From Abstract to Concrete: Co-infections, Comorbidities and Complications from CROI 2024

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Disclosures

- None

- I intend to discuss unlabeled/unapproved use of drugs or products

Outline

- Cardiovascular disease
  - REPRIEVE and associated substudy data
  - Hypertension
  - Left ventricular diastolic dysfunction
- Semaglutide
  - Metabolic dysfunction-associated steatotic liver disease
  - Weight loss
- HCV
- HBV vaccination
- Other complications: Kidney, lung, and cancer (prostate)
- DoxyPEP
- Mpox

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Pitavastatin to Prevent Cardiovascular Disease in HIV Infection

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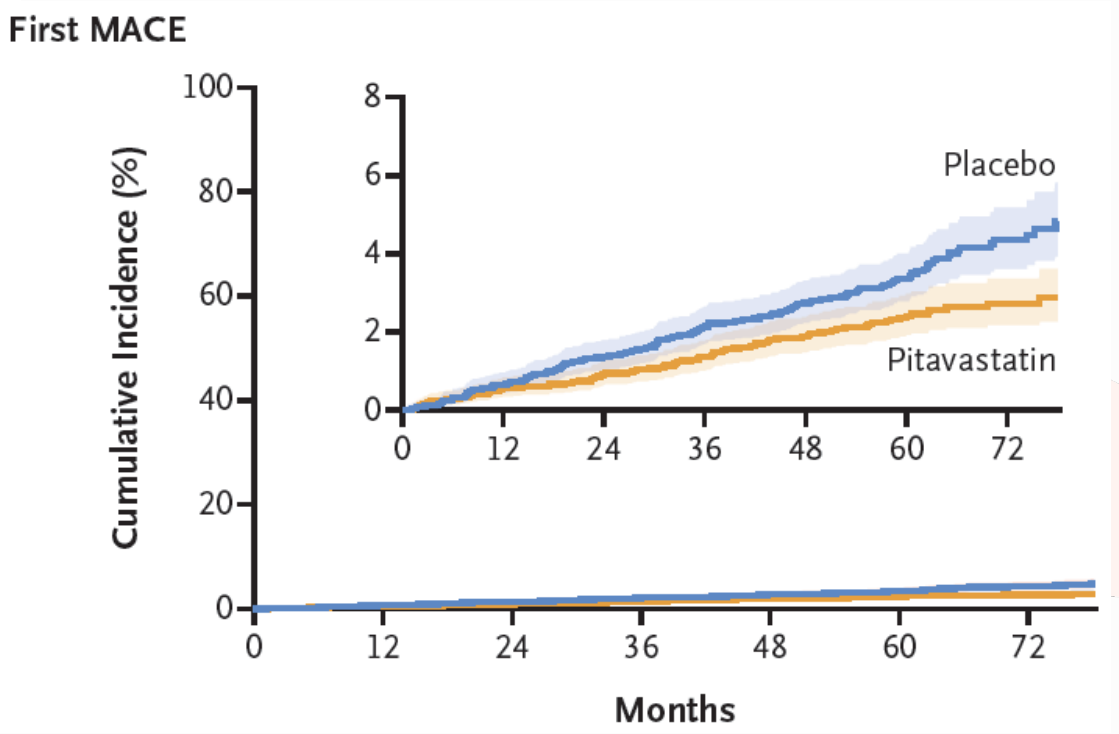


JAMA Cardiology | Original Investigation

Effects of Pitavastatin on Coronary Artery Disease and Inflammatory Biomarkers in HIV

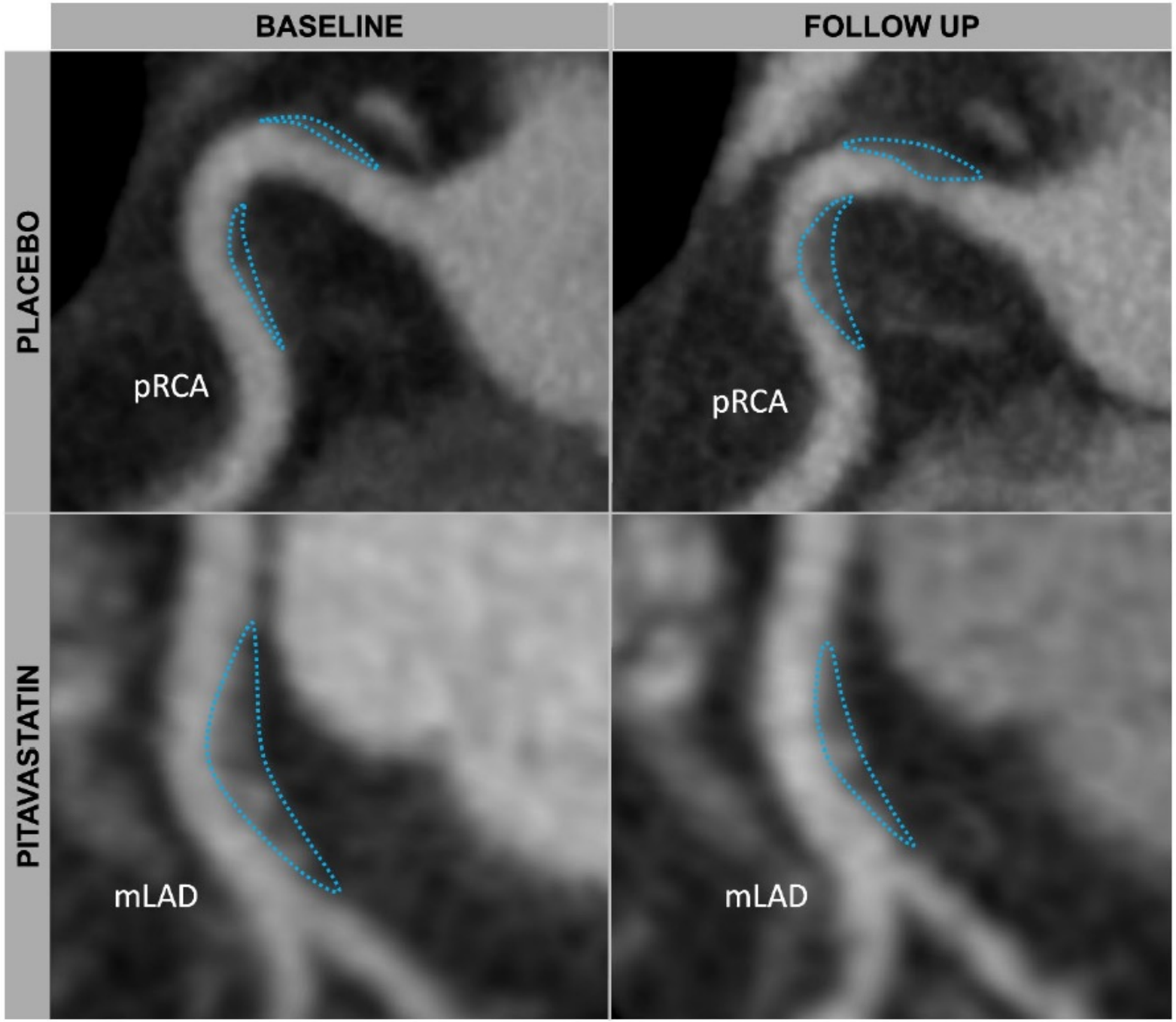
Mechanistic Substudy of the REPRIEVE Randomized Clinical Trial

Michael T. Lu, MD, MPH; Heather Ribaudo, PhD; Borek Foldyna, MD; Markella V. Zanni, MD; Thomas Mayrhofer, PhD; Julia Karady, MD, PhD; Jana Taron, MD; Kathleen V. Fitch, MSN; Sara McCallum, MPH; Tricia H. Burdo, PhD; Kayla Paradis, MBA; Sandeep S. Hedgire, MD; Nandini M. Meyersohn, MD; Christopher DeFilippi, MD; Carlos D. Malvestutto, MD, MPH; Audra Sturniolo, MS; Marissa Diggs, BA; Sue Siminski, MBA; Gerald S. Bloomfield, MD; Beverly Alston-Smith, MD; Patrice Desvigne-Nickens, MD; Edgar T. Overton, MD; Judith S. Currier, MD; Judith A. Aberg, MD; Carl J. Fichtenbaum, MD; Udo Hoffmann, MD, MPH; Pamela S. Douglas, MD; Steven K. Grinspoon, MD; for the REPRIEVE Trial Writing Group

JAMA Cardiol. doi:10.1001/jamacardio.2023.5661
Published online February 21, 2024. Corrected on February 28, 2024.

N = 661

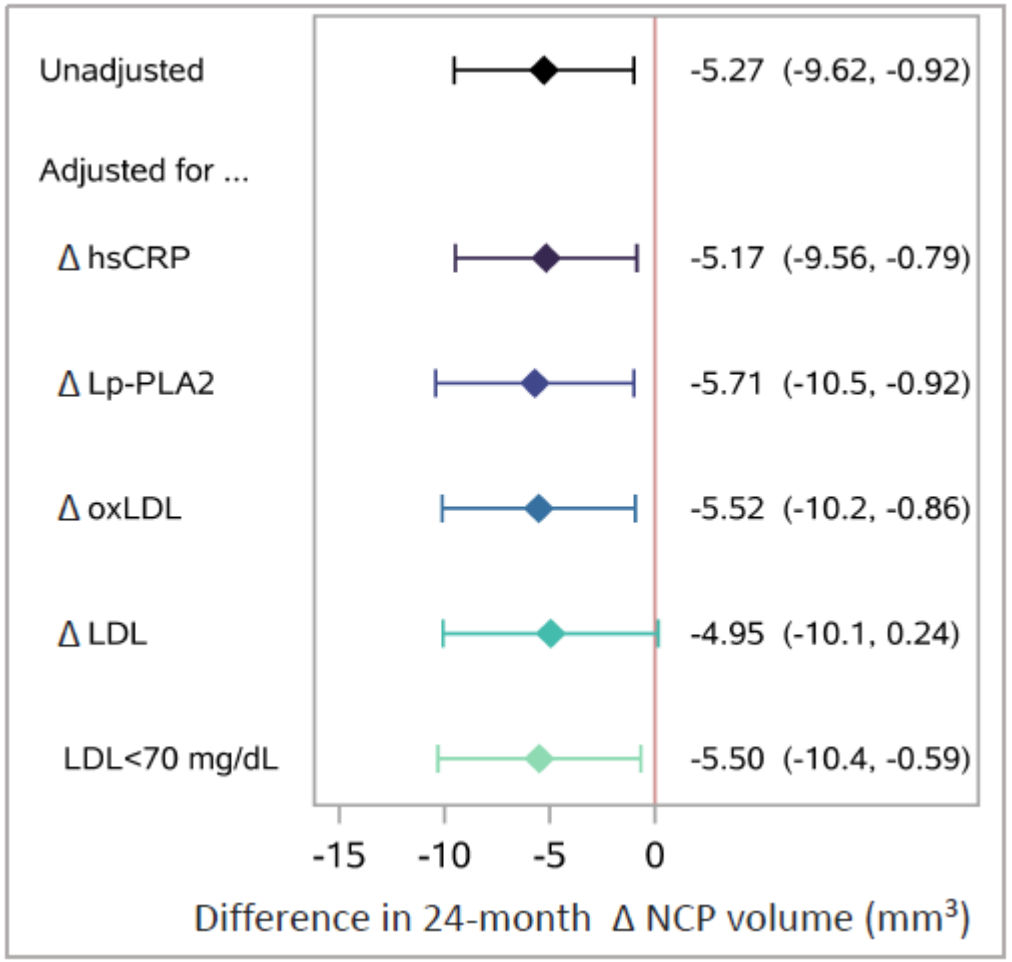
- Progression of non-calcified plaque 33% less likely with pitavastatin and 7% greater reduction in plaque volume
- Oxidized LDL and lipoprotein-associated phospholipase A2 (Lp-PLA2) decreased



Relating Pitavastatin Effects on Inflammatory Biomarkers to Plaque Changes in REPRIEVE

Pitavastatin significantly reduced LDL and key biomarkers of lipid oxidation and arterial inflammation in people with HIV, but these changes were not associated with changes in noncalcified or total plaque volumes.

What then may be mediating the changes in plaque volume?

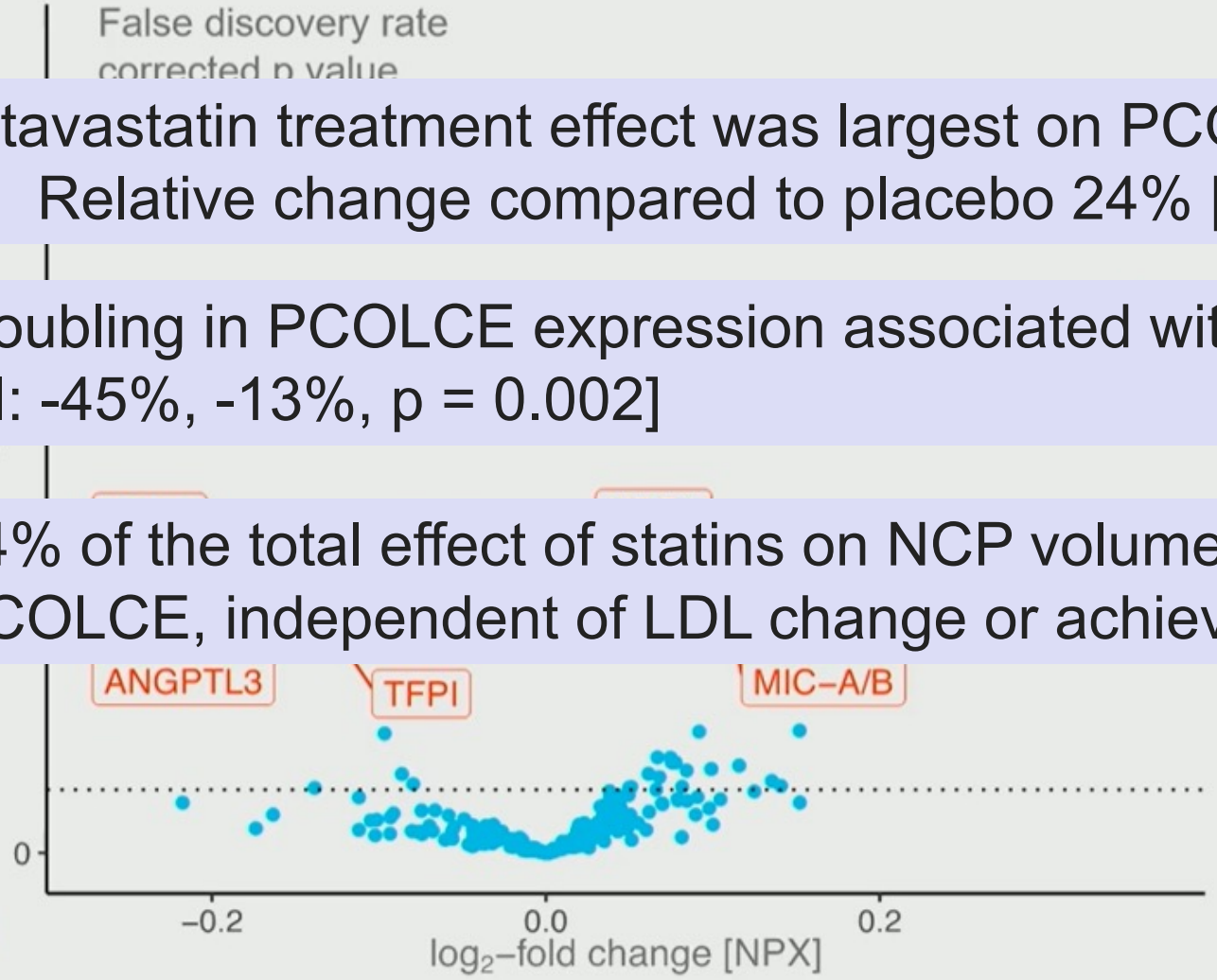


Proteins differentially expressed over time between treatment groups

Pitavastatin treatment effect was largest on PCOLCE:
Relative change compared to placebo 24% [95% CI: 18%, 31%, p < 0.001]

Doubling in PCOLCE expression associated with decrease in NCP by 31% [95% CI: -45%, -13%, p = 0.002]

84% of the total effect of statins on NCP volume change was mediated through PCOLCE, independent of LDL change or achieved LDL



Proteins showing differential expression between treatment groups	
Decreased expression	
ANGPTL3	*Angiopoietin-related protein 3*: Involved in regulation of lipid and glucose metabolism
TFPI	Xa directly. It possesses an antithrombotic
Increased expression	
	MHC class I polypeptide-related sequence A-B:
NRP1	development of the cardiovascular system, in angiogenesis.
PCOLCE	*Procollagen C-endopeptidase enhancer 1*: Binds to the C-terminal propeptide of type I procollagen and enhances procollagen C-proteinase activity

