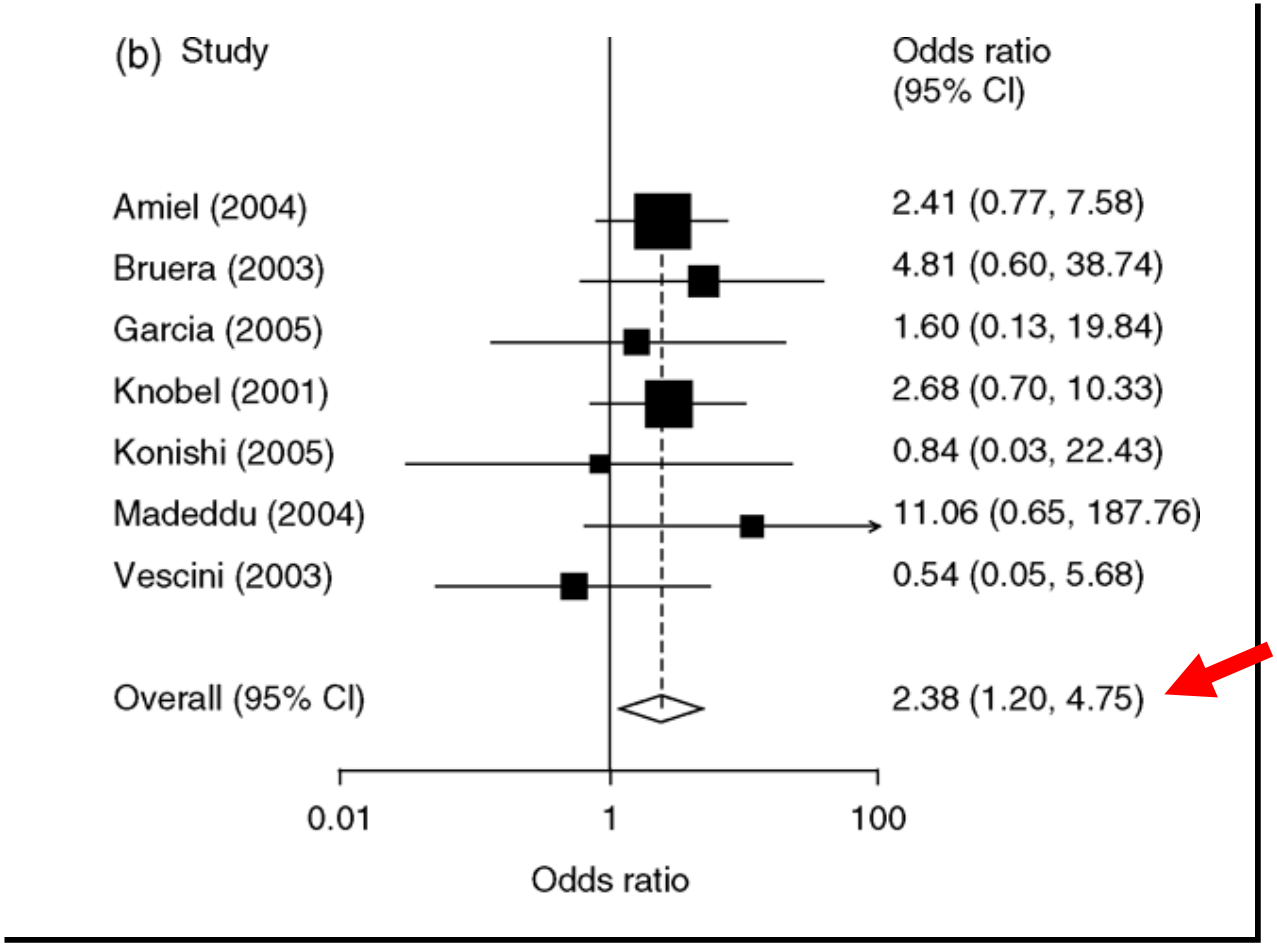


Odds of osteoporosis: HIV+ vs. HIV-



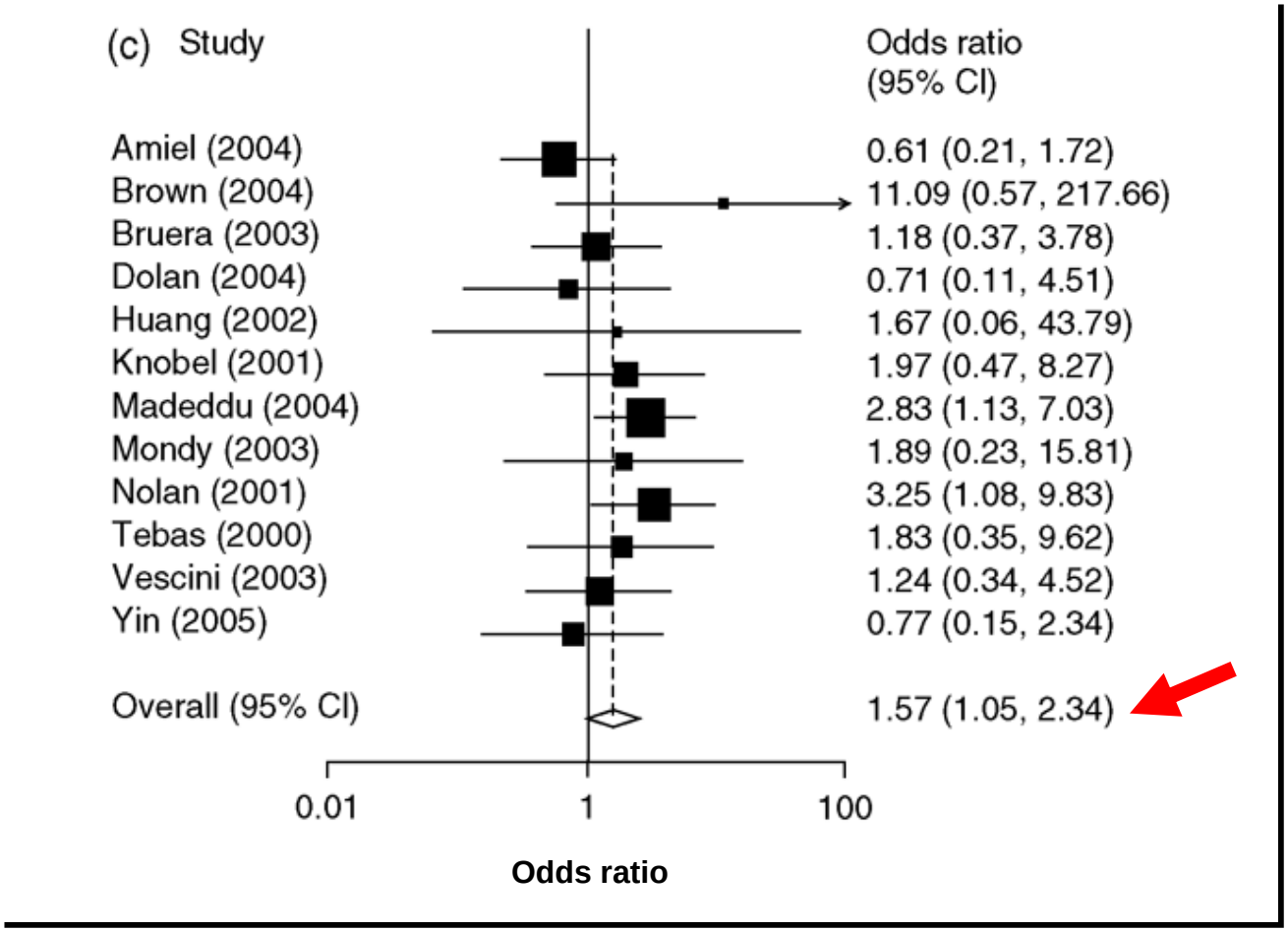
Brown and Qaqish. AIDS 2006;20:2165-74

Odds of osteoporosis in HIV-infected patients on ART compared with ART-naïve patients



