Envejecimiento, inflamación y comorbilidades

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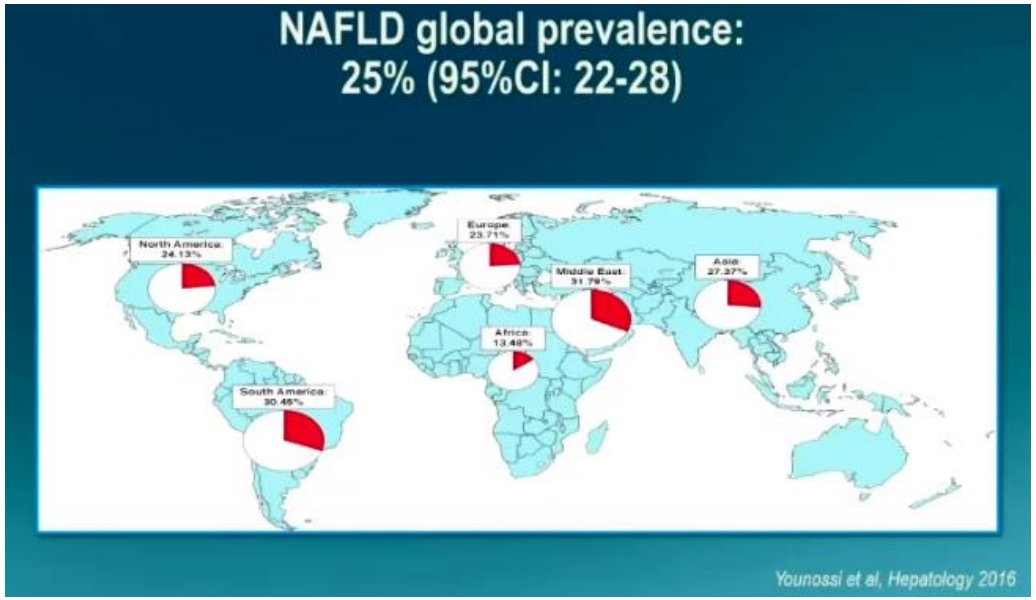
Fundació Lluita contra la SIDA i les Malalties Infeccioses
H Germans Trias i Pujol, Badalona

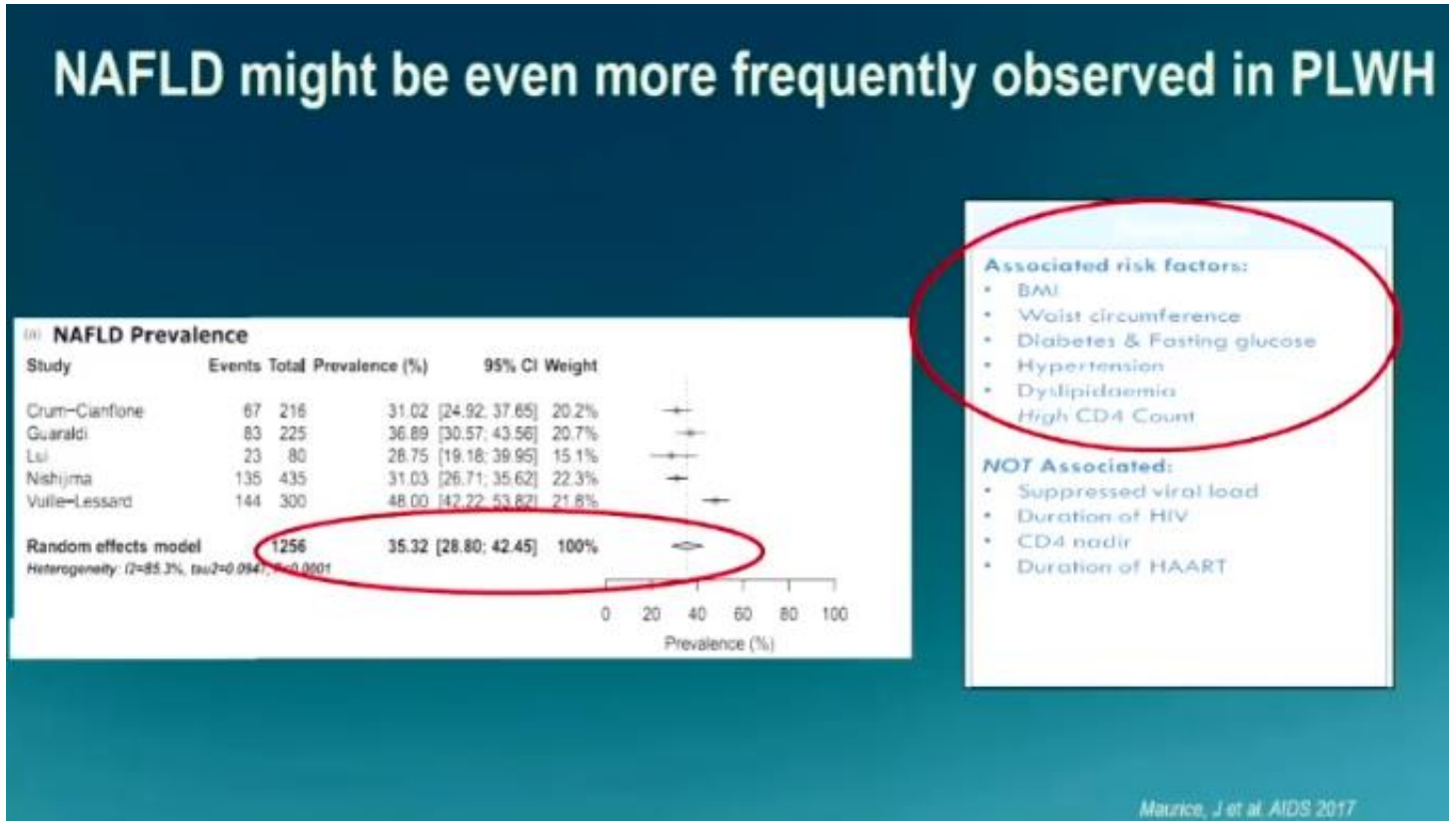
ESTEATOSIS HEPÁTICA

Liver Steatosis
in People Living with HIV

Maud Lemoine, MD, PhD, FRCP
Imperial College London, UK

1- Elevada prevalencia en población general y mayor en VIH





2- Diagnóstico: terminologia

MAFLD
Metabolic (dysfunction) Associated Fatty Liver Disease

JOURNAL OF HEPATOLOGY

A new definition for metabolic dysfunction-associated fatty liver disease: An international expert consensus statement

A new controversial entity

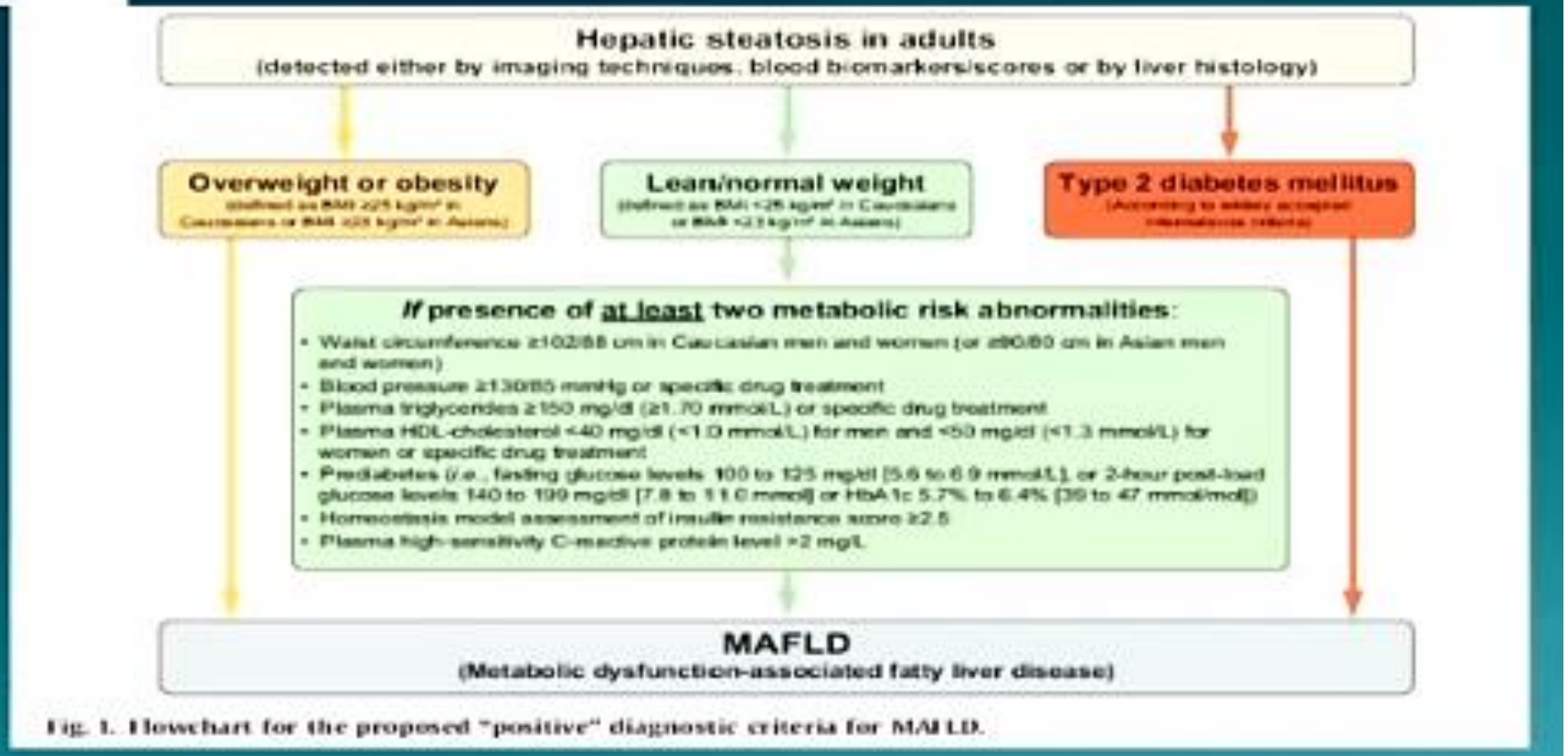
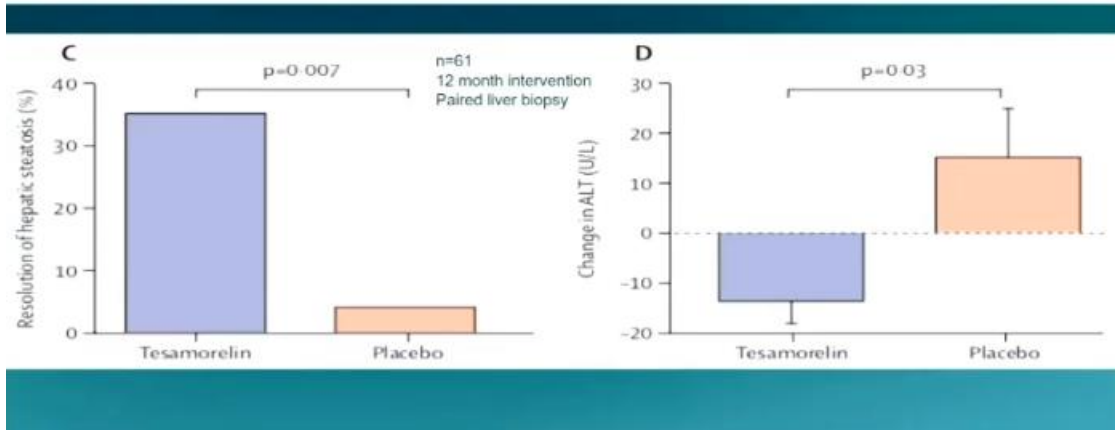


Fig. 1. Flowchart for the proposed "positive" diagnostic criteria for MAFLD.

3- Tratamiento

Effects of tesamorelin on non-alcoholic fatty liver disease in HIV: a randomised, double-blind, multicentre trial

Takara L Stanley*, Lindsay T Fourman*, Meghan N Feldpausch, Julia Purdy, Isabel Zheng, Chelsea S Pan, Julia Aepfelbacher, Colleen Buckless, Andrew Tsao, Anela Kellogg, Karen Branch, Hang Lee, Chia-Ying Liu, Kathleen E Corey, Raymond T Chung, Martin Torriani, David E Kleiner, Colleen M Hadigan†, Steven K Grinspoon†

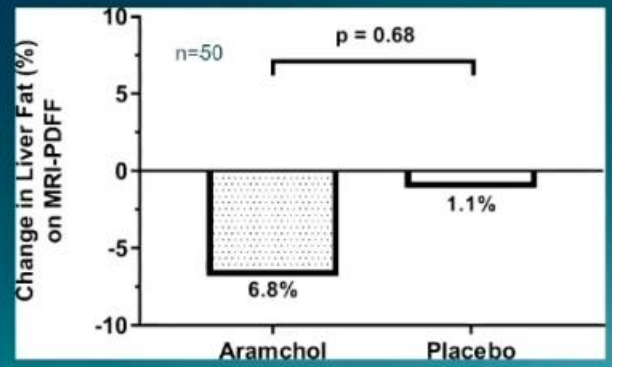


Aramchol - ARRIVE Trial

Double-blind, randomized, placebo-controlled trial
12 weeks with 600 mg of oral Aramchol daily

NAFLD defined **by MRI-PDFF≥ 5%**
+ at least one risk factor for severe NAFLD

(dyslipidemia, ALT>ULN, overweight, prediabetes/diabetes)



Ajmera et al, Hepatology 2019

Vitamin E in HIV-associated NASH

n=27 HIV mono-infected patients with a diagnosis of **NASH based on CAP and cytokeratin-18**
Single arm trial of 24 Vitamin E 800 IU/L daily during 24 weeks

Sebastiani et al, AIDS 2020

Weight Loss (WL) is key

n=261 (non HIV patients)
12 months intervention
paired liver biopsy

Reduced steatosis

NASH Resolution

NASH & Fibrosis Regression

Poster 00520

NAFLD IS COMMON AND ASSOCIATED WITH CARDIOVASCULAR RISK IN REPRIEVE PARTICIPANTS

Carl J. Fichtenbaum, MD[1] Heather J. Ribaudo, PhD[2] , Jana Taron, MD[3], Jorge Leon-Cruz, MS[2], Netanya S. Utay, MD[4] Ken S. Ho, MD, MSc[5], Anne F. Luetkemeyer, MD[6], Shobha Swaminathan, MD[7], Carrie D. Johnston, MD, MSc[8], Evelynne S. Fulda, BA[9], Emma Kileel, MPH[9], Michael T. Lu, MD, MPH[10], Steven K. Grinspoon, MD[9], Jordan E. Lake, MD[11], and REPRIEVE Trial Investigators. [1]University of Cincinnati, [2]Harvard T.H. Chan School of Public Health, [3]University Medical Center Freiburg, [4]University of Texas Southwestern Medical Center, [5]University of Pittsburgh School of Medicine, [6]University of California, San Francisco, [7]Rutgers New Jersey Medical School, [8]Weil Cornell School of Medicine, [9]Massachusetts General Hospital, [10] Harvard Medical School, [11]University of Texas Health Science Center.

Objective

The objective of this analysis was to estimate the prevalence and cardiometabolic characteristics of NAFLD among REPRIEVE participants who underwent computed tomography (CT).

Methods

- The REPRIEVE Mechanistic substudy is embedded within an international primary CVD prevention RCT of pitavastatin calcium vs. placebo among 7,770 PWH ages 40-75 years on antiretroviral therapy (ART).
- A subset of 655 U.S. participants had non-contrast CT with measurement of hepatic steatosis defined as a mean hepatic attenuation <40 HU or liver/spleen ratio <1.0.

Figure 2 – Risk Factors of NAFLD

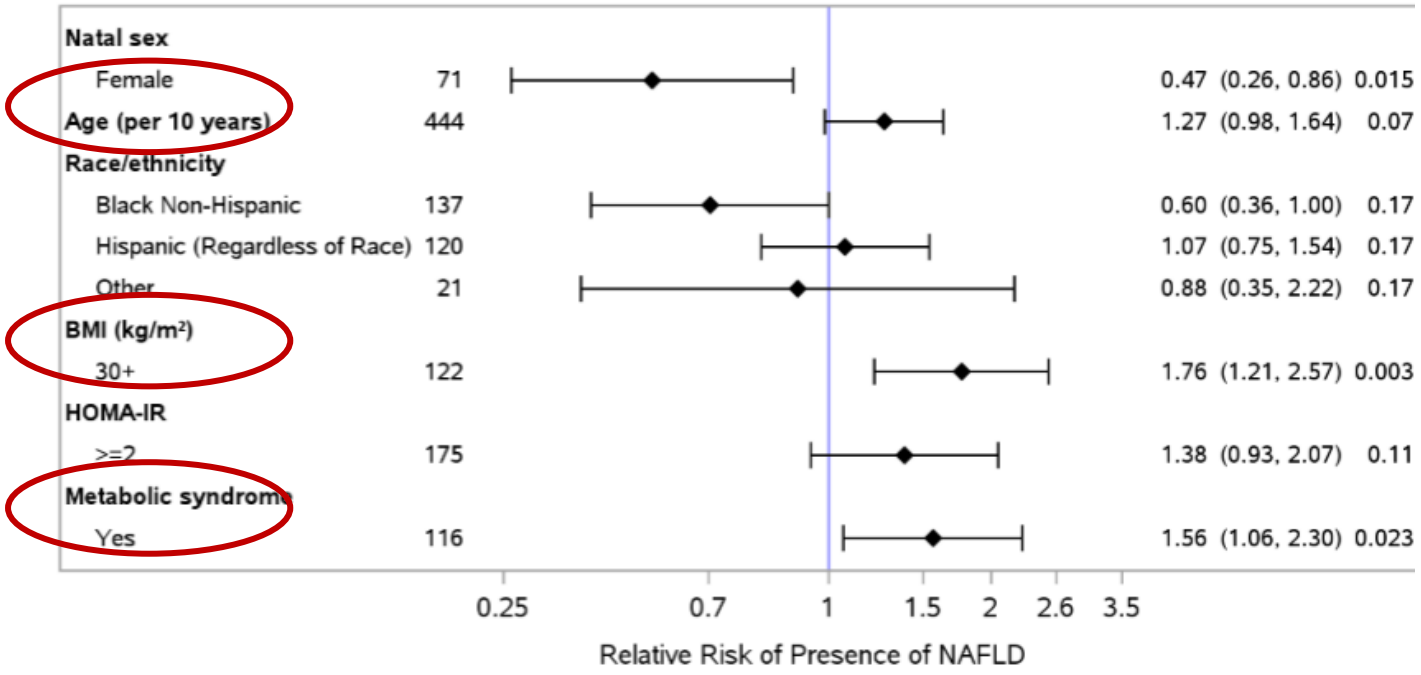


Table 4 – Immune / Inflammatory Indices

	Hepatic Steatosis			NAFLD		
	Total (N=655)	No (N=516)	Yes (N=139)	Total (N=477)	No (N=380)	Yes (N=97)
LpPLA-2 (ng/mL)	131 (92.2, 169)	129 (90.1, 165)	140 (99.4, 176)	132 (95.9, 171)	130 (91.1, 168)	144 (107, 187)
P-value			*0.025*			*0.013*
sCD163 (ng/mL)	846 (626, 1096)	846 (616, 1078)	845 (666, 1204)	852 (649, 1120)	851 (634, 1113)	860 (674, 1215)
P-value			*0.34*			*0.50*
sCD14 (ng/mL)	1818 (1527, 2174)	1827 (1537, 2176)	1721 (1483, 2120)	1818 (1506, 2173)	1831 (1536, 2194)	1699 (1440, 2085)
P-value			*0.39*			*0.18*
MCP-1 (pg/mL)	186 (147, 242)	185 (145, 236)	193 (157, 256)	186 (146, 245)	185 (144, 239)	199 (155, 267)
P-value			*0.09*			*0.11*
IL-6 (pg/mL)	1.63 (1.02, 2.89)	1.63 (1.00, 2.85)	1.68 (1.18, 3.33)	1.62 (1.01, 2.93)	1.58 (0.99, 2.80)	1.66 (1.15, 3.73)
P-value			*0.24*			*0.20*
D-Dimer (ng/mL)	243 (146, 397)	242 (144, 397)	249 (147, 391)	251 (153, 424)	249 (153, 431)	257 (149, 420)
P-value			*0.98*			*0.84*

Conclusions

- In this cohort with controlled HIV, high CD4 counts, and low to moderate cardiovascular risk, NAFLD (20%) was common including 45% with higher ALT values
- NAFLD was more prevalent with older age, and those self-identified as males and non-black race; it was also associated with higher BMI and metabolic syndrome.
- NAFLD was associated with selected indices of inflammation and metabolic disturbances but not HIV specific indices or ART.
- Elevated LpPLA-2 and hsCRP levels suggest a correlation between NAFLD and cardiovascular risk in PWH.