Performance of the ACC/AHA Pooled Cohort Equations for Risk Prediction in the Global REPRIEVE Trial

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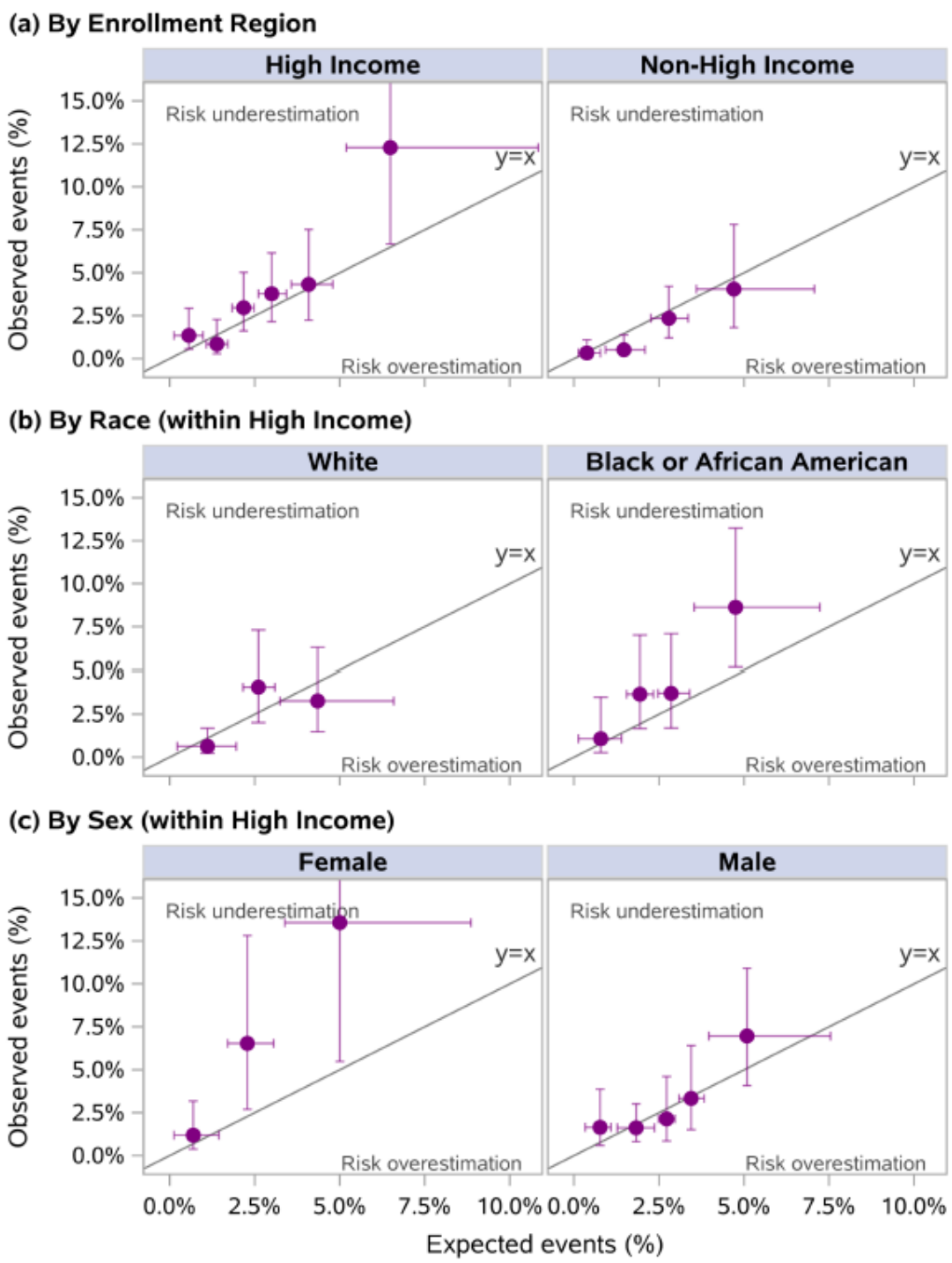
	Observed/Expected Events			
	Obs.	Exp.	O:E Ratio	P-value
Overall	**84**	**81**	**1.03**	**0.81**
Overall Female	21	14	1.42	0.44
Overall Male	64	67	0.95	0.74
Non-High Income	22	32	0.69	0.015
High Income	63	49	1.30	0.21
High Income White	22	24	0.92	0.79
High Income Black	37	23	1.66	0.13
High Income Female	17	7	2.56	0.05
High Income Male	46	42	1.10	0.70

Among a global cohort of PWH, the Pooled Cohort Equation over-predicted events among participants in non-High Income regions and under-predicted events in female and Black or African American participants from High Income regions.



Pitavastatin Has No Effect on Physical Function: REPRIEVE PREPARE Substudy

We hypothesized that physical function would decline with time, but PWH randomized to pitavastatin would have slower declines compared to placebo

Physical function (10x chair rise, 4-m gait, balance, grip strength, mSPPB) was evaluated annually for up to 5 years

- Among a relatively young population of PWH, physical function changed only minimally over 5 years, with no effects of pitavastatin vs placebo.
- There was a low prevalence of myalgias reported both in PREPARE and in the overall REPRIEVE population.
- ***In combination, these findings support the long-term safety of statin therapy on muscle, when used for primary prevention among PWH.***

Erlandson K, abstr 152

Recommendations for the Use of Statin Therapy as Primary Prevention of Atherosclerotic Cardiovascular Disease in People with HIV

Statement released: February 27, 2024

For people with HIV who have low-to-intermediate (<20%) 10-year atherosclerotic cardiovascular disease (ASCVD) risk estimates

- Age 40–75 years
  - When 10-year ASCVD risk estimates are 5% to <20%, the Panel for the Use of Antiretroviral Agents in Adults and Adolescents with HIV (the Panel) recommends initiating at least moderate-intensity statin therapy **(AI).**
    - Recommended options for moderate-intensity statin therapy include the following:
      - Pitavastatin 4 mg once daily **(AI)**
      - Atorvastatin 20 mg once daily **(AII)**
      - Rosuvastatin 10 mg once daily **(AII)**
  - When 10-year ASCVD risk estimates are <5%, the Panel favors initiating at least moderate-intensity statin therapy **(CI).** The absolute benefit from statin therapy is modest in this population; therefore, the decision to initiate a statin should take into account the presence or absence of HIV-related factors that can increase ASCVD risk.[a]
    - Same options for moderate-intensity statin therapy as recommended for 10-year ASCVD risk estimates of 5% to <20% (see above)

Key Recommendations for the General Population (Including People with HIV) Based on AHA/ACC/Multisociety Guidelines

For people age 40–75 years who have high (≥20%) 10-year ASCVD risk estimates

- Initiate high-intensity statin therapy.

For people age 20–75 years who have low-density lipoprotein cholesterol (LDL-C) ≥190 mg/dL

- Initiate high-intensity statin therapy at maximum tolerated dose.

For people age 40–75 years with diabetes mellitus

- Initiate at least moderate-intensity statin therapy. Perform further risk assessment to consider using a high-intensity statin.

Table 1: Number Needed to Treat over 5 Years Based on REPRIEVE

	Population	N	NNT_5
10-Year Atherosclerotic Cardiovascular Disease Risk Score	>10%	563	35
	5–10%	2,995	53
	2.5% to <5.0%	2,055	149
	0% to <2.5%	2,156	199
Overall		7,769	106

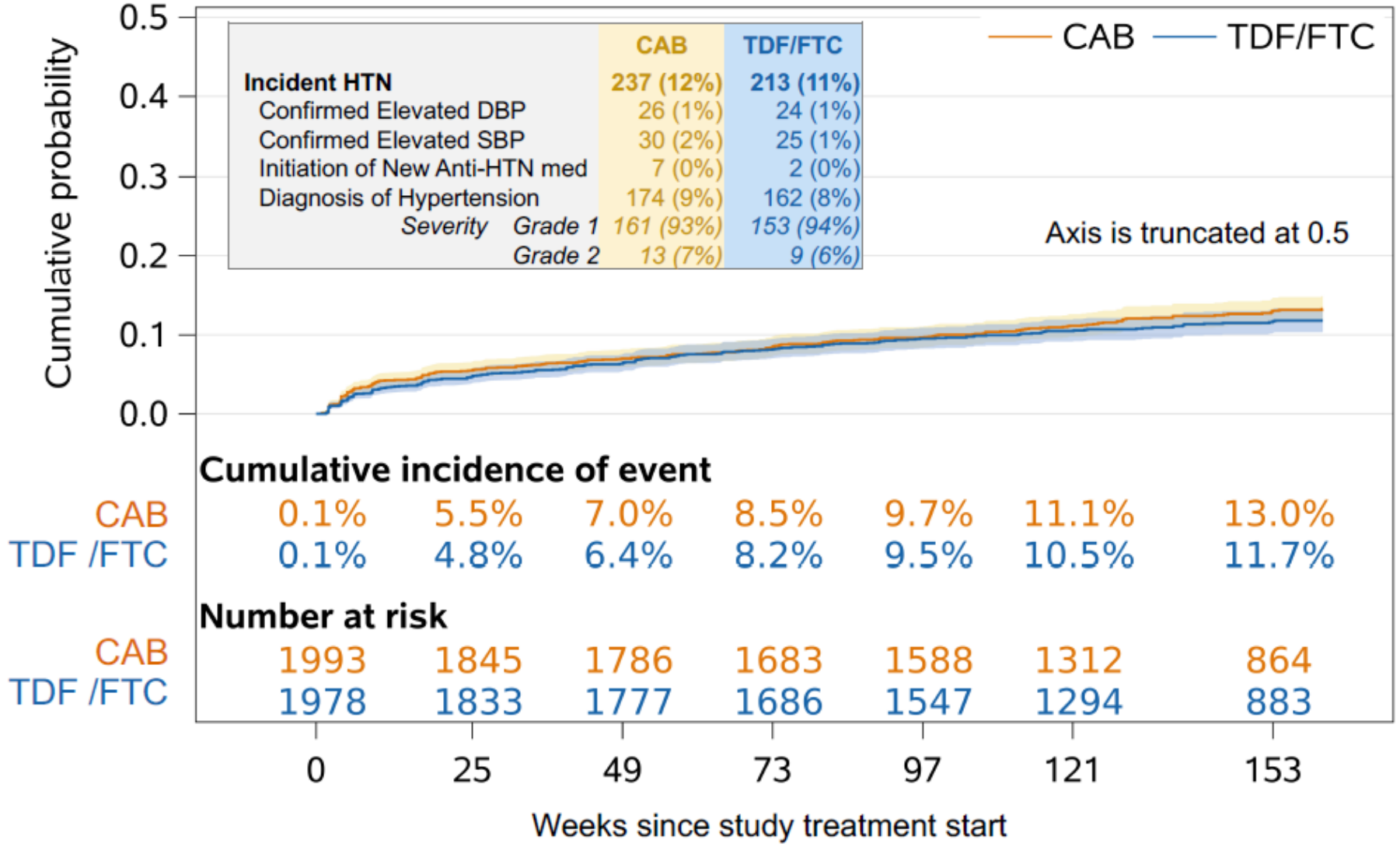
Key: NNT_5 = number needed to treat over 5 years

	High Intensity	Moderate Intensity	Low Intensity
LDL-C Lowering	**≥50%**	**30% to 49%**	**<30%**
	Atorvastatin[a] 40–80 mg Rosuvastatin[a] 20–40 mg	**Pitavastatin 4 mg (AI)**[b] **Atorvastatin 20 mg (AII)**[a,b] **Rosuvastatin 10 mg (AII)**[a,b] Fluvastatin XL 80 mg Fluvastatin 40 mg twice daily Lovastatin[c] 40–80 mg Pravastatin 40–80 mg Simvastatin[c] 20–40 mg	Pravastatin 10–20 mg Simvastatin[c] 10 mg Fluvastatin 20–40 mg Lovastatin[c] 20 mg

No Increased Risk for Hypertension with CAB-LA Compared to TDF/FTC for HIV PrEP in HPTN 083

0789

Figure 2. Cumulative Incidence of First HTN Event



	CAB	TDF/FTC
Incident HTN	**237 (12%)**	**213 (11%)**
Confirmed Elevated DBP	26 (1%)	24 (1%)
Confirmed Elevated SBP	30 (2%)	25 (1%)
Initiation of New Anti-HTN med	7 (0%)	2 (0%)
Diagnosis of Hypertension	174 (9%)	162 (8%)
Severity Grade 1	*161 (93%)*	*153 (94%)*
Grade 2	*13 (7%)*	*9 (6%)*

Table 2. Associations between Repeated Use of Individual Substances and Left Ventricular Diastolic Dysfunction (LVDD)

	Unadjusted OR(95% CI)	Adjusted OR(95% CI) Saturated Model①	Adjusted OR(95% CI) Parsimonious Model②
Tobacco	1.70 (1.05, 2.77)*	1.71 (1.01, 2.91)*	1.86 (1.09, 3.16)*
Alcohol	1.09 (0.66, 1.80)	1.05 (0.61, 1.82)	
Cannabis	1.12 (0.66, 1.89)	0.89 (0.49, 1.62)	
Stimulant	2.11 (1.14, 3.91)*	1.91 (1.18, 3.09)*	1.92 (1.17, 3.16)*
Opioid	0.49 (0.07, 3.63)	0.21 (0.02, 1.75)	
Sedative	2.73 (1.18, 6.32)*	2.12 (0.89, 5.07)	

Table 3. Association between Repeated Co-Use of Stimulants + Tobacco and Left Ventricular Diastolic Dysfunction (LVDD)

	Unadjusted OR(95% CI)	Adjusted OR(95% CI) Parsimonious Model②
Stimulant + Tobacco co-use	1.44 (0.88, 2.37)	2.45 (1.25, 4.80)*

Repeated co-use of stimulants (e.g., cocaine, meth) and tobacco is a potent risk factor for left ventricular dysfunction (LVDD) in women with HIV

N=1,162 women with HIV • Mean age (SD): 49 years (9)