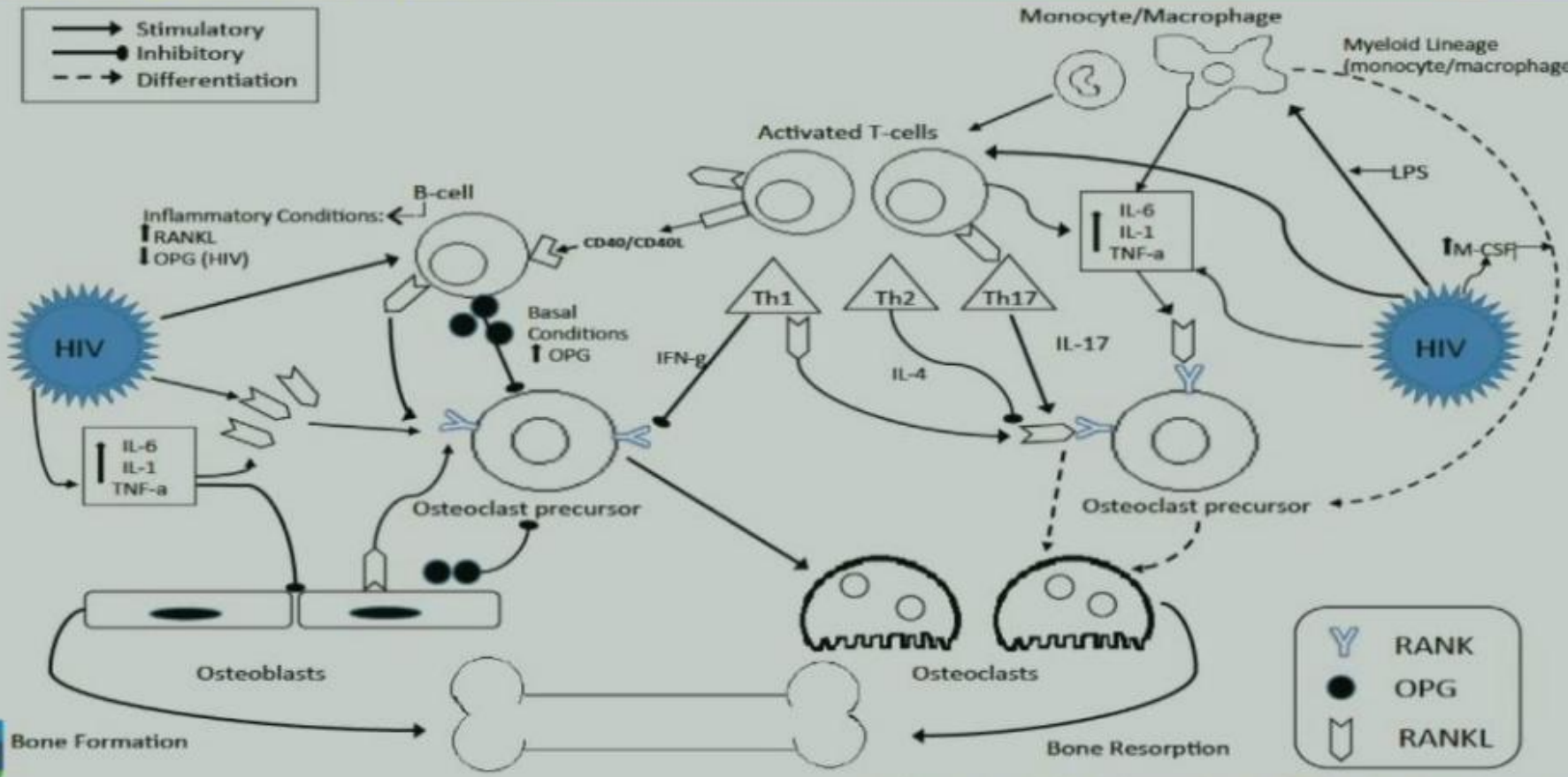
Brown and Qaqish. AIDS 2006;20:2165-74

Odds of osteoporosis in HIV-infected patients on PIs



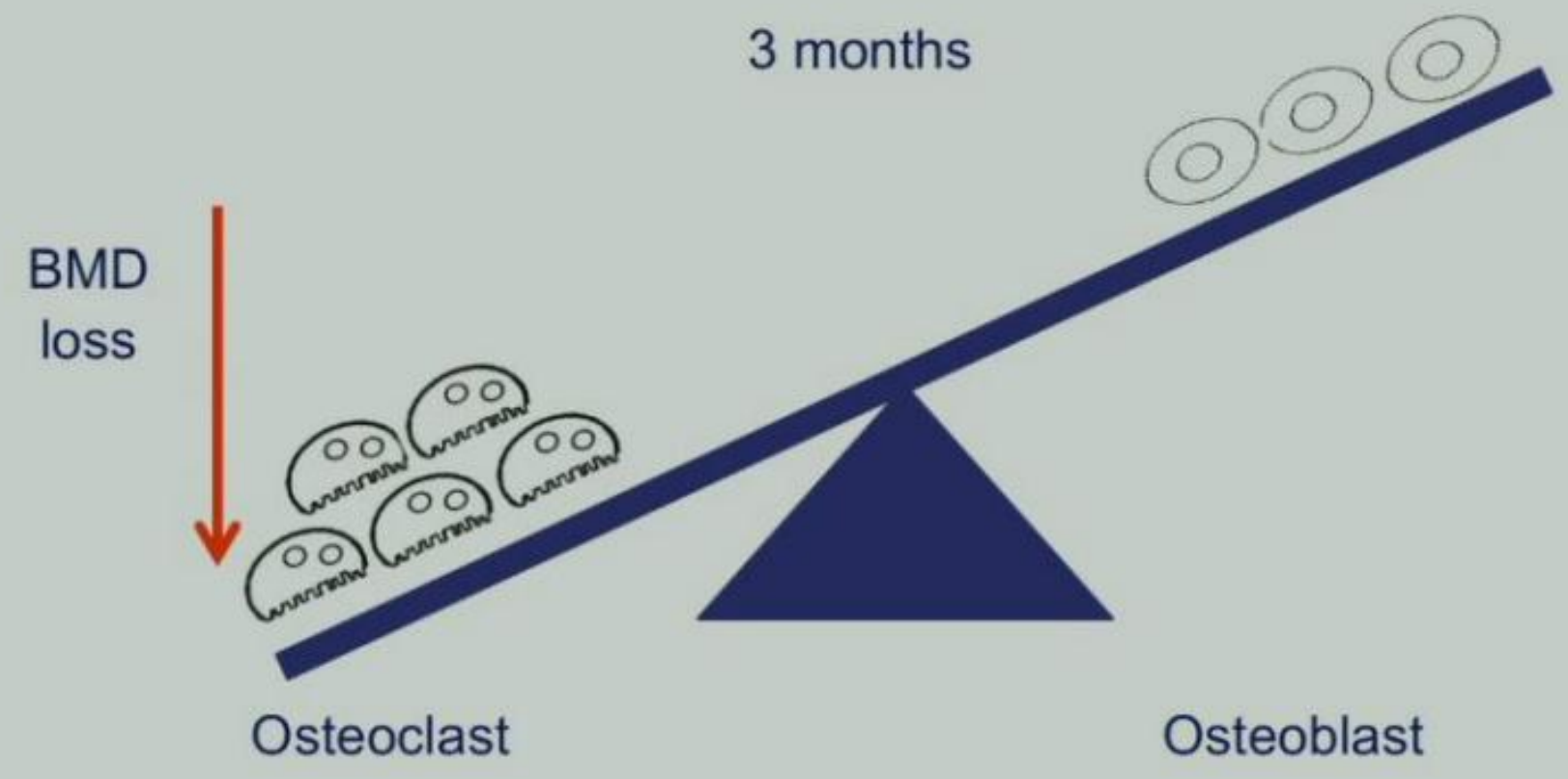
Brown and Qaqish. AIDS 2006;20:2165-74

How little we know……

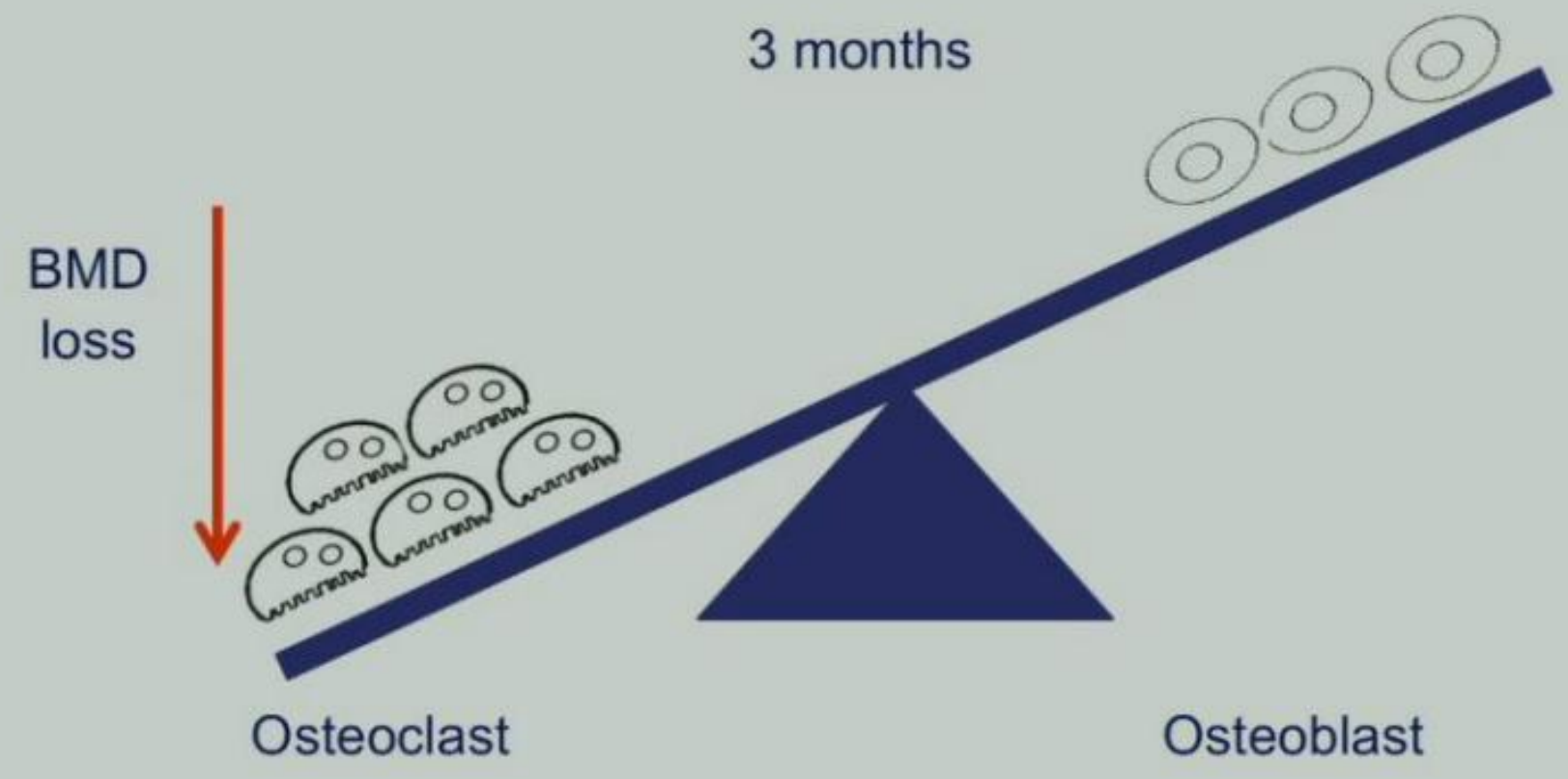


McGinty T et al. Curr Opin HIV AIDS. 2016. [Epub ahead of print].

ART initiation and Bone Turnover



ART initiation and Bone Turnover

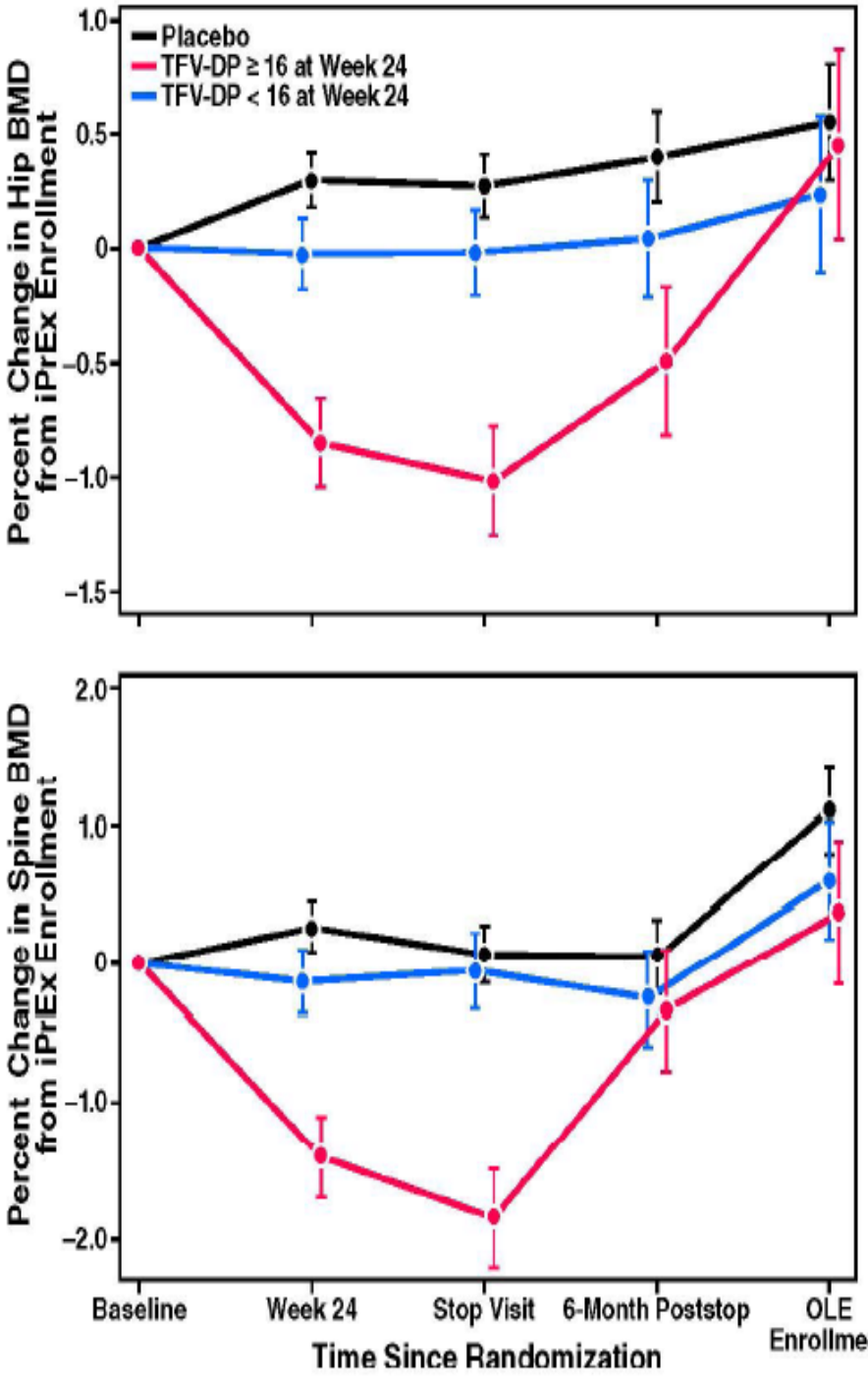


ART initiation and Bone Turnover

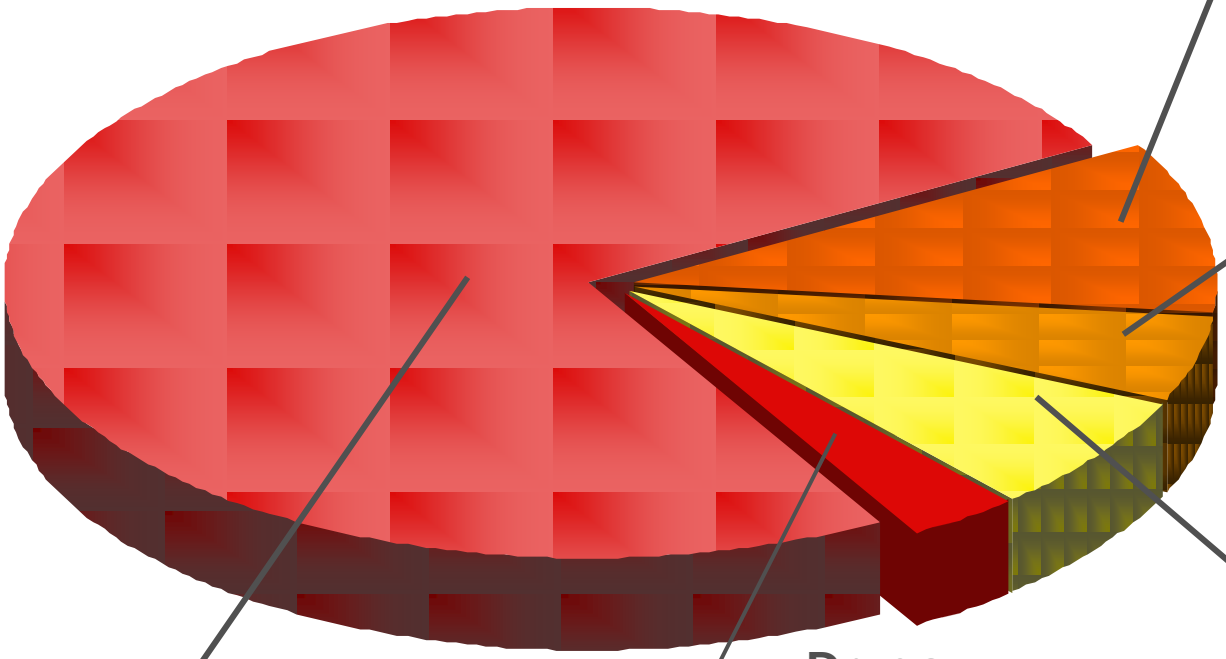
#47

I Ofotokun

A single dose zolendronic acid prevents antiretroviral–induced bone loss



Bone Mass Determinants



Diseases
- Celiac disease
- Renal Disorders
- HIV

Hormones
- Estrogen
- Testosterone
- GH
- Thyroid
- Glucocorticoids
- Vitamin D

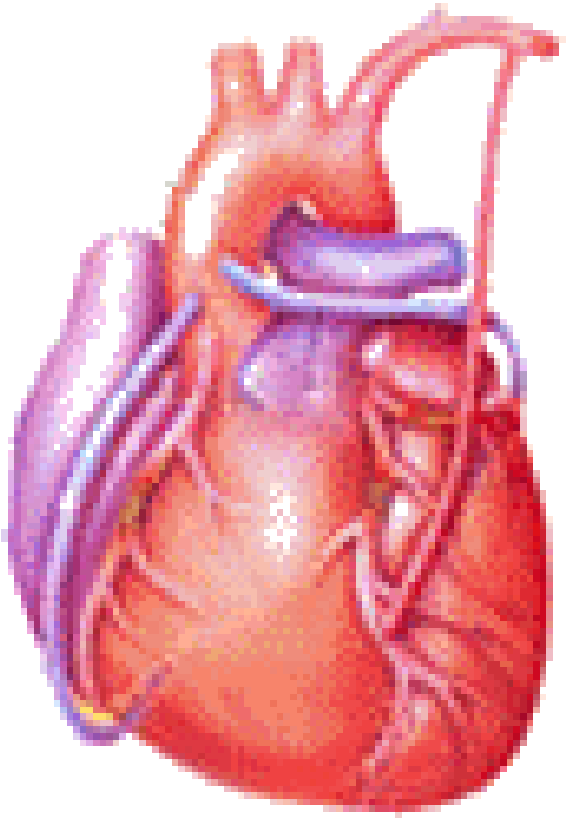
Behaviour
- Physical exercise
- Diet
- Smoke
- Alcohol