Determinants of liver steatosis in people living with HIV on antiretroviral therapy

01955

Riebensahm C[1,2], Berzigotti[3,4], Surial B[1], Günthard H[5,6], Tarr, P.E.[7], Furrer H[1], Rauch A[1], Wandeler, G[1,8], Swiss HIV Cohort Study

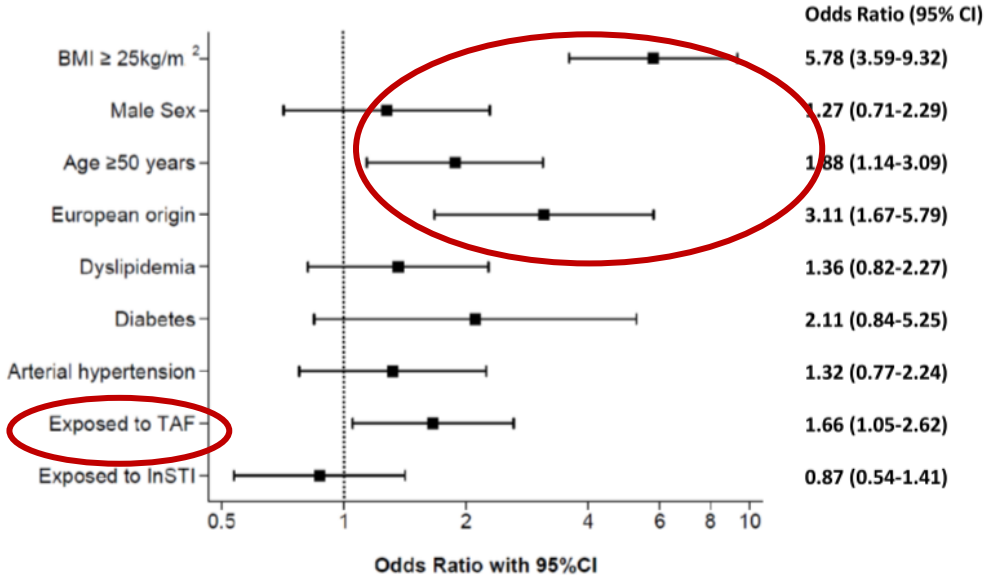
[1]Department of Infectious Diseases, Bern University Hospital, University of Bern, Switzerland, [2]Graduate School of Health Sciences, University of Bern, Switzerland, [3]Department for Visceral Surgery and Medicine, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, Switzerland, [4]Hepatology, [4]Department of BioMedical Research, University of Bern, Bern, Switzerland, [5]Division of Infectious Diseases and Hospital Epidemiology, University Hospital Zurich, University of Zurich, [6]Institute of Medical Virology, University of Zurich, [7]University Department of Medicine, Kantonsspital Bruderholz, University of Basel, [8]Institute of Social and Preventive Medicine, University of Bern, Switzerland

Table 1. Baseline characteristics, stratified by BMI category

Characteristics	BMI <25 kg/m²	BMI ≥25 kg/m²
	N= 204	N= 212
Median age, years (IQR)	51 (42-59)	52 (46-59)
Female sex (%)	52 (25.5)	61 (28.8)
Region of origin (%)		
Europe	154 (75.5)	151 (71.2)
Africa	27 (13.2)	52 (24.5)
Other	23 (11.3)	9 (4.2)
HIV transmission group (%)		
MSM	112 (54.9)	90 (42.5)
Other	92 (45.1)	122 (57.5)
Arterial hypertension (%)	49 (24.0)	72 (34.0)
Diabetes (%)	9 (4.4)	28 (13.2)
Dyslipidemia (%)	59 (28.9)	98 (46.2)
Median BMI, kg/m² (IQR)	22.1 (20.8-23.9)	29.6 (26.6-31.5)
Median ALT, U/L (IQR)	28.0 (19.0-30.5)	33.2 (22.0-40.0)
Hazardous alcohol consumption (%)	41 (22.2)	42 (22.0)
Median current CD4+ count, cells/µl (IQR)	740 (535-897)	792 (577-985)
Median eGFR in mL/min (IQR)	91 (75-104)	89 (71-100)
ART duration, years (IQR)	13.3 (7.0-20.0)	12.0 (6.0-19.0)
Exposed to TAF (%)	103 (50.5)	126 (59.4)
Exposed to InSTI (%)	141 (69.1)	138 (65.1)

Overall, 212 (51.0%) participants had liver steatosis, including 143 with severe steatosis. The proportion of individuals with liver steatosis was 69.8% in patients with a BMI ≥25 kg/m² and 31.4% in individuals with a BMI <25 kg/m². Of all participants, 179 (43.0%) met the criteria for MAFLD.

Figure 1. Multivariate analysis of factors associated with liver steatosis



Abbreviations: BMI, body mass index, TAF; tenofovir alafenamide; InSTI, integrase-strand transfer inhibitor; OR, odds ratio; CI, confidence interval

Conclusion

Our data show a high prevalence of liver steatosis among PLWH on ART in Switzerland.

In addition to well-established risk factors such as age, ethnicity and obesity, the use of TAF was significantly associated with hepatic steatosis.

Overall, MAFLD was diagnosed in 43% of participants, including in 17% of individuals with a BMI <25 kg/m² and liver steatosis.

ENVEJECIMIENTO

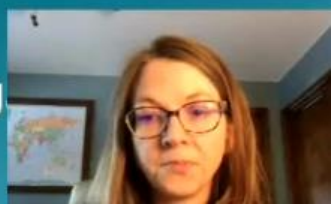
Geographical Differences in Functional Impairment of People with HIV

Kristine M. Erlandson, MD MS
University of Colorado- Anschutz Medical Campus
Aurora, CO, USA

- Measures of physical function can provide a better estimate of the impact of aging than chronologic age
  - Strongly associated with morbidity and mortality, including cardiovascular disease
- Physical function impairments occur earlier in people with HIV
- Little is known about how functional impairments differ between geographic regions
  - ART timing or regimens
  - Gender differences

Methods

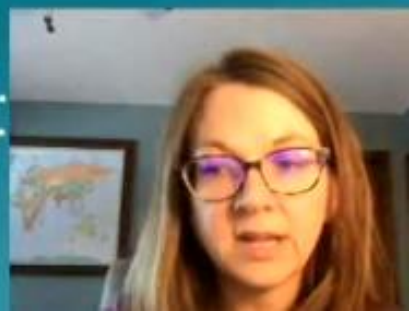
- REPRIEVE is a prospective, double-blind, randomized, placebo-controlled multicenter study comparing pitavastatin vs placebo
- Eligibility includes PWH on ART, age between 40 and 75 years, CD4 ≥100 cells/mm^3, and no known CVD
- Global burden of disease (GBD) super regions defined by WHO classifications:
  - *High income*: U.S. (excluding Puerto Rico), Canada, and Spain
  - *Latin America/Caribbean*: Puerto Rico, Brazil, Peru, and Haiti
  - *South Asia*: India
  - *Southeast/East Asia*: Thailand
  - *Sub-Saharan Africa*: Botswana, South Africa, Zimbabwe, and U

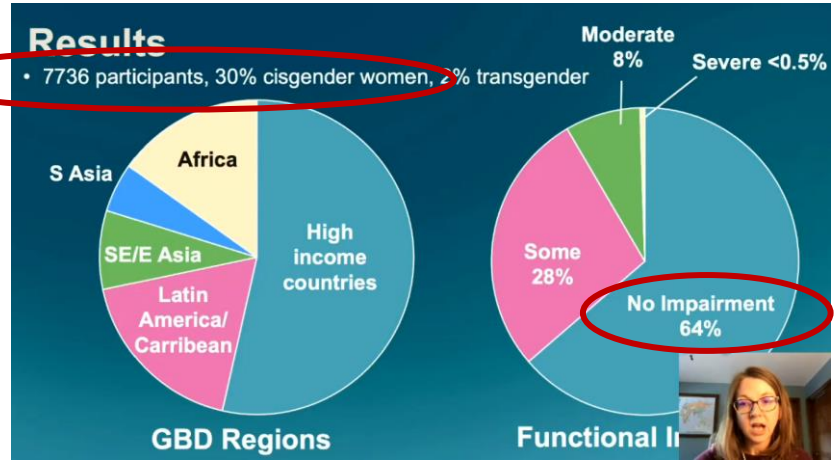


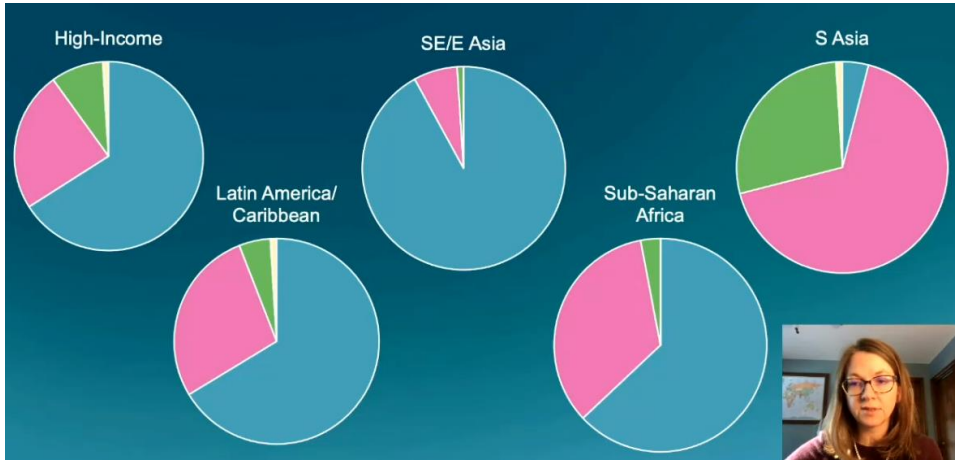
Methods: Duke Activity Status Instrument (DASI)

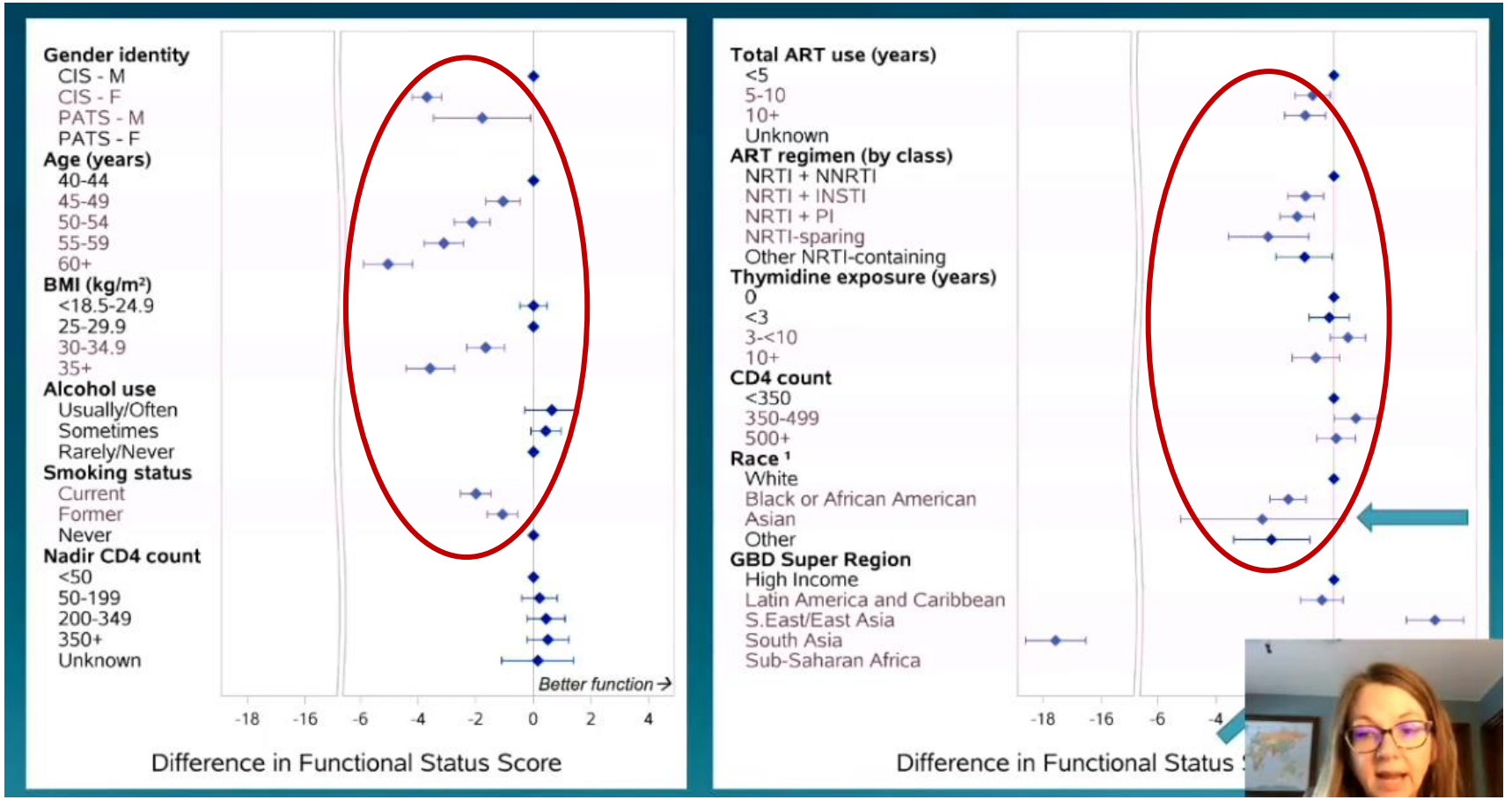
Can you…	MET
1. Take care of yourself, that is, eating, dressing, bathing, and using the toilet?	2.75
2. Walk indoors, such as around your house?	1.75
3. Walk a block or two on level ground?	2.75
4. Climb a flight of stairs or walk up a hill?	5.50
5. Run a short distance?	8.00
6. Do light work around the house like dusting or washing dishes?	2.70
7. Do moderate work around the house like vacuuming, sweeping floors, carrying groceries?	3.50
8. Do heavy work around the house like scrubbing floors, or lifting or moving heavy furniture?	8.00
9. Do yard work like raking leaves, weeding or pushing a power mower?	4.50
10. Have sexual relations?	5.25
11. Participates in moderate recreational activities, like golf, bowling, dancing, doubles tennis, or throwing baseball or football?	6.00
12. Participate in strenuous sports like swimming, singles tennis, football, basketball or skiing?	7.50

- No impairment (58.2)
- Some impairment (34.7 to <58.2), no difficulty with activities with MET <7.
- Moderate impairment (9.95 to <34.7), no difficulty with activities with MET
- Severe (0 to <9.95), difficulties with activities inside the house

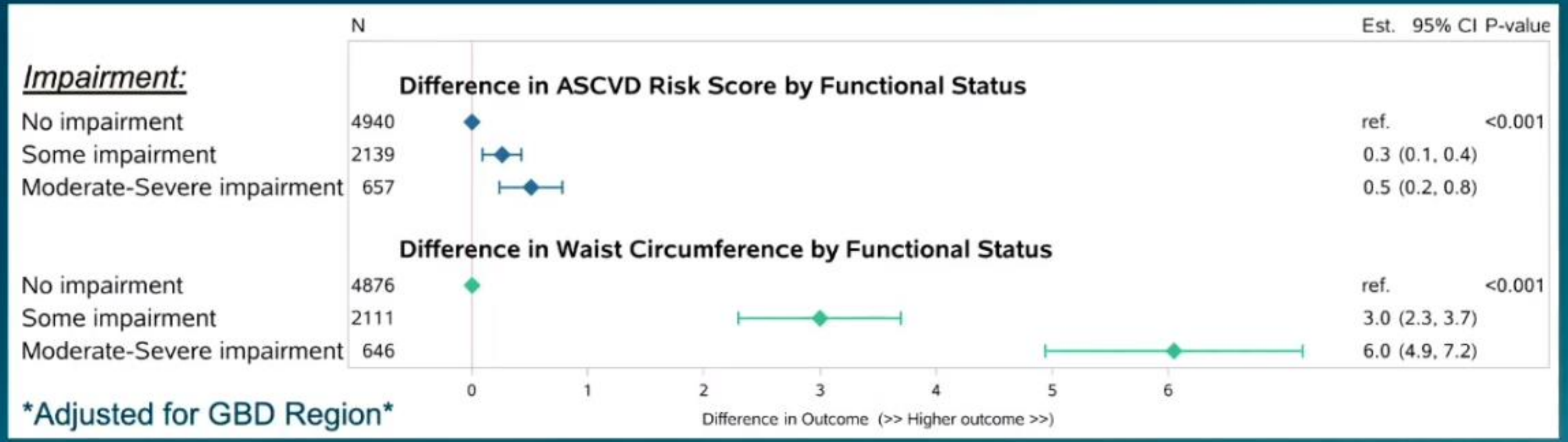



Results
• 7736 participants, 30% cisgender women, 2% transgender
S Asia
Africa
SE/E Asia
Latin America/ Carribean
High income countries
GBD Regions
Moderate 8%
Severe <0.5%
Some 28%
No Impairment 64%
Functional I