Parsimonious model: adjusted for age, SBP, DM, eGFR < 60

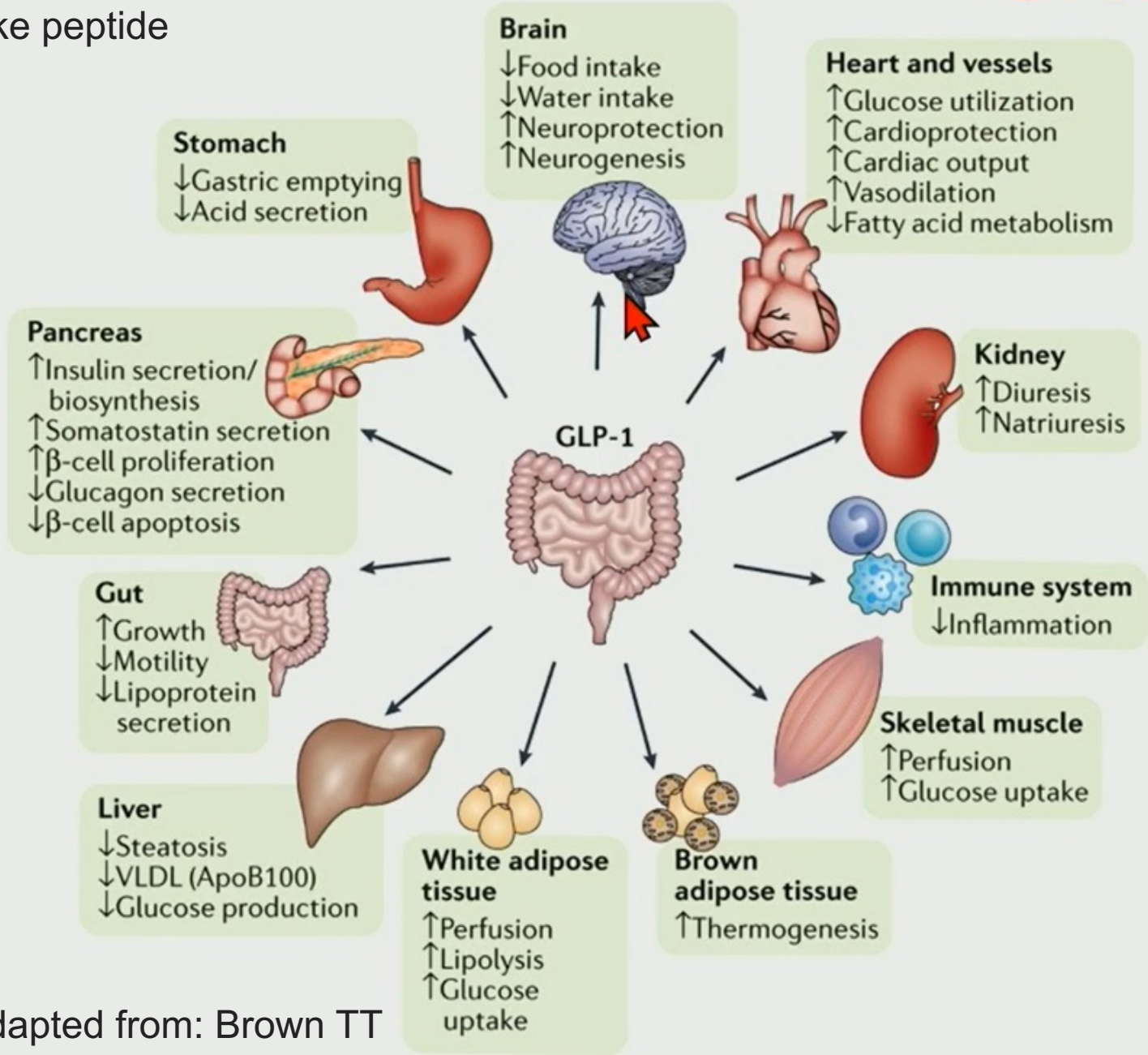
WIHS Women's Interagency HIV Study

Riley E, abstr 793

CROI 2024

Gut-derived incretin hormone glucagon-like peptide

Multiple Sites of Action of GLP-1 RA



Muskiet, NatureReviewsNephrology, 2017

Adapted from: Brown TT

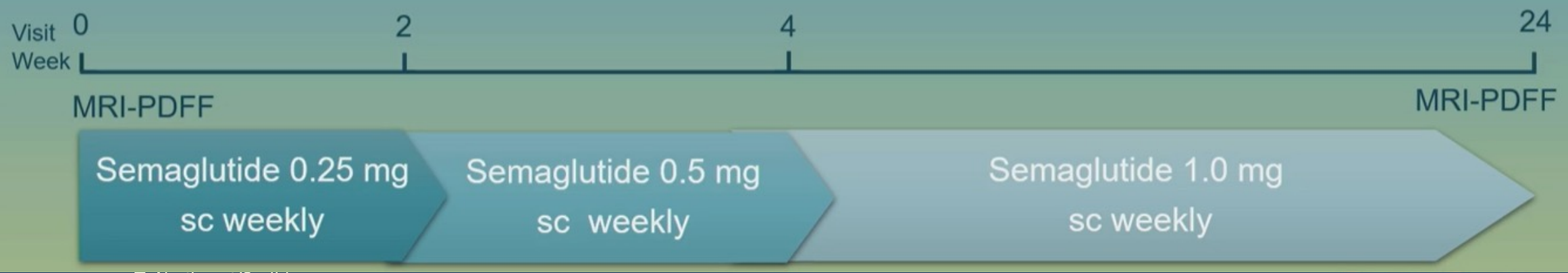
Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)

ACTG A5371, the SLIM LIVER study, was a phase IIb, single-arm, open-label, pilot study of the effects of semaglutide on magnetic resonance imaging-proton density fat fraction (MRI-PDFF)-quantified intrahepatic triglyceride (IHTG) content

Inclusion Criteria

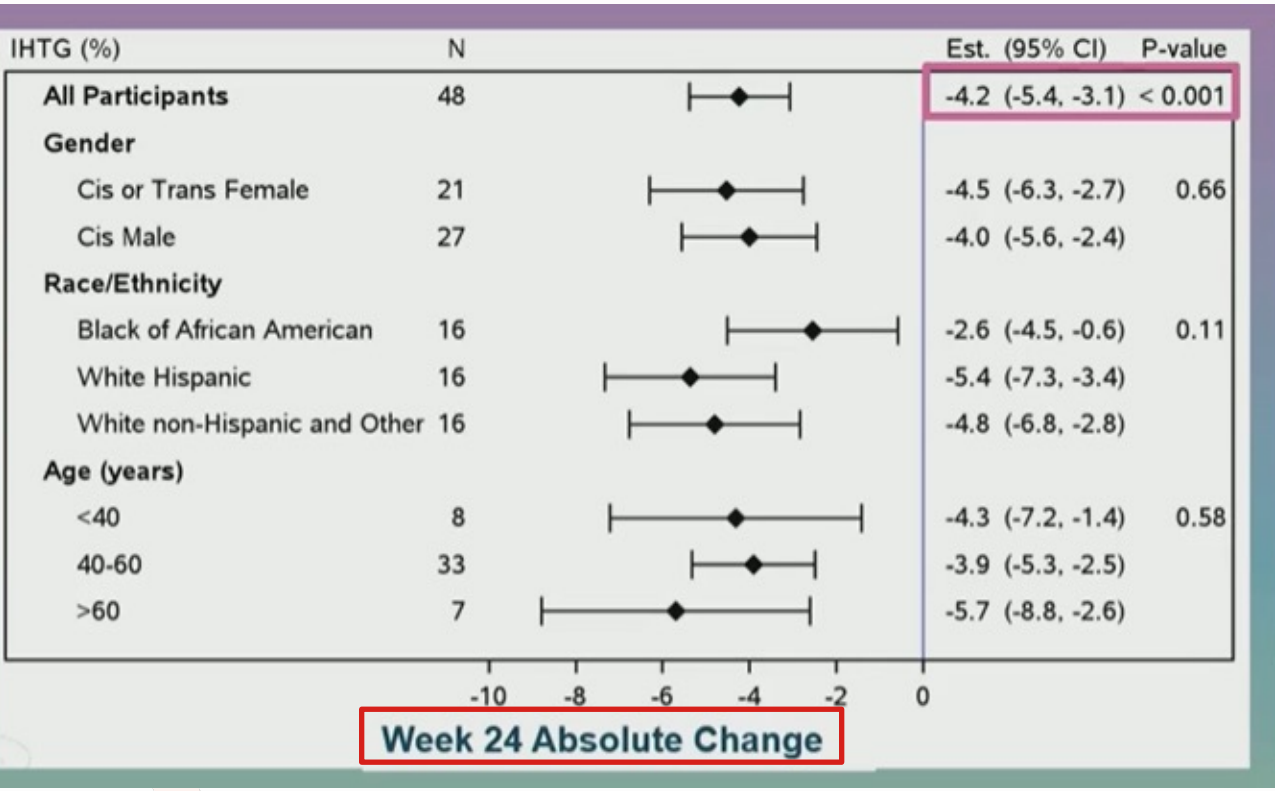
- Adult PWH on suppressive ART
- Elevated minimum waist circumference
  - -WC≥95 cm ♂ / WC 94≥cm ♀
- Insulin resistance or pre-diabetes
- ≥5% IHTG on MRI-PDFF

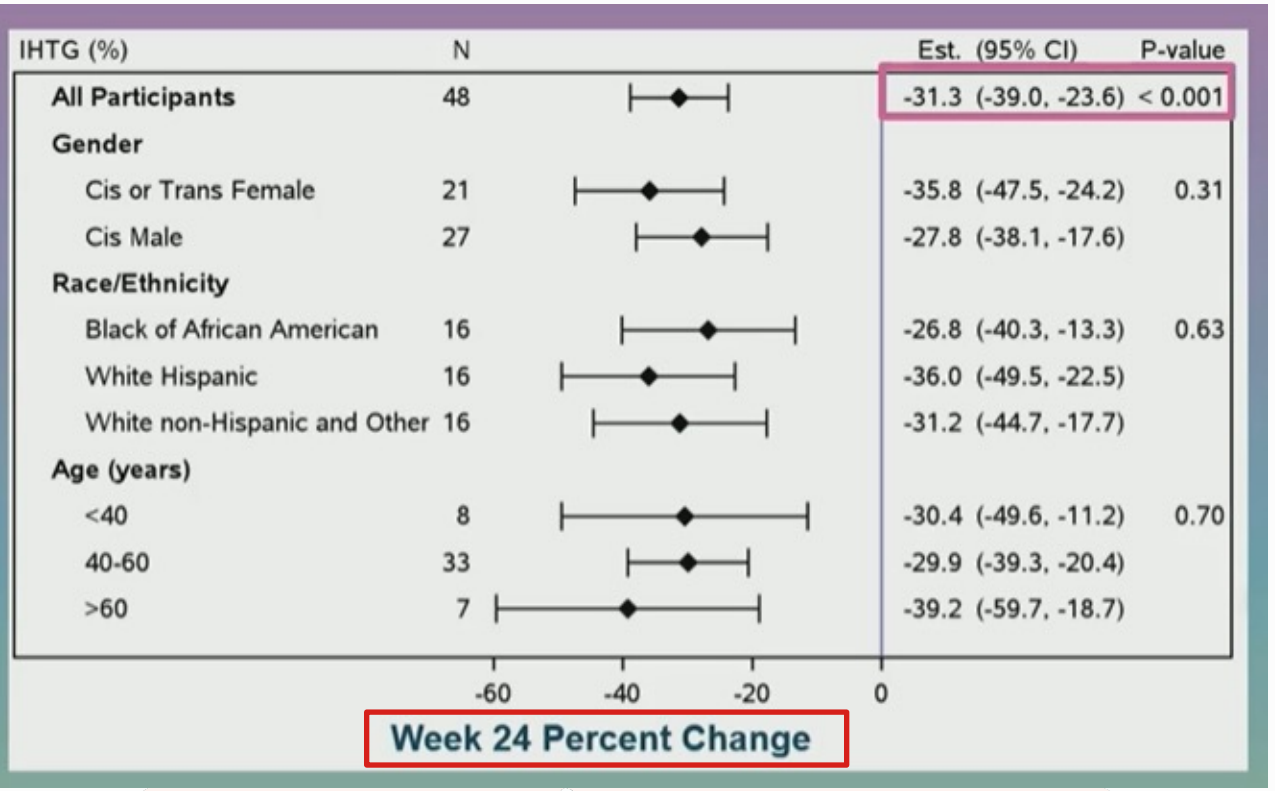
- **51 enrolled, 49 completed per-protocol**
- **Reasons for exclusion from analysis:**
  - -Nausea Grade 3 (n=1)
  - -Withdrawal of Informed Consent (n=1)



Northeast/Caribbean

Lake J, abstr 159





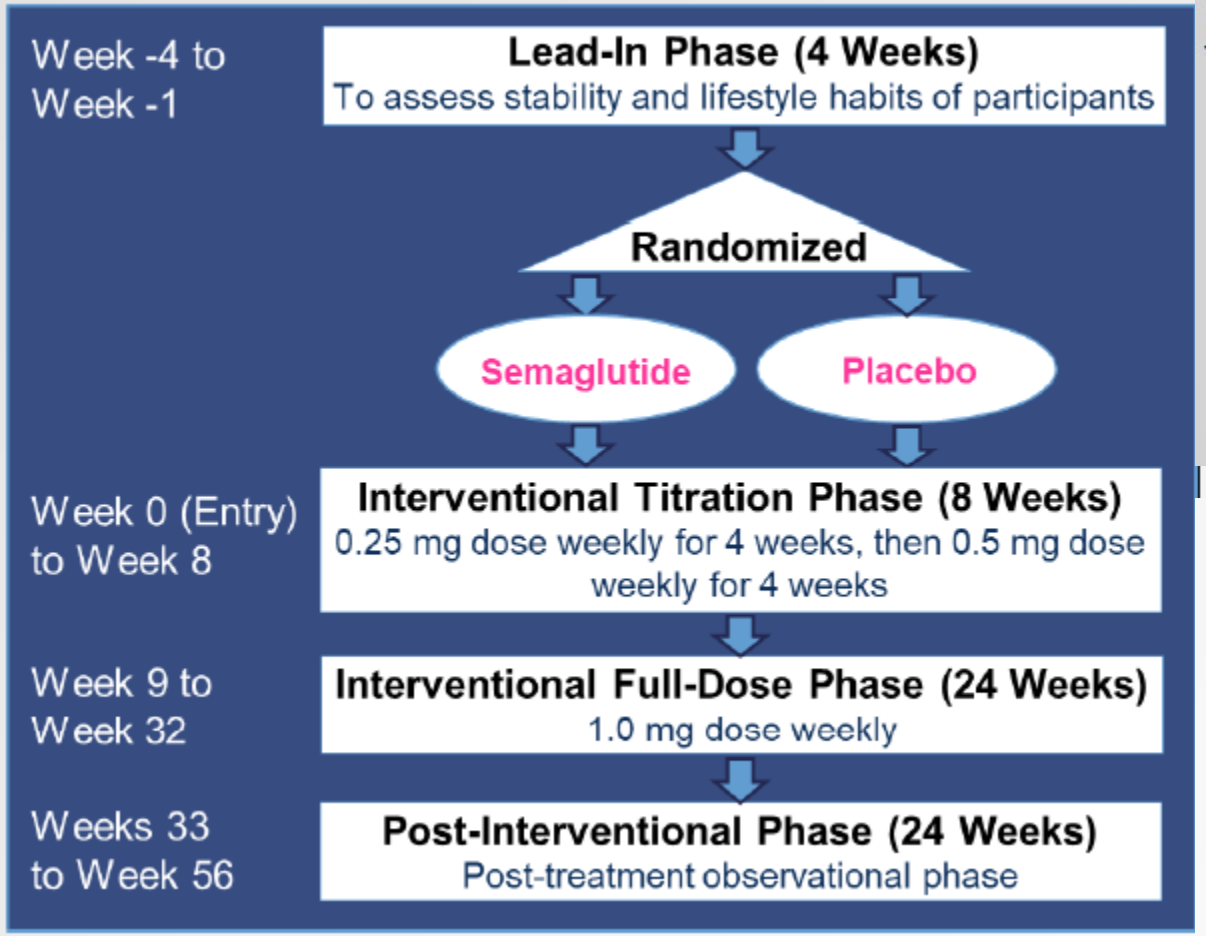
58% of participants had a ≥30% relative reduction in IHTG
29% of participants had complete MASLD resolution (absolute IHTG <5%)

Mean weight loss was 7.8 kg (17 lbs) over 24 weeks

IHTG improvements correlated with weight loss (r=0.54, p<0.0001)

EFFECTS OF SEMAGLUTIDE ON INFLAMMATION AND IMMUNE ACTIVATION IN HIV-ASSOCIATED LIPOHYPERTROPHY

#798



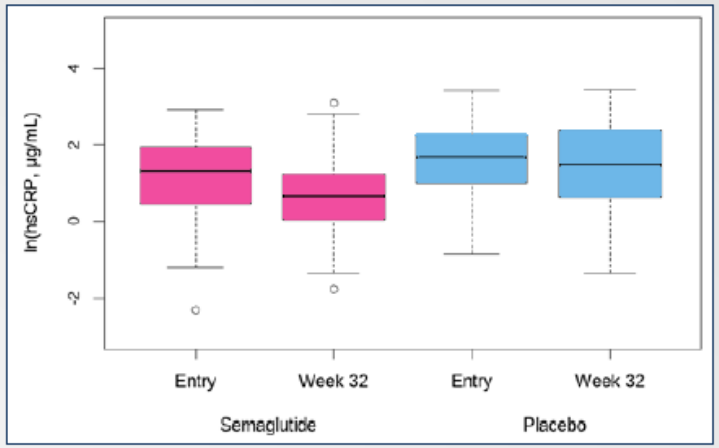
KEY INCLUSION/EXCLUSION CRITERIA

- **Inclusion:** Age ≥18 years, HIV RNA <400 copies/mL ≥6 months, stable ART ≥12 weeks, BMI ≥25 kg/m^2, WC >95 cm (men) and >94 cm (women), WHR >0.94 (men) and >0.88 (women), subjective abdominal girth increase after ART initiation
- **Exclusion:** Diabetes, known cardiovascular disease, pregnancy, history of pancreatitis, thyroid cancer, multiple endocrine neoplasia syndrome type 2, or severe HIV-associated lipoatrophy

