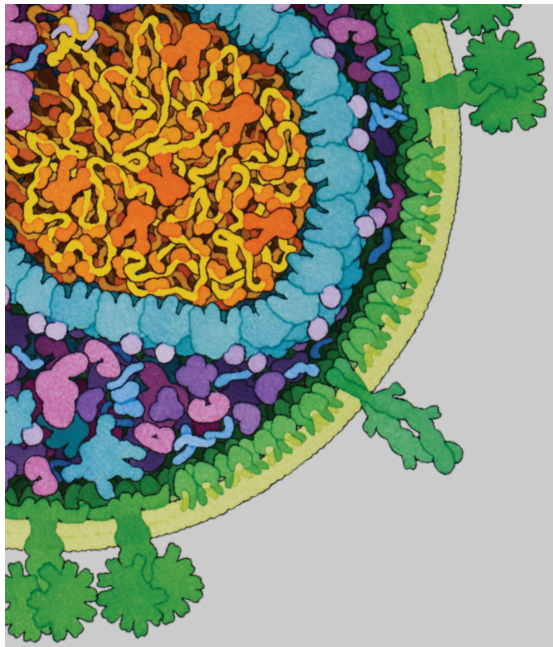
Community feedback: CROI 2019

Simon Collins
HIV i-Base
www.i-Base.info

CROI 2019: selection

- UK case of remission
- ART: Long-acting injections, strategies and pipeline drugs
- Integrase and weight
- PrEP: TAF, bNAbs, vaginal insert, retention

Slides are all from CROI 2019 original talks.



SUSTAINED HIV-1 REMISSION FOLLOWING HOMOZYGOUS CCR5 DELTA32 ALLOGENIC HSCT

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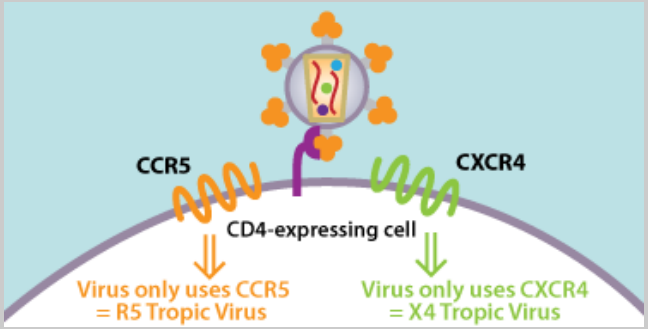
Disclosure: Self: Research grant/grant pending from Wellcome Trust; consulting or advisor fees from ViiV Healthcare, Inc.; speaker's bureau for Gilead Sciences

CROI 2019

HIV-1 and CCR5 as a target for remission



- CCR5 is the most commonly used coreceptor used to enter CD4+ target cells
- △ 32 mutation is a 32 base pair deletion in CCR5, preventing expression.
- 1% of Europeans are △32 homozygous and resistant to R5 HIV-1