Drugs
- Diuretics
- Antiretrovirals
- Anticonvulsants
- Corticosteroids

Heredity

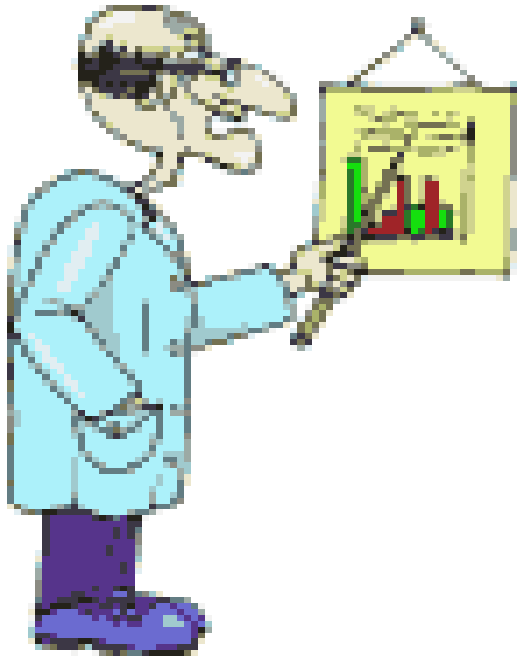
Ruffing JA, 2006; McGuigan FE 2002

2. Il cuore

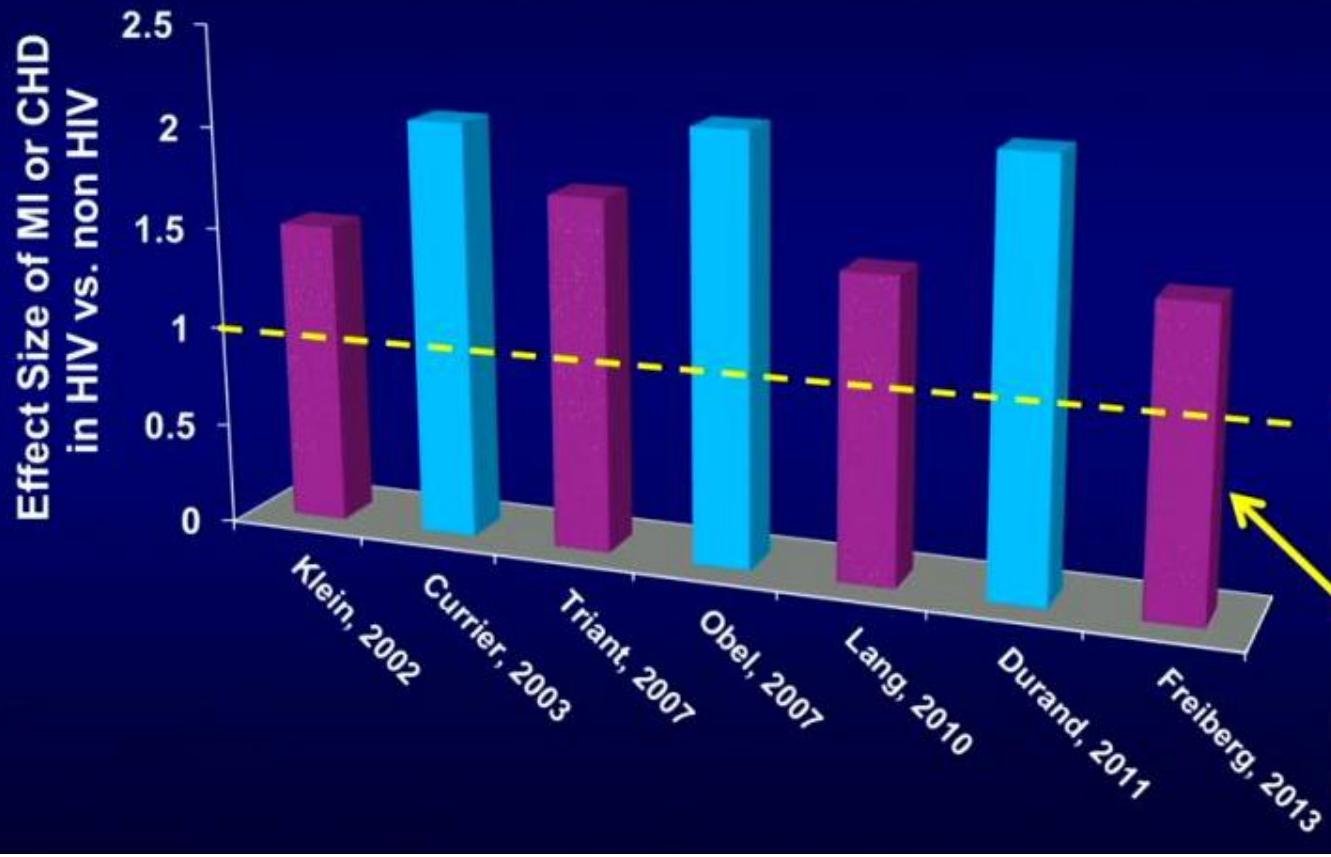


Cuore 1/4:

- Le dimensioni del fenomeno



CVD Risk in HIV-Infected Patients is Beyond That Predicted by Traditional Risk Factors



In the VACS cohort, the HR of MI was 1.48 in HIV vs. non-HIV veterans after adjusting for FRS, comorbidities, and substance use (95% CI 1.27-1.72). (Freiberg, 2013)

#641

DR Drozd

Myocardial infarction risk in the NA-ACCORD compared to MESA (multi-ethnic study of aterosclerosis) **and ARIC** (atherosclerosis risk in communities)

had significantly higher incidence of MI

Table 1. Adjusted incidence rate ratios (aIRR) and 95% confidence intervals comparing NA-ACCORD to MESA and ARIC

	aIRR [95% CI]	
Variable	MESA	ARIC
Cohort		
NA-ACCORD	2.40 [1.79, 3.20]	1.33 [1.10, 1.61]
Age		
40-49	1.00	1.00
50-59	1.94 [1.52, 2.49]	2.02 [1.62, 2.50]
>=60	3.83 [2.81, 5.23]	3.75 [2.99, 4.70]
Sex		
Male	1.00	1.00
Female	0.52 [0.40, 0.67]	0.62 [0.56, 0.68]
Race		
Non-black	1.00	1.00
Black	0.77 [0.62, 0.96]	1.13 [1.01, 1.26]
Smoking		
Never	1.00	1.00
Ever	1.56 [1.22, 1.98]	1.54 [1.38, 1.72]
Missing	1.32 [0.92, 1.89]	1.22 [0.89, 1.66]

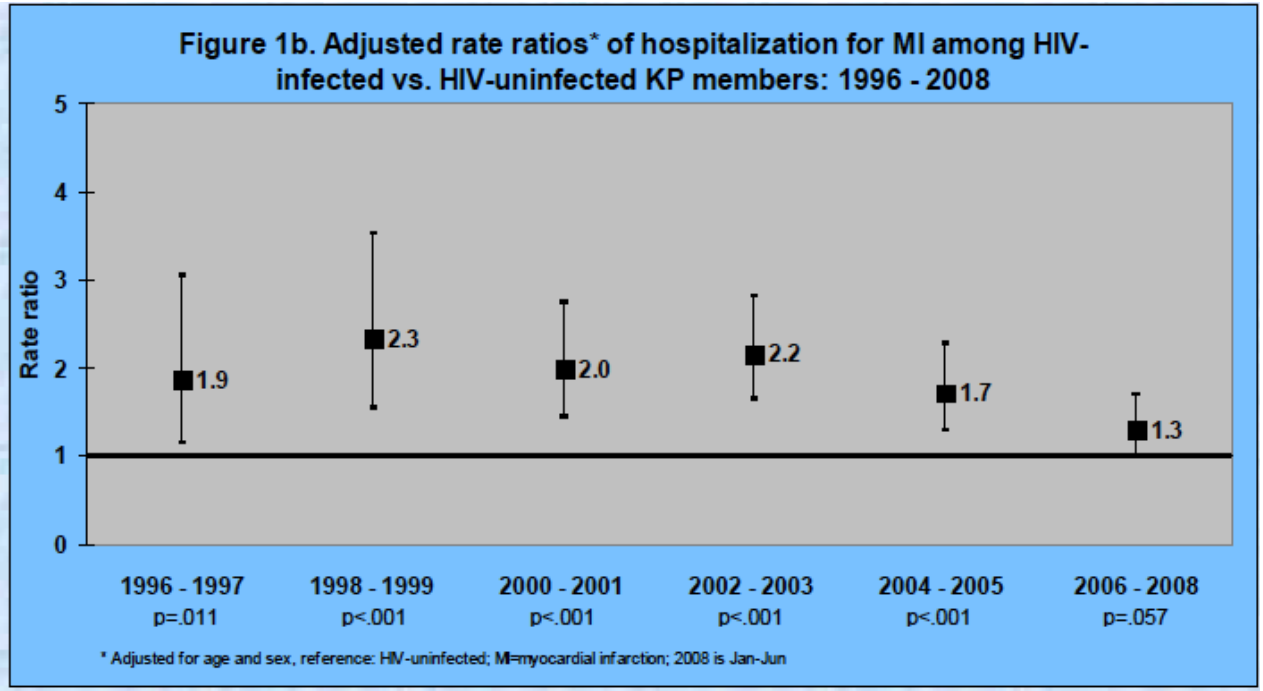
Clin Infect Dis 2015 Jan 16.

Declining Relative Risk for Myocardial Infarction Among HIV-Positive Compared With HIV-Negative Individuals With Access to Care.

Klein DB
Kaiser Permanente, Los Angeles, California.

Concerns remain for an increased myocardial infarction (MI) risk among individuals infected with human immunodeficiency virus (HIV).
We conducted a cohort study evaluating MI risk from 1996 to 2011 by HIV status. **The adjusted MI rate ratio for HIV status declined over time, reaching 1.0 (95% confidence interval, .7-1.4) in 2010-2011**, the most recent study period

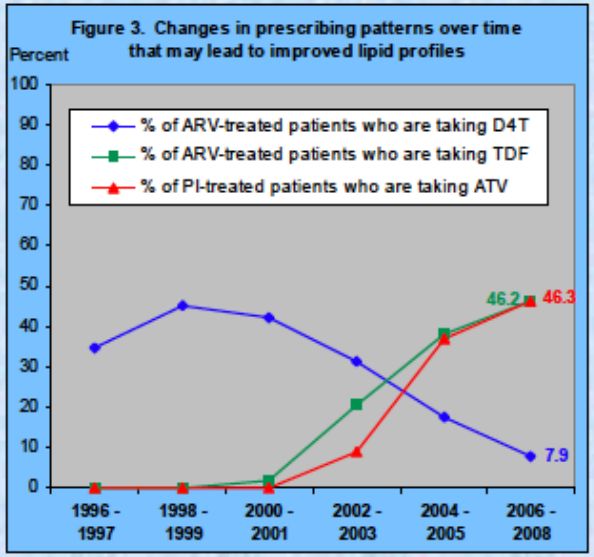
Surveillance of Cardiovascular and Cerebrovascular Event Rates among HIV-infected and HIV-uninfected Californians: 1996-2008

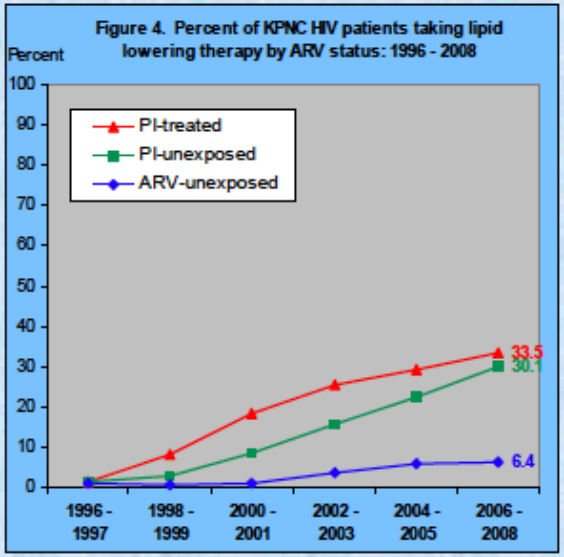


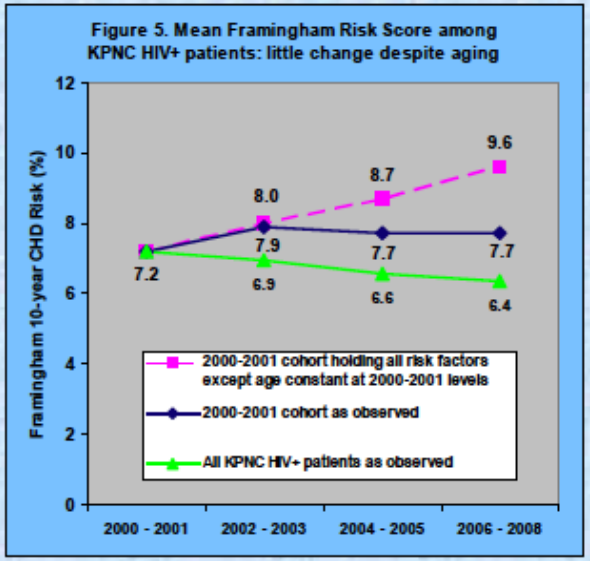
- Kaiser Permanente identified hospital myocardial infarction among 20,305 adult HIV+ KP members and among 203,050 year-, age-and sex-matched HIV-KP members from 1996 through June, 2008. 2
- For the period 1996--2008, MIs among our HIV+ population and were uncommon, occurring at a rate of 3.0 per 1000 per person years.
- During 1996-2008, the rates of MI among HIV+ and HIV- patients converged such that in 2006-2008 the difference in rates between the two groups became statistically non-significant