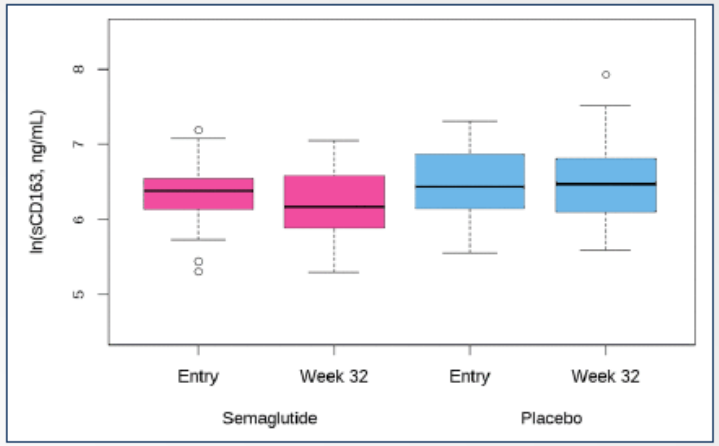
Summary of 32-week multiplicative regression models for primary outcome measures

Outcome variable	β[a]	SE	95% CI	p	% change[b]
Abdominal TAT, cm^2	−72·1	19·3	−109·9, −34·3	**<0·0001**	−15·1%
Abdominal SAT, cm^2	−42·0	17·1	−75·5, −8·5	**0·014**	−11·2%
Abdominal VAT, cm^2	−30·8	9·9	−50·1, −11·5	**0·002**	−30·6%
Lean body mass, kg	−2.98	2.00	−6.8, 0.86	0.129	−5.7%

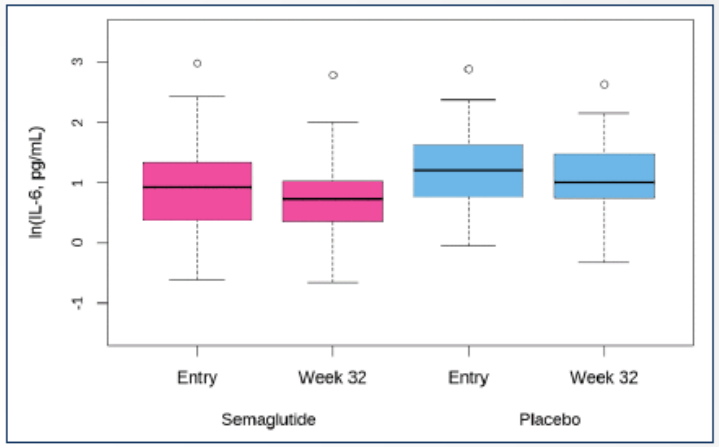
hsCRP
-39.9%



IL-6
-18.8%

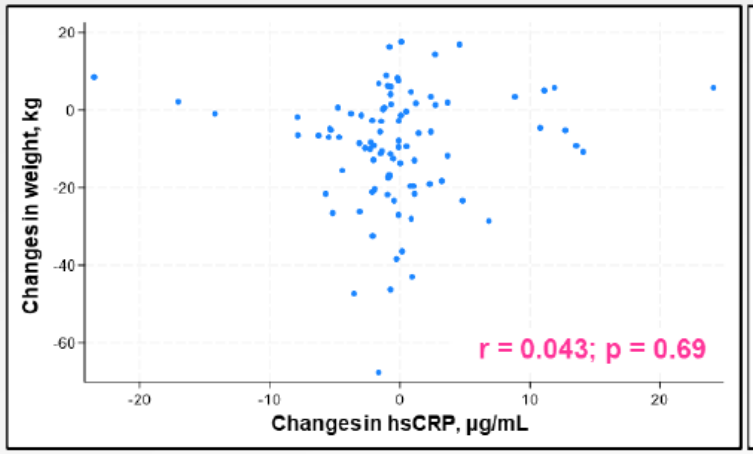


sCD163
-12.3%

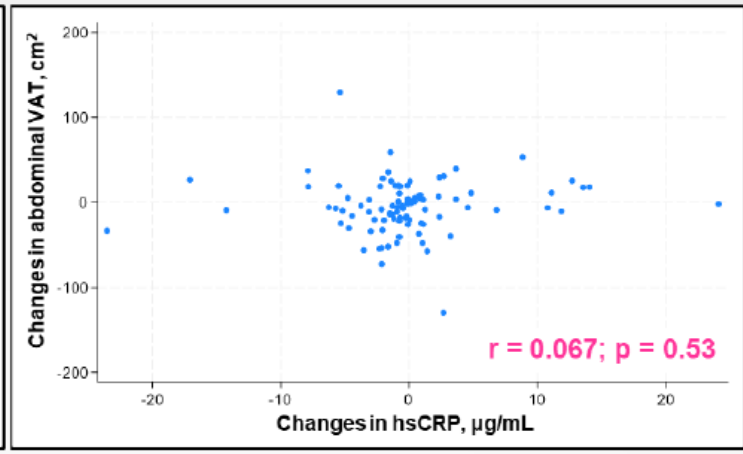


Semaglutide use caused notable decreases in several key inflammatory markers independent of abdominal VAT & weight loss in people with ***HIV-associated lipohypertrophy*** and without diabetes.

A. CORRELATION BETWEEN CHANGES IN hsCRP & CHANGES IN WEIGHT



B. CORRELATION BETWEEN CHANGES IN hsCRP & CHANGES IN ABDOMINAL VAT



Ross Eckhard A, abstr 798

Impact of Semaglutide on Weight Change Among People with HIV: A Stratified Analysis by Baseline BMI

797

Baseline Characteristics

N=222

25% female
75% male

Mean follow-up: 1.1 years

Mean age: 53 years (SD: 10)

77% diabetic

89% virally suppressed

Table 1. Weight loss results stratified by BMI class

BMI Class	n (%)	Weight loss, kg (95% CI)
Normal (18.5 – 24.9 kg/m²)	11 (4.9)	-4.1 (-7.9, -0.2)
Overweight (25.0 – 29.9 kg/m²)	36 (16.2)	−4.6 (−6.9, −2.3)

- For those with information on dose, most (87 of 111) PWH received low doses of subcutaneously injected semaglutide (0.25, 0.5, 1 mg), while 24 PWH received high doses (1.7, 2, 2.4 mg)
- There were no significant interactions for weight loss over time with diabetes status or dose
  - **With diabetes**: -6.18 (-7.48, -4.89) kg ($p < 0.001$) vs. **Without diabetes**: −8.57 [−11.45, −5.68] kg ($p < 0.001$); *p for interaction=0.12*
  - **Low dose**: -8.95 (-10.84, -7.06) kg ($p < 0.001$) vs. **High dose**: −12.06 [−17.49, −6.63] kg ($p < 0.001$); *p for interaction=0.27*

Treatment with semaglutide was associated with average ***weight loss of 6.5kg*** and ***bodyweight reduction of 5.7%*** at 1 year among PWH

Haidar L, Crane HM, abstr 797

Effects of Semaglutide on Muscle Structure and Function in the SLIM Liver Study

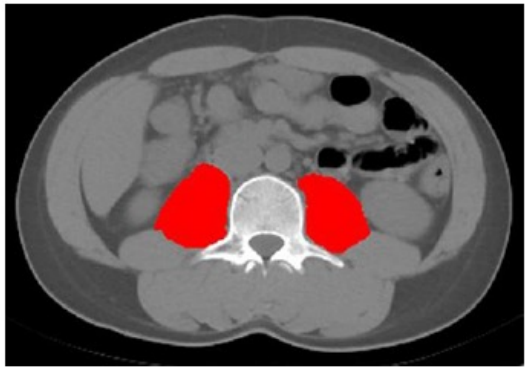
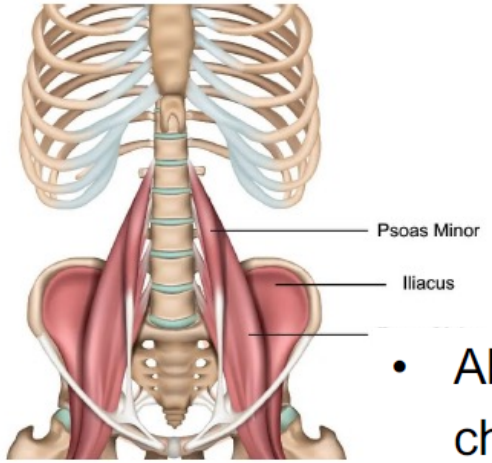


Figure 1. Psoas major muscle on MRI, in red.



- Absolute psoas muscle volume decreased by 1.49 mL (CI: -2.15, -0.83); no significant change seen in absolute psoas muscle fat
- PWH >60 years old had greatest decrease in muscle volume, but there were no statistically significant differences between other subgroups

Table 1. Change in physical function.

Parameter	Baseline	Week 24	Change, Baseline to Week 24	P-value
5x Chair Rise (seconds)				0.077
10x Chair Rise (seconds)				0.069
Gait speed (meters/second)				0.078
Presence of slow gait speed (<1 meters/second)				0.029

Physical function was **preserved** despite loss of muscle volume among people with HIV taking semaglutide.

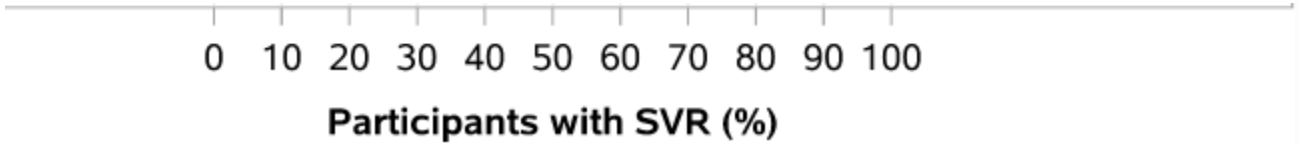
A Phase II Trial of 4 Weeks of Glecaprevir/Pibrentasvir for Early Hepatitis C Virus (ACTG A5380) 00696

PURGE-C

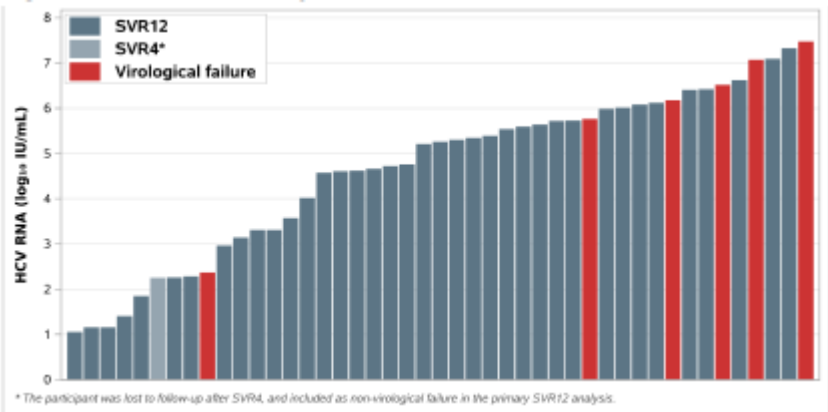
A5380 was powered to conclude that the SVR12 proportion is >80% using the 90% Wilson confidence interval (CI).

Figure 1. SVR12 Proportion

	Total N	SVR N	SVR% (90% CI)
Overall			
Primary approach[1]	45	38	84.4% (73.6%, 91.3%)
Planned supplementary[2]	44	38	86.4% (75.7%, 92.8%)

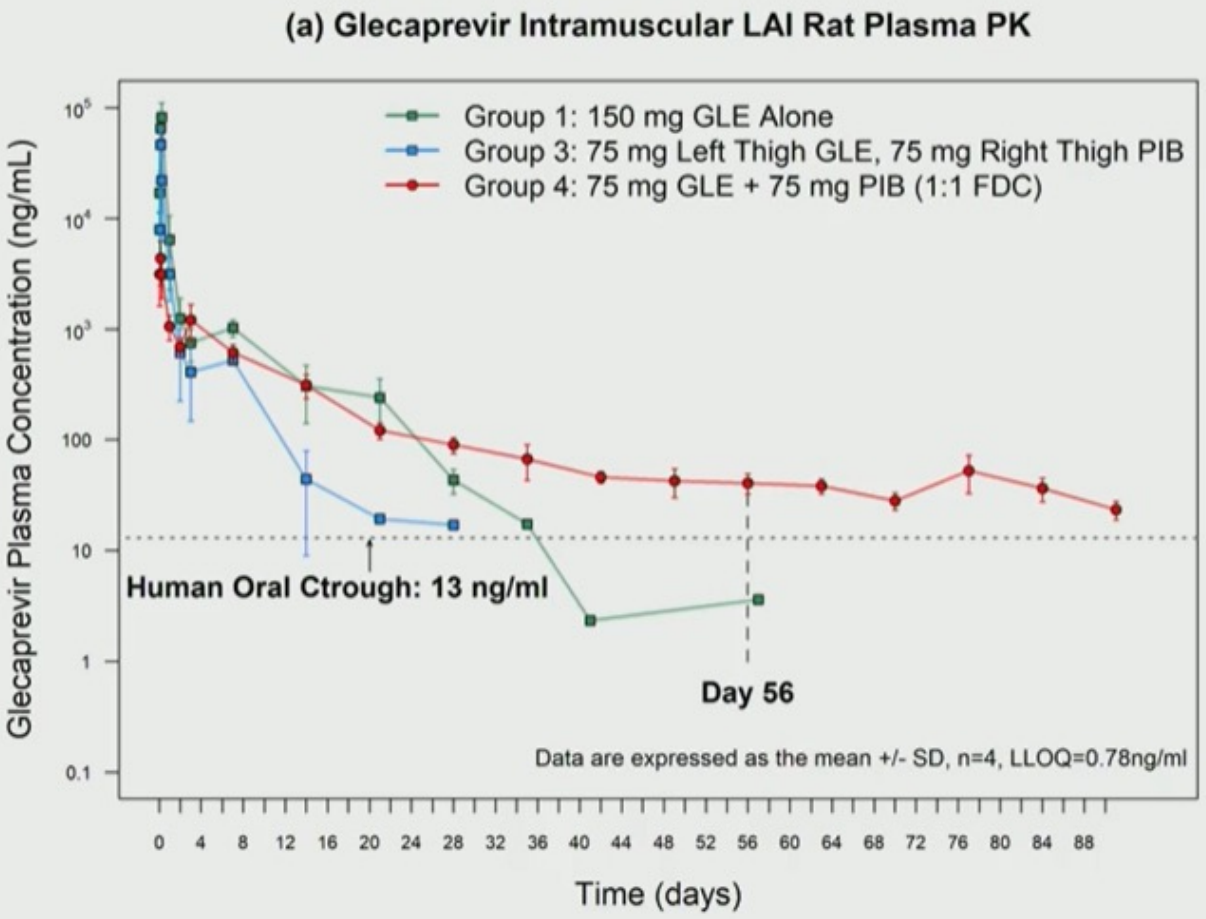


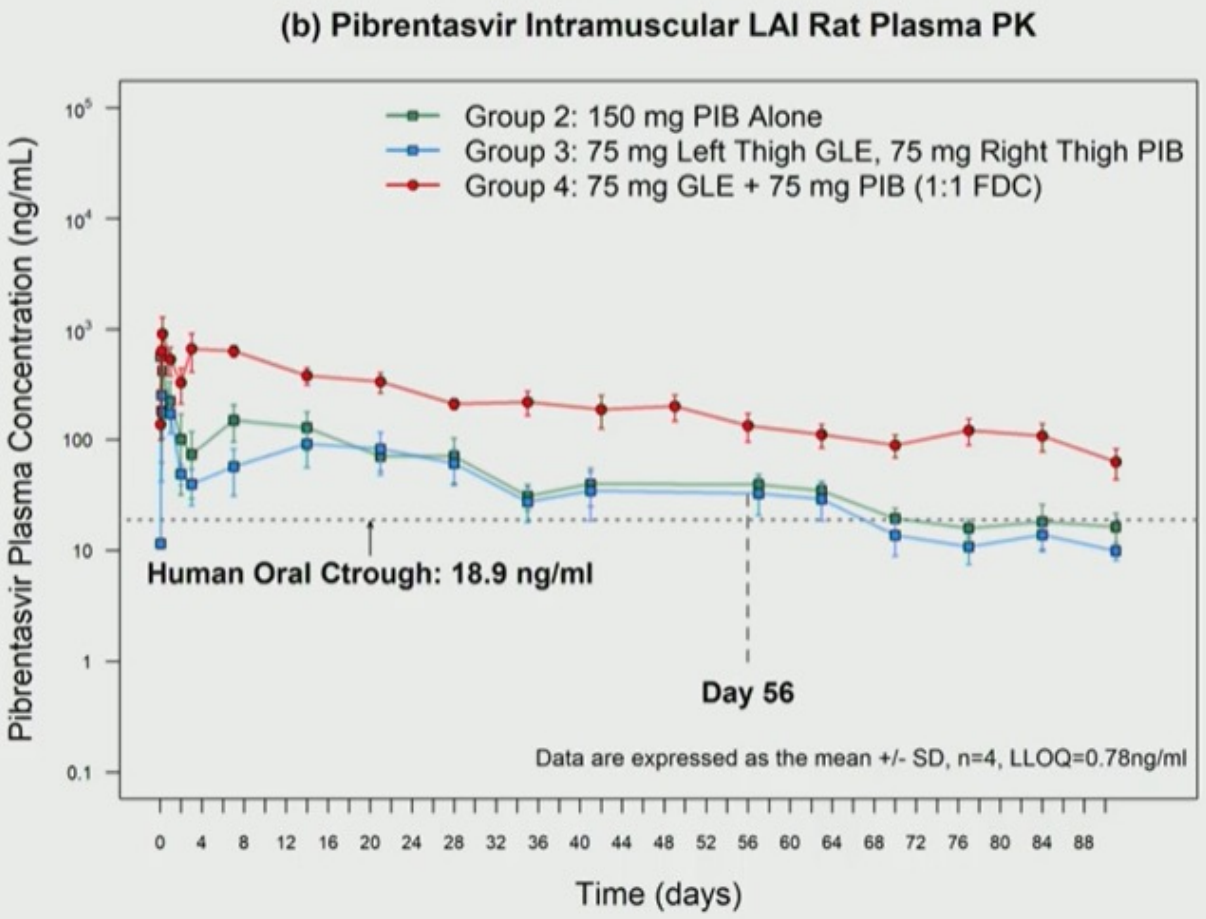
[1] Primary approach: all participants who initiated study treatment.
[2] Planned supplementary approach excluding premature study discontinuations.