Samson, Parmentier et al. Nature 1996; Deng, Landau et al

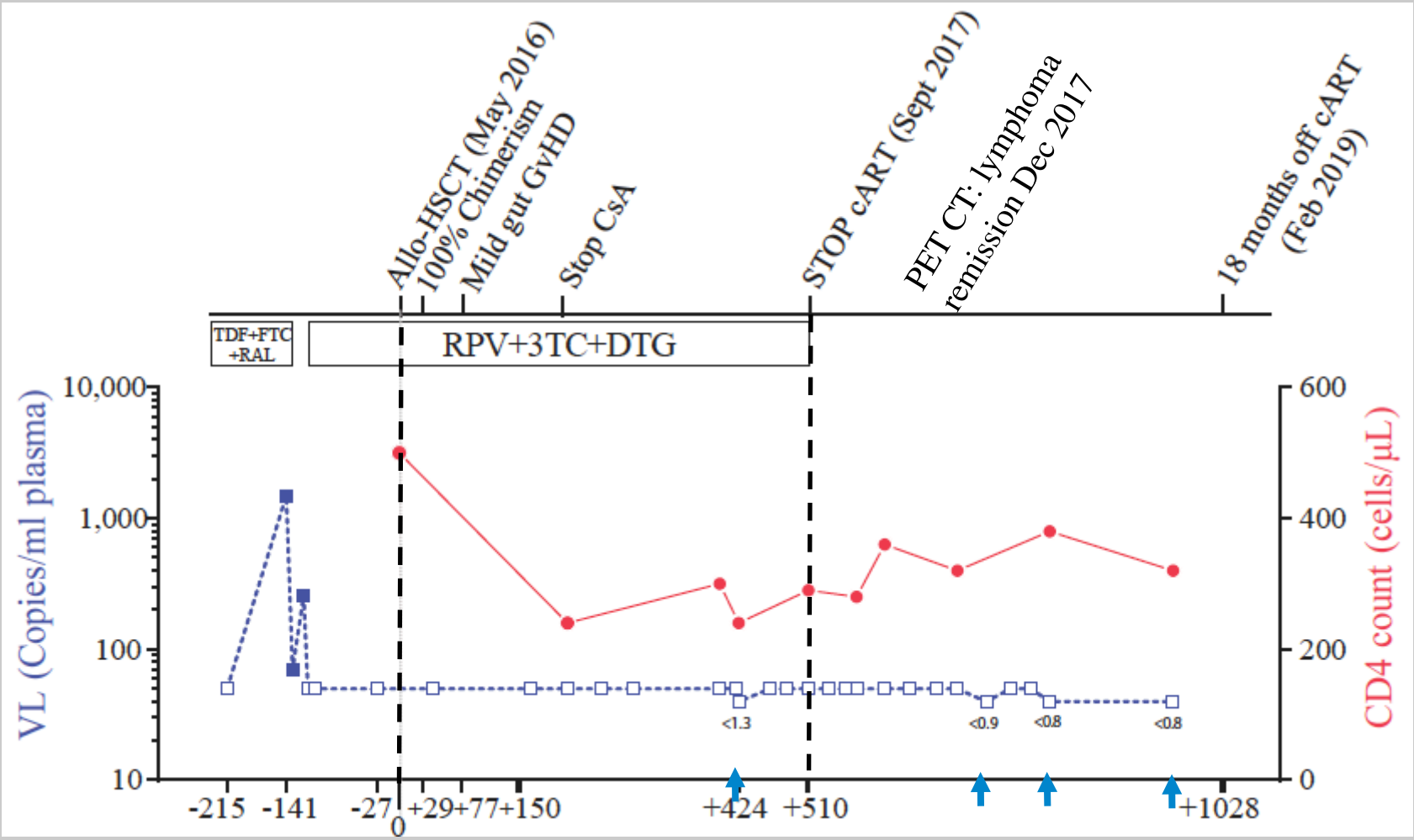
Case History

- **HIV-1 Diagnosis 2003**
- **2013:** Stage IVb Hodgkin lymphoma

  Atripla initiated. Viral suppression achieved

  Switch to TDF/FTC/Raltegravir (ABVD chemo)

- Failed multiple lines of chemotherapy and mobilisation for auto SCT
- Donor registry search for allo HSCT
  - Unrelated 9/10 HLA high-resolution match.
  - Donor homozoygous CCR5-d32 mutation


Allo-HSCT (May 2016)
100% Chimerism
Mild gut GvHD
Stop CsA
STOP cART (Sept 2017)
PET CT: lymphoma remission Dec 2017
18 months off cART (Feb 2019)
TDF+FTC +RAL
RPV+3TC+DTG
VL (Copies/ml plasma)
10,000
1,000
100
10
CD4 count (cells/µL)
600
400
200
0
<1.3
<0.9
<0.8
<0.8
-215
-141
-27
0
+29+77+150
+424
+510
+1028

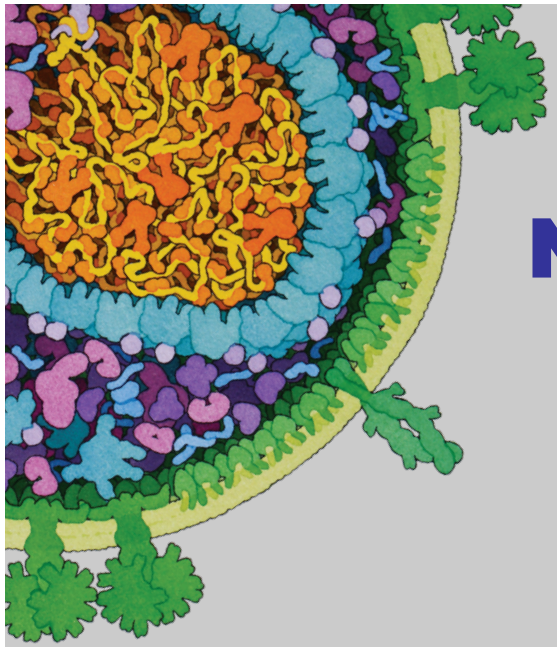
'The London Patient' Timothy Brown

- Homozygous for wild type CCR5
- Infection with R5 using virus
- Hodgkin Lymphoma
- Single HSCT
- No irradiation
- Reduced intensity conditioning
- T cell depletion with aCD52
- Mild GVH
- 100% T cell donor chimerism

- Heterozygous for ▵32
- Infection with R5 using virus
- Acute Myelogenous Leukemia
- Two HSCT
- Total Body Irradiation
- Full intensity conditioning
- T cell depletion with ATG
- Mild GVH
- 100% T cell donor chimerism

CROI 2019: ART and drugs

- Persistent low level viral load
- Cabotegravir/rilpivirine LA injections
- ART: Long-acting injections, strategies and pipeline drugs
- Maturation inhibitor, capsid inhibitor, PGT-121 bNAb
- ART and weight gain