L Hurley CROI 2009, abstract 710

Surveillance of Cardiovascular and Cerebrovascular Event Rates among HIV-infected and HIV-uninfected Californians: 1996-2008



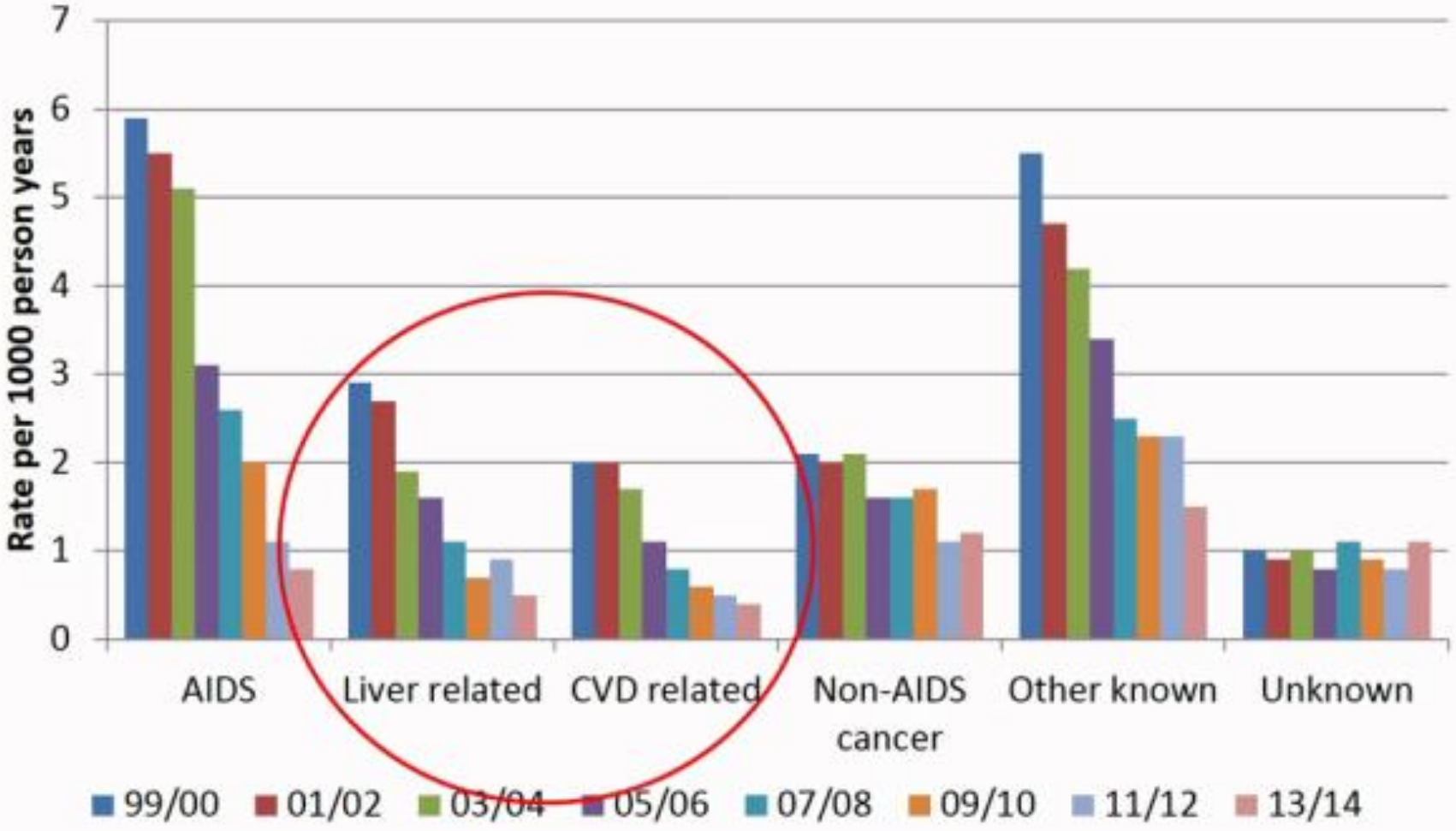




Among HIV+ patients, the observed decline in rate of MI consistent with
1.a shift to more lipid friendly antistroke antiretroviral regimens
2.increased use of lipid lowering therapy
3.effective management of traditional cardiovascular risk factors as evidenced by stable Framingham risk scores despite an aging population.

L Hurley CROI 2009, abstract 710

Age-adjusted rates of death

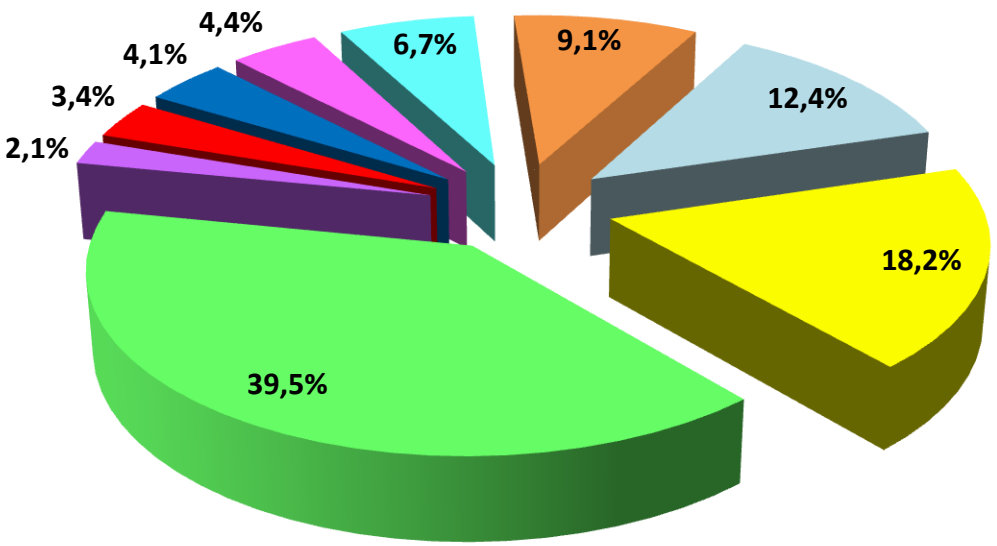


D:A:D: Smith *et al*, Lancet 2014

Likely explanations to decreasing trends in CVD in aging cohort

- Better management of modifiable traditional risk factors
  - Less smoking
  - Better dyslipidaemia control
  - Screening & tx for hypertension and diabetes if indicated
- Less use of ARVs related to CVD development in high risk individuals
  - Switch from PI to mainly NNRT based ART
    - If PI-based: focus on more recently introduced drugs
  - less use of abacavir in high underlying CVD risk populations

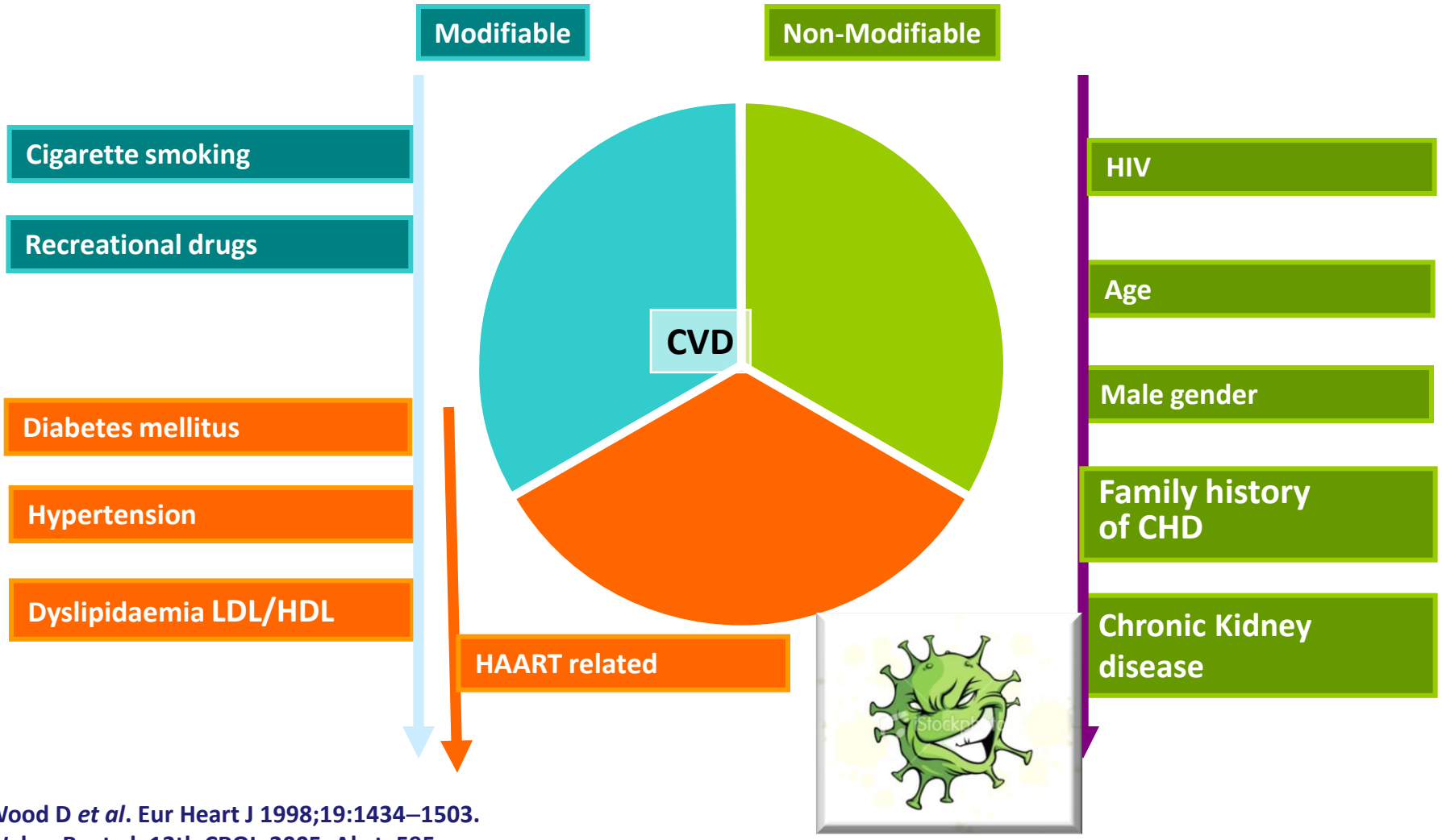
Cause of death, n= 702



- Drug abuse
- Suicide
- Cardio-cerebro-vascular
- Non HIV related infections
- Non-AIDS malignancies (excluded HCC)
- Unknown
- Other
- Hepatic
- HIV related

Dec 2014 Report

Cuore 2/4: HIV come fattore di rischio indipendente



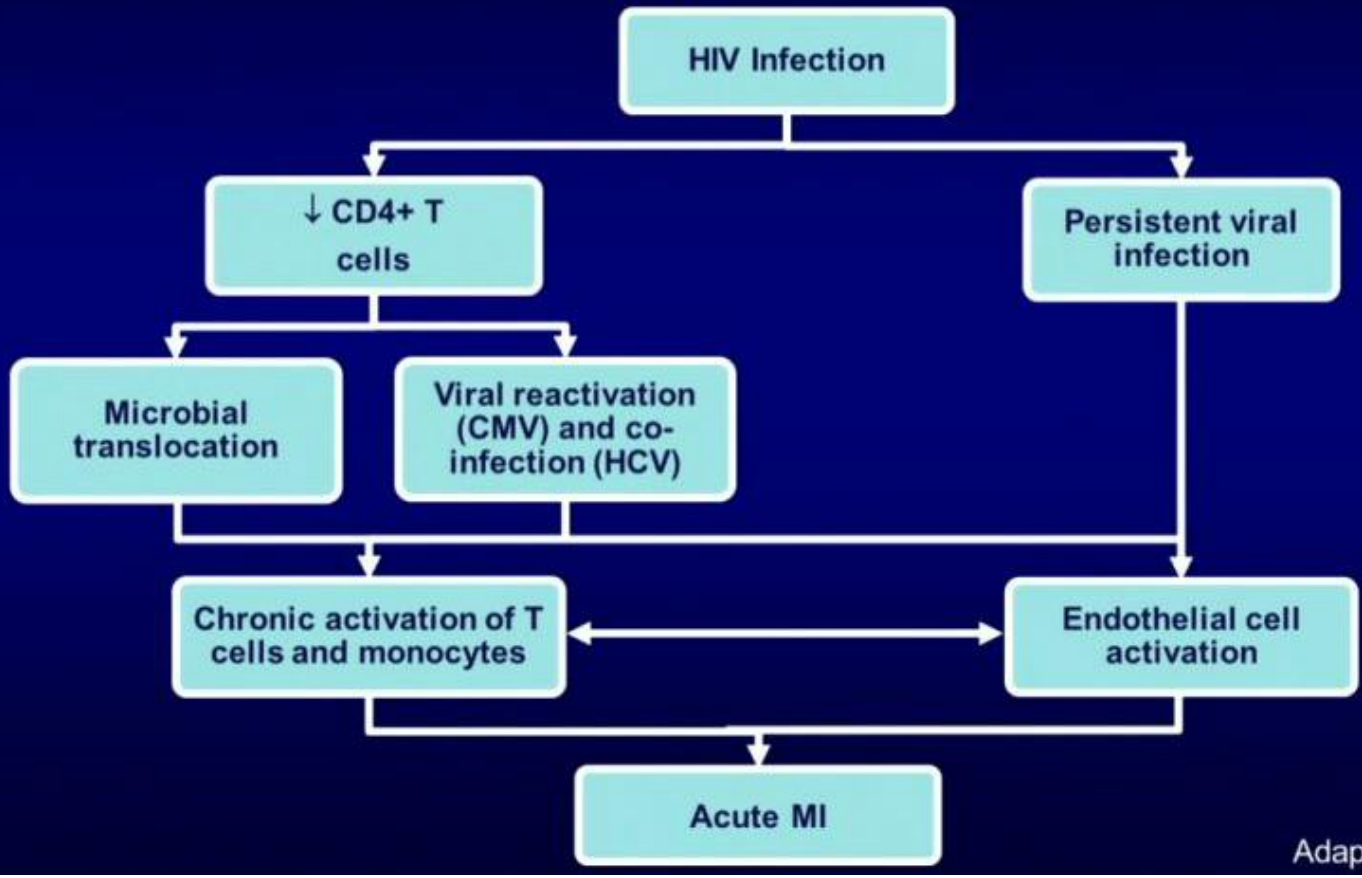
Wood D *et al*. Eur Heart J 1998;19:1434–1503.
Weber R. et al. 12th CROI, 2005; Abst. 595

Inflammation:
The keystone of aging and chonic diseases

Inflammation predicts disease in treated HIV infection, as it does in the general population

- Mortality (Kuller, PLoS Med, 2008, Sandler JID 2011, Tien JAIDS 2011)
- **Cardiovascular Disease** (Baker, CROI 2013)
- Lymphoma (Breen, Cancer Epi Bio Prev, 2010)
- Venous Thromboembolism (Musselwhite, AIDS, 2011)
- Type II Diabetes (Brown, Diabetes Care, 2010)
- Cognitive Dysfunction (Burdo AIDS 2012)
- Frailty (Erlandson, JID 2013)

HIV: a State of Immune Activation and Suppression



Adapted from Hsue JID 2012

How is HIV Unique?
Look to your guts!