Preclinical PK of a HCV LA-Injectable Formulation

Green – Either GLE or PIB alone in both thighs Blue – GLE to left thigh PIB to right thigh RED – GLE/PIB 1:1 FDC administered to both thighs





The combination of both drugs within an FDC maintains a longer terminal half-life for GLE and improves exposure for PIB, maintaining plasma concentrations **above the human oral C_{trough}**

Arashad U, abstr 161

ACTG A5379 (BEeHIVe): Background

Conventional vaccine, which consists of recombinant Hepatitis B surface antigen (HBsAg) and an alum adjuvant, achieves seroprotection (Anti-HBs ≥10 mIU/mL) in 35-80% in people with HIV

- Predictors of non-response include older age, low CD4 count, HIV viremia

HepB-CpG (HEPLISAV-B®) contains recombinant HBsAg (20 mcg) and CpG 1018® adjuvant

- Adjuvant binds to TLR9 (sensing receptor for innate immune responses) expressed on plasmacytoid dendritic cells and memory B cells
- Approved as 2 dose series for adults 18 years and older

100% seroprotection achieved with 3 doses of HepB-CpG in people with HIV and no prior vaccination (A5379 Group B results)

Marks et al, Clin Infect Dis. 2023

Adapted from Marks K, abstr 209

ACTG

Study Design

Group A – Non-response to conventional vaccine (n=561)

- Participants randomized 1:1:1 to receive
  - **HepB-CpG 2 doses** at entry and week 4 (n=187)
  - **HepB-CpG 3 doses** at entry and at weeks 4 and 24 (n=187)
  - **HepB-alum** 3 doses at entry and at weeks 4 and 24 (n=187).
- Group A stratified by sex at birth and diabetes
- Participants on study for 72 weeks

HepB-CpG administered IM as 0.5 mL dose (contains 20 mcg of HBsAg and 3000 mcg CpG 1018® adjuvant)
HepB-alum administered as 1.0 ml dose (contains 20 mcg of HBsAg)

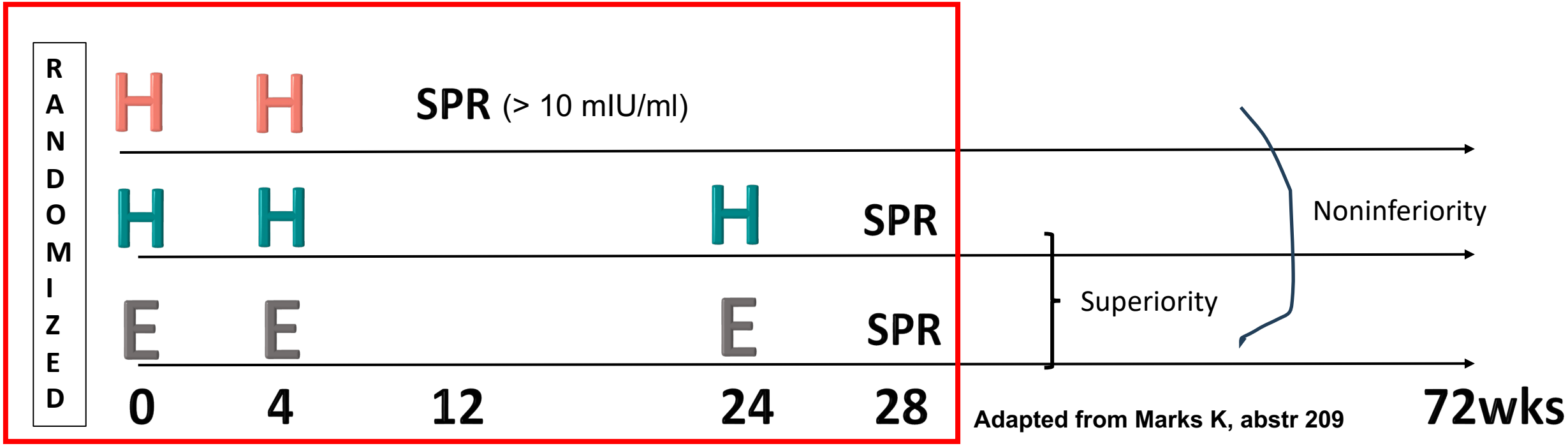
41 sites in 10 countries

ACTG

Primary Objectives – Non-responders

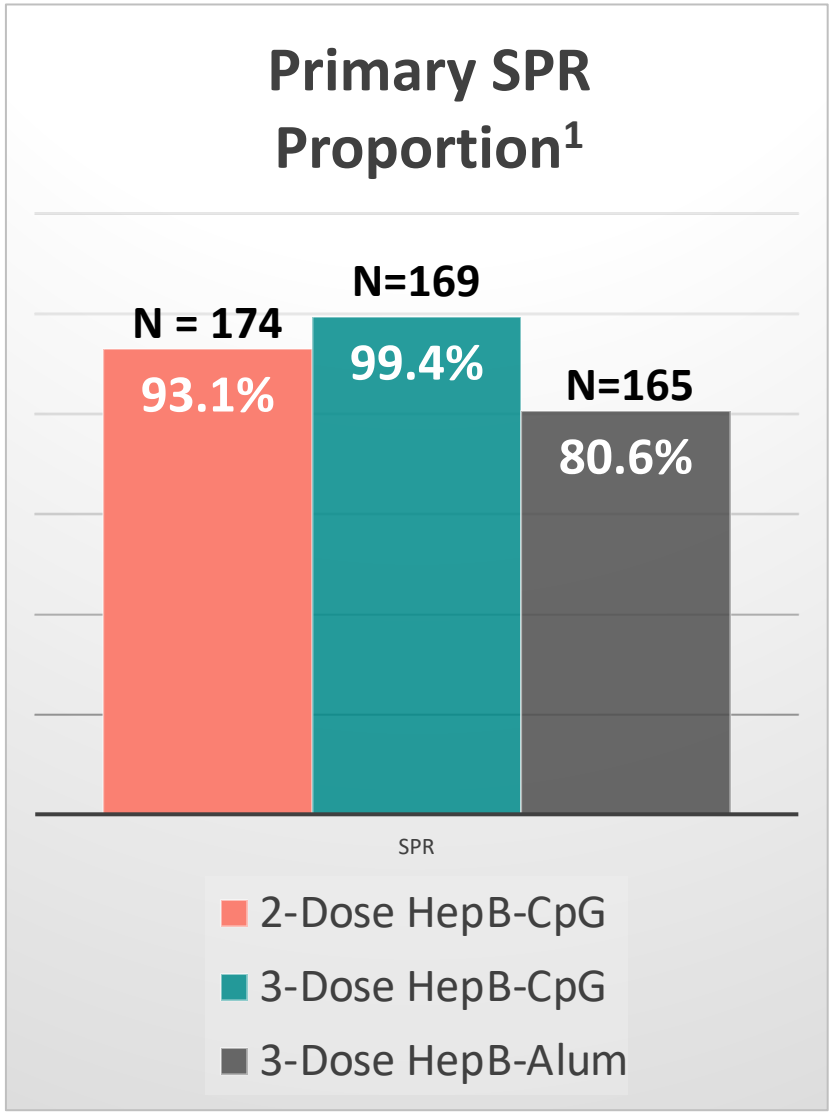
- **To compare the seroprotection response (SPR) of 2-dose HepB-CpG to 3-dose HepB-alum (non-inferiority)**
- **To compare SPR of 3-dose HepB-CpG to 3-dose HepB-alum (superiority)**
- **To describe safety**

Documentation of HBV vaccination
No serum HBsAb level ≥10 mIU/mL at any time
Serum HBsAb level <10 mIU/mL, "negative", or indeterminant within 45 days of study entry

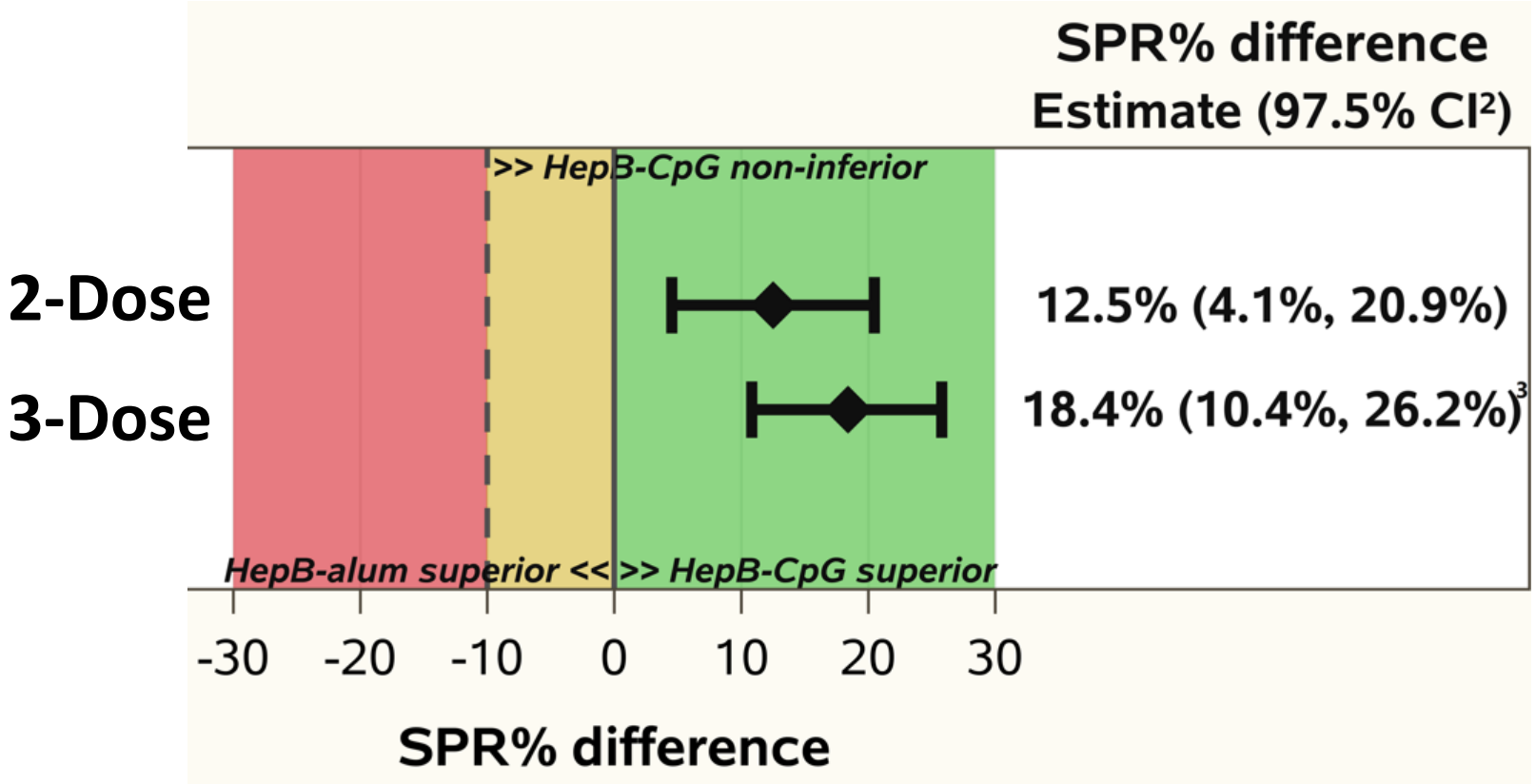


Adapted from Marks K, abstr 209

Primary Results



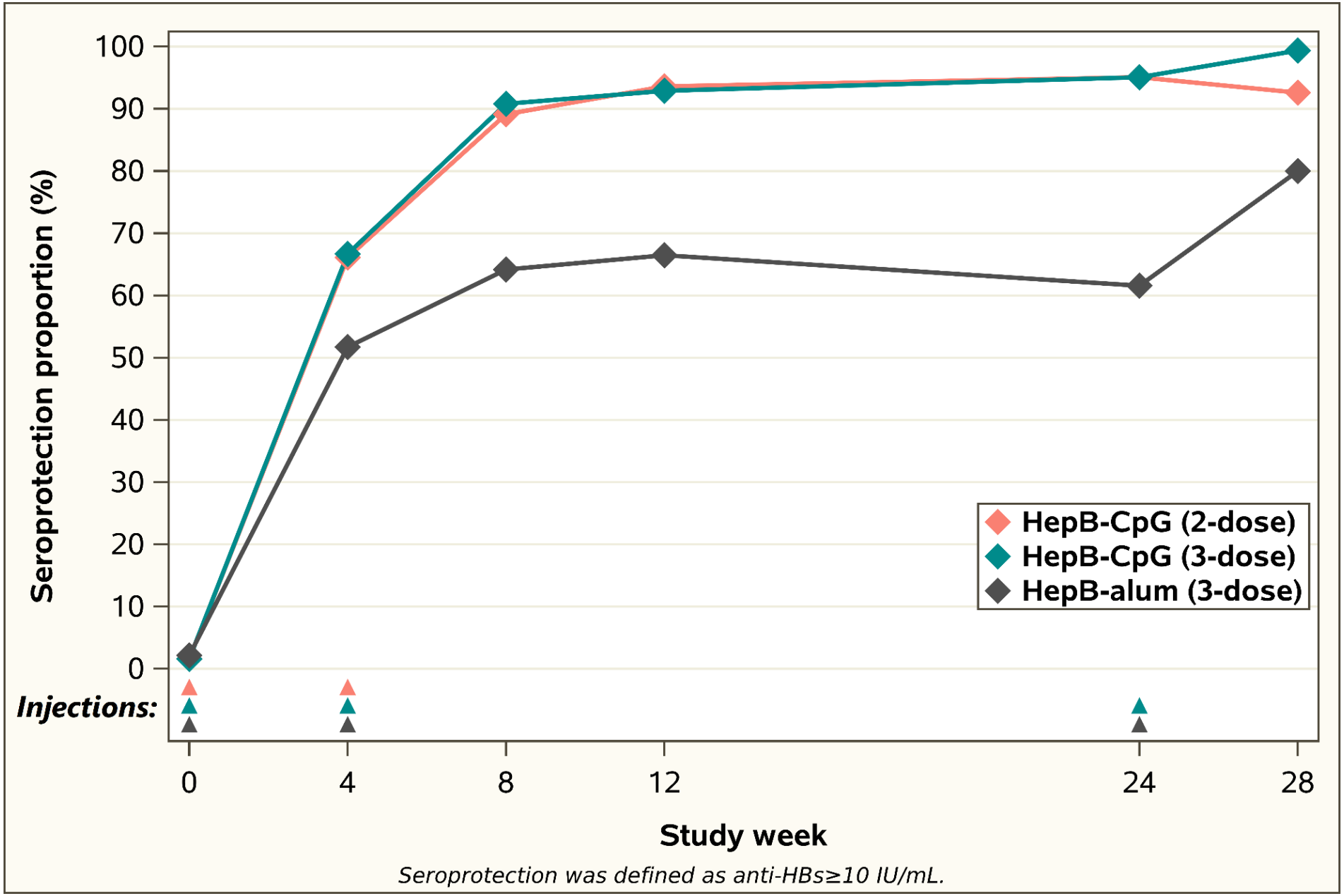
HepB-CpG SPR Comparison to HepB-Alum



[1] N denotes the number of participant in the Analysis Set
[2] 97.5% Newcombe CI
[3] Repeated CI adjusted for group sequential monitoring

ACTG

SPR Proportion at Study Visits



ACTG

Safety

- Gr 2/3 AEs that occurred in 5% or more of participants by study arm:

	2-Dose HepB-CpG	3-Dose HepB-CpG	3-Dose HepB-Alum
Injection Site Pain	5%	11%	5%
Fatigue	5%	9%	6%
Headache	7%	7%	8%
Malaise	6%	6%	5%
Myalgia	5%	6%	4%

One or more AEs <u>related to vaccines</u> were experienced by 33%, 46% and 36%, respectively, mostly Gr 1 and 2. Vaccination site pain, fatigue, headache, malaise and myalgia were most frequent

- Grade 3 in 3%, 1% and 4% and no deaths occurred

Adapted from Marks K

ACTG

Conclusions

In this study of PWH with non-response to conventional HBV vaccine, both 2 and 3 doses of HepB-CpG achieved superior SPR compared to 3 doses of HepB-alum

- Three doses of HepB-CpG achieved a higher proportion with titers >1000 mIU/ml compared to two doses, and to 3 doses of HepB-alum

No unexpected safety issues or deaths

- Participants remain in follow-up through 72 weeks to assess durability of response and safety

ACTG

Safety of Tenofovir Alafenamide in individuals with a history of Proximal Renal Tubulopathy on TDF

828

TDF-associated PRT was defined as two or more of:

- normoglycemic glycosuria [>1+ on dipstick]
- proteinuria [>1+ on dipstick or urine protein/creatinine ratio >30 mg/mmol]
- hypophosphatemia [serum phosphate <0.64 mmol/L)
- rapid eGFR decline [>5 mL/min/1.73 reduction from baseline]

or a renal biopsy showing acute tubular by other causes, with clinical resolution following TDF discontinuation.