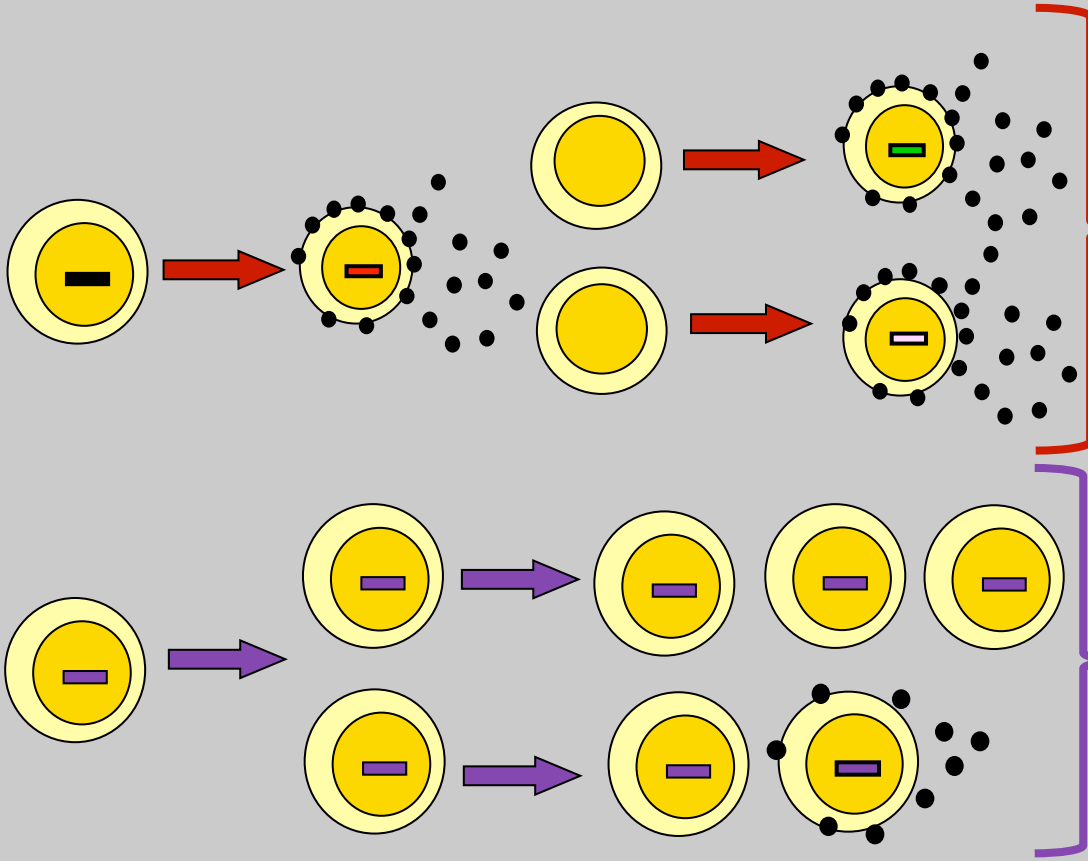
NONSUPPRESSIBLE VIREMIA ON ART FROM LARGE CELL CLONES CARRYING INTACT PROVIRUSES

Elias K. Halvas
University of Pittsburgh
Pittsburgh, PA, USA

Disclosure: Nothing to Disclose

CROI 2019

Viral Replication vs. Cellular Proliferation



Non-Suppressible Viremia

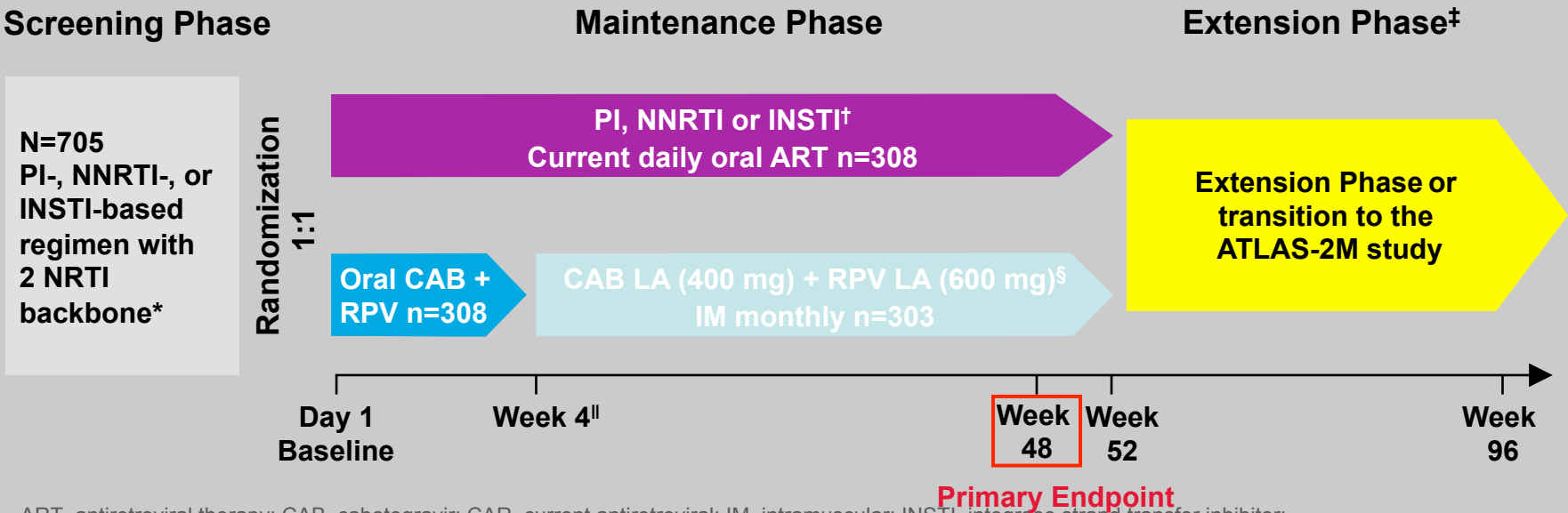
- **Can be caused by clonal proliferation of $CD4^+$ T-cells carrying replication-competent proviruses: "Repliclones"**
  - Some cells within the clones are producing virions
  - Clones are large (10^7-10^8 cells) but overall are rare integrants (0.03 -1%)
  - Intact proviruses are intragenic, within introns and in either orientation to gene
- **Clinical Implications**
  - Clinically-detectable viremia may not be due to non-adherence or drug resistance
- **Cure Implications**
  - Smaller clones may be producing infectious virus throughout lymphoid organs
  - May fuel rapid viremia rebound off ART
  - Need to eliminate or suppress repliclones!
  - Have the potential to regrow.
- **Unanswered Questions**
  - Mechanisms of clonal escape?
  - Latency? CTL or antibody resistance?