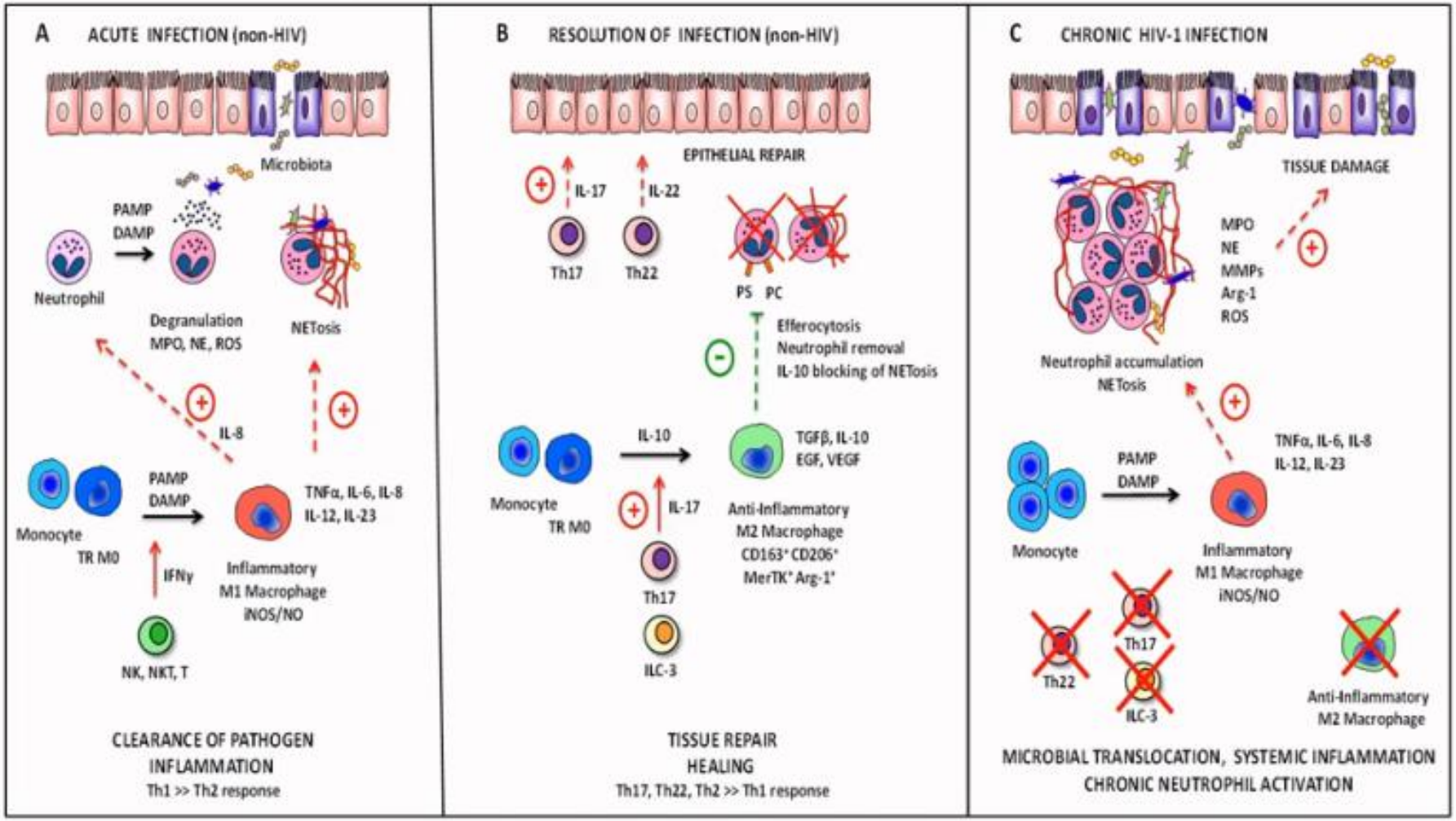
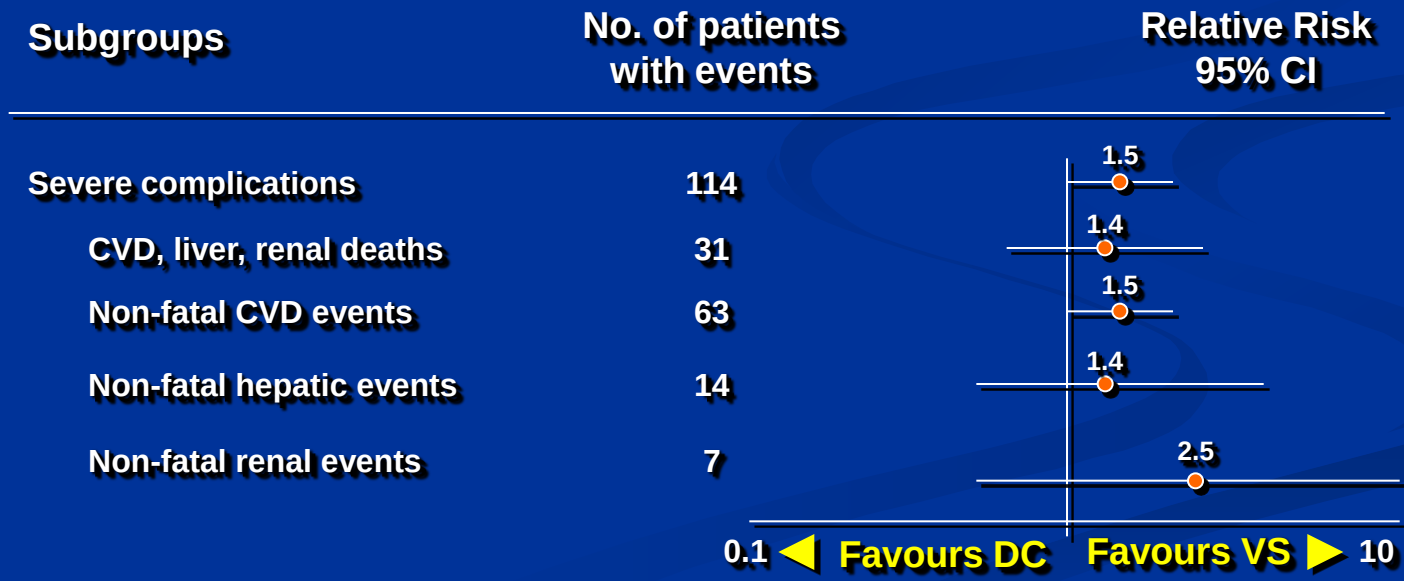


Figure courtesy of Dr. Zdenek Hel.

SMART Study: Short-term CD4+ guided episodic use of ART is inferior to continuous therapy

- CD4+ guided drug conservation (DC) strategy was associated with significantly greater disease progression or death compared with continuous viral suppression (VS): RR 2.5 (95% CI: 1.8–3.6; $p<0.001$)
- Includes increased CVD-, liver- and renal-related deaths and non-fatal CVD events

Severe complications endpoint and components



El-Sadr W, *et al. 13th CROI*, Denver 2006, #106LB

START Design

HIV-infected individuals who are ART-naïve with CD4+ count > 500 cells/mm^3

Early ART Group

Initiate ART immediately following randomization

N=2,326

Deferred ART Group

Defer ART until the CD4+ count declines to < 350 cells/mm^3 or AIDS develops

N=2,359

Primary composite endpoint, target = 213

- Serious AIDS or death from AIDS
- Serious Non-AIDS Events and death not attributable to AIDS
  - CVD, ESRD, decompensated liver disease, & non-AIDS defining cancers

INSIGHT/STAT: Babiker et al 2012

Atherosclerosis

The Search for Biomarkers

- Learning from the Statin Experience
  - Magnitude of CVD reduction exceeds lipid lowering effect (not linearly related)
  - Anti-inflammatory effects prevent atherosclerosis progression
- Potential inflammatory pathways to target
  - IL-6 signaling pathway → CRP
  - Alternative pathways (Phospholipase inhibitors (PLA_2))
  - Oxidative stress, i.e. Antioxidants
  - Monocyte phenotypes
- Key issues for targeting CRP
  - Limited specificity for atherosclerosis-associated inflammation
  - Poor prognostic value in secondary prevention
  - Changes in CRP may not reflect changes in arterial inflammation
- **Residual CVD risk ≠ Residual inflammation**

Passacquale G, Di Giosia, Ferro. Cardiovascular Research. 2015. 12: 709-21.

A5350: Effect of Probiotics on Gut Microbiome and Immune Activation Markers

Protocol Co-Chairs: Turner Overton and Adriana Andrade

The trial will randomize 90 HIV-infected adults 18 years of age and older
- On ART, with CD4 count >200 c/mm^3, and HIV VL < **50cp/mL**

ACTG AIDS CLINICAL TRIALS GROUP

Blinded

45 participants on ART + probiotic X 24 weeks

45 participants on ART + placebo X 24 weeks

Followed for an additional 12 weeks off study therapy after completion of probiotic./placebo

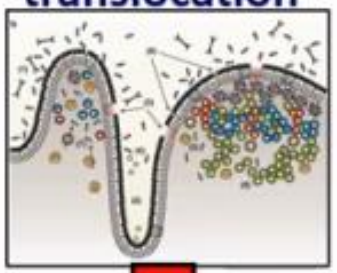
Key Study Objectives

- Assess changes in inflammatory biomarkers
- Assess changes in microbial translocation markers
- Assess changes in T cell phenotypes
- Assess changes in monocyte phenotypes
- Assess changes in microbial diversity
- Assess changes in gut permeability

Relevance to CVD?

- Potential to increase Th17 T cell population in gut
- Potential to shift monocyte population
- Mediated through improved gut permeability

Microbial translocation



Inflammation

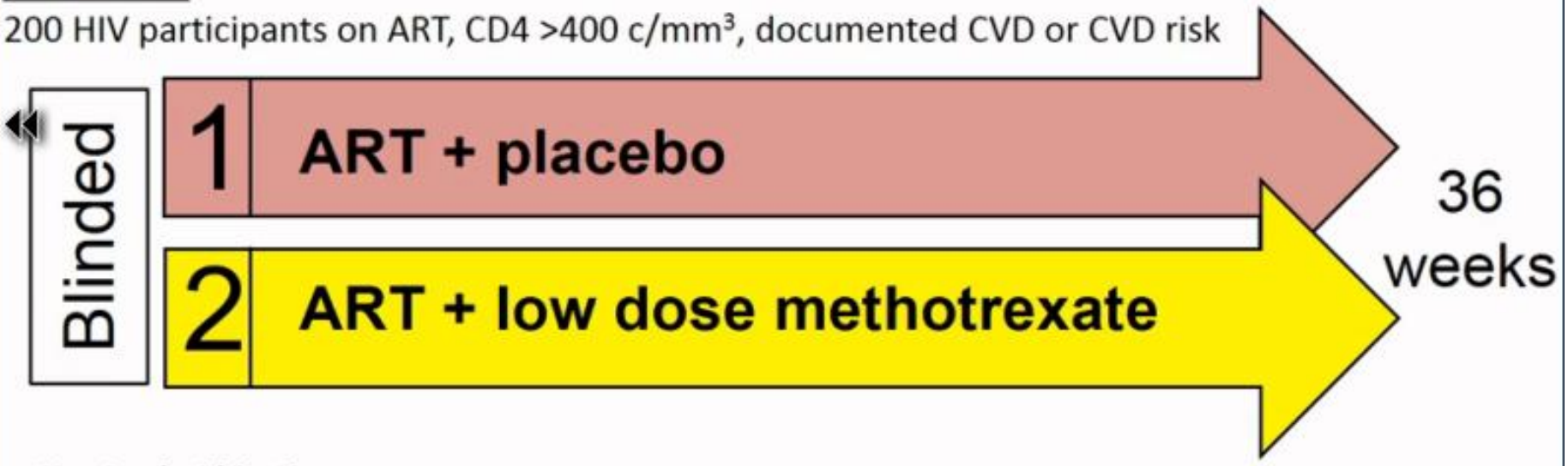
↑ Monocyte activation
↑ T cell activation
Dyslipidemia
Hypercoagulation

A5314: Effect of Reducing Inflammation with Low Dose Methotrexate on Inflammatory Markers and Endothelial Function in Treated and Suppressed HIV Infection

Protocol Co-Chairs: Priscilla Hsue, MD, and Judith Currier, MD, MSc

Enrollment:

200 HIV participants on ART, CD4 >400 c/mm^3, documented CVD or CVD risk



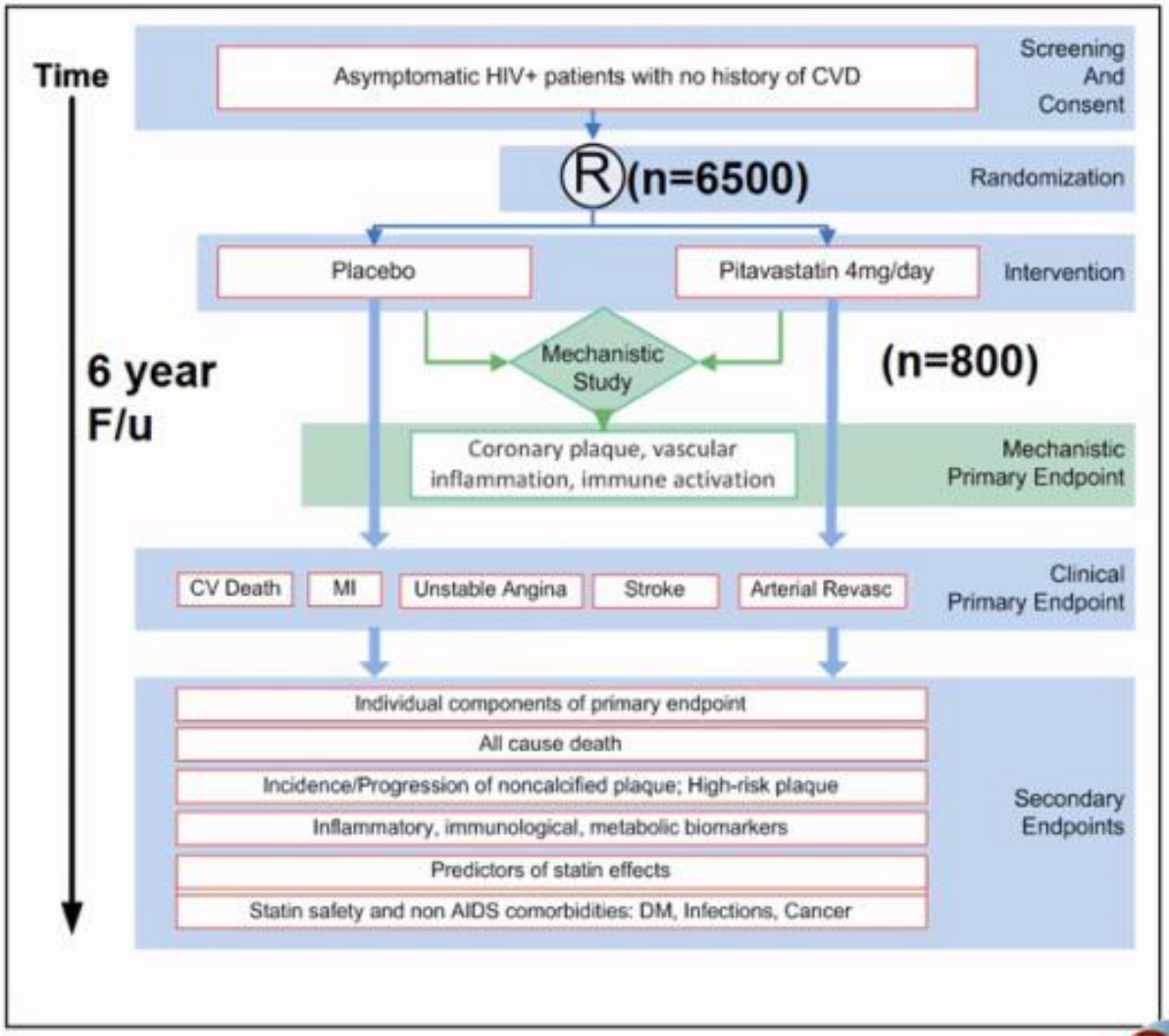
Key Study Objectives

- To evaluate safety of low dose methotrexate (LDMTX) therapy
- To demonstrate LDMTX improves endothelial function (brachial artery FMD) Secondary
- To estimate the effects of LDMTX on cardiovascular markers related to CVD risk, inflammation, and coagulation, including hsCRP, IL-6, sCD163, and D-dimer
- To investigate the impact of LDMTX on additional soluble and cellular markers of inflammation, coagulation, monocytes activation, reactivation of CMV, and HIV-1 persistence

153/200 participants enrolled

Randomized Trial to Prevent Vascular Events in HIV
REPRIEVE (A5332)

Principal Investigators:
Steven Grinspoon, MD
Pamela S Douglas, MD
Udo Hoffmann, MD, MPH
Heath Ribaudo, PhD



Funded by NHLBI and NIAID. Supported by KOWA Pharmaceuticals.

ACTG
AIDS CLINICAL TRIALS GROUP

3/4
Prevedere il rischio…

747.
Cardiovascular Disease Risk Prediction in the HIV Outpatient Study (HOPS)

Angela M.Thompson-Paul

Results and Conclusions

HOPS Patients	10-Year CVD Risk Estimation			
	FPS	ACC/AHA	SCORE	D:A:D
Any length follow-up (n=2,392)				
Expected events	126	147	19	193
Observed events	149	178	23	256
Ratio expected/observed*	0.85	0.83	0.83	0.75
Hosmer-Lemeshow X^2 *p*-value†	0.002	< 0.001	0.02	< 0.001
C-statistic‡	0.71	0.71	0.57	0.72
≥10 years of Follow Up (n= 725)				
Expected events	41	45	6	60
Observed events	63	77	1	87
Ratio expected/observed*	0.65	0.58	--	0.69
Hosmer-Lemeshow X^2 *p*-value†	0.11	0.17	--	0.01
C-statistic‡	0.70	0.68	--	0.70

- **The four risk prediction equations underestimated the 10-year risk of CVD in our large, diverse HIV cohort.**
- **To better estimate CVD risk in HIV-infected persons in the United States, additional risk factors (e.g. immunologic markers, virologic status) may need to be considered.**

746.
Cumulative HIV Care Measures Highly Associated With Acute Myocardial Infarction

Jorge L. Salinas (VACS)

- **Cumulative measures** of viral load, CD4 count and VACS Index provide added information about risk of AMI, of these, VACS Index is the most comprehensive.

Complications from Head to Toe

Comparing Cardiovascular Disease Risk Scores for Use in HIV-Infected Individuals

Heidi M. Crane

University of Washington, Seattle, WA, United States

Risk scores

Risk Score	Population	Target Cardiovascular Events	Variables Included
FRS- CHD (Framingham)	30 – 74 years	Angina, MI, CHD death, coronary insufficiency	Age, Total Cholesterol, HDL-C, BP, Diabetes status, Smoking, Gender
ATP3-FRS-CHD (ATP3)	>20 years	MI, CHD death	Age, Total Cholesterol, HDL-C, BP, Smoking, Gender, Antihypertension Medication use
DAD (DAD)	HIV, European	MI	Age, Total Cholesterol, HDL-C, BP, Diabetes status, Smoking, Gender, Abacavir use, Duration of indinavir use, Duration of lopinavir use
2013 ACC/AHA ASCVD Pooled Cohort Equations (ASCVD)	40 – 79 years	MI, CHD death, stroke	Age, Total Cholesterol, HDL-C, BP, Diabetes status, Smoking, Gender, White or African American, Antihypertension Medication use

Conclusion

- The large size, comprehensive clinical data and central adjudication of MI by type in CNICS allows for direct comparison of clinical risk scores
- The addition of specific antiretroviral medications in the DAD score did not improve discrimination or calibration compared with ASCVD

  -however inclusion of different HIV-specific measures may lead to improvements and should be tested

  -see for example Hunt et al., poster #671 on CD4/CD8 ratio and MI
- Current standard of care for primary CVD prevention such as prescribing a statin is to use the ASCVD score in the general population, no one knows how this works in HIV but these findings suggest that it works fairly well
- ASCVD performed better than the other risk scores, doing better than both older more outdated scores and an HIV score with antiretroviral medications

Cuore 4/4:
Gli interventi farmacologici

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association.

2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Neil J. Stone, Jennifer Robinson, Alice H. Lichtenstein, C. Noel Bairey Merz, Conrad B. Blum, Robert H. Eckel, Anne C. Goldberg, David Gordon, Daniel Levy, Donald M. Lloyd-Jones, Patrick McBride, J. Sanford Schwartz, Susan T. Shero, Sidney C. Smith, Jr, Karol Watson and Peter W.F. Wilson

4 Statin Benefit Groups

1- Individui con evidenze cliniche di malattia cardiovascolare aterosclerotica (infarto miocardico, stroke)
→ che corrispondono a pazienti a rischio molto alto secondo le linee europee

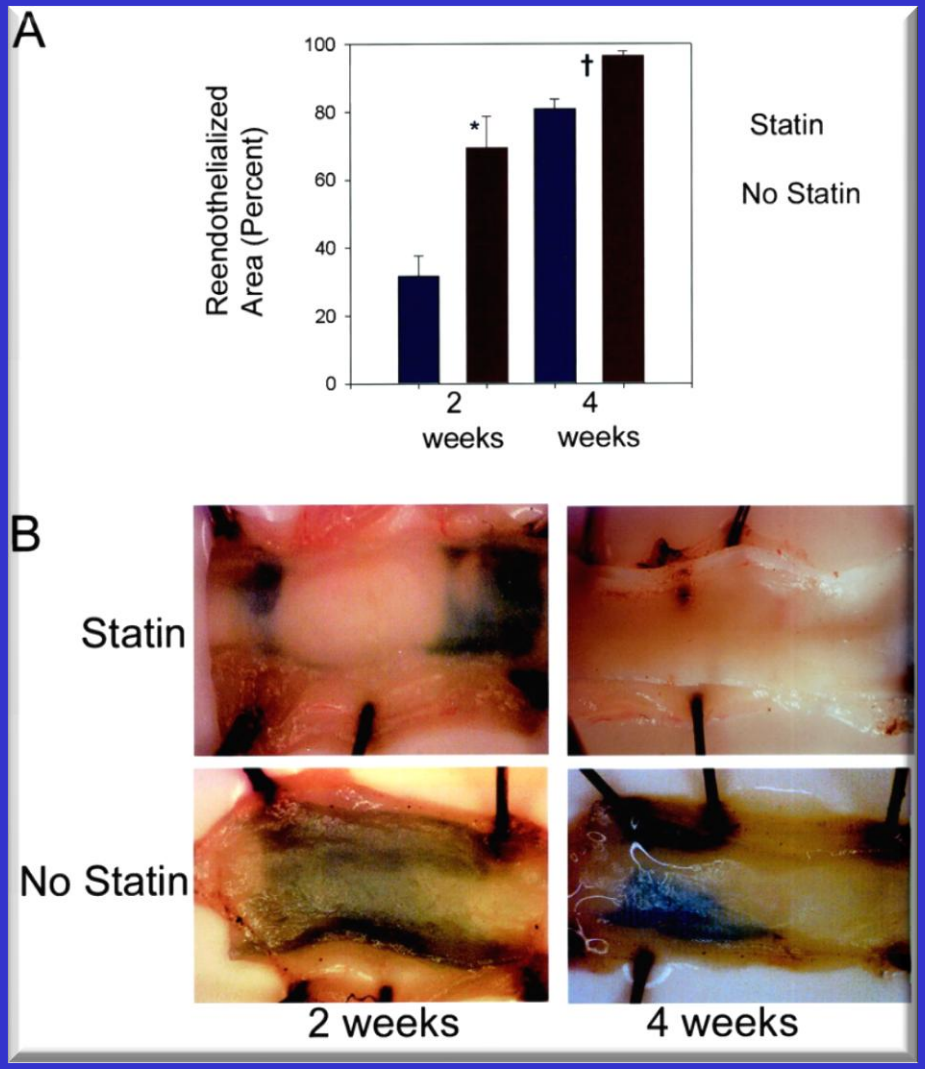
2- Individui con aumento primario de c-LDL oltre 190 mg/dL
Valore molto alto che spesso sono paziente con dislipidemie familiari considerati ad alto rischio

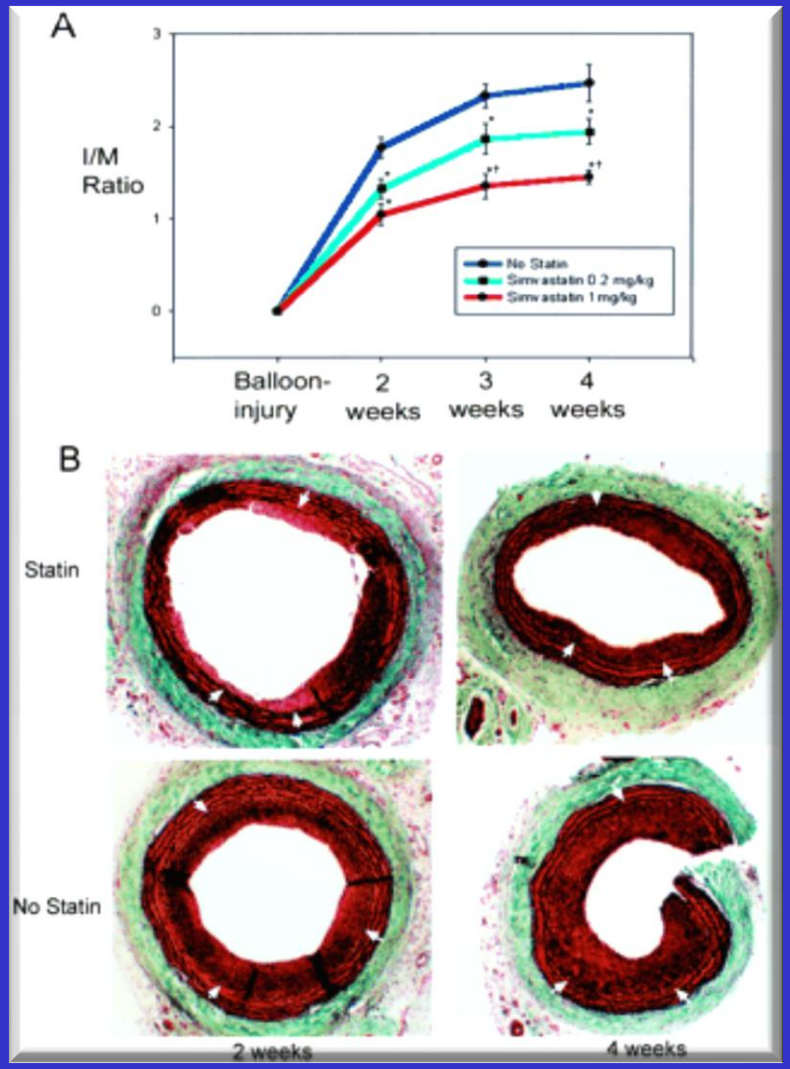
3- Diabetici nella fascia di età 40-75 anni e con c-LDL > 70 mg/dL senza evidenze cliniche di ASCVD → rischio almeno alto

4- Individui senza ASCVD o diabete, con c-LDL >70mg/dL e rischio stimato di ASCVD a 10 anni ≥7,5%

Re-endotelizzazione mediata dalle Statine.