Non-diabetic adults with HIV RNA <200 estimated glomerular filtration rate (eGF mL/min/1.73m², and urine protein/creat mg/mmol who were no longer receiving TAF initiated TAF-based antiretroviral therapy (ART) regimen and were followed annually for five years.

Key findings:

28 patients who developed Proximal Renal Tubulopathy / Fanconi syndrome on TDF initiated a TAF-based regimen and were followed up for 5 years.

- **None developed recurrent PRT**
- **Kidney function remained stable**

AIDS Linked to the IntraVenous Experience

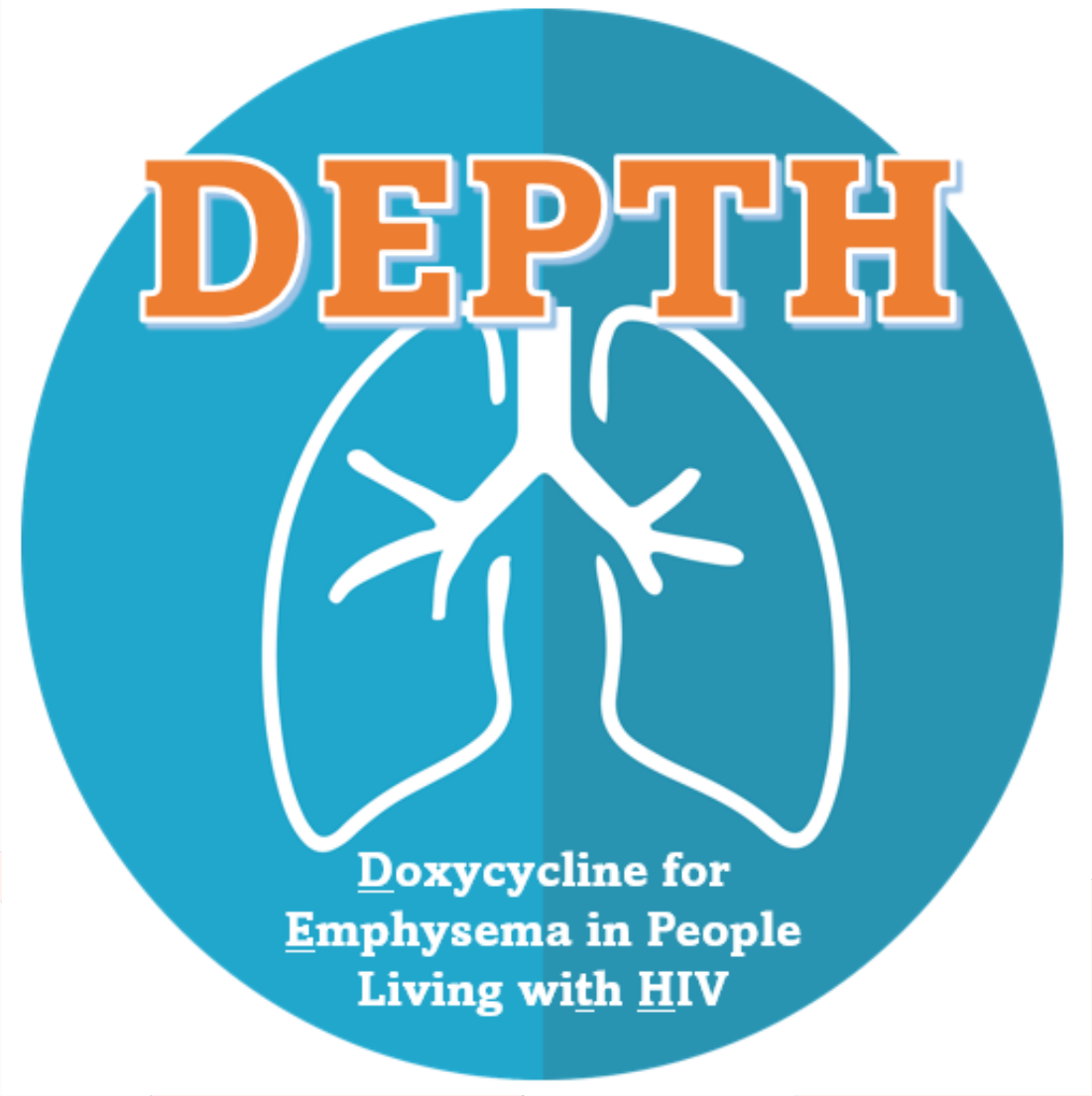
alive

shield

Mortality Cause	All-Cause Mortality	
	Hazard Ratio (95% CI)	P-Value
Lung Function Measure		
Absolute FEV_1**	1.95 (1.38, 2.75)	**<0.001**
FEV_1Q**	1.90 (1.38, 2.61)	**<0.001**
FEV_1 % (<70%)	1.86 (1.47, 2.36)	**<0.001**
FEV_1 z-score (z<-2.5)	1.81 (1.36, 2.40)	**<0.001**

- Pulmonary disease is an important comorbidity among PLWH
- Lung function is a strong predictor of mortality even after accounting for other comorbidities and exposures
- Associations between lung function and all-cause mortality were consistent and robust w/ recent changes in interpretation strategies

Raju S, abstr 153



https://depth-trial.com/

depth@med.cornell.edu

Prostate Cancer Characteristics and Outcomes for Veterans with HIV

Characteristic	PWH n=791	PWoH n=2,778	p
PSA at dx, median	6.8	6.3	0.005
Metastatic at dx, %	4.1	2.7	0.048

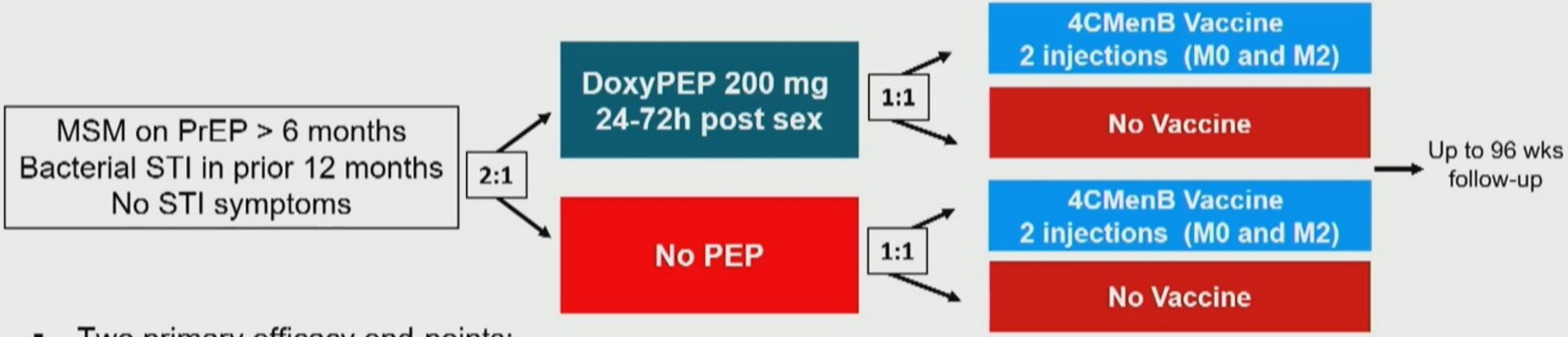
Adjusting for age and calendar year, 1.25 fewer PSA tests for PWH versus PWoH (p<0.001)

D'Amico Risk Group	PWH n=759	PWoH n=2,703	Hazard Ratio (95% CI)	p
All-cause (%)				
Low	19	16	1.3 (0.9-1.8)	0.11
Intermediate	21	16	1.7 (1.3-2.2)	<0.001
High	26	25	1.3 (1.0-1.9)	0.01
Prostate cancer (%)				
Low	0.4	0.5	1.0 (0.9-1.1)	0.92
Intermediate	1	2	0.9 (0.3-2.3)	0.80
High	7	8	1.1 (0.6-2.2)	0.41

Age-adjusted Cox proportional hazards multivariable models

Sigel K, abstr 154

ANRS DOXYVAC Study Design



- Two primary efficacy end-points:
  - **Impact of DoxyPEP on time to a first episode of syphilis or chlamydia**
  - **Impact of the 4CMenB vaccine on time to a first episode of *N. gonorrhoeae* infection.**

Molina JMG, abstr 124

PRESS RELEASE

ANRS DOXYVAC: final analysis may modify interim results of this trial assessing the effectiveness of meningococcal B vaccination in preventing gonococcal infections

ANRS | Emerging Infectious Diseases will commission an independent audit

Paris, May 15, 2023

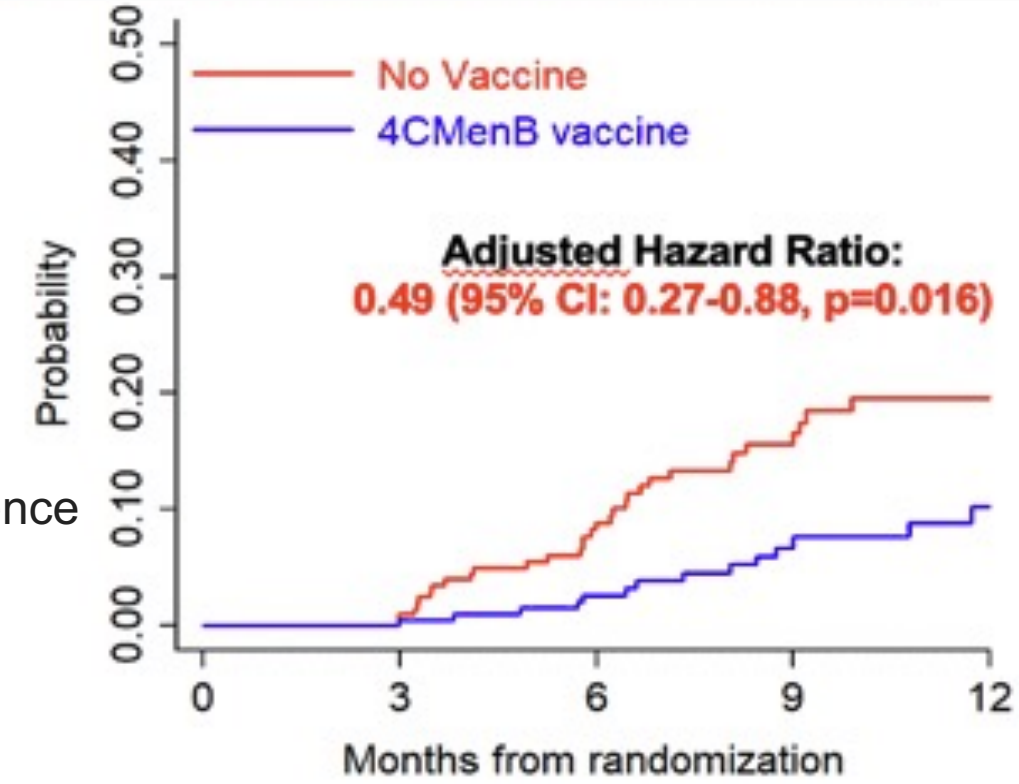
4CMenB Vaccine: Time to 1st GC Infection

No interaction between Doxy PEP and 4CMenB vaccine (p=0.41)

49 subjects infected
32 in No Vaccine arm
(incidence: 19.7/100 PY),
17 in 4CMenB vaccine arm
(incidence: 9.8/100 PY)

GC infections were considered from M3 visit (1 month after 2nd vaccine dose)

GC incidence



Number at risk

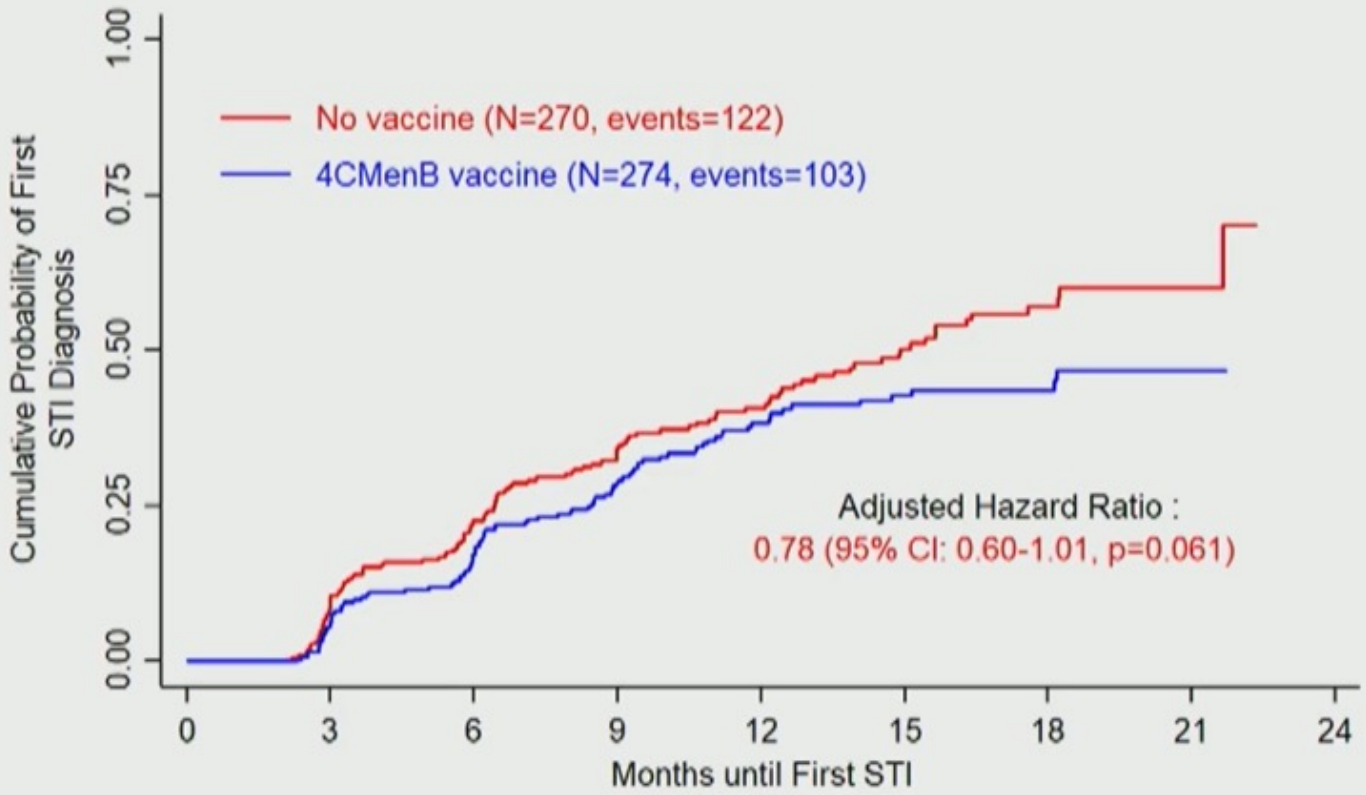
No Vaccine	245	208	150	91	49
4CMenB vaccine	257	208	170	102	49