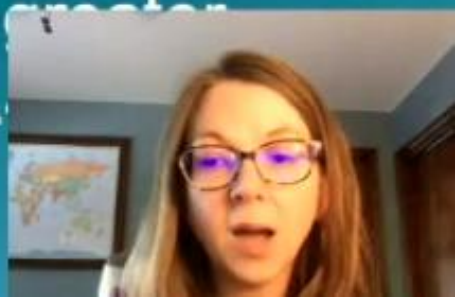

High-Income
SE/E Asia
S Asia
Latin America/ Caribbean
Sub-Saharan Africa


Gender identity
CIS - M
CIS - F
PATS - M
PATS - F
Age (years)
40-44
45-49
50-54
55-59
60+
BMI (kg/m²)
<18.5-24.9
25-29.9
30-34.9
35+
Alcohol use
Usually/Often
Sometimes
Rarely/Never
Smoking status
Current
Former
Never
Nadir CD4 count
<50
50-199
200-349
350+
Unknown
Better function →
-18 -16 -6 -4 -2 0 2 4
Difference in Functional Status Score
Total ART use (years)
<5
5-10
10+
Unknown
ART regimen (by class)
NRTI + NNRTI
NRTI + INSTI
NRTI + PI
NRTI-sparing
Other NRTI-containing
Thymidine exposure (years)
0
<3
3-<10
10+
CD4 count
<350
350-499
500+
Race ¹
White
Black or African American
Asian
Other
GBD Super Region
High Income
Latin America and Caribbean
S.East/East Asia
South Asia
Sub-Saharan Africa
-18 -16 -6 -4
Difference in Functional Status

Functional Impairment and Cardiometabolic Risk



- Moderate to severe impairment was associated with 0.5 point greater ASCVD risk score, 6 cm greater waist circumference, and a 1.5 odds of metabolic syndrome

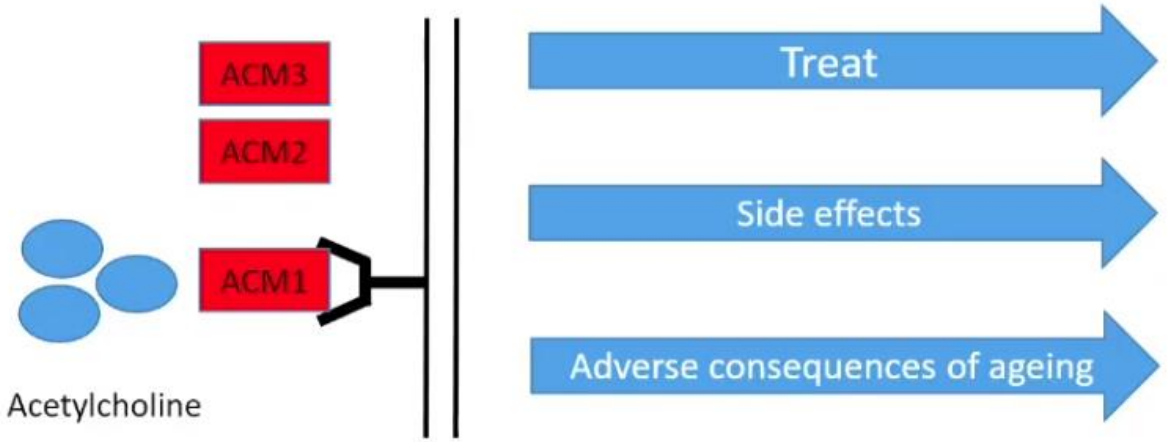


ANTICHOLINERGIC MEDICATIONS ASSOCIATED WITH FALLS AND FRAILTY IN PEOPLE WITH HIV (PWH)

Jessica Doctor
Guy's and St Thomas' Hospital
London, United Kingdom

The POPPY Study Group

Anticholinergic Medications (ACM)



POPPY

Are PWH at risk of adverse consequences of aging secondary to ACM?

- Limited studies to date in PWH
- Prevalence 15-30% of ACM use
- Associations with neurocognitive dysfunction[1]

1 Cooley AIDS 2021

Methods: Statistical Analysis

POPPY

Pharmacokinetic and clinical observations in people over 50

Cross-sectional analysis of data collected at study entry using **Stata version 16**

Participant taking **any ACM**: Score ≥ 1 on any scale

1. Anticholinergic Risk Score
2. Anticholinergic Burden Score
3. Scottish Intercollegiate Guidelines Network

Main Exposure

1. **Recurrent falls**: ≥ 2 self reported falls within the previous 28 days
2. **Frailty**: Modified Fried's criteria

Outcomes

Confounders considered

Socio-demographic
Lifestyle factors
HIV related indices
Co-morbidities
Co-medications
PROMS: PHQ 9

2 stage logistic regression

1. Socio-demographic/lifestyle covariates which showed a significant association with exposure
2. Co-morbidities, Co-medications, PROMS: PHQ-9 added in a stepwise manner

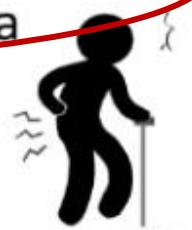
Demographics of PWH ≥ 50

Variable	N=699
Age (median (IQR)), years	57 (53-62)
Male, n (%)	612 (88)
White, n (%)	603 (86)
Unemployed, n (%)	99 (14)
High education, n (%)	479 (69)
Rec drugs last 6 months, n (%)	177 (25)

Prevalence of outcome

9% (63/673) reported recurrent falls

32% (126/609) met frailty criteria



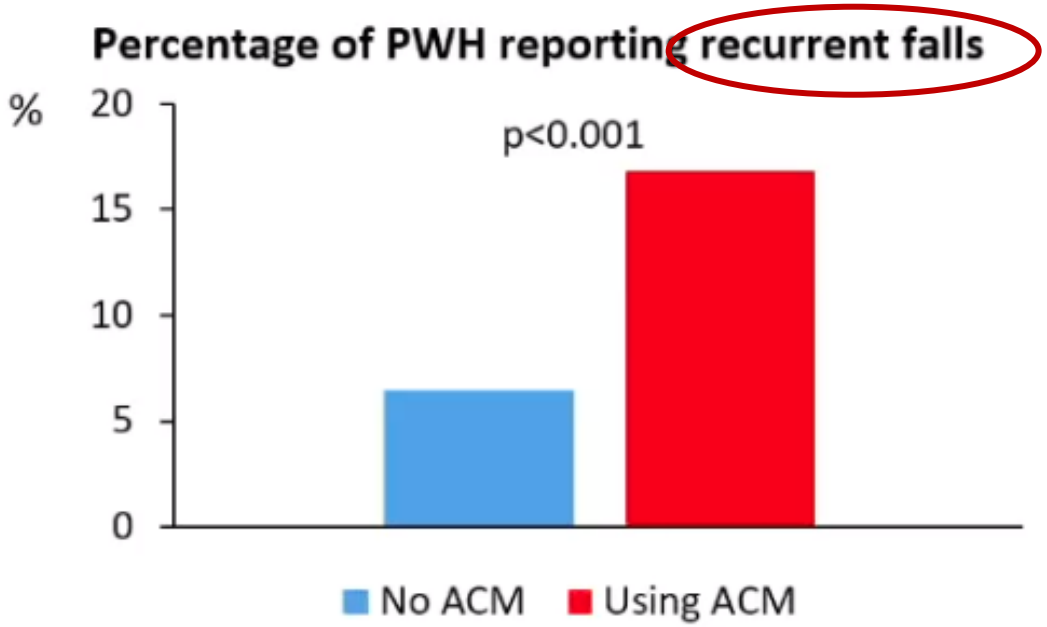
Number of ACM prescribed

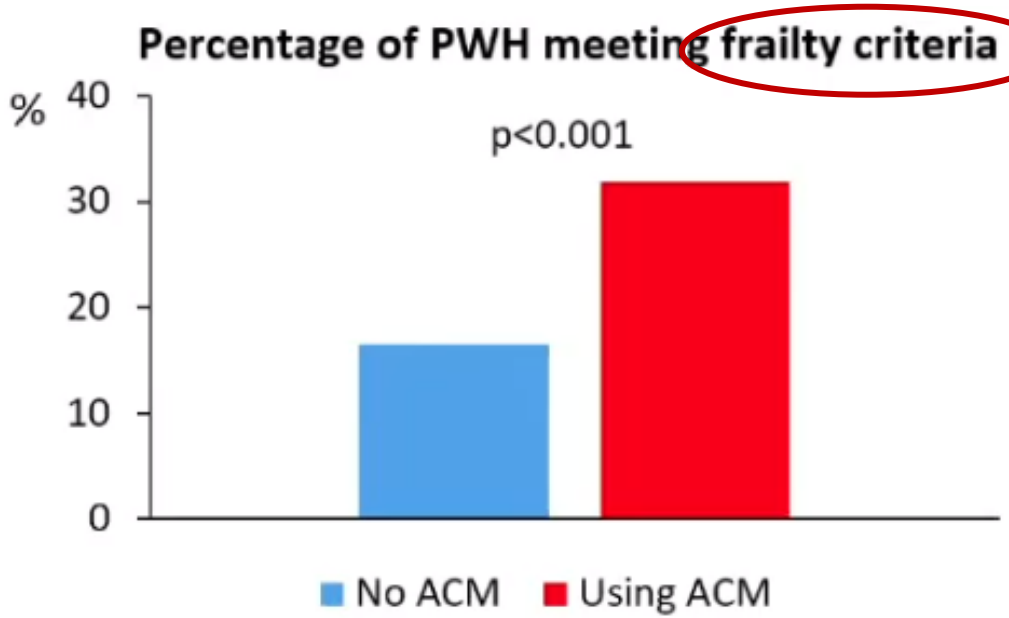
ACM number	Frequency n (%)
0	507 (73)
1	129 (18)
≥2 (maximum 9)	63 (9)

Commonest ACM prescribed

ACM	Frequency n (%)
Codeine	36 (12)
Citalopram	34 (12)
Loperamide	25 (9)
Amitriptyline	21 (7)
Diazepam	17 (6)
Cetirizine	16 (5)

Variable	Prescribed an ACM		P value
	No (n=506)	Yes (n=193)	
Age (median [IQR]), years	57 (53-62)	56 (52-61)	0.56
Male, n (%)	441 (87)	171 (89)	0.61
Single, n (%)	301 (60)	134 (69)	0.01
Unemployed, n (%)	67 (13)	32 (17)	0.05
High education, n (%)	348 (69)	131 (68)	0.82
Rec drugs last 6 months, n (%)	118 (23)	59 (31)	0.05
Moderate severe/severe depressive symptoms, n (%)	49 (10)	31 (16)	0.001
Number of comorbidities (mean [SD])	2.76 (1.6)	4.19 (1.51)	<0.001
Number of non ACM co-medications (≥5)	44 (9)	70 (36)	<0.001





Final regression model of the association of using any ACM with recurrent falls and frailty

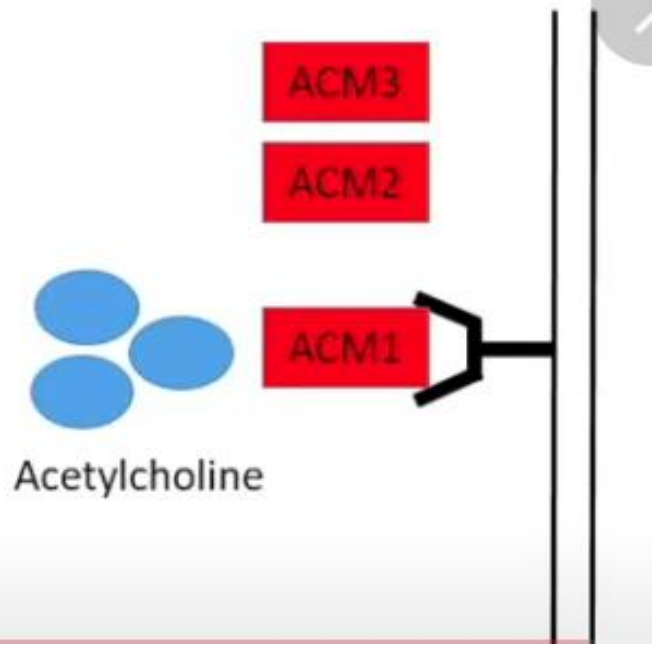
Adjustment	ACM	Recurrent falls			Frailty		
		OR	CI	P value	OR	CI	P value
Unadjusted	none	1	n/a		1	n/a	
	Any	3.3	1.9 - 5.9	<0.001	2.3	1.5 - 3.6	<0.001
Demographic/lifestyle	Any	2.5	1.3 - 4.6	0.004	1.8	1.1 – 3.0	0.02
Demographic/lifestyle and clinical factors	Any	1.9	0.9 - 4.0	0.08	1.7	0.9 – 3.0	0.08

Summary

- ACMs are prescribed in a quarter of the population of PWH
- Evidence of an association with recurrent falls and, to a lesser extent, frailty
- Our findings support most worldwide data in the general geriatric population
- Clinicians to be aware of this association and reduce exposure to ACM where possible

- **Limitations**
  - Cross-sectional analysis
  - Unable to account for duration of use or dose of ACM
  - Self-reported exposure and some outcome measures

- **Future Work**
  - Investigation of temporal relationships
  - Investigation of possible association between ACM and cognitive impairment



CARDIOVASCULAR y INFLAMACIÓN

Trends in Myocardial Infarction Risk by HIV Status in Two US Healthcare Systems

Michael J. Silverberg

Kaiser Permanente Northern California
Oakland CA USA

Study Objective

To quantify changes over time in MI incidence rates comparing PWH and PWoH identified from two large healthcare systems in California and Massachusetts, with participants selected to have similar baseline risks of MI.

Kaiser Permanente Northern California (KPNC)

Integrated healthcare delivery system serving San Francisco Bay Area

4.5 million current members, with ~30,000 cumulative members with HIV

Mass General Brigham (Partners)

- Integrated health care system serving Boston, MA and surrounding regions
- Brigham and Women's and Massachusetts General Hospitals and affiliated outpatient centers
- 1.5 million served annually; ~7,000 cumulative with HIV

Methods

- Study design: cohort study
- Study population:
  - PWH: adults (≥18 years) identified between 2005-2017 from KPNC or Partners. Those with history of CVD excluded.
  - PWoH: 3:1 propensity-matched in KPNC and 4:1 in Partners, with propensity scores informed by baseline* demographics (age, race, sex, year) and baseline* Framingham risk score components (total cholesterol, HDL, diabetes, systolic BP, hypertension treatment, smoking)

  *baseline: The first year Framingham risk score components were measured, anchored at lipids date
- Outcome: New diagnosis of MI during 2005-2020 (all events adjudicated at Partners; validated case definition at KPNC)
- Exposure: HIV status and baseline calendar era (2005-2009 and 2010-2017)
- Follow-up: From baseline until earliest of: MI, death, loss-to-follow-up, 5 years after baseline, or administrative end of follow-up (2020)

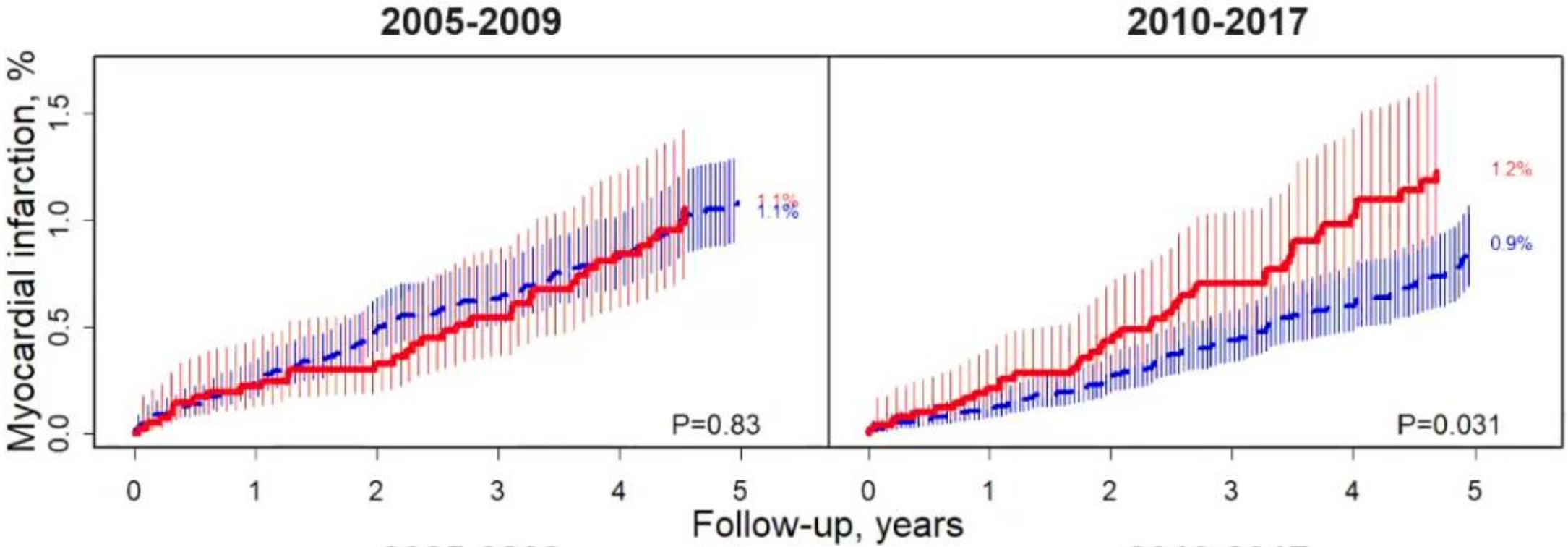
Baseline Characteristics by HIV and Calendar Era
reflects matching by HIV status

	PWH		PWoH	
Baseline Calendar Era	2005-2009	2010-2017	2005-2009	2010-2017
N	4,280	5,121	14,059	15,359
Mean age, years	44.5	43.7	44.2	43.3
Men, %	87	89	85	90
White / Black / Other, %	53 / 17 / 30	49 / 18 / 34	51 / 19 / 30	49 /17 / 34
Mean total cholesterol, mg/dL	182.6	177.2	182.9	178.4 ⬇
Mean HDL cholesterol, mg/dL	42.6	45.8	43.7	45.4 ⬆
Mean systolic blood pressure, mmHg	123.0	123.6	123.8	123.0
Current smoker, %	27	22	28	23 ⬇
Hypertension medications, %	26	25	28	23 ⬇
Diabetes, %	7	5	6	6

HIV-specific Baseline Characteristics

	PWH	
Baseline Calendar Era	2005-2009	2010-2017
N	4,280	5,121
HIV RNA>400 copies/mL, %	39	23 ⬇
Mean CD4, cells/μL	470	587 ⬆
ART use, %	76	88 ⬆
Mean years HIV	7.8	9.1 ⬆
Prior ART Class experience (among ART users), %		
NNRTI	52	46 ⬇
PI	54	27 ⬇
INSTI	3	40 ⬆⬆

Cumulative incidence of MI similar by HIV status in 2005-2009 but higher for PWH compared with PWoH in 2010-2017



2005-2009

	KPNC		Partners		Overall	
HIV Status	PWH	PWoH	PWH	PWoH	PWH	PWoH
N	3,584	10,740	696	3,319	4,280	14,059
MI events	33	105	2	12	35	117
MI rate*	0.24	0.25	0.08	0.10	0.21	0.22

* per 100 person-years

2010-2017

	KPNC		Partners		Overall	
HIV Status	PWH	PWoH	PWH	PWoH	PWH	PWoH
N	4,615	13,857	506	1,502	5,121	15,359
MI events	39	81	4	6	43	87
MI rate*	0.25	0.17	0.22	0.12	0.25	0.16

* per 100 person-years

Adjusted* HRs for MI by HIV Status (PWoH reference), and stratified by Calendar era and Cohort

	KPNC		Partners		Overall	
Era	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
2005-2009	1.0 (0.7, 1.5)	0.90	1.2 (0.3, 5.8)	0.82	1.1 (0.8, 1.5)	0.61
2010-2017	1.6 (1.1, 2.4)	0.02	2.1 (0.6, 7.5)	0.28	1.6 (1.1, 2.4)	0.007

*Stepwise adjusted models considering demographics and Framingham risk score components.