LONG-ACTING CABOTEGRAVIR + RILPIVIRINE FOR MAINTENANCE THERAPY: ATLAS WEEK 48 RESULTS

S Swindells,[1] JF Andrade-Villanueva,[2] GJ Richmond,[3] G Rizzardini,[4] A Baumgarten,[5] M Masiá,[6] G Latiff,[7] V Pokrovsky,[8] JM Mrus,[9] J Huang,[10] KJ Hudson,[9] DA Margolis,[9] KY Smith,[9] P Williams,[11] WR Spreen[9]

[1]University of Nebraska Medical Center, Omaha, NE, United States; [2]University of Guadalajara, Guadalajara, Mexico; [3]Broward Health Medical Center, Fort Lauderdale, FL, United States; [4]Fatebenefratelli Sacco Hospital, Milan, Italy; [5]Center for Infectious Diseases, ZIBP, Berlin, Germany; [6]Hospital General Universitario de Elche, Alicante, Spain; [7]Maxwell Centre, Durban, South Africa; [8]Central Research Institute of Epidemiology, Moscow, Russian Federation; [9]ViiV Healthcare, Research Triangle Park, NC, United States; [10]GlaxoSmithKline, Mississauga, ON, Canada; [11]Janssen Research and Development, Beerse, Belgium

ATLAS Study Design: Randomized, Multicenter, International, Open-Label, Noninferiority Study in Adults with Virologic Suppression (Ongoing)

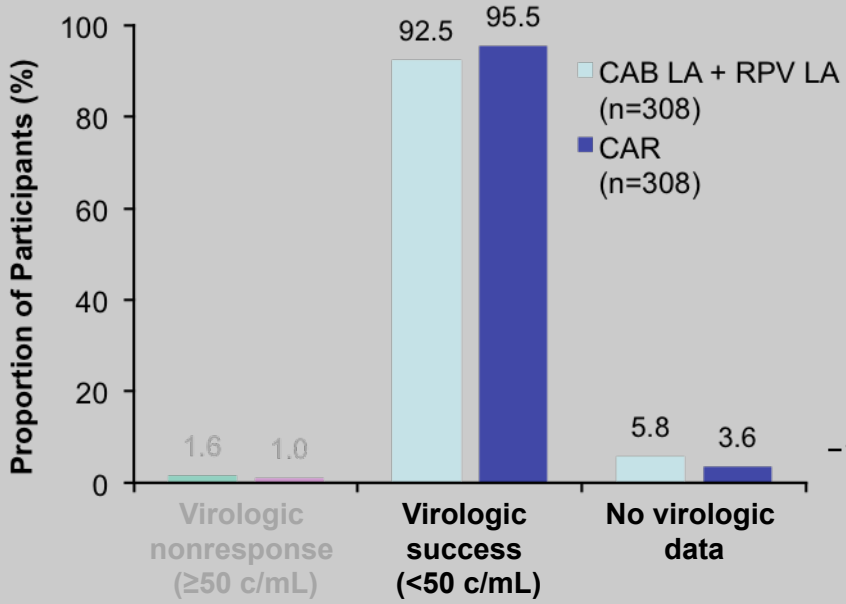


ART, antiretroviral therapy; CAB, cabotegravir; CAR, current antiretroviral; IM, intramuscular; INSTI, integrase strand transfer inhibitor; LA, long-acting; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside RTI; PI, protease inhibitor; RPV, rilpivirine; VL, viral load.