4CMenB Vaccine
Time to First GC infection

No interaction between Doxy PEP and 4CMenB vaccine (p=0.82)

225 subjects infected
122 in No Vaccine arm
(incidence: 77.1/100 PY),
103 in 4CMenB vaccine arm
(incidence: 58.3/100 PY)

Interim analyis:
49 subjects infected, aHR: 0.49
(95%CI: 0.27 - 0.88)



Number at risk									
No Vaccine	270	234	194	131	94	58	30	4	0
4CMenB vaccine	274	251	212	159	105	68	37	6	0

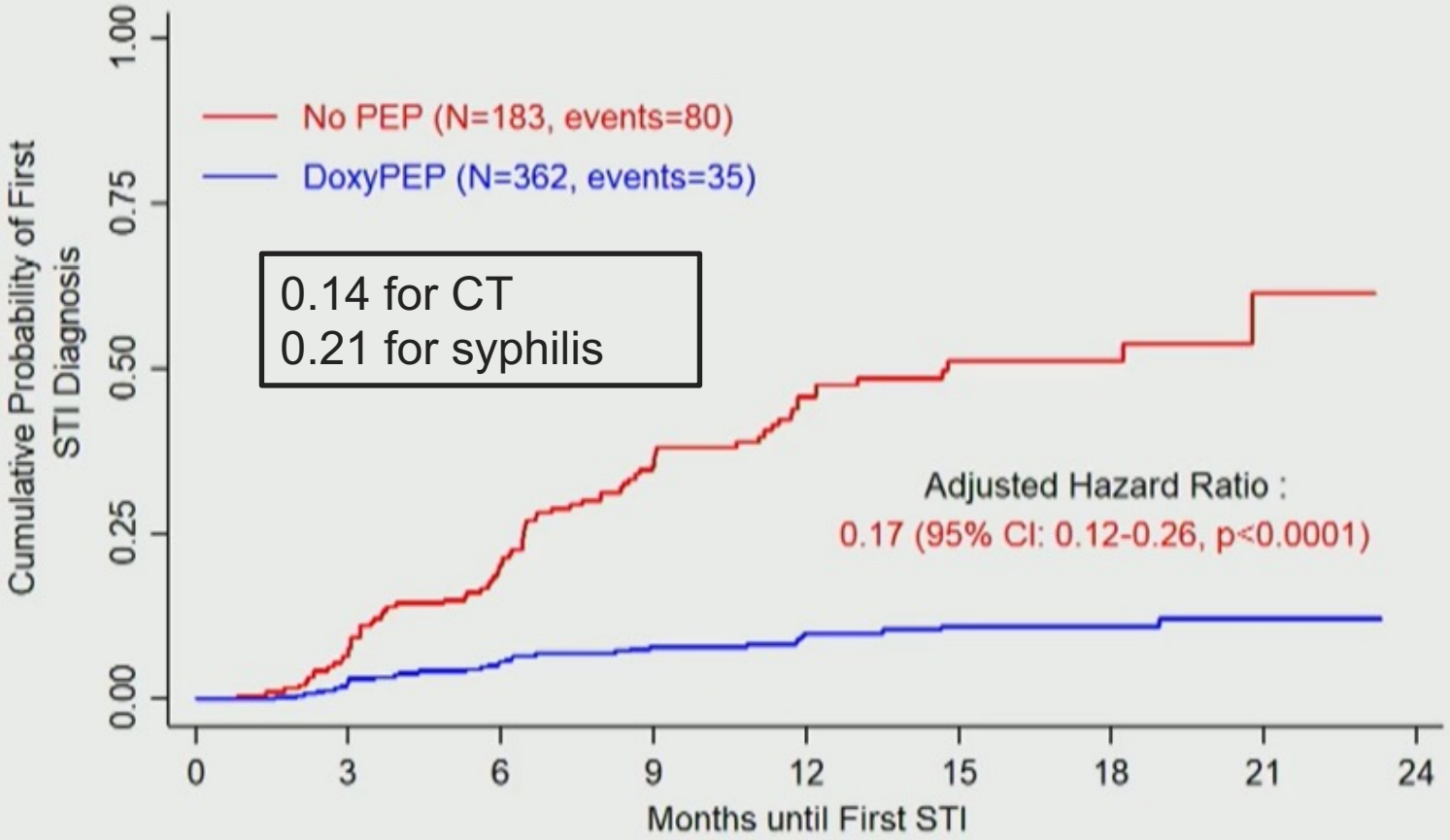
GC infections were considered from M3 visit (1 month after 2nd vaccine dose) and multi-sites infection = 1 single event

Doxycycline PEP
Time to First CT or Syphilis Infection

No interaction between Doxy PEP and 4CMenB vaccine (p=0.83)

Median follow-up:
14 months (IQR: 9-18)

115 subjects infected
80 in No PEP arm
(incidence: 53.2/100 PY),
35 in Doxy PEP arm
(incidence: 8.8/100 PY)



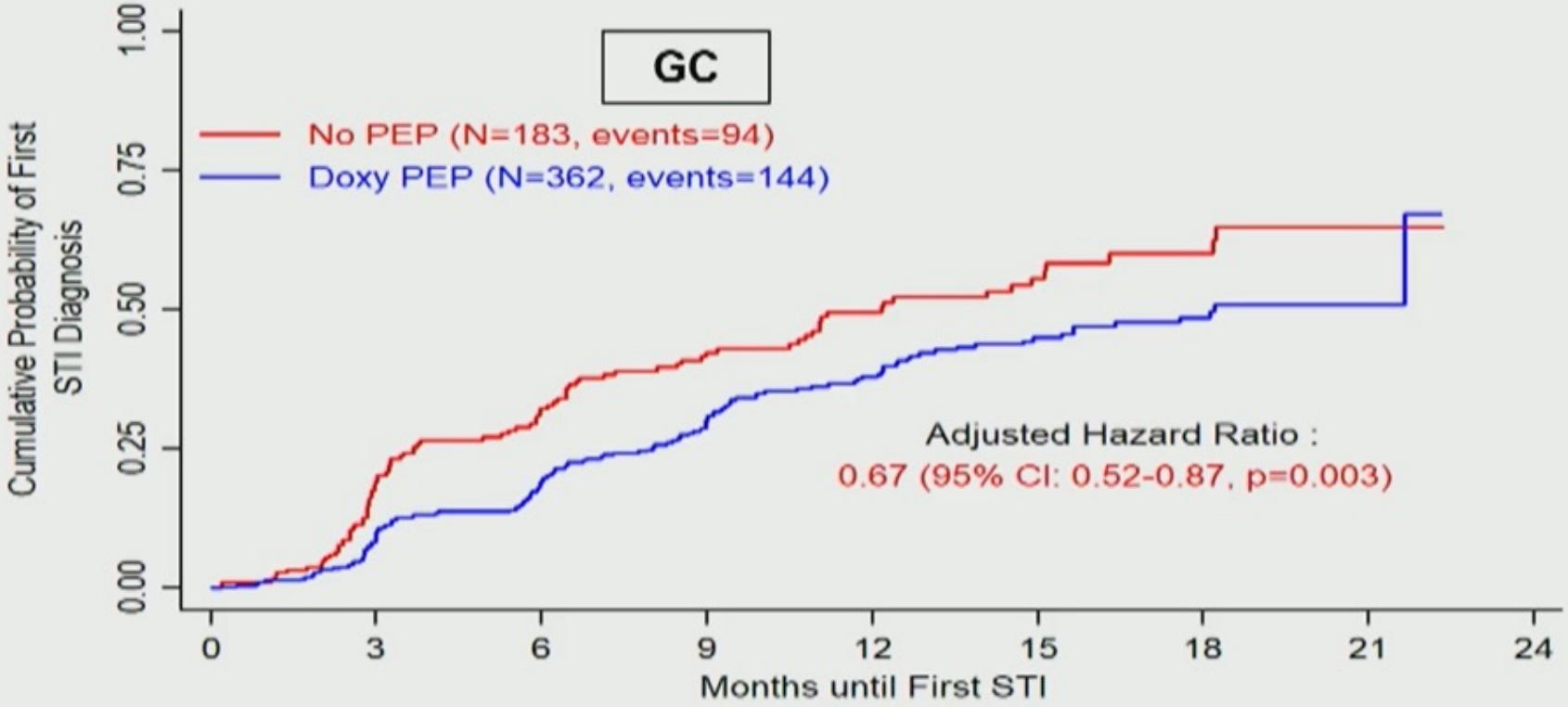
Number at risk

No PEP	183	164	135	92	60	32	20	4	0
DoxyPEP	362	339	316	264	206	146	90	19	0

Interim analyis:
49 subjects infected, aHR: 0.16

For CT multi-sites infection = 1 single event

Doxycycline PEP
Time to First GC



Number at risk

No PEP	183	143	117	82	57	32	18	4	0
DoxyPEP	362	317	270	196	134	88	47	6	0

238 subjects infected
94 in No PEP arm (incidence: **68.4/100** PY)
144 in Doxy PEP arm (incidence: 45.5 /100 PY)

Interim analyis:
84 subjects infected, aHR: 0.49

GC multi-sites infection = 1 single event

DoxyPEP study design and results

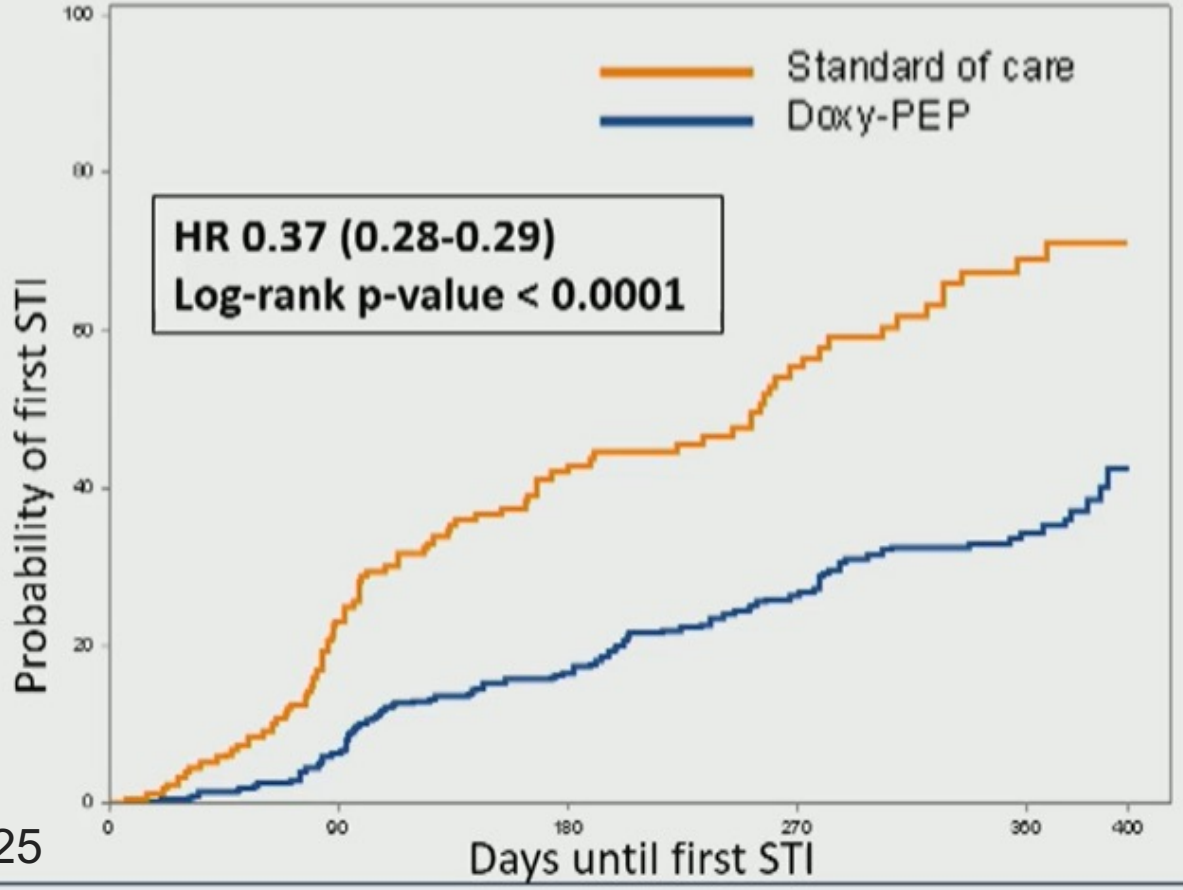
Intervention: Open label doxycycline 200 mg as PEP within 72 hours after condomless sexual contact, max 200mg /daily

MSM & TW living with HIV *or* without HIV on PrEP

2:1 randomization

DoxyPEP Results

- **Overall 65% ↓ reduction in bacterial STIs each quarter**
- **≈ 80% ↓ chlamydia & syphilis**
- **≈ 50% ↓ gonorrhea**
- **Effectiveness independent of HIV serostatus**



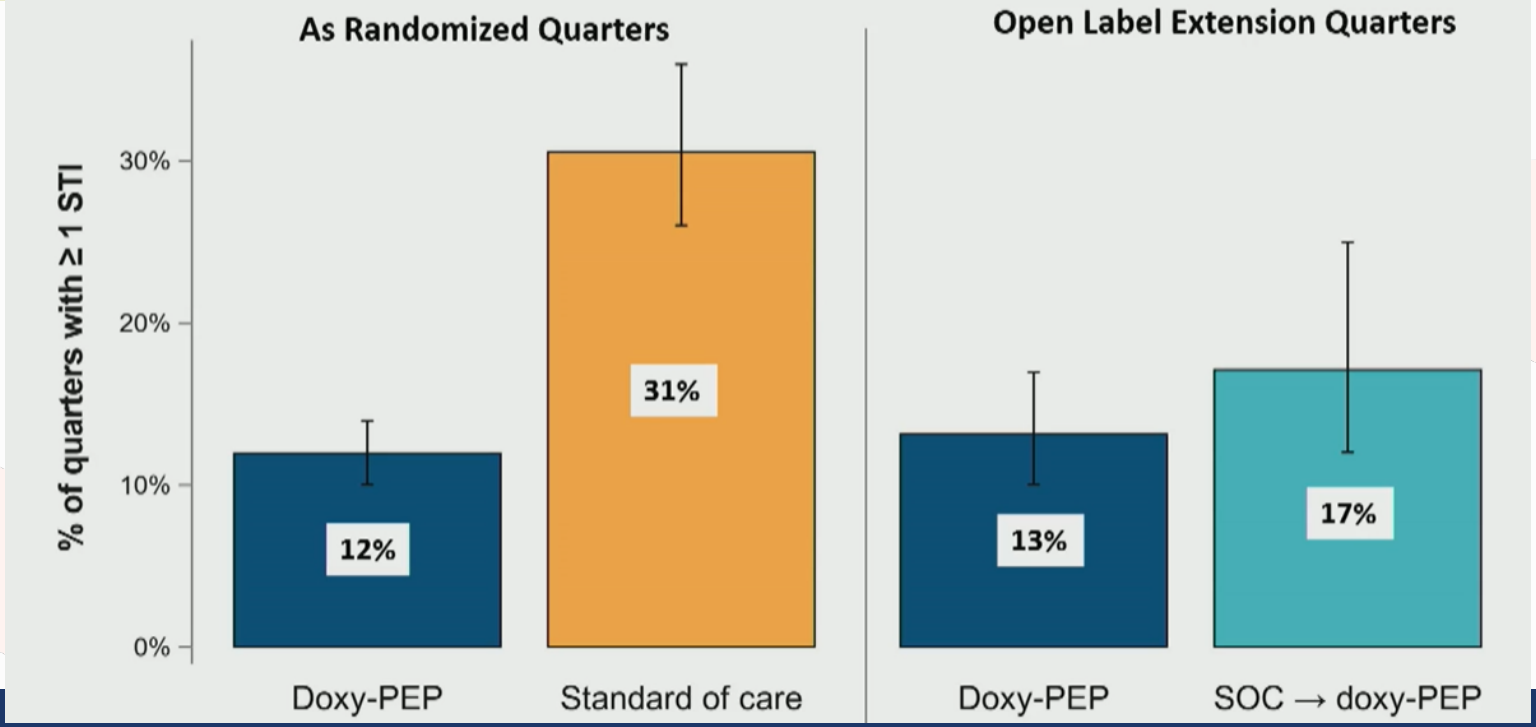
DOXYPEP

Luetkemeyer A, abstr 125

DoxyPEP open label extension

- Objective: Assess doxy-PEP effectiveness, use, and changes in sexual behavior in the setting of participants' awareness of efficacy from the DoxyPEP Study