Summary / Conclusions

- Among PWH and PWoH with similar CVD risk profiles at baseline, we observed no difference in MI risk for baseline years 2005-2009, and a 60% higher risk in PWH for years 2010-2017
- Results appear to be driven by decrease in MI risk for PWoH, that was not seen for PWH
- HIV-specific factors, such as longer HIV duration and newer ART (e.g., INSTIs), may have prevented PWH from realizing the same improvements in MI risk as PWoH
- Clinical implications for PWH include continued surveillance for CVD and primary prevention, including possibly more aggressive interventions.

GUT MICROBIOTA, PLASMA METABOLOMICS, AND ATHEROSCLEROSIS IN HIV INFECTION

Zheng Wang , Ph.D.

Albert Einstein College of Medicine
Bronx, New York, USA

Aims

- Gut Microbiota Alteration and Plaque (To identify specific taxa which associated with plaque)
- Plaque-associated Microbial Taxa and Host Plasma Metabolomic profiles
- Microbial-associated Host Metabolites and Plaque
- Gut microbiota Functional components and potential underlying mechanisms
  (To reveal key enzymes and mechanisms)

Methods

Gut Microbiome measurement

- Amplicon sequencing: 16S rRNA V4 region.
  QIIME 2 + PICURSt 2 pipeline
- 84 Microbial Genera which consisted of 660 amplicon sequence variants (ASVs)
- 1952 GMB Functional Enzymes
- CSS / CLR transformation

Plasma Metabolomics profiling

- Liquid chromatography– mass spectrometry (LC-MS)
  Progenesis QI + TraceFinder
- 211 lipids and 167 polar metabolites
- Inverse normal transformation

Carotid Artery Plaque Ascertainment

- High-resolution B-mode ultrasound
- Focal plaque assessed at 8 locations
  Near and far walls of common carotid, internal carotid , external carotid, bifurcation

Methods

Cross- sectional

n= 361

Number of plaque cases = 97
WIHS participants
2017- 2019

- Gut Microbiota and Plaque
- Plaque-associated Microbial Taxa and Plasma Metabolomic profiles
- Gut microbiota Taxa, Functional components, Plasma Metabolites and Plaque

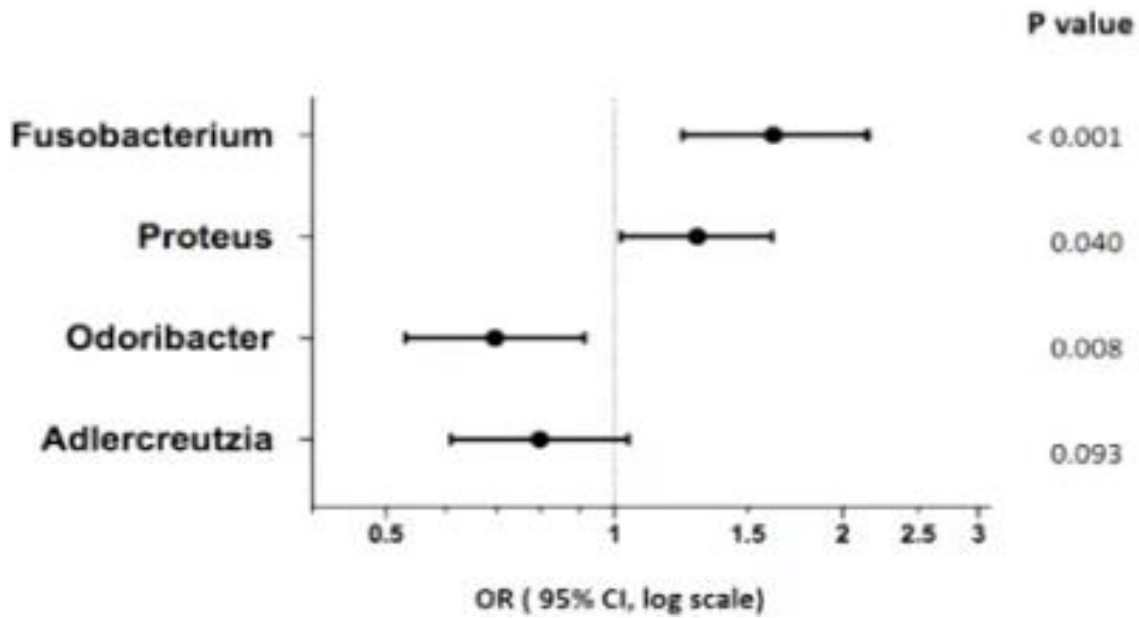
Prospective

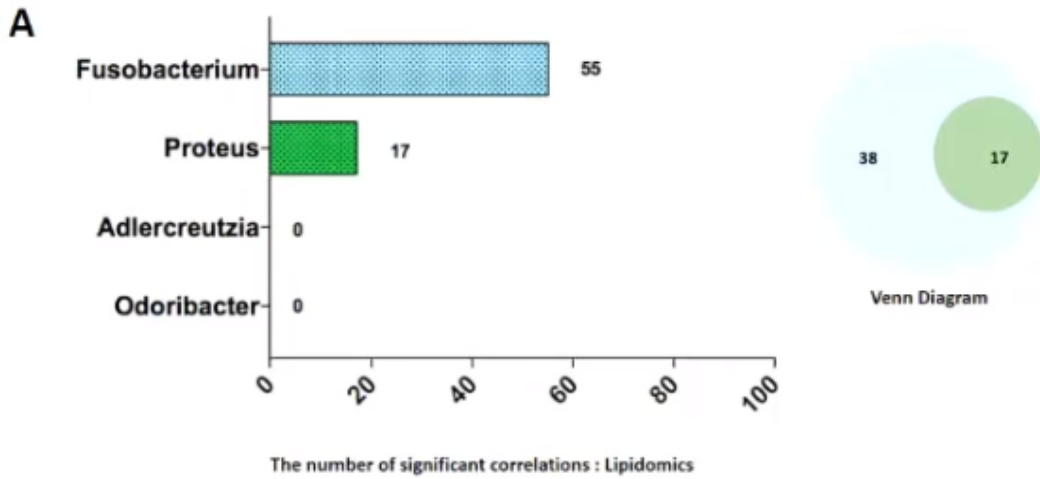
n= 737

Identified 112 incident plaque cases
~7-years follow-up
MWCCS participants
Base line 2004 - 2006
Follow up 2011 - 2013

- Microbial-associated Metabolites and incident Plaque

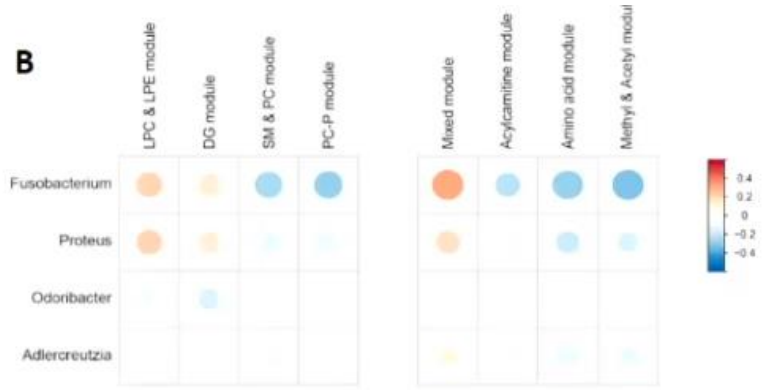
- Potential Mechanisms


P value
Fusobacterium
Proteus
Odoribacter
Adlercreutzia
< 0.001
0.040
0.008
0.093
0.5
1
1.5
2
2.5
3
OR (95% CI, log scale)

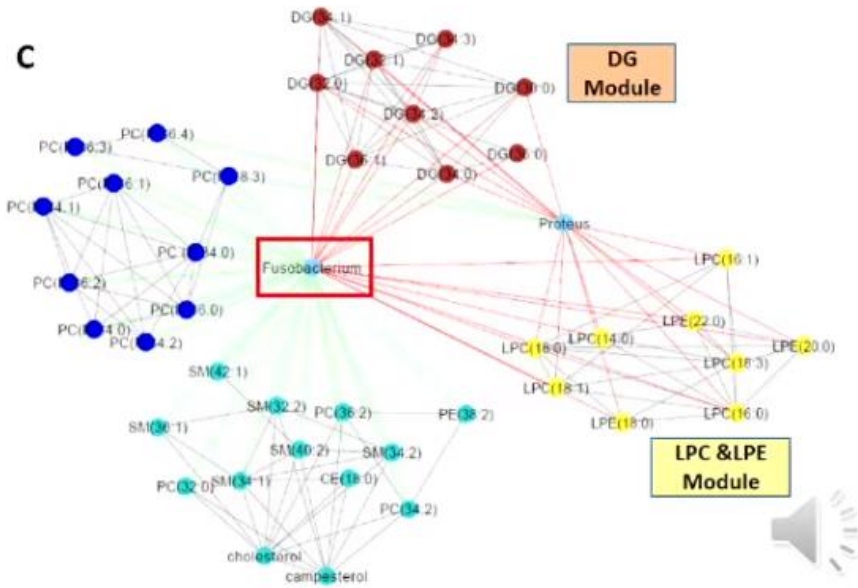

A
Fusobacterium
Proteus
Adlercreutzia
Odoribacter
55
17
0
0
0
20
40
60
80
100
The number of significant correlations : Lipidomics

38
17
Venn Diagram

B



C



Section 3 : Bacteria-associated Host Plasma Metabolites and Risk of Carotid Artery Plaque

- **Prospective data** ; N= 737 ; Over 7-year follow-up, identified 112 incident plaque cases.

		All (n= 737)		
Module		**RR**	**95% CI**	**p value**
DG module	Model 1	1.24	(1.02 - 1.51)	0.030
	Model 2	1.24	(1.02 - 1.51)	0.029
LPC & LPE module	Model 1	1.34	(1.09 - 1.64)	0.005
	Model 2	1.32	(1.07 - 1.63)	0.008
PC-PE module	Model 1	1.37	(1.11 - 1.69)	0.003
	Model 2	1.34	(1.08 - 1.67)	0.008
SM & PC module	Model 1	1.08	(0.88 - 1.32)	0.466
	Model 2	1.12	(0.92 - 1.38)	0.264
Amino acid module	Model 1	0.93	(0.76 - 1.14)	0.491
	Model 2	0.99	(0.79 - 1.23)	0.910
Acylcarnitine module	Model 1	1.12	(0.87 - 1.44)	0.392
	Model 2	1.14	(0.88 - 1.48)	0.329
Methyl & Acetyl module	Model 1	1.06	(0.83 - 1.36)	0.638
	Model 2	1.06	(0.83 - 1.36)	0.635
Mixed module	Model 1	0.95	(0.76 - 1.18)	0.632
	Model 2	0.97	(0.78 - 1.21)	0.797

The data are adjusted risk ratios (RR) and 95% CI of carotid artery plaque per standard deviation increment in metabolite modules (inverse-normal transformed).
Model 1: Adjusted for age, gender, race, study site, education, and Smoking status.
Model 2: Further adjusted for ART use, CD4 counts, HIV viral load, crack cocaine use, injected drug use, HCV infection.

Higher levels of DG module, LPC & LPE module ,were longitudinally associated with increased risk of plaques,
after adjusting for demographic , behavioral factors and HIV Variables.

No interactions by HIV+/HIV- status.

Conclusions & Future perspective

- Among individuals with or at high risk of HIV, we identified altered gut microbiota and related functional capacities in the lipid metabolism, associated with disrupted plasma lipidomic profiles and carotid artery atherosclerosis.

- Although the association between Gut Fusobacterium and CVD has not been reported before, Fusobacterium was detected in human carotid artery plaque tissues (Chhibber, J. et al.,2016) .
  Our findings provide new evidence supporting that gut Fusobacterium might be one of the potential sources of Fusobacterium in carotid artery plaque

- Revealed the Potential mechanisms
  E.g. Fusobacterium --- phospholipaseA1/A2 --- LPCs & LPEs --- atherosclerosis

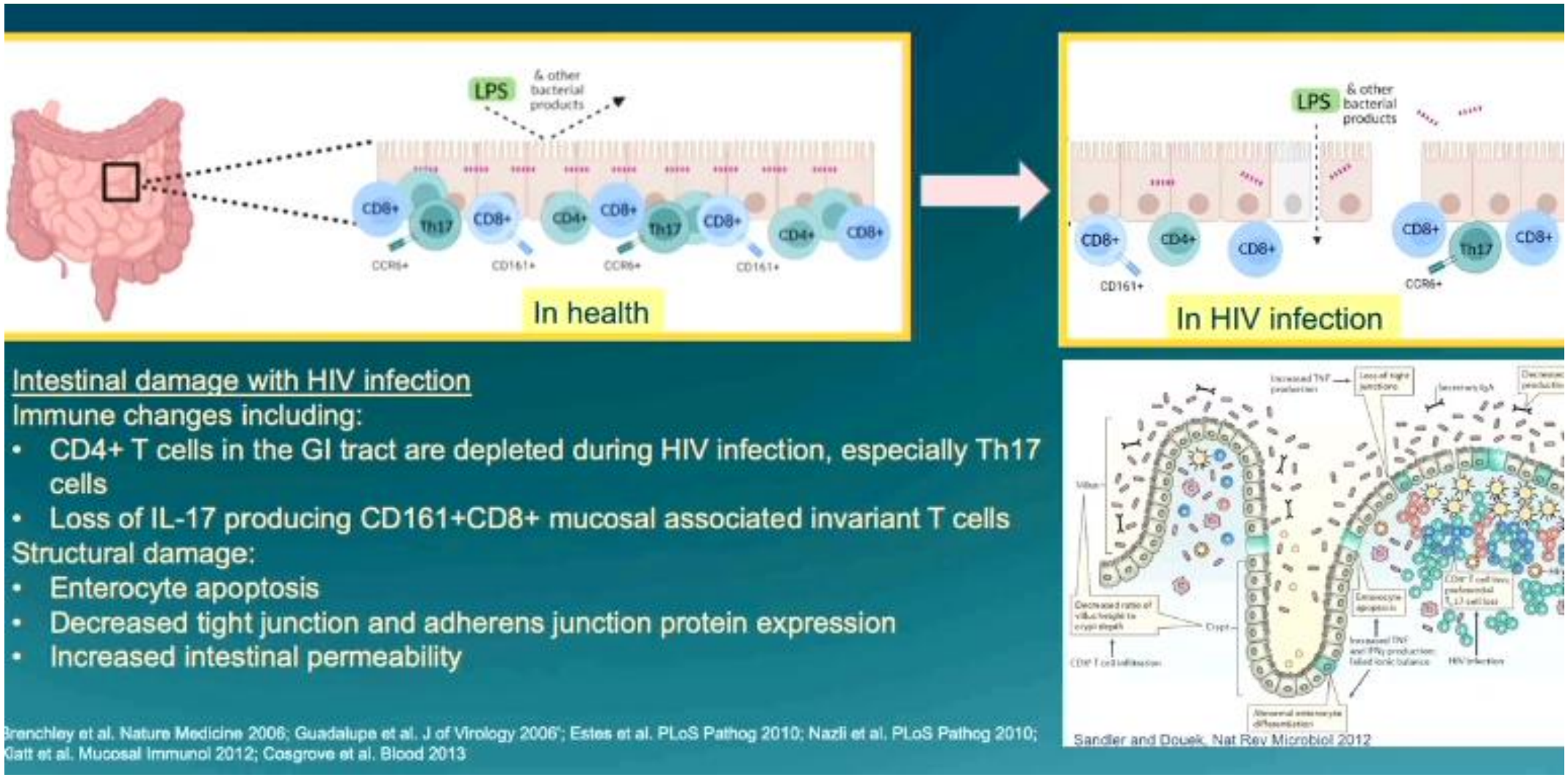
- Integrated Multi-omics analyses including Gut Microbiome , host Metabolomics, and host Genetics hold the potential to reveal the underlying mechanisms. Our study also supports the concept of a potential therapeutic role of modulating the gut microbiota and related microbial metabolites in the prevention of atherosclerosis and CVD. eg. Probiotics, tailoring diet modulations and fecal microbiota transplantation, etc.

IMPROVING INTESTINAL BARRIER USING GLUCAGON-LIKE PEPTIDE-2 ANALOG REDUCES ARTERIAL INFLAMMATION IN PEOPLE WITH HIV

Coauthors: Caroline Diggins, Shibani Mukerji, Douglas Kwon, Charles Saylor, Lediya Cheru, Jae Sim, Meaghan Flagg, Björn Corleis, Emily Rudmann, Shady Abohashem, Ahmed Tawakol

Janet Lo, M.D., M.MSc.