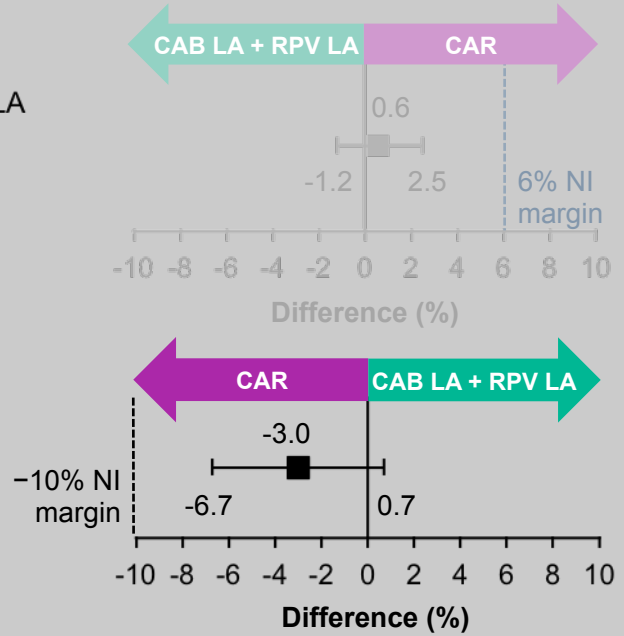
*Uninterrupted ART 6 months and VL <50 c/mL at Screening, 2× VL <50 c/mL ≤12 months; †INSTI-based regimen capped at 40% of enrollment; Triumeq excluded from study; ‡Optional switch to CAB LA + RPV LA at Week 52 for those on CAR; §Participants who withdraw/complete IM CAB LA + RPV LA must complete
52 weeks of follow-up; ‖Participants received an initial loading dose of CAB LA (600 mg) and RPV LA (900 mg) at Week 4b. From Week 8 onwards, participants received CAB LA (400 mg) + RPV LA (600 mg) injections every 4 weeks.

ATLAS Virologic Snapshot Outcomes at Week 48 for ITT-E: Noninferiority Achieved for Primary and Secondary Endpoints

Virologic Outcomes



Adjusted Treatment Difference (95% CI)*



Primary endpoint:

LA noninferior to CAR (HIV-1 RNA ≥50 c/mL) at Week 48

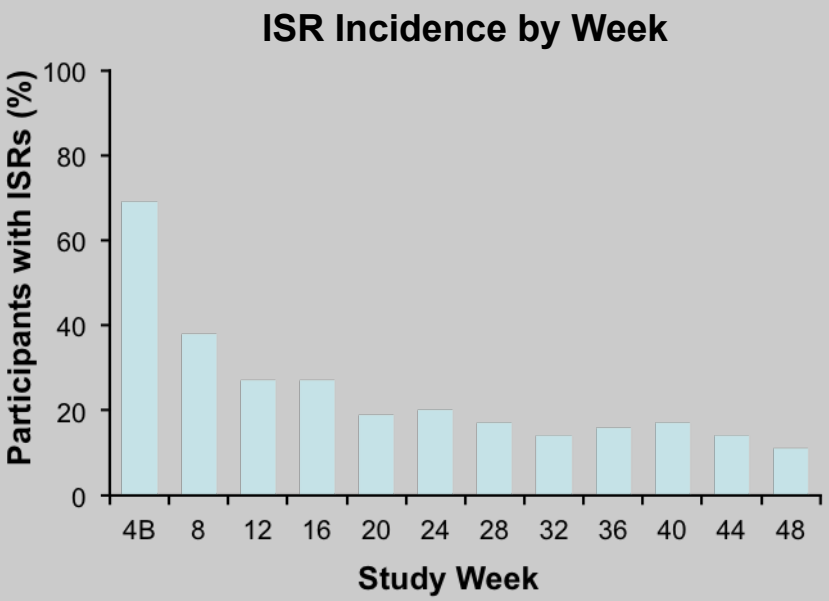
Key secondary endpoint:

LA noninferior to CAR (HIV-1 RNA <50 c/mL) at Week 48

CAB, cabotegravir; CAR, current antiretroviral; CI, confidence interval; ITT-E, intention-to-treat exposed; LA, long-acting; NI, noninferiority; RPV, rilpivirine.
*Adjusted for sex and baseline third agent class.

Swindells S, et al. CROI 2019; Seattle, WA. Abstract 1475.

ATLAS Injection Site Reactions



Event	CAB LA + RPV LA N=308
Participants receiving injections	303
Injections given, n	6978
ISR events, n (%)	1460 (20.9)
Pain	1208 (82.7)
Nodule	54 (3.7)
Induration	54 (3.7)
Swelling	48 (3.3)
Grade 3 ISR pain, no. of events (%)	20 (1.7)
Median duration of ISRs, days	3
Participants with ISR leading to withdrawal, n (%)	4 (1.3)

- The majority (99%,1439/1460) of ISRs were grade 1–2 and most (88%) resolved within ≤7 days

CAB, cabotegravir; IM, intramuscular; ISR, injection site reaction; LA, long-acting; RPV, rilpivirine.
Bars represent incidence of onset ISRs relative to the most recent IM injection visit.