Segmenti di carotidi di ratto lesionate meccanicamente.



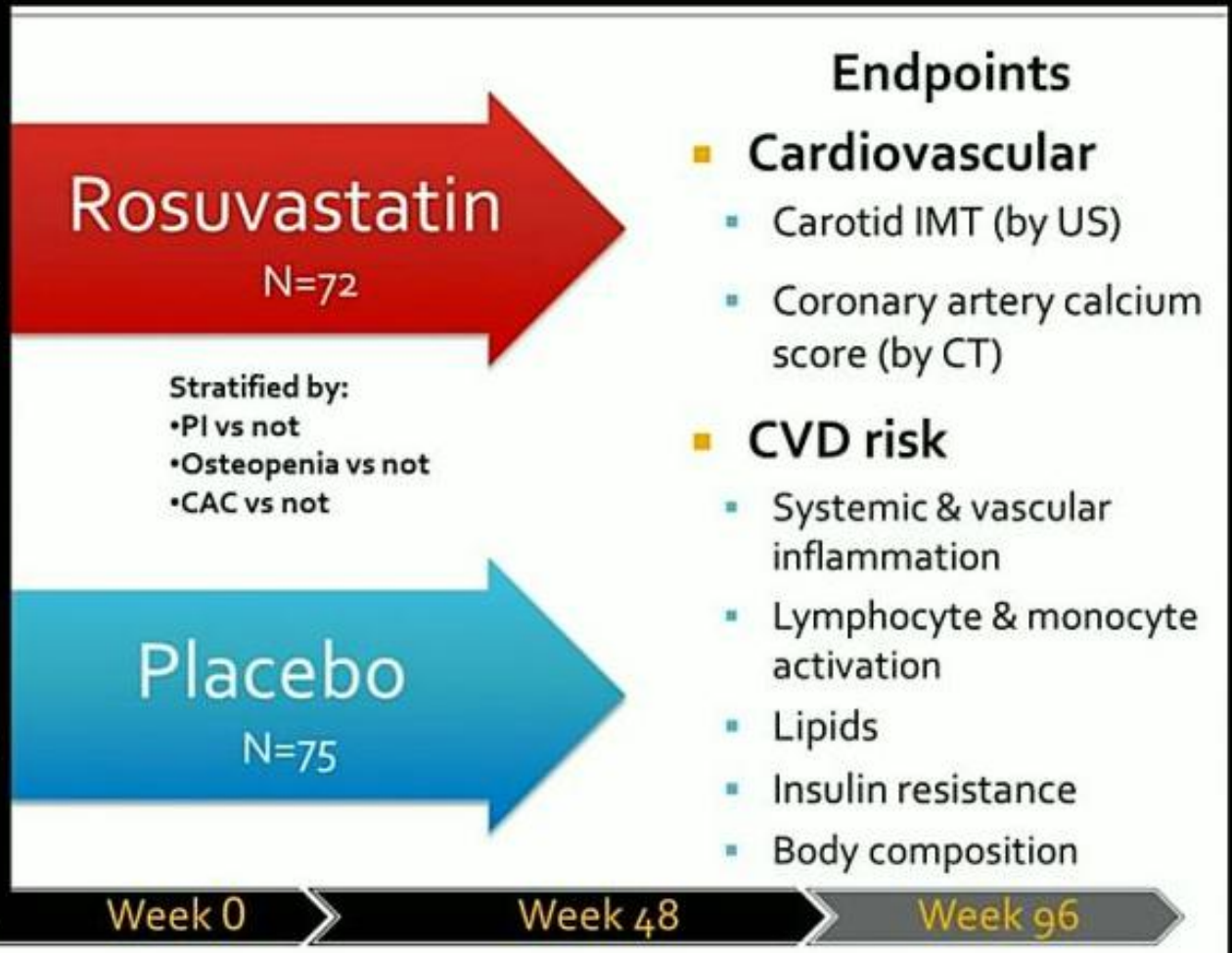


Walter, Circulation 2002

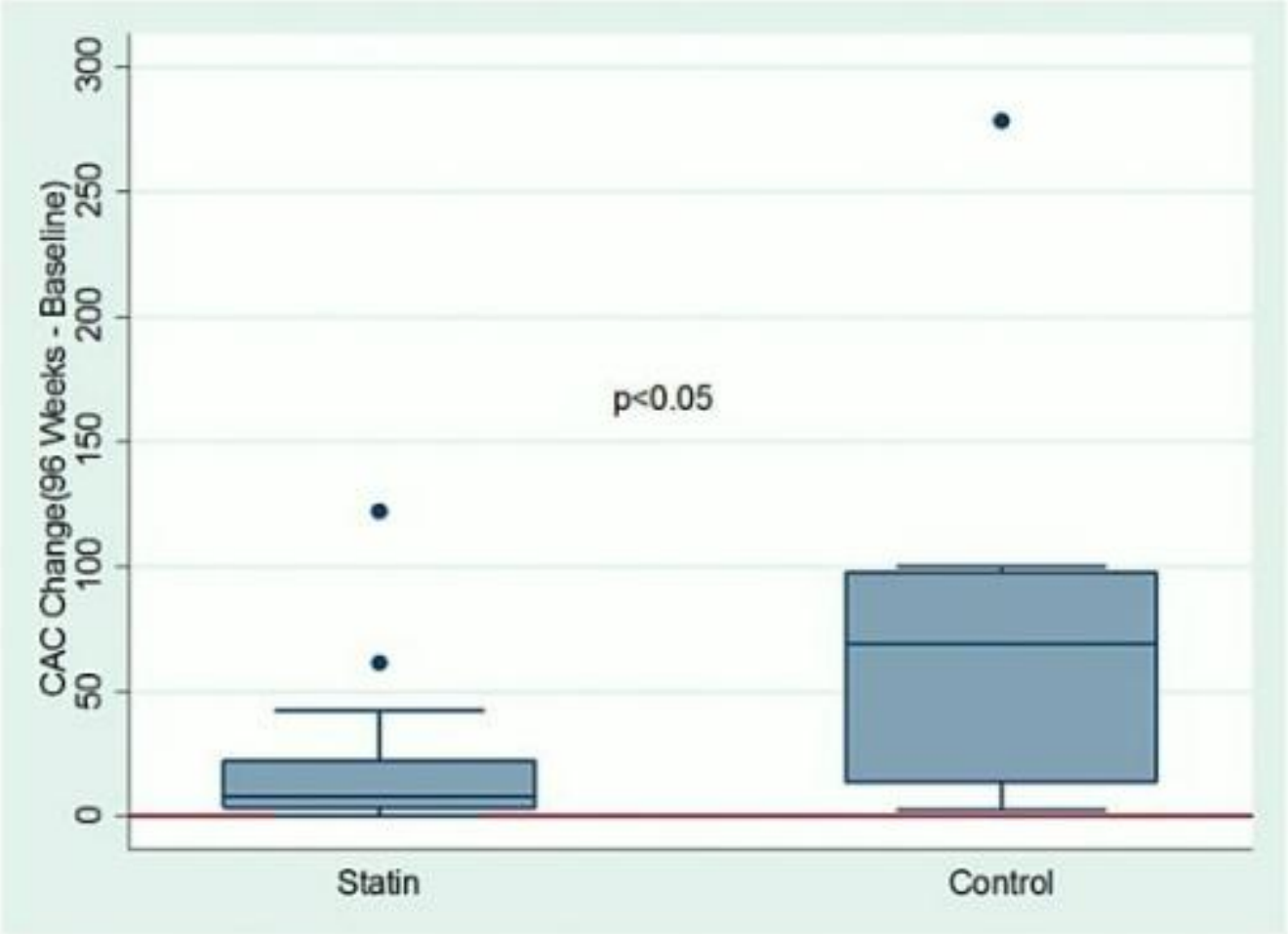
SATURN-HIV Design

Inclusion

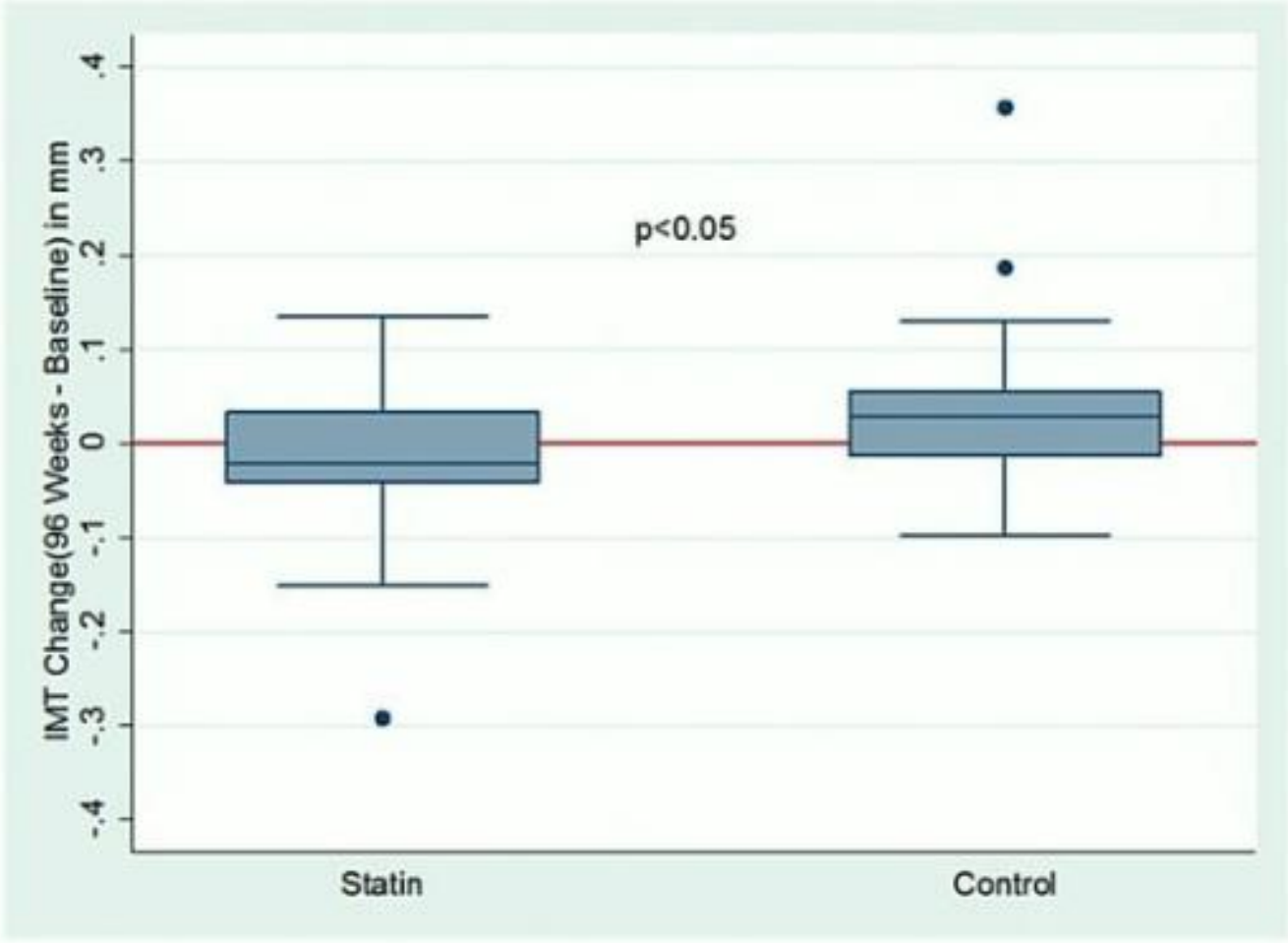
- HIV-1 & ≥18 years
- On ART >6mo & HIV-1 RNA ≤1000 cps/ml
- Fasting LDL-C≤130mg/dl
- Heightened immune activation (CD8+CD38+DR+ ≥19% or hsCRP ≥2µg/ml)
- No CVD or diabetes
- No fragility fractures
- No immunomodulatory, bone tx, or hypolipemics



Change in CAC Score in the subset with CAC at baseline



Change in Mean CCA IMT in Subset with Baseline CAC



#674

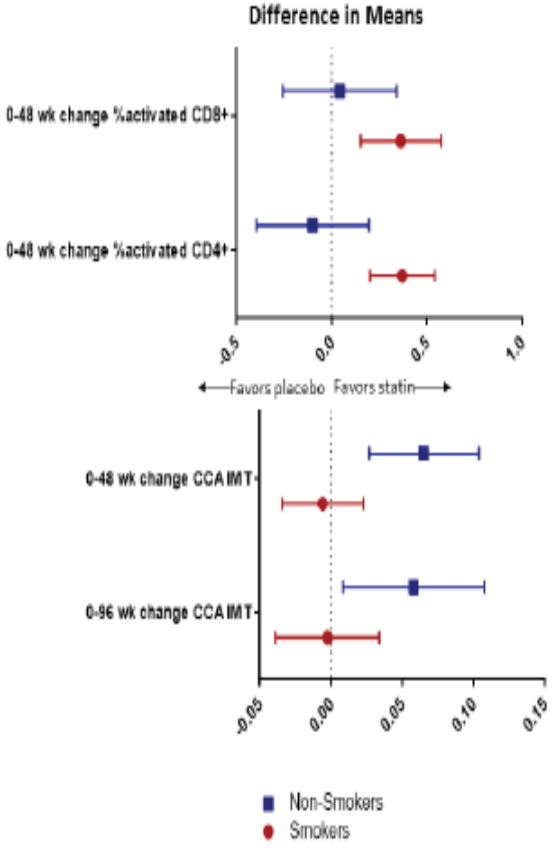
CO Hileman

The effect of rosuvastatin on vascular disease differs by smoking status SATURN-HIV

Mean Change in T cell Activation and Carotid Intima Media Thickness for Rosuvastatin and Placebo Groups by Smoking Status

	Rosuvastatin	Placebo	p-value
Activated CD4+T Cells			
0-48 wk change			
Smokers	-0.511	-0.138	<0.01
Non-smokers	-0.365	-0.463	0.51
Activated CD8+T Cells			
0-48 wk change			
Smokers	-0.613	-0.248	<0.01
Non-smokers	-0.506	-0.462	0.77
CCA IMT			
0-48 wk change			
Smokers	0.018	0.012	0.7
Non-smokers	-0.024	0.042	<0.01
0-96 wk change			
Smokers	0.018	0.016	0.9
Non-smokers	0.008	0.066	0.02

Values shown are mean absolute change from baseline in log-transformed outcome adjusted for the baseline value of that outcome. P-values are for between group t tests.