Massachusetts General Hospital and Harvard Medical School
Boston, MA / USA



Intervention: Glucagon-like peptide-2

- GLP-2 is a gastrointestinal hormone released by intestinal L-cells that regulates intestinal epithelial cell growth and functions related to absorption of nutrients
- GLP-2 restores intestinal epithelium and promotes mucosal healing
- In animal models of intestinal injury, GLP-2 reduces intestinal permeability, microbial translocation and intestinal inflammation
- A GLP-2 analog, teduglutide, is FDA approved for short bowel syndrome

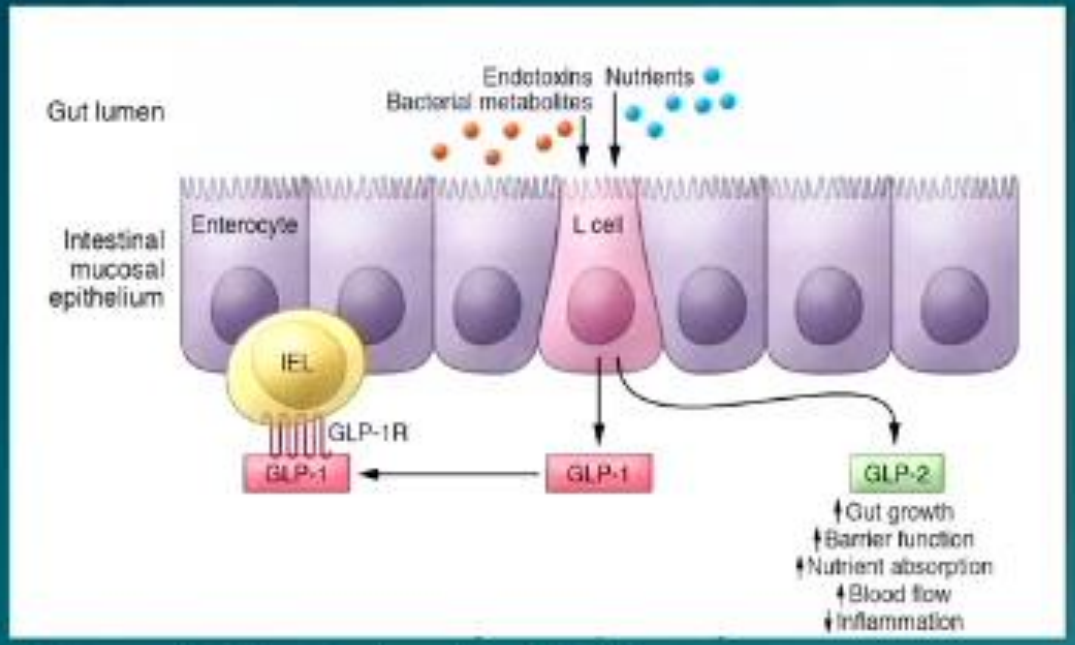
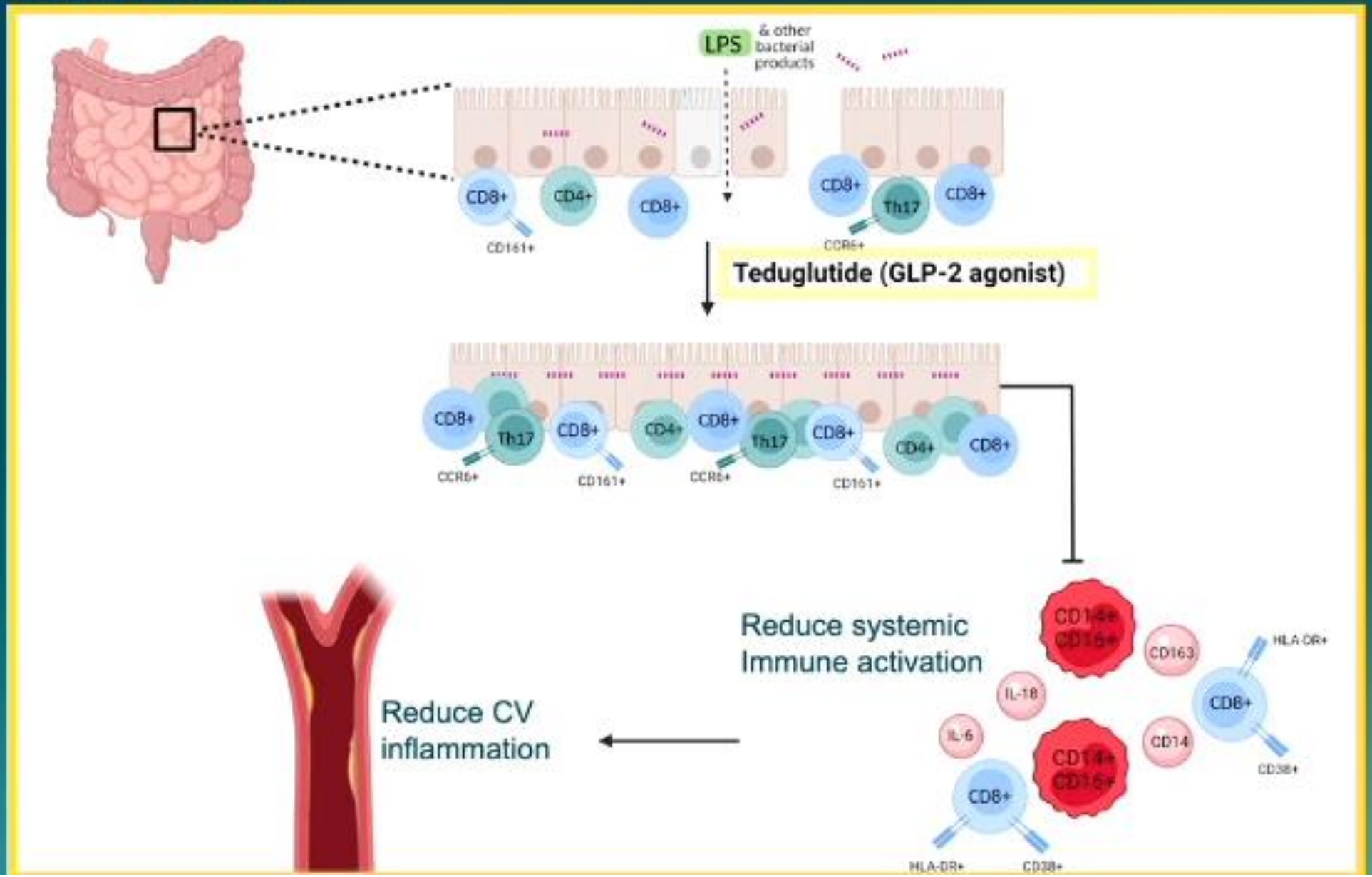


Figure modified from Drucker et al. JCI 2017

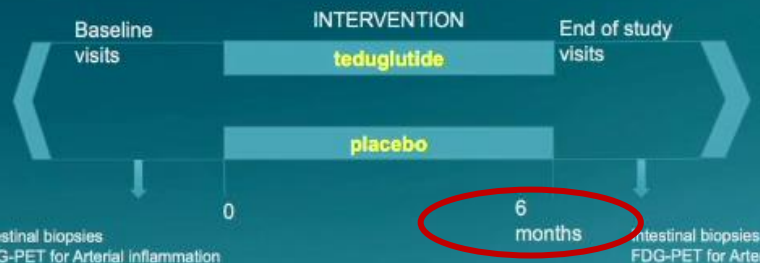
Drucker et al. AJP 1999
Cani et al. Gut 2009
Drucker et al. JCI 2017

Hypothesis


LPS
& other bacterial products
CD8+
CD4+
CD8+
CD161+
CD8+
Th17
CD8+
CCR6+
Teduglutide (GLP-2 agonist)
CD8+
Th17
CD8+
CD4+
CD8+
Th17
CD8+
CD4+
CD8+
CCR6+
CD161+
CCR6+
CD161+
Reduce systemic Immune activation
CD163
HLA-DR+
IL-18
CD8+
IL-6
CD14
CD8+
CD38+
HLA-DR+
CD38+
Reduce CV inflammation

Study Design

Double-blind, placebo-controlled, randomized (1:1) proof of concept trial of GLP-2 analog teduglutide 0.05mg/kg/day SC vs placebo in PWH on ART



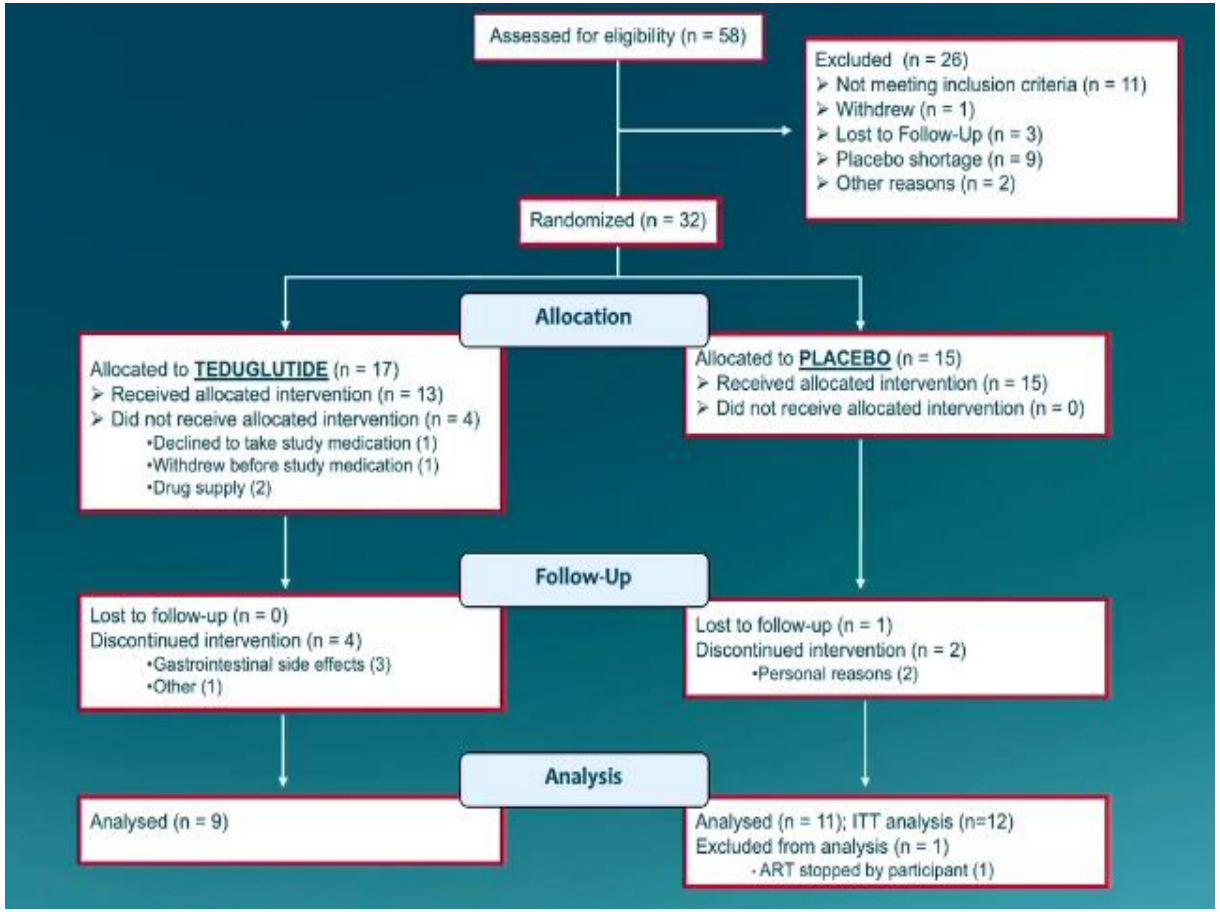
Inclusion Criteria

1. Men and women with HIV age 21-65
2. Stable anti-retroviral therapy (ART) as defined by no changes in ART regimen for > 6 months
3. HIV viral load < 200 copies/mL
4. To be **eligible for endoscopy** procedure, laboratory values that meet the following criteria:
   a. Hemoglobin > 9.0 g/dL
   b. Absolute neutrophil count ≥ 1000/mm^3
   c. Platelet count ≥ 100,000/mm^3
   d. Prothrombin time < 1.2 x ULN
   e. Partial thromboplastin time < 1.5 x ULN
5. Ability and willingness to give written **informed consent** and to comply with study requirements

Exclusion Criteria

1. History of clinically significant gastrointestinal disease
2. Use of **immunomodulatory agents** within 30 days prior to study enrollment
3. High intensity statin
4. Initiation of statin therapy or change in statin dose <90 days prior to entry
5. History of requiring **antibiotic prophylaxis** for invasive procedures
6. Currently taking **anticoagulants**
7. Subject taking any of the following **medications**: systemic steroids, interleukins, systemic interferons, systemic chemotherapy including oral chemotherapeutic agents, methotrexate, octreotide, growth hormone, antiarrhythmics including digoxin, antiepileptics, immunosuppressants, vancomycin, rifampin, aminoglycosides, clonidine, prazosin, lithium
8. History of **malignancy**

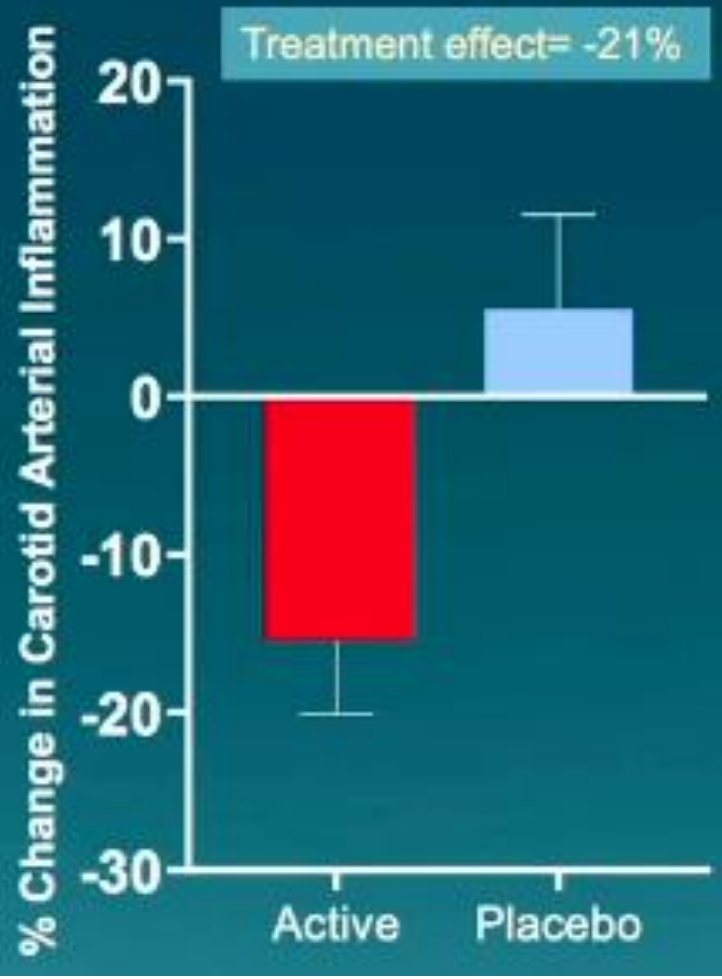
And others



Baseline Characteristics

	Teduglutide (N = 17)	Placebo (N = 15)	p-value
Age, years	58.3 [50.1-59.8]	54.6 [49.5-59.2]	0.62
Sex (male), %	76.5	80.0	0.81
Race, %			0.32
White	64.7	40.0	
Black/African American	23.5	46.7	
More than one race	11.8	6.7	
Other	0.00	6.7	
Active smoker, %	29.4	40.0	0.53
Viral load < 200 cp/mL, %	100.0	100.0	
Current ART use, %	100.0	100.0	
NNRTI, %	17.7	33.3	0.31
PI, %	23.5	26.7	0.84
INSTI, %	76.5	60.0	0.32
CD4+ T-cell Count	639 ± 165	685 ± 225	0.51
Nadir CD4 Count (reported)	199 [20.5-382.5]	200 [50-350]	0.98
BMI (kg/m^2)	27.1 ± 5.0	28.6 ± 4.4	0.36
Current statin use, %	41.2	26.7	0.39
HbA1c, %	5.5 ± 0.4	5.6 ± 0.3	0.54
Total Cholesterol, mg/dL	180.82 ± 32.78	186.33 ± 35.04	0.65
LDL Cholesterol, mg/dL	102.53 ± 27.93	113.93 ± 33.28	0.30
HDL Cholesterol, mg/dL	50.94 ± 16.54	48.33 ± 17.54	0.67
Triglycerides, mg/dL	129 [83.5-174.5]	105 [95-141]	0.43

Results: Primary Endpoint
Change in Arterial Inflammation



Primary analysis

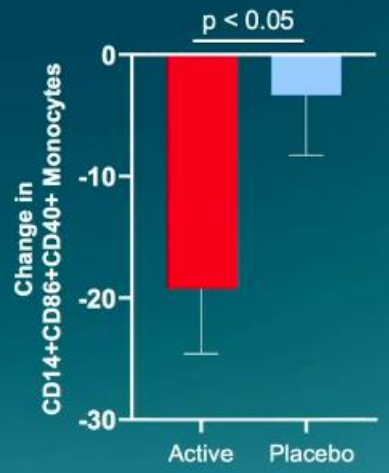
Carotid arterial inflammation:
Target-to-background ratio of most diseased segment of index carotid vessel,
ANCOVA p=0.01

ITT (including participant in placebo group who stopped ART)
ANCOVA p=0.03

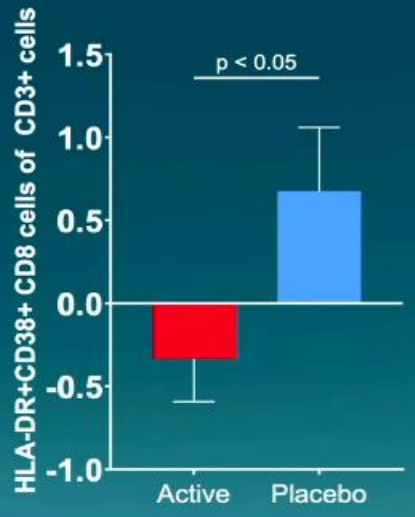
Sensitivity analysis:

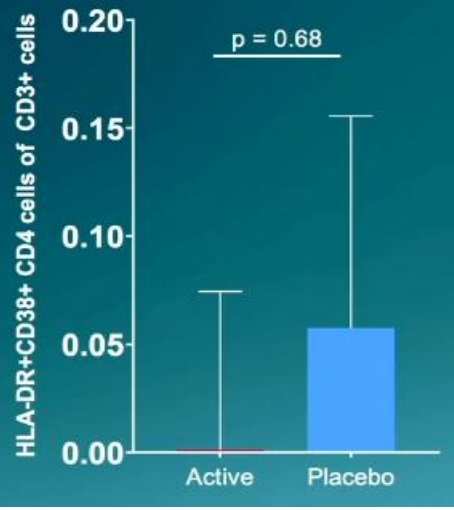
- Adjusting for statin use, carotid arterial inflammation decreased with teduglutide compared to placebo (p=0.02)
- Adjusting for smoking status, carotid arterial inflammation decreased with teduglutide compared to placebo (p=0.03)