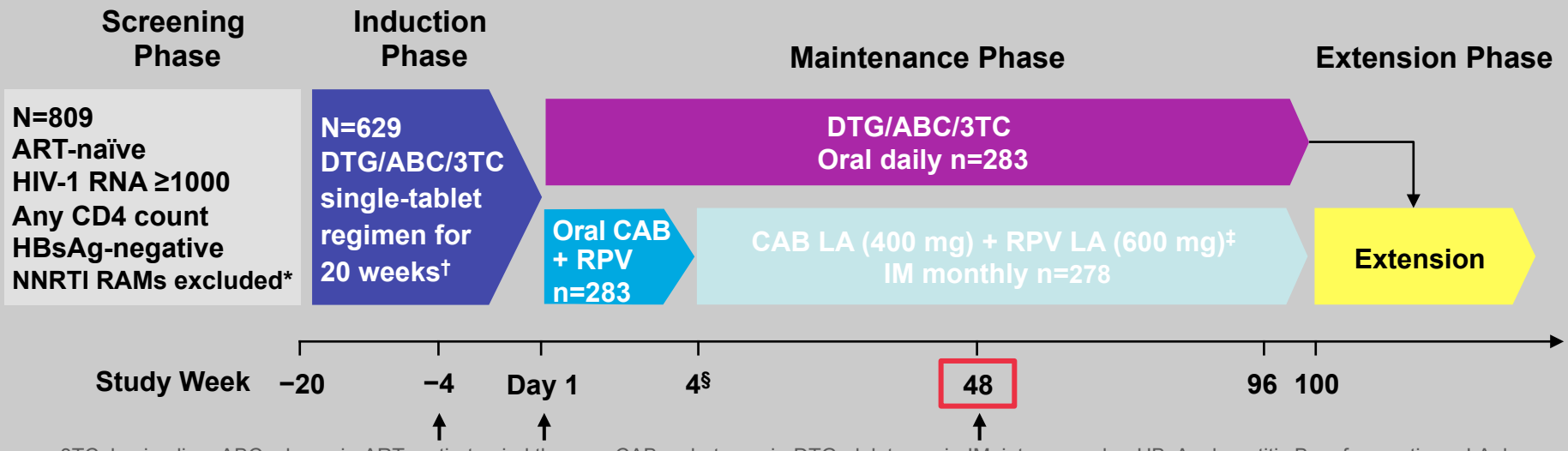
Swindells S, et al. CROI 2019; Seattle, WA. Abstract 1475.

LONG-ACTING CABOTEGRAVIR + RILPIVIRINE FOR HIV MAINTENANCE: FLAIR WEEK 48 RESULTS

Chloe Orkin,[1] Keikawus Arasteh,[2] Miguel Górgolas Hernández-Mora,[3] Vadim Pokrovsky,[4] Edgar T. Overton,[5] Pierre-Marie Girard,[6] Shinichi Oka,[7] Ronald D'Amico,[8] David Dorey,[9] Sandy Griffith,[8] David A Margolis,[8] Peter Williams,[10] Wim Parys,[10] William R Spreen[8]

[1]Queen Mary University, London, United Kingdom; [2]EPIMED GmbH, Berlin, Germany; [3] Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain; [4]Central Institute of Epidemiology, Moscow, Russian Federation; [5]University of Alabama at Birmingham, Birmingham, AL, United States; [6]Hôpital Saint Antoine, Paris, France; [7]National Center for Global Health and Medicine, Tokyo, Japan; [8]ViiV Healthcare, Research Triangle Park, NC, United States; [9]GlaxoSmithKline, Mississauga, Ontario, Canada; [10]Janssen Research and Development, Beerse, Belgium

FLAIR Study Design: Randomized, Multicenter, International, Open-Label, Noninferiority Study in ART-Naïve Adults (Ongoing)