289 participants contributed to OLE
82/83 SOC participants chose to start doxy-PEP
Median OLE quarters per participant: 2 (IQR 1-3)

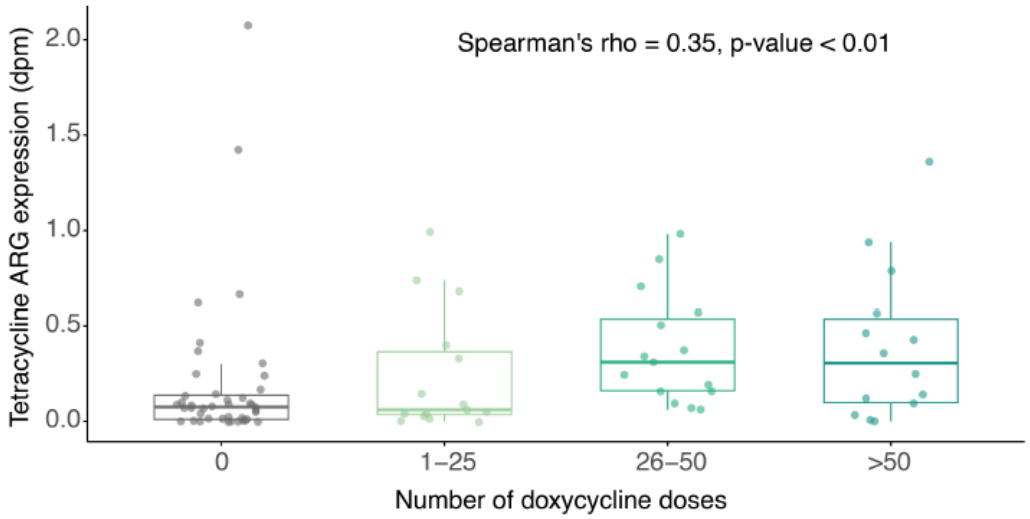


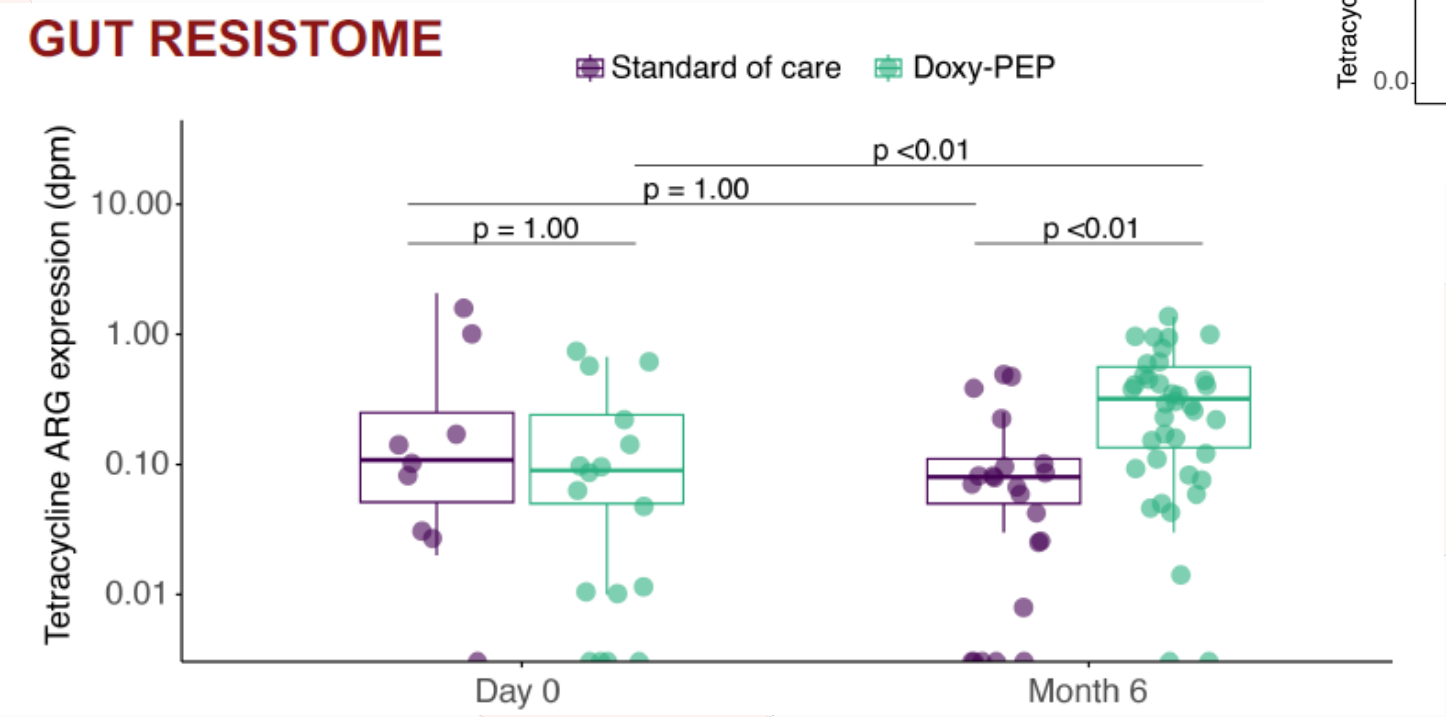
Luetkemeyer A, abstr 125

Impact of Doxycycline as STI Postexposure Prophylaxis on the Gut Microbiome and Antimicrobial Resistance Gene Expression

1154

Doxy-PEP use minimally affected the gut microbiome over 6 months. **Increased expression of tetracycline antimicrobial resistance genes was observed,** *and future research is necessary to determine clinical significance.*





Clinical Implementation of DoxyPEP

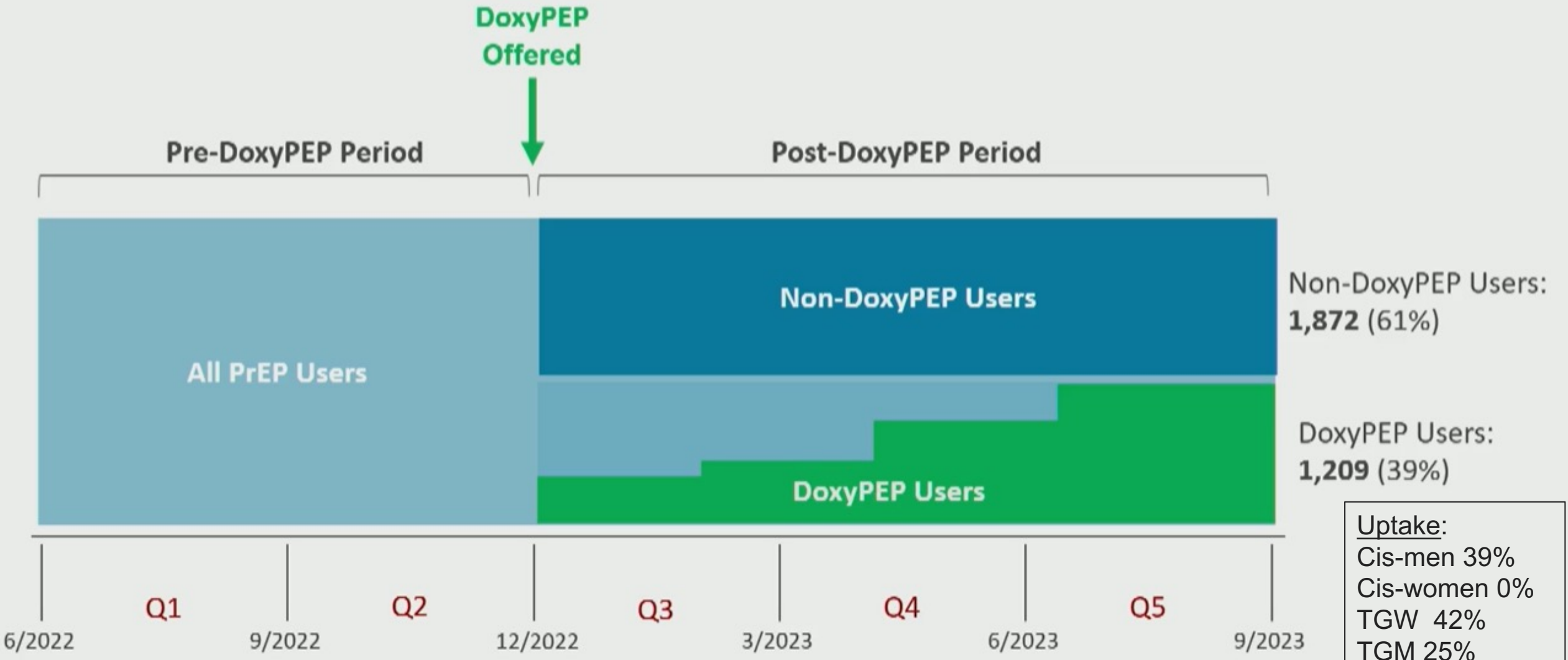
Magnet Clinic @ Strut - San Francisco AIDS Foundation

Large sexual health clinic located in the Castro Neighborhood.

- >8,000 clients seen annually for sexual health services
- ~3,000 active PrEP users

DoxyPEP rollout started in November 2022.

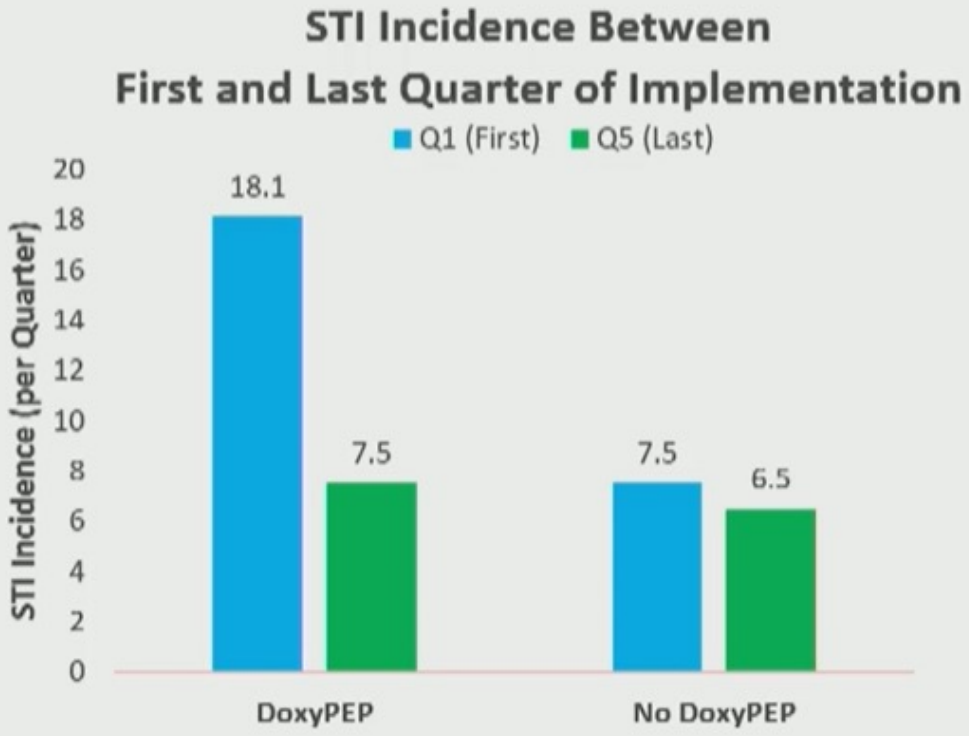
Scott H, abstr 126



Uptake:
Cis-men 39%
Cis-women 0%
TGW 42%
TGM 25%

Scott H, abstr 126

STI Incidence among DoxyPEP Users (Pre-Post Analysis)



	IRR	95% CI	p-value
Any STI	0.42	0.24 - 0.74	0.003
Chlamydia	0.33	0.23 - 0.46	<0.001
Syphilis	0.22	0.09 - 0.54	0.001
Gonorrhea	0.89	0.69 - 1.15	0.383

Scott H, abstr 126

Mpox Potpourri

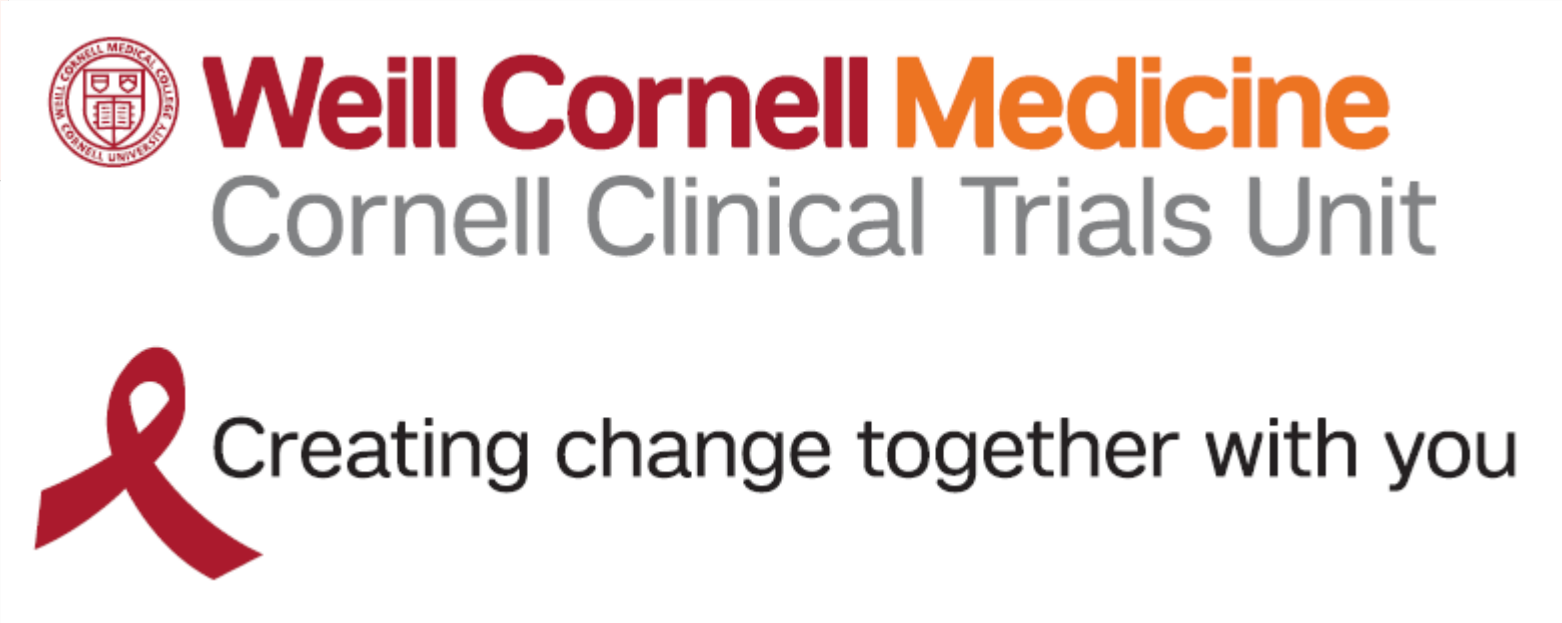
STOMP
Study of Tecovirimat for Mpox

- PWH prescribed tecovirimat within 7 d of sx onset (n = 56) less likely to have mpox progression than propensity score-matched PWH (n = 56) who were not treated early[1]
  - Aldred B, JAMA Intern Med. 2024 Mar 1;184(3):275-279.
    - See: Zucker J, Fischer WA 2nd, Wilkin T. Tecovirimat for Mpox-Promise and Limitations. JAMA Intern Med. 2024 Mar 1;184(3):279-280.
- 2 cases with advanced HIV, severe mpox treated with tecovirimat[2]
  - Both rebounded a few days after 14 d course
    - 1 with adequate levels had no resistance mutations; other with low levels developed multiple mutations (A290V, D294V, I372N, Y252C)
- CNICS: Detectable viremia, lack of ART, CD4 ≤ 350 associated w/ hospitalization[3]
- Tecovirimat exposures were lower in people with mpox than healthy adults, although concentrations remained above the effective Cmin for the drug in non-human primates[4]

[1] Aldred B, abstr 419; [2] Marot S, abstr 422; [3] Montano MA, abstr 423; [4] Wei Z, abstr 428

Acknowledgments

- Kristen Marks, MD, MS for sharing A5379 slides
- All of the investigators and participants who contributed to the studies presented tonight



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