Change in CD86+CD40+CD14+ Monocytes

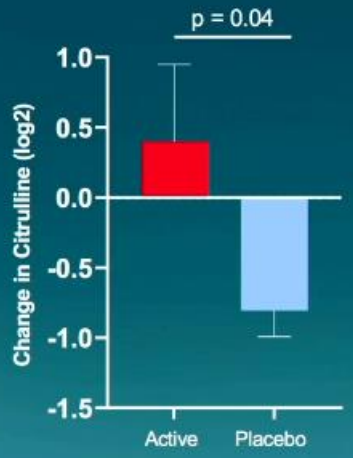


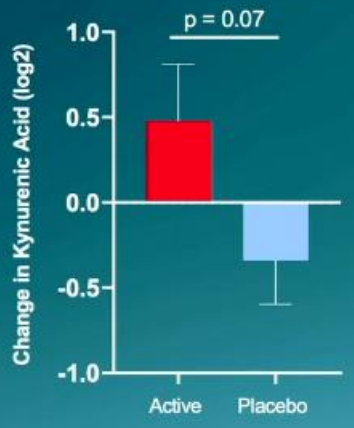
Teduglutide reduced peripheral activated CD8+ cells



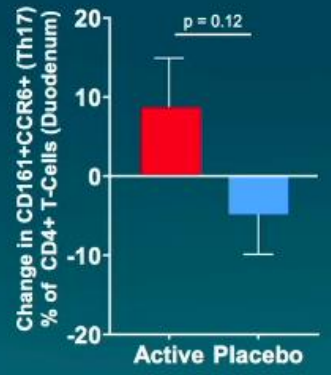


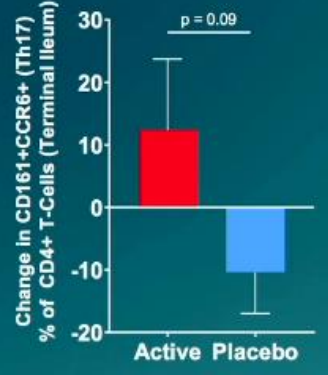
Teduglutide prevented the decline of citrulline, a measure of small intestinal functional mass





Change in intestinal Th17 cells





In teduglutide treated group, change in duodenal Th17 cells related to change in citrulline, a marker of small bowel health: **r = 0.98, p = 0.002**

Adverse Events

	Received Teduglutide (n = 13)	Received Placebo (n = 15)
Adverse Event, n (%)	10 (76.9)	10 (66.7)
Serious Adverse Event, n (%)	0 (0.0)	0 (0.0)
Discontinued Study Medication Due to Adverse Event, n (%)	5 (38.5)	0 (0.0)
Abdominal bloating and discomfort	1	
Bloating, burping, gas; tarry stool related to intestinal biopsy	1	
Constipation, abdominal cramps, diarrhea/loose stool	1	
Nausea, emesis, bloating, abdominal discomfort	1	
Bloating, burping, constipation, abdominal discomfort	1	
Injection Site Adverse Event, n (%)	2 (15.4)	5 (33.3)
Bruising, n	2	3
Numbness, n		1
Bleeding, n		1
Itching, n		1
Burning, n		1
Gastrointestinal Adverse Event, n (%)	9 (69.2)	7 (46.7)
Gastroenteritis, n		1
Abdominal bloating, constipation, cramping, pain, discomfort, n	7	5
Burping and/or gas, n	3	1
Decreased appetite, n	1	
Diarrhea/loose stools, n	2	3
Nausea, vomiting, n	2	
Gastritis, n		1
Esophagitis (incidentally detected on study EGD), n	1	
Gastrointestinal Polyps (detected on study colonoscopy)		
At baseline, n	2	3
At endpoint, n	2	5

Limitations

- Small final sample size due to placebo supply shortage for subcutaneously administered medication
- Gastrointestinal side effects of teduglutide in this study population

Conclusions

In this proof-of-concept randomized study, intestinotrophic GLP-2 analog, teduglutide, reduced arterial inflammation in carotid arteries of individuals with HIV

Teduglutide reduced circulating activated monocytes and activated CD8+ cells

Teduglutide prevented loss of enterocyte functional mass as measured by citrulline

Increase in citrulline related to increase in intestinal Th17 cells among participants with HIV treated with teduglutide

GI side effects may limit the use of teduglutide in PWH, however, other future therapeutic strategies to enhance GLP-2 pathway may be worth exploring

Future larger studies are needed to target the GI epithelial barrier in PWH

SNC

ACTG A5324: A RANDOMIZED TRIAL OF ART INTENSIFICATION FOR COGNITIVE IMPAIRMENT IN PWH

Scott Letendre, M.D.
University of California, San Diego

- **ACTG 5324 (the InMIND Trial)**
  - Randomized, double-blind, placebo-controlled trial
  - **Primary aim:** Determine if ART intensification improves neuropsychological (NP) test performance in PWH on suppressive ART with cognitive impairment

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Methods

- 14 U.S. and 11 international sites
- Eligibility criteria
  - Women and men with HIV infection
  - Taking ART that did not contain an integrase inhibitor or maraviroc (MVC)
  - Plasma HIV RNA < 50 copies/mL
  - Performance > 1 standard deviation below the normative mean on two NP tests in different domains
  - No cause of impairment other than HIV infection
- Design
  - Participants were randomized to add dolutegravir (DTG)+MVC, DTG+placebo, or dual placebo to their existing antiretroviral therapy regimen
  - **Repeat NP testing** at weeks 24, 48, 72, and 96
  - **Primary outcome:** Change from baseline to week 48 on the normalized total z-score
  - **Also measured:** Beck Depression Inventory-II (BDI-II), Plasma HIV RNA, blood CD4+ and CD8+ T-cells, and soluble biomarkers in blood and CSF

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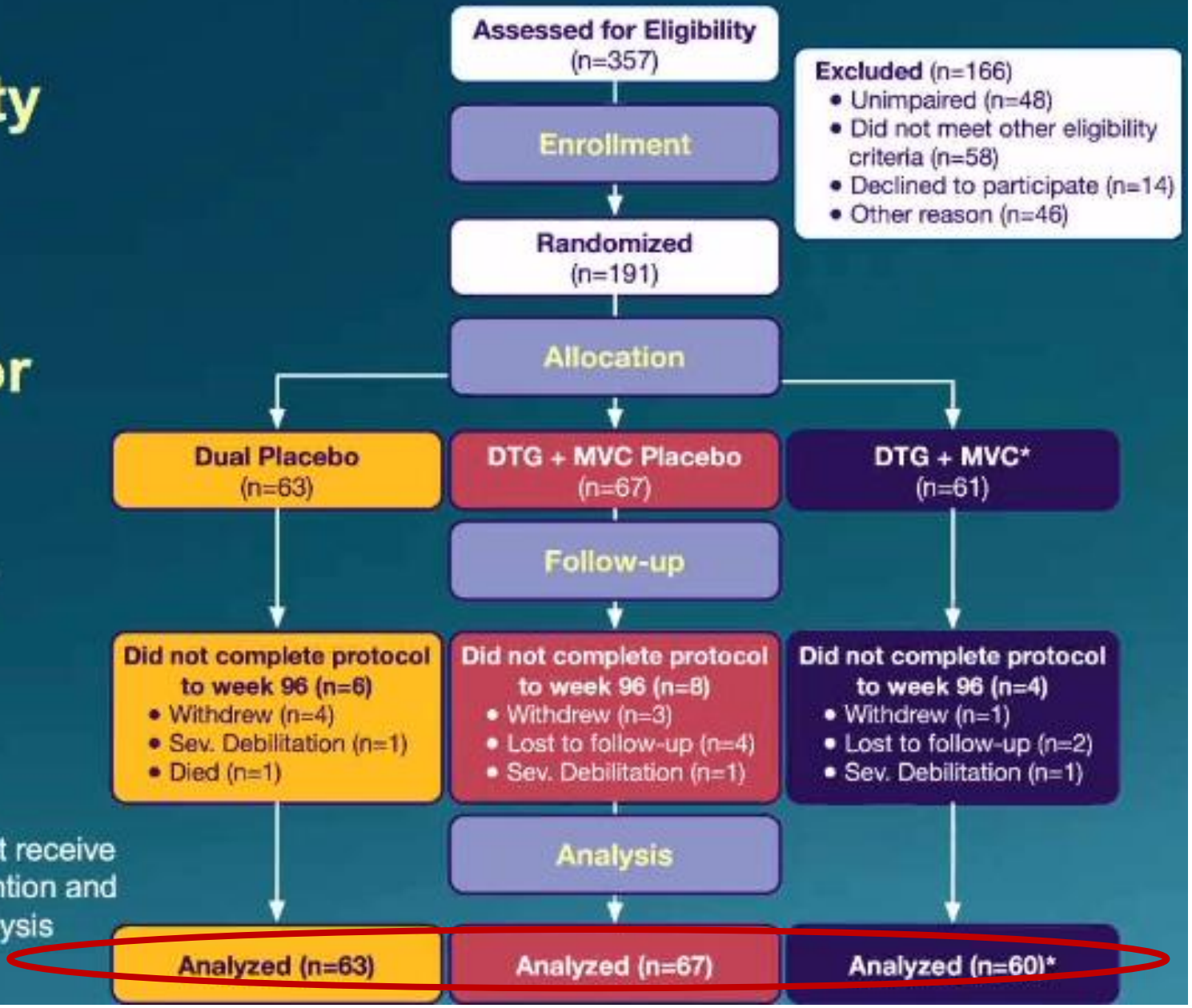
- 357 assessed for eligibility
- 191 (53.5%) enrolled
- 82% from the U.S.
- Most common reasons for screen failure
  - Unimpaired (n=48)
  - Did not meet other eligibility criteria (n=58)



* One participant did not receive the randomized intervention and was excluded from analysis

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Results – Primary and Secondary Outcomes

- Total z-score improved over time and did not differ between arms at week 48 or other timepoints ($p > 0.10$)
- BDI-II and PHQ-9 improved over time and did not differ between arms at week 48 or other timepoints ($p > 0.10$)
- Sex, race, study site, efavirenz use, or baseline z-score did not influence results

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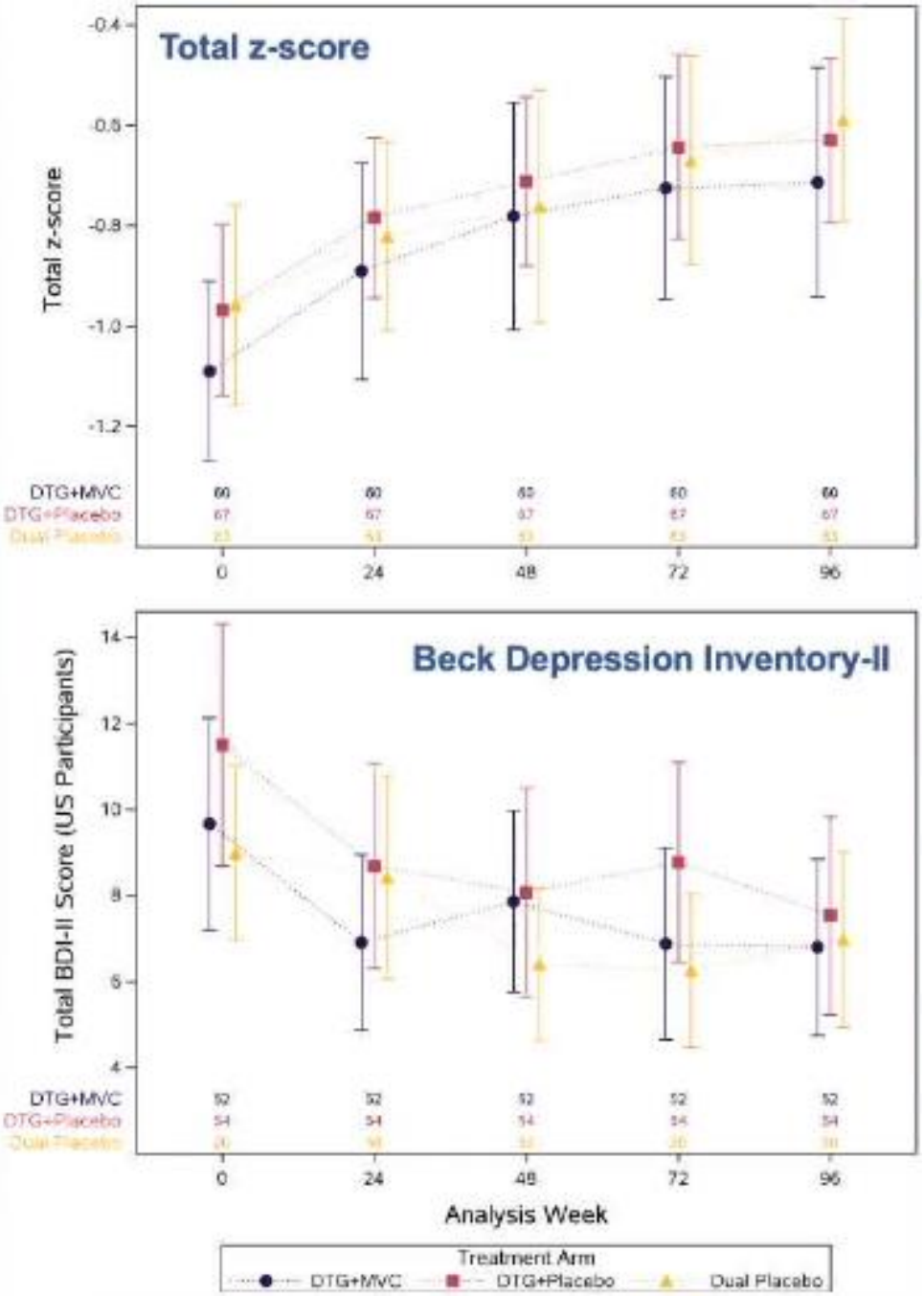
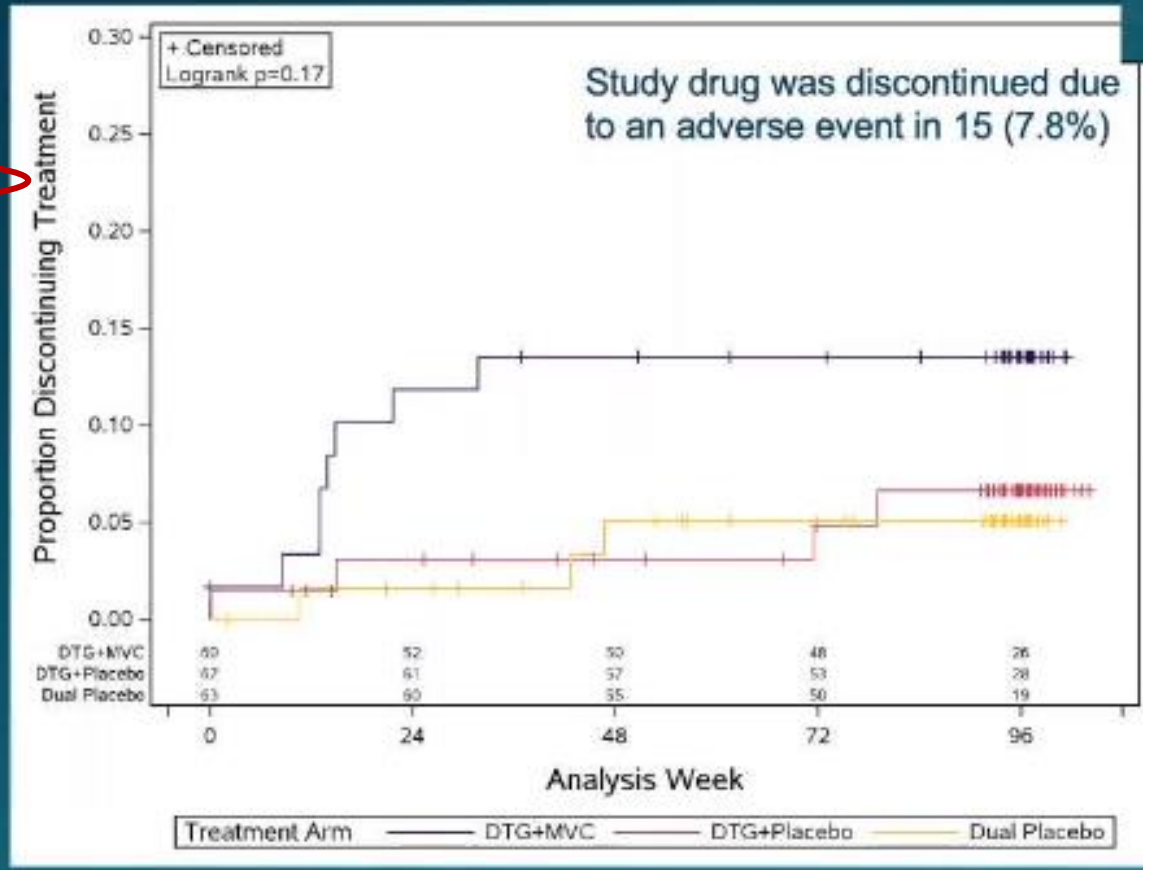
Primary analysis timepoint: 48 weeks



Adverse Events Related to Study Drug	Dual Placebo (n=63)	DTG+ Placebo (n=67)	DTG+ MVC (n=61)
Overall	3 (4.8%)	5 (7.5%)	7 (11.5%)
Gastrointestinal disorders	2 (3.2%)	2 (3.0%)	1 (1.6%)
Nervous system disorders	0 (0%)	1 (1.5%)	0 (0%)
Psychiatric disorders	0 (0%)	0 (0%)	1 (1.6%)
Respiratory disorders	1 (1.6%)	0 (0%)	0 (0%)
Urinary tract infection	0 (0%)	0 (0%)	1 (1.6%)
Laboratory Investigations			
Creatinine clearance decreased	0 (0%)	2 (3.0%)	4 (6.6%)
Serum bilirubin increased	1 (1.6%)	0 (0%)	0 (0%)
Virologic Investigations			
Confirmed virologic failure	4 (6%)	0 (0%)	1 (2%)

All values are number (percent)



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IS THERE A ROLE OF NOVEL ART REGIMENS IN THE DECLINING PREVALENCE OF HAND?

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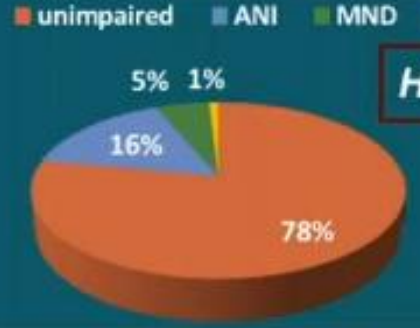
Rome, Italy

I. The **primary aim** was to estimate **prevalence of HAND** in more recent years of ART

II. The **secondary aim** was to assess the relationships between HAND and several socio-demographic, clinical, laboratoristic and therapeutic variables, in order to identify potentially **predictive factors for HAND**.