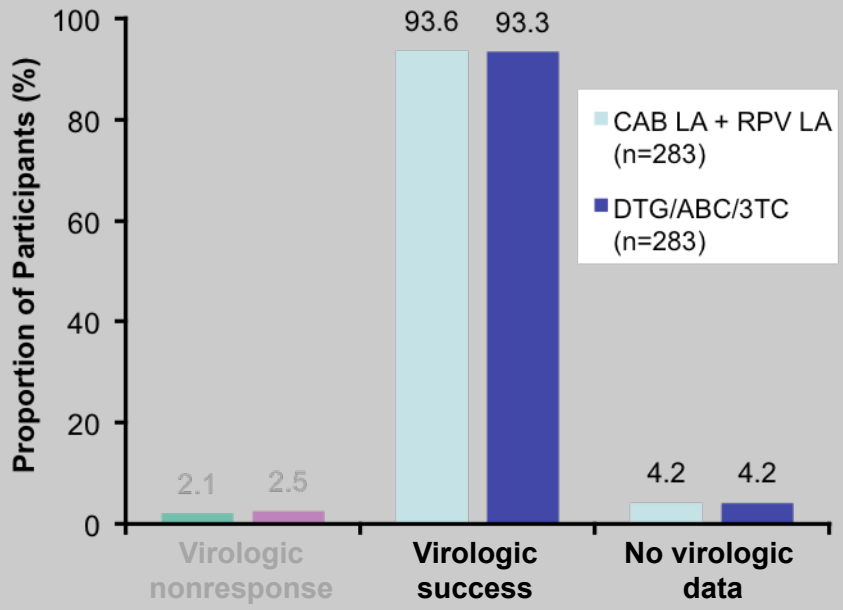
3TC, lamivudine; ABC, abacavir; ART, antiretroviral therapy; CAB, cabotegravir; DTG, dolutegravir; IM, intramuscular; HBsAg, hepatitis B surface antigen; LA, long-acting;
NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; RAM, resistance-associated mutation; RPV, rilpivirine.

*NNRTI RAMS but not K103N were exclusionary; †DTG plus 2 alternative non-ABC NRTIs was permitted if participant was intolerant or HLA-B*5701-positive (n=30 as last regimen during induction: n=2 discontinued during induction, n=14 randomized to CAB LA + RPV LA, n=14 randomized to DTG/ABC/3TC arm and continued on DTG plus 2 alternative non-ABC NRTIs
in Maintenance Phase); ‡Participants who withdraw/complete CAB LA + RPV LA enter 52-week long-term follow-up; §Participants received initial loading doses of CAB LA 600 mg and
RPV LA 900 mg at Week 4. Beginning Week 8, participants received CAB LA 400 mg + RPV LA 600 mg injections every 4 weeks.

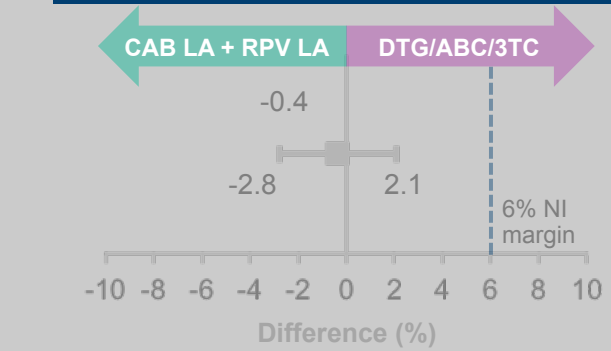
Orkin C, et al. CROI 2019; Seattle, WA. Abstract 3947.

FLAIR Virologic Snapshot Outcomes at Week 48 for ITT-E:
Noninferiority Achieved for Primary and Secondary Endpoints

Virologic Outcomes

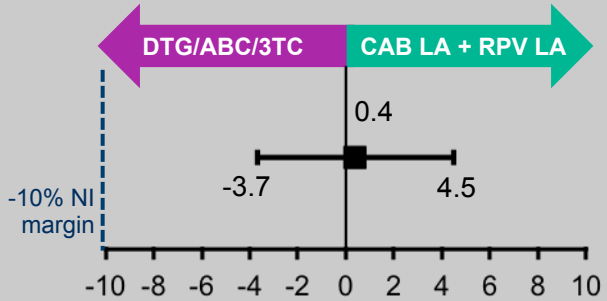


Adjusted Treatment Difference (95% CI)*



Primary endpoint:

LA noninferior to DTG/ABC/3TC (≥50 c/mL) at Week 48



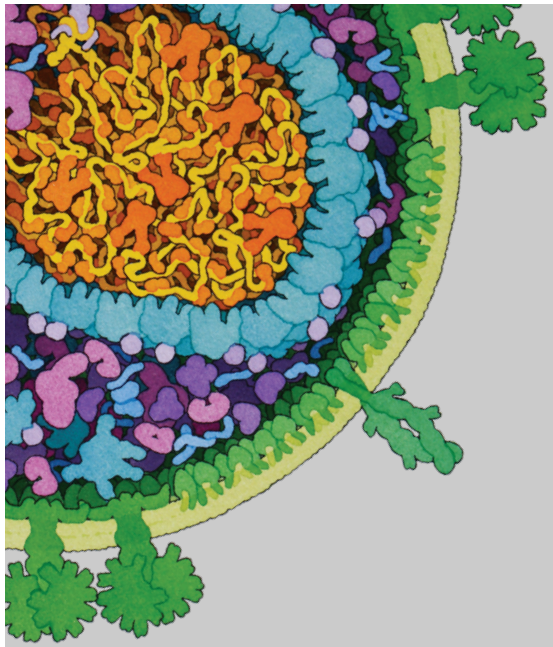
Key secondary endpoint:

LA noninferior to DTG/ABC/3TC (<50 c/mL) at Week 48

3TC, lamivudine; ABC, abacavir; CAB, cabotegravir; CI, confidence interval; DTG, dolutegravir; ITT-E, intent-to-treat-exposed; LA, long-acting; NI, noninferiority; RPV, rilpivirine.