Active smoking modified the effect of rosuvastatin **(beneficial effect not apparent in smokers)**

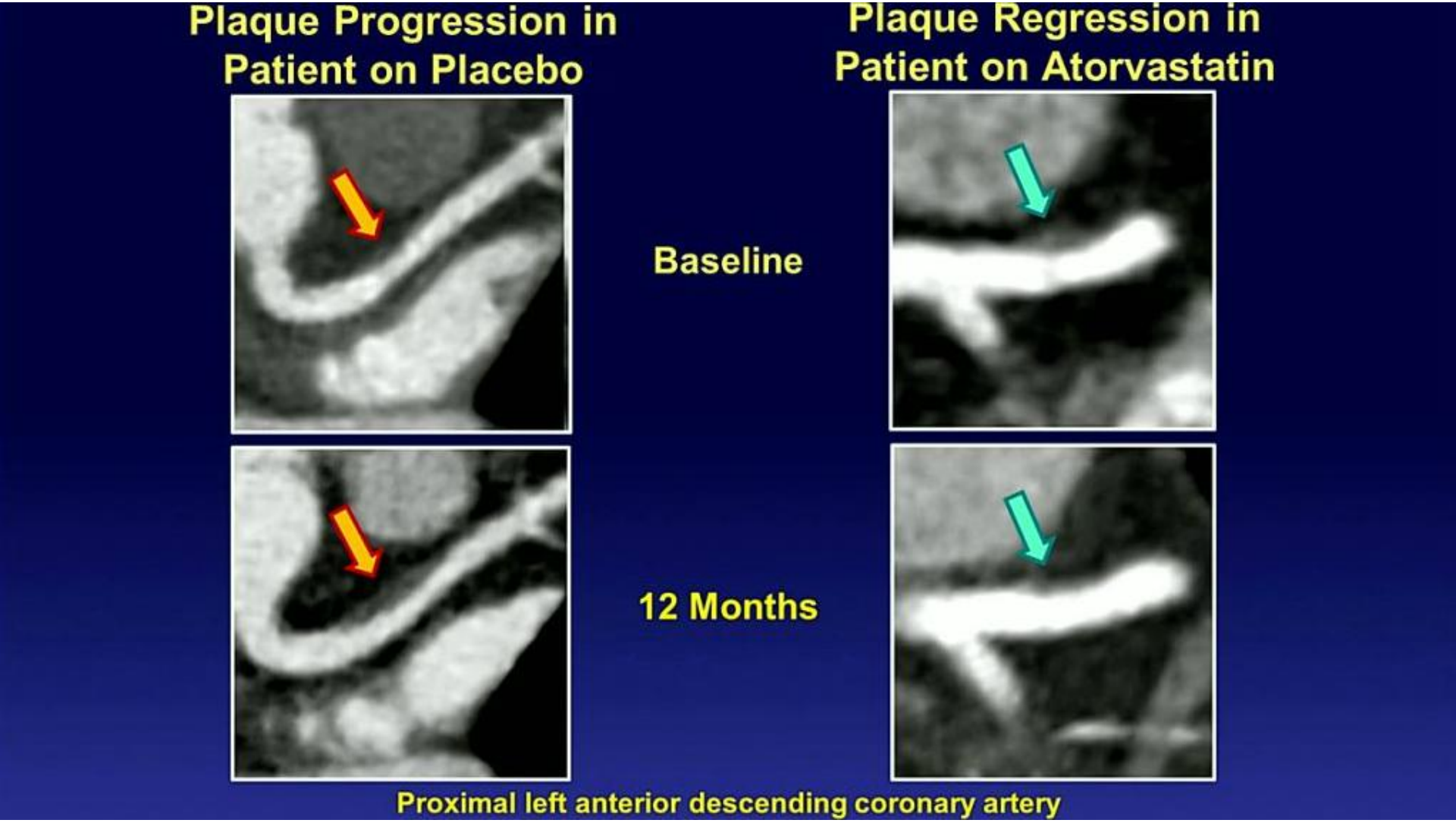
However T-cell activation improves more in smokers

Cardiovascular, Bone, and Kidney Health

Statin Therapy Reduces Coronary Noncalcified Plaque Volume in HIV Patients: A Randomized Controlled Trial

Janet Lo

Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States


Plaque Progression in Patient on Placebo
Plaque Regression in Patient on Atorvastatin
Baseline
12 Months
Proximal left anterior descending coronary artery

#673

E Nou

Statin effects on oxLDL in relationship to plaque and arterial inflammation in HIV

over 12 months oxLDL decreases with **atorvastatin**

Reduction in serum oxLDL is associated with changes in non-calcific plaque volume total plaque volume positively remodeled plaque and low attenuation plaque

The relationship between oxLDL and non calcified plaque volume is independent of 10-year FRS, VL, CD4 and change in direct LDL

Table 1: Spearman Correlations Between Change in Plaque Characteristics and Change in Lipids and Inflammatory Markers

	Change in Non-calcified Plaque Volume (mm3)	Change in Total Plaque Volume (mm3)	Change in Positively Remodeled Plaque (# segments)	Change in Low Attenuation Plaque (# segments)
Change in oxLDL (U/L)	**ρ= 0.50; p= 0.002**	**ρ= 0.34; p= 0.04**	**ρ= 0.34; p= 0.047**	**ρ= 0.41; p= 0.02**
Change in Lp-PLA$_2$ (ng/mL)	**ρ= 0.44; p= 0.007**	**ρ= 0.34; p= 0.04**	**ρ= 0.34; p= 0.04**	**ρ= 0.36; p= 0.03**
Change in Direct LDL (mg/dL)	ρ= 0.26; p= 0.12	ρ= 0.27; p= 0.11	ρ= 0.17; p= 0.31	ρ= 0.14; p= 0.41
Change in Total Cholesterol (mg/dL)	ρ= 0.16; p= 0.34	ρ= 0.14; p= 0.43	ρ= 0.09; p= 0.59	ρ= 0.29; p= 0.09
Change in HDL Cholesterol (mg/dL)	**ρ= -0.32; p= 0.05**	ρ=-0.20 ; p= 0.23	ρ= -0.20; p= 0.24	ρ= -0.30; p= 0.07
Change in Triglycerides (mg/dL)	ρ= 0.23; p= 0.16	ρ= 0.06; p= 0.71	ρ= -0.16; p= 0.35	ρ= 0.29; p= 0.09

Data are Spearman's rank correlation coefficients. Significant p-values are shown in bold.

Abbreviations: oxLDL = oxidized LDL, CRP = C-reactive protein, Lp-PLA$_2$ = Lipoprotein Phospholipase-A$_2$, LDL = Low-density lipoprotein, HDL = High-density lipoprotein, sCD14 = soluble CD14, sCD163 = soluble CD163.

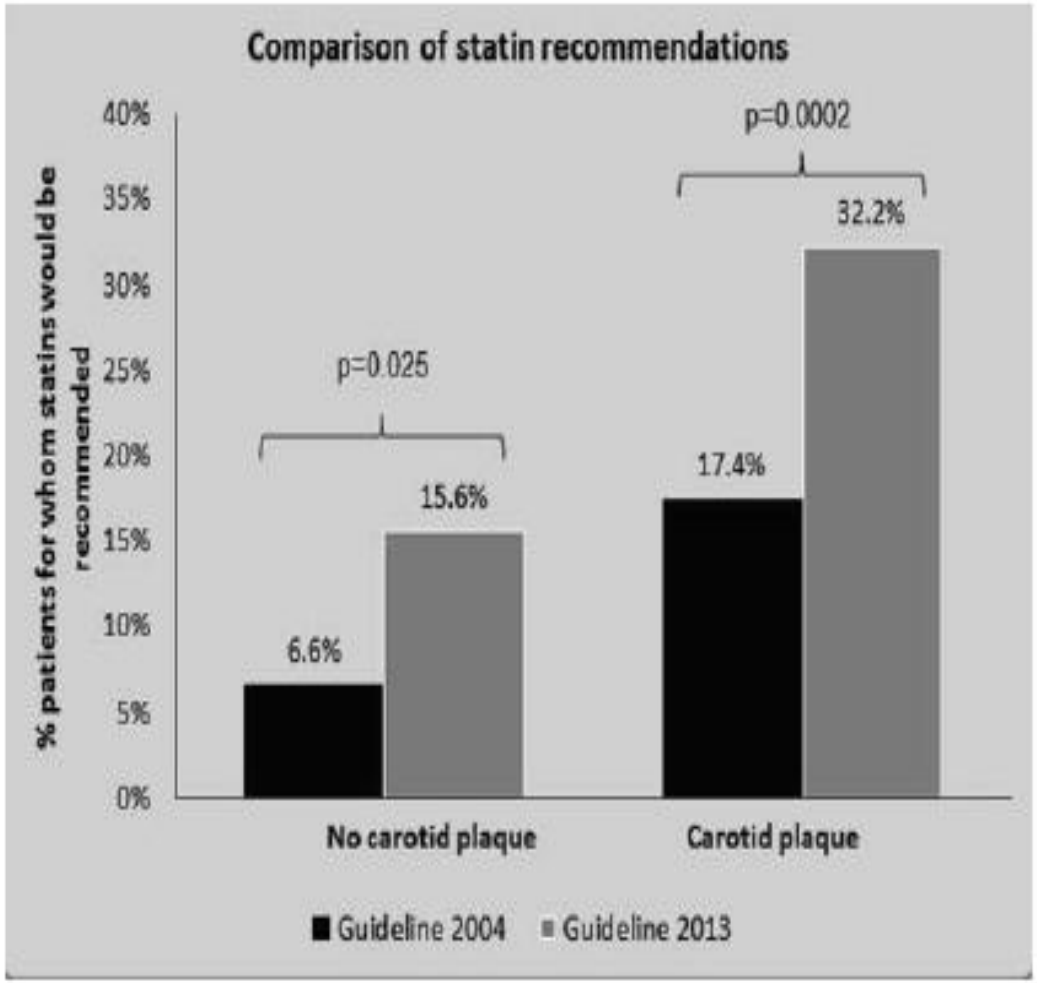
Data relating change in oxLDL to plaque parameters exclude two outliers in the placebo group. Sensitivity analyses including these subjects show similar results in terms of directionality and significance of relationship for non-calcified plaque volume.

#643

B Weigel

2013 ACC/AHA guideline undertreats HIV-infected adults with atherosclerosis

HIV specific colesterol guidelines that include detection of subclinical atherosclerosis may help to identify HIV-infected adults who are at increased ASCVD risk



Complications from Head to Toe

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

Meagan K. O'Brien

Icahn School of Medicine at Mount Sinai, New York, NY, United States

	Fold Change from Baseline to Week 12 (95 % CI)				
	Placebo (N=37)	Aspirin 100mg (N=38)	P Value[1]	Aspirin 300mg (N=38)	P value[1]
	1.21 (0.86, 1.70)	0.21 (0.16, 0.30)	<0.001	0.28 (0.20, 0.39)	<0.001
sCD14 (ng/mL)	0.97 (0.93, 1.02)	1.03 (0.98, 1.08)	0.70	0.99 (0.94, 1.04)	0.70
sCD163(ng/mL)	0.98 (0.89, 1.07)	1.03 (0.94, 1.13)	0.44	1.12 (1.03, 1.23)	0.037
IL-6(pg/mL)	1.03 (0.87, 1.21)	1.13 (0.96, 1.33)	0.096	1.03 (0.87, 1.21)	0.38
D-dimer (ng/mL)	1.02 (0.91, 1.13)	0.99 (0.89, 1.10)	0.69	1.08 (0.97, 1.19)	0.46
KT ratio (nM/uM)[2]	-1.3 (-3.6, 1.1)	-3.0 (-5.3, -0.7)	0.30	0.5 (-1.8, 2.7)	0.30
%CD38+HLA-DR+ CD8+ T cells[2]	-0.4 (-2.2, 1.3)	-1.5 (-3.2, 0.2)	0.40	-1.2 (-2.9, 0.5)	0.56
FMD (%)[2]	-0.5 (-1.3, 0.4)	-1.2 (-2.1, -0.4)	0.091	-0.5 (-1.3, 0.4)	0.61

[1] P value tests difference between Aspirin arm and placebo arm

[2] Changes in KT ratio, CD8 activation, and FMD were modeled as absolute changes (not relative changes).

Grazie per l'attenzione