	Complaining (n=791, 33.2%)	Not-complaining (n=1592, 66.8%)		Complaining (n=791, 33.2%)	Not-complaining (n=1592, 66.8%)
Male gender, n (%)	620 (78.4%)	1333 (83.7%)	**HIV-RNA cp/mL <40 at NPA, n (%)**	615 (77.8%)	1419 (89.1%)
Age, years, median (IQR)	49 (43-56)	51 (43-56)	**Type of current ART regimen**,n (%)**		
MSM, n (%)	314 (39.7%)	767 (48.2%)	*NNRTI-based*	247 (31.2%)	761 (47.8%)
Years of education, median (IQR)	13 (8-13)	13 (10-16)	*PI/r-based*	231 (29.2%)	226 (14.2%)
Years of HIV infection, median (IQR)	8.7 (2.2-19.3)	10.7 (4.6-19.9)	*INSTI-based*	106 (13.4%)	323 (20.3%)
HCV-Ab positivity, n (%)	159 (20.1%)	358 (22.5%)	*dual therapy*	94 (11.9%)	94 (5.9%)
Nadir CD4 < 200 cell/mm^3, n (%)	404 (51.1%)	437 (27.5%)	*bPI monotherapy*	33 (4.2%)	113 (7.1%)
CD4 cell/mm^3 at NPA, n (%)			**Years of NPA, n (%)**		
≤350	232 (29.3%)	198 (12.4%)	*2009-2011*	142 (18.0%)	145 (9.1%)
351-500	135 (17.1%)	257 (16.1%)	*2012-2014*	257 (32.5%)	482 (30.3%)
501-700	187 (23.6%)	525 (33.0%)	*2015-2017*	192 (24.3%)	366 (23.0%)
>700	218 (27.6%)	599 (37.6%)	*2018-2020*	200 (25.3%)	599 (37.6%)

HAND prevalence



HAND 22%

all study population

HAND prevalence according to calendar period

HAND 40%

complaining

HAND 13%

not complaining

RESULTS – *HAND predictors*

	AOR*	95% CI		p-value
Age, 10 years increase	1.16	1.03	1.30	0.013
CD4⁺ at NPA (cells/mm³)				
≤ 350	1.00			
351-500	0.66	0.46	0.95	0.025
501/700	0.50	0.36	0.71	<0.001
> 700	0.45	0.31	0.64	<0.001
Education (per 1 year more)	0.84	0.81	0.86	<0.001
HCV Ab				
negative	1.00			
positive	1.44	1.09	1.92	0.011
Type of current ART regimen				
NRTI+NNRTI	1.00			
NRTI+bPI	1.15	0.85	1.55	0.376
NRTI+INSTI	0.67	0.46	0.97	0.035
dual therapy	0.59	0.38	0.93	0.024
bPI monotherapy	0.74	0.44	1.23	0.242
Years of NPA				
2009-2011	1.00			
2012-2014	0.73	0.52	1.02	0.067
2015-2017	0.48	0.33	0.70	<0.001
2018-2020	0.43	0.29	0.63	<0.001
Complaining	3.83	3.01	4.86	<0.001

***Multivariable logistic regression, adjusted for:**

- gender,
- mode of HIV transmission (MSM, heterosexual, intravenous drug users),
- years from HIV test,
- nadir CD4+ (< or ≥ 200 cells/mm³),
- HIV-RNA at NPA (≤ or > 40 cp/mL).

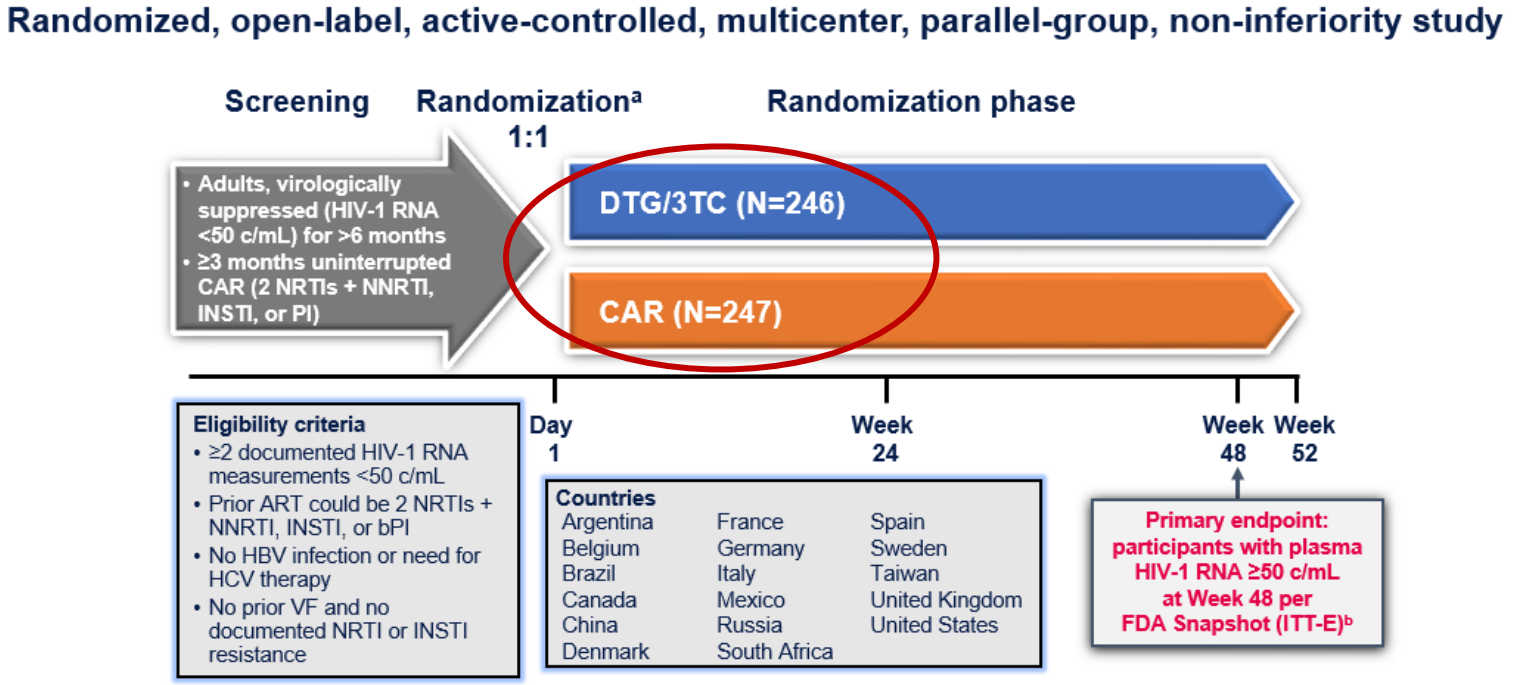
Neuropsychological assessment (NPA)

AUMENTO de PESO

WEEK 48 METABOLIC HEALTH AFTER SWITCH TO DTG/3TC VS CAR BY BASELINE REGIMEN (SALSA)

Debbie Hagins,[1] Cristina Mussini,[2] Fujie Zhang,[3] Princy N. Kumar,[4] Laurent Hocqueloux,[5] Nuria Espinosa,[6] Christoph Wyen,[7] James Oyee,[8] Lori A. Gordon,[9] Gilda Bontempo,[9] Brian Wynne,[9] Elizabeth Blair,[9] Mounir Ait-Khaled,[10] Jean van Wyk[10]

[1]Georgia Department of Public Health, Coastal Health District, Chatham CARE Center, Savannah, GA, USA; [2]Clinic of Infectious Diseases, AOU Policlinico, and University of Modena and Reggio Emilia, Modena, Italy; [3]Beijing Ditan Hospital, Capital Medical University, Beijing, China; [4]Georgetown University Medical Center, Washington, DC, USA; [5]Centre Hospitalier Régional d'Orléans, Orléans, France; [6]Hospital Universitario Virgen del Rocío, Instituto de Biomedicina de Sevilla (IBiS), Sevilla, Spain; [7]Praxis am Ebertplatz, Cologne, Germany; [8]GlaxoSmithKline, Brentford, UK; [9]ViiV Healthcare, Research Triangle Park, NC, USA; [10]ViiV Healthcare, Brentford, UK



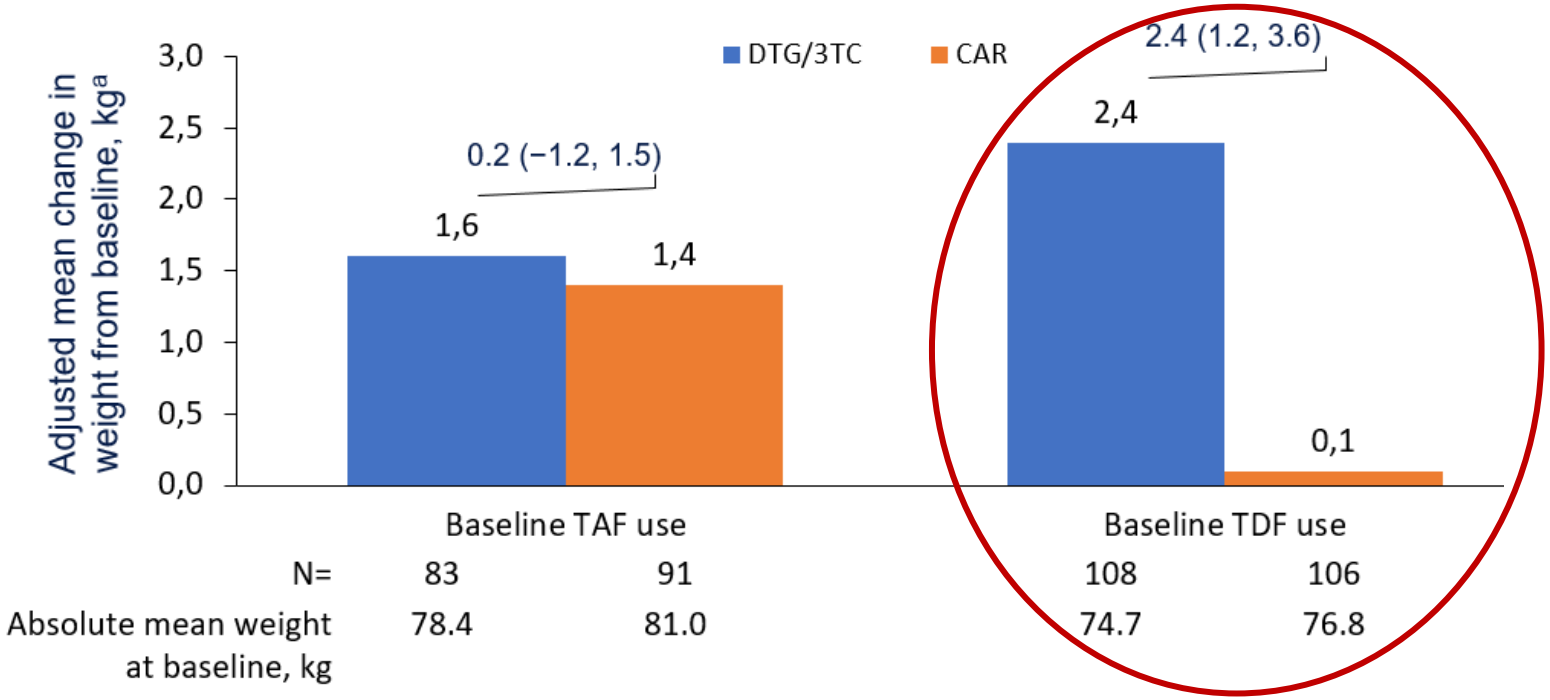
- In the ITT-E population, 493 participants were randomized to switch to DTG/3TC (N=246)
  or continue CAR (N=247)
- Demographics, baseline characteristics, and baseline TAF or TDF use were similar between groups
  - Characteristics were similar between the baseline TAF and TDF use groups

Baseline Demographics and Clinical Characteristics: ITT-E Population

Characteristic	DTG/3TC (N=246)	CAR (N=247)
Age, median (range), y	45 (22-74)	45 (23-83)
Female, n (%)	108 (44)	84 (34)
Race, n (%)		
African American/African heritage	45 (18)	48 (19)
Asian	31 (13)	39 (16)
White	149 (61)	144 (58)
Other races[a]	21 (9)	16 (6)
CD4+ cell count, median (range), cells/mm^3	675 (154-2089)	668 (94-1954)
CD4+ cell count, cells/mm^3, n (%)		
<500	60 (24)	63 (26)
≥500	185 (75)	184 (74)
Duration of ART before Day 1, median (range), mo	63 (4-240)	71 (12-253)
ART received at screening, n (%)		
TDF[b]	109 (44)	109 (44)
EFV	66 (27)	58 (23)
TAF	83 (34)	91 (37)
Unboosted INSTI (BIC, DTG,[c] or RAL)	27 (11)	30 (12)
Boosted INSTI (EVG/c)	24 (10)	25 (10)
Weight, median (range), kg	73 (43-154)	75 (36-160)
BMI, median (range), kg/m^2	25 (18-51)	26 (14-69)
Metabolic syndrome, n (%)[d]	20 (8)	35 (14)
Fasting insulin, geometric mean (95% CI)	1.93 (1.78-2.10)	2.12 (1.92-2.35)
Fasting glucose, median (range), mmol/L	5.2 (3.7-10.3)	5.2 (3.2-18.7)
HbA_{1c}, median (range)	5.3 (3.7-9.0)	5.4 (3.7-12.1)
HOMA-IR, median (range)	1.84 (0.40-15.0)	2.05 (0.40-65.80)

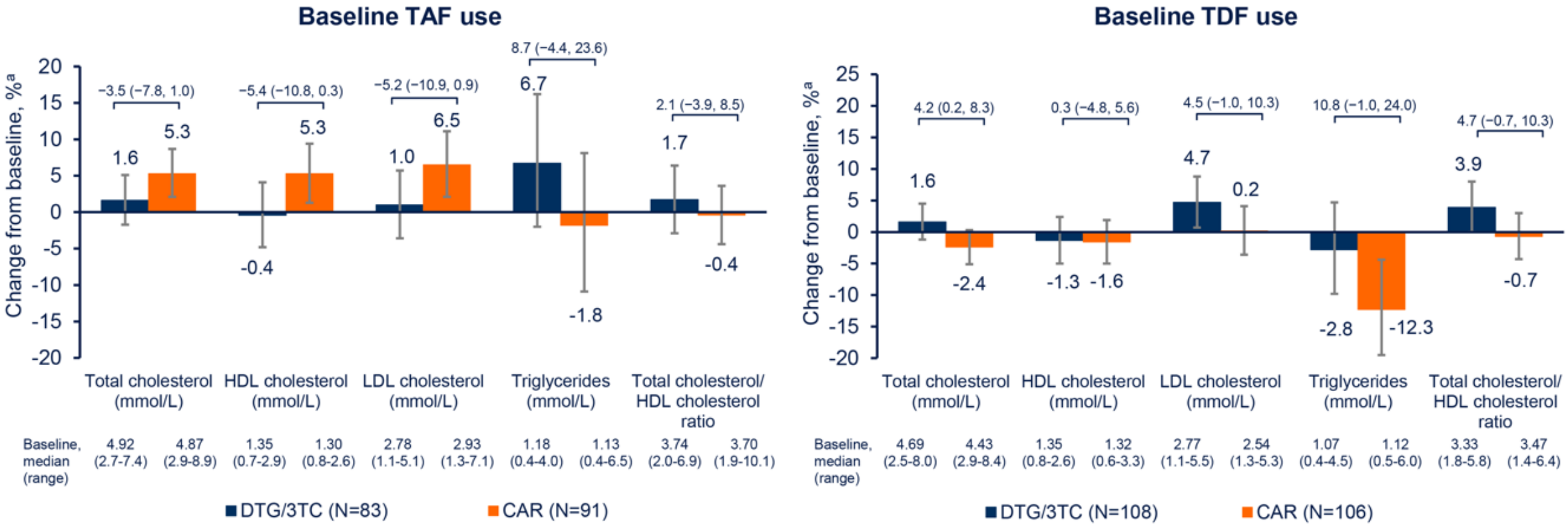
[a]Includes American Indian or Alaska Native or individuals of multiple races. [b]Includes tenofovir disoproxil succinate (DTG/3TC, n=1; CAR, n=3). [c]DTG regimens, n/N (%): DTG + FTC + TAF (DTG/3TC, 1/246 [<1]; CAR, 3/247 [1]); DTG + 3TC + TAF (DTG/3TC, 0/246 [0]; CAR, 1/247 [<1]); DTG + FTC + TAF + BIC + FTC + TDF (DTG/3TC, 1 [<1]; CAR, 0 [0]). [d]Participants who have BMI ≥30 kg/m^2 and satisfy any 2 of the raised/reduced factors within the baseline visit window: raised triglycerides, ≥150 mg/dL or treatment; reduced HDL, <40 mg/dL (men), <50 mg/dL (women), or treatment; raised blood pressure, systolic ≥130 mm Hg or diastolic ≥85 mm Hg, or treatment for hypertension; raised fasting plasma glucose, ≥100 mg/dL or previous diagnosis of type 2 diabetes.

Weight Changes



- Overall, adjusted mean change in weight from baseline to Week 48 was 2.1 vs 0.6 kg in the DTG/3TC vs CAR groups (treatment difference, 1.49 kg; 95% CI, 0.70-2.28); weight change was similar between groups in participants with baseline TAF use and was greater in the DTG/3TC group for those with baseline TDF use
- In the overall analysis, proportion of participants with ≥10% weight gain was 12% (27/230) vs 4% (9/224) in the DTG/3TC vs CAR groups, respectively
- Proportions of participants with ≥10% weight gain were similar in the baseline TAF use subgroup (DTG/3TC, 8% [6/79] vs CAR, 7% [6/86]) and higher with DTG/3TC vs CAR (14% [14/98] vs 3% [3/95]) in the baseline TDF use subgroup

Percent Change From Baseline in Fasting Lipids at Week 48 by Baseline TAF or TDF Use



Adjusted mean treatment difference (95% CI) displayed above treatment groups. [a]Estimated adjusted ratio (Week 48 to baseline) in each group calculated using MMRM applied to change from baseline in $\log_e$-transformed data adjusting for treatment, $\log_e$-transformed baseline value, age, sex, race, baseline third agent class, CD4+ cell count, subgroup, treatment-by-visit interaction, $\log_e$-transformed baseline value-by-visit interaction, treatment-by-subgroup interaction, subgroup-by-visit interaction, and subgroup-by-treatment-by-visit interaction, with visit as the repeated factor.

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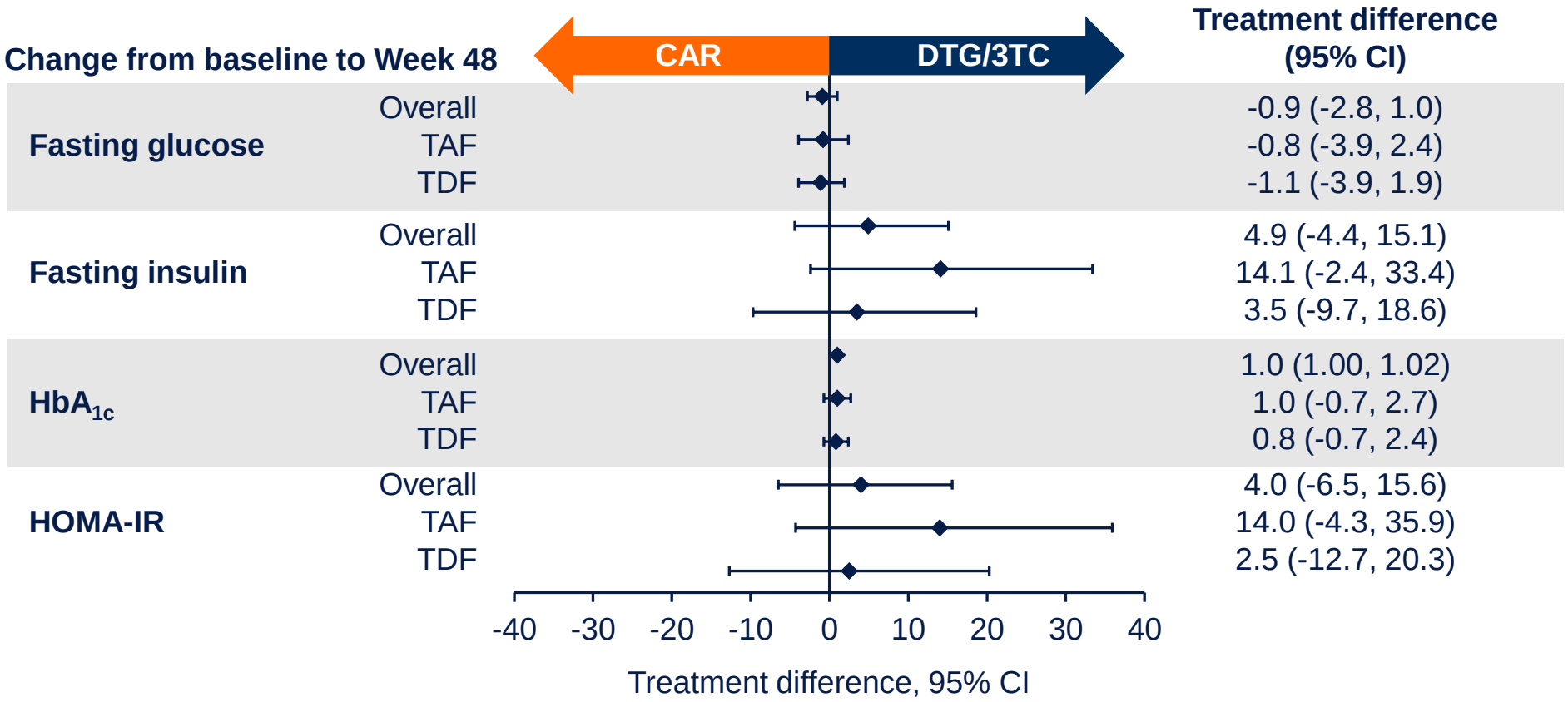
Fasting Glucose and Insulin, HbA_{1c}, and HOMA-IR



Overall and subgroup analyses based on estimated adjusted ratio (Week 48 to baseline) in each group calculated using MMRM applied to change from baseline in log_e-transformed data adjusting for treatment, visit, baseline third agent class, CD4+ cell count, age, sex, race, BMI, presence of hypertension, log_e-transformed baseline value, treatment-by-visit interaction, and log_e-transformed baseline value-by-visit interaction, with visit as the repeated factor. HbA_{1c} outcomes also adjusted for presence of diabetes mellitus. Subgroup analyses also adjusted for subgroup, treatment-by-subgroup interaction, subgroup-by-visit interaction, and subgroup-by-treatment-by-visit interaction.

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48-WEEK BODY COMPOSITION CHANGES IN PLWH SWITCHING FROM 3DR TO DTG + 3TC: DOLAM STUDY

598

Elisa de Lazzari[1], Adrià Curran[2], Eugenia Negredo[3], Pere Domingo[4], Nadia Abdulghani[5], Jose M Gatell[6], Jose L Blanco[1] and Esteban Martínez[1] on behalf of the DOLAM study group

Hospital Clínic, Barcelona[1]; Hospital Vall d'Hebron, Barcelona[2]; Hospital Germans Trías I Pujol, Badalona[3]; Hospital de Sant Pau, Barcelona[4]; Hospital Arnau de Vilanova, Lleida[5]; ViiVHealthcare, Barcelona. Spain.

BACKGROUND

In DOLAM study, 48-week weight change from baseline increased significantly in DTG+3TC (2DR) arm (mean change 1·6 kg [95% CI 0·9 to 2·4], p<0·0001) but not in triple therapy (3DR) arm (0·1 kg [–0·6 to 0·8], p=0·78).

The difference between 2DR versus 3DR in mean weight change at 48 weeks was 1.5 kg (95% CI 0·5 to 2·5, p<0.005).

A pre-planned dual-X-absorptiometry (DXA) sub-study aimed to assess 48-week body composition changes.

COMPARISON OF THE CHANGE BETWEEN THE GROUPS. INTERACTION BETWEEN TIME AND TREATMENT GROUP.

DXA scan		Ratio of ratios	95% CI	P value
FAT (g)	Total body	1.04	0.94-1.14	0.451
	Trunk	1.17	0.93-1.47	0.182
	Limb	1.04	0.93-1.15	0.511
LEAN MASS (g)	Total body	0.98	0.92-1.03	0.418
	Trunk	0.99	0.97-1.02	0.620
	Limb	0.99	0.94-1.03	0.584
BMD (g/cm²)	Lumbar spine	1.0019	0.9915-1.0125	0.716
	Total hip	0.9956	0.9820-1.0095	0.535

RESULTS

180 (68%) of 265 participants contributed to the sub-study.

Baseline characteristics did not differ between groups andfrom those of the main study.

At 48 weeks vs. baseline, weight (2DR vs. 3DR) ratio of ratios was 1.0151 (95%CI 1.0009-1.0294) P=0.037

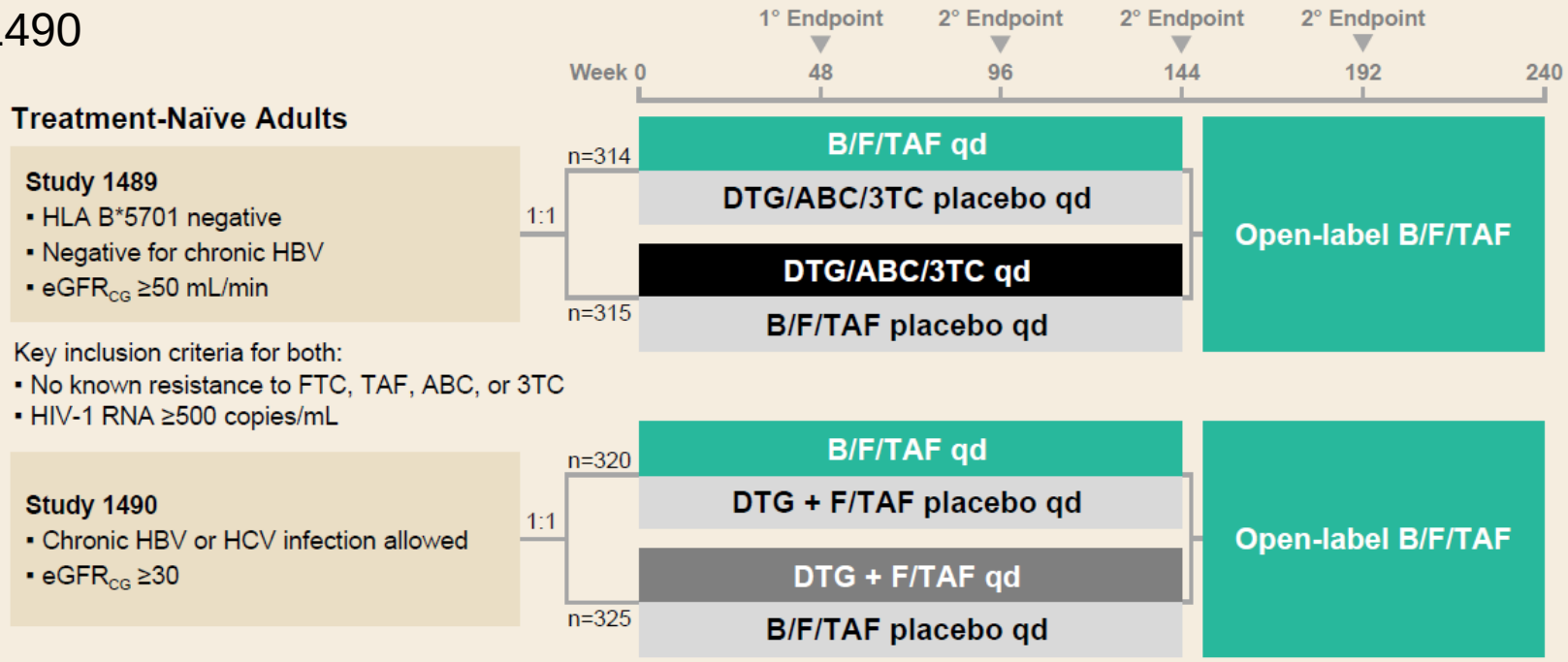
B/F/TAF Five-Year Outcomes in Treatment-Naïve Adults

David A. Wohl,[1] Anton Pozniak,[2] Kimberly Workowski,[3] Debbie Hagins,[4] Eric S. Daar,[5] Chloe Orkin,[6] Ellen Koenig,[7] Karam Mounzer,[8] Samir Gupta,[9] Hailin Huang,[10] Rima K. Acosta,[10] Jason Hindman,[10] Jared Baeten,[10] Hal Martin,[10] Paul E. Sax[11]

[1]UNC School of Medicine, Chapel Hill, NC; [2]Chelsea and Westminster Hospital, London, UK; [3]Emory University, Atlanta, GA; [4]Chatham County Health Department, Savannah, GA; [5]The Lundquist Institute, Torrance, CA; [6]Ambrose King Centre Barts Health NHS Trust, The Royal London, UK; [7]Instituto Dominicano de Estudios Virólgicos, Santo Domingo, Dominican Republic; [8]Philadelphia FIGHT Community Health Centers, Philadelphia, PA; [9]Indiana University School of Medicine, Indianapolis, IN; [10]Gilead Sciences, Inc., Foster City, CA; [11]Brigham and Women's Hospital, Boston, MA

Study Designs: Randomized, Double Blind, Active Controlled

Studies 1489 and 1490



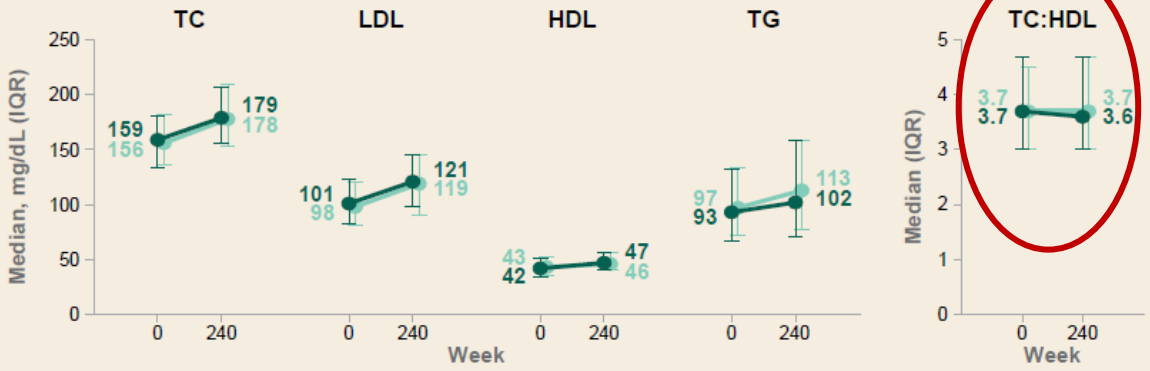
Objectives

- To assess 5-year outcomes (144 wk of blinded treatment plus 96 wk in OLE [aka Week 240]) from Studies 1489 and 1490
- The present analysis focuses on those participants originally randomized to B/F/TAF to gain further insight into long-term safety and efficacy

Characteristics at B/F/TAF Start*

	Study 1489 B/F/TAF: n=314	Study 1490 B/F/TAF: n=320
Median age, y (range)	31 (18–71)	33 (18–71)
Female sex at birth, n (%)	29 (9)	40 (13)
Race/ethnicity, n (%)		
Black or African descent	114 (37)	97 (30)
Hispanic/Latinx ethnicity	72 (23)	83 (26)
Median body weight, kg (IQR)	77 (68, 88)	76 (68, 87)
Median HIV-1 RNA, log_{10} copies/mL (IQR)	4.4 (4.0, 4.9)	4.4 (4.0, 4.9)
HIV-1 RNA >100,000 copies/mL, n (%)	53 (17)	66 (21)
Median CD4 cells/μL (IQR)	443 (299, 590)	440 (289, 591)
CD4 count <200 cells/μL, n (%)	36 (11)	44 (14)
Asymptomatic HIV infection, n (%)	286 (91)	286 (89)
Median $eGFR_{CG}$, mL/min (IQR)	126 (108, 146)	120 (101, 142)

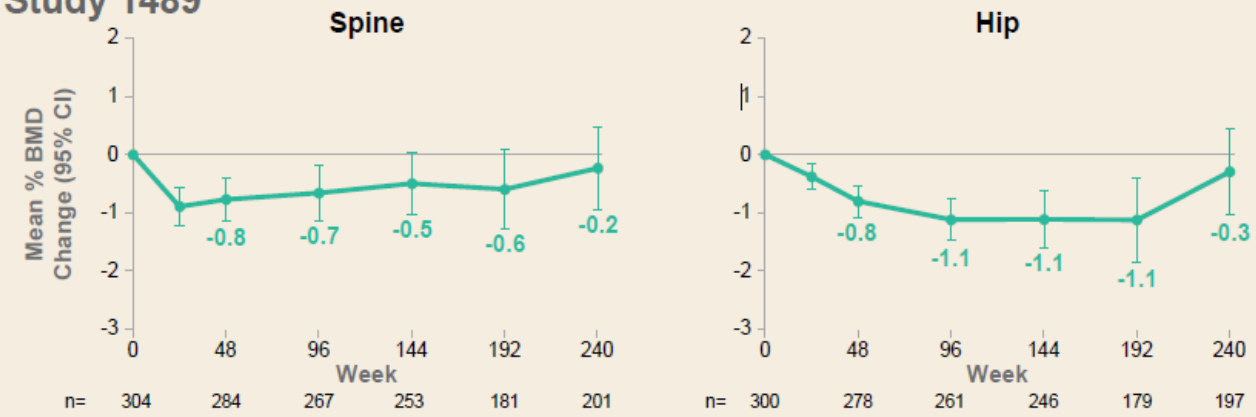
Fasting Lipid Changes Through Week 240*



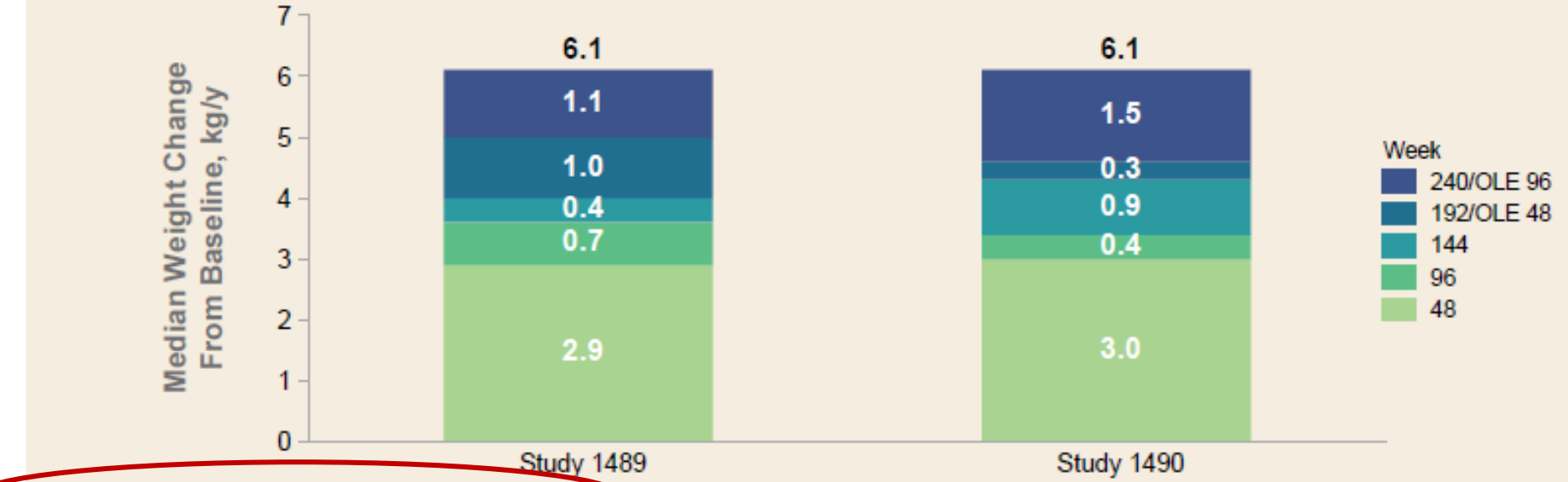
Participants on Lipid-Lowering Agents, %	At Baseline	Initiated				
		Week 48	Weeks 48–96†	Weeks 96–144†	Weeks 144–192†	Weeks 192–240†
Study 1489: n=314	4	3	2	1	2	1
Study 1490: n=320	7	2	2	1	2	1

Spine and Hip BMD Changes Through Week 240

Study 1489*



Weight Changes From Randomized Phase Baseline Through Week 240*



*Includes only participants initially randomized to B/F/TAF.

Conclusions

- In treatment-naïve people living with HIV through 5 y of follow-up among those originally randomized to B/F/TAF, we observed:
  - High rates of virologic suppression with no treatment-emergent resistance in the final resistance analysis population
  - ≤1% occurrence of study drug-related AEs leading to D/C and no renal-related D/Cs
  - Stable $eGFR_{CG}$ after organic cation transporter-2–related initial declines and no reported cases of proximal renal tubulopathy
  - Small changes in fasting lipids, with stable TC:HDL ratios and few participants initiating lipid-lowering agents
  - Median cumulative weight gain of 6.1 kg; ~3 kg in first 48 wk, followed by ~0.3–1.5 kg/y, consistent with data from previous studies in treatment-naïve populations[11-16]
    - Weight gains after Week 48 are consistent with what is seen in the general population[10]
  - Minimal impact on longitudinal trends of spine and hip BMD from baseline, with mean decreases that did not exceed 0.29% at Week 240
- These results confirm the long-term safety and efficacy of B/F/TAF

¡MUCHAS GRACIAS!

Eugenia Negredo

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