*Adjusted for sex and baseline HIV-1 RNA (< vs ≥100,000 c/mL).

Orkin C, et al. CROI 2019; Seattle, WA. Abstract 3947.



A PHASE IIA STUDY OF NOVEL MATURATION INHIBITOR GSK2838232 IN HIV PATIENTS

Edwin DeJesus

Orlando Immunology Center
Orlando, FL, USA

Disclosure: Self: Consulting or advisor fees from Gilead Sciences, Janssen Therapeutics, Theratechnologies Inc.; speaker's bureau for Gilead Sciences, Theratechnologies Inc.

CROI 2019

Background and Objectives

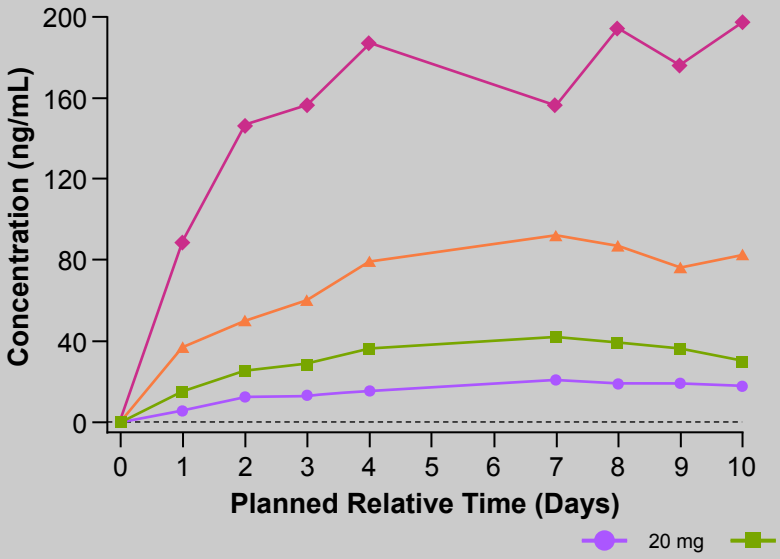
- In vitro, GSK2838232 has been found to have:[1]
  - A mean 50% maximal inhibitory concentration (IC_{50}) value of 1.6 nM (range: 0.8 to 4.3 nM)
  - Minimal impact of protein binding
  - A broad spectrum and potent virologic profile
  - Inhibited HIV-1 strains containing the polymorphism in the consensus Sp1 QVT region
- Clinical studies in healthy volunteers have found GSK2838232 co-administered with ritonavir:[2]
  - Has a mean half-life of 34 hours
  - Achieved steady-state by Day 4 to 7 for the once-daily dose
  - Has a well-defined PK, safety, and tolerability profile
- This **proof-of-concept Phase IIa study** assessed the safety and tolerability, antiviral activity and PK of GSK2838232 co-administered once daily orally with cobicistat in HIV-1-infected adults

HIV, human immunodeficiency virus; PK, pharmacokinetics.

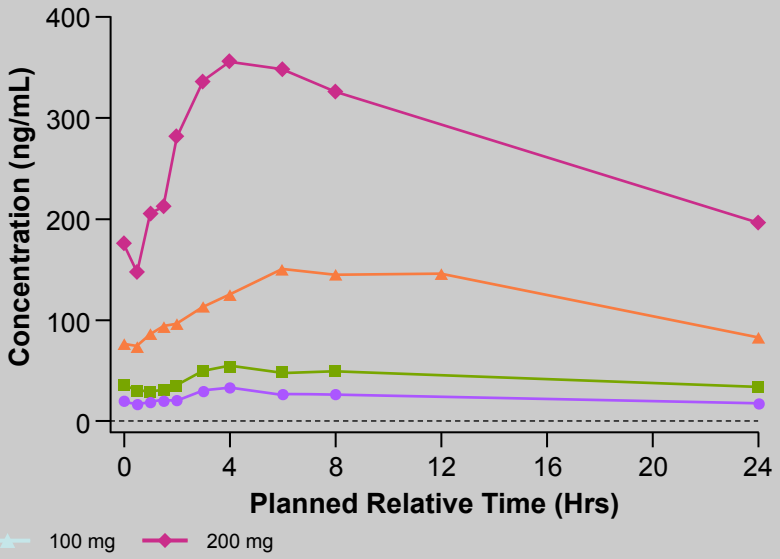
[1]Jeffrey J, et al. Conference on Retroviruses and Opportunistic Infections. February 23–26, 2015, Seattle, Washington, Abstract #538;
[2]Johnson M, et al. J Infect Dis. Epub ahead of print. 2018. PMID: 30407

Pharmacokinetics of GSK'232 With Cobicistat

Median Predose (Trough) Plasma Concentrations of GSK'232



Median Plasma Concentration of GSK'232 Over Time (Day 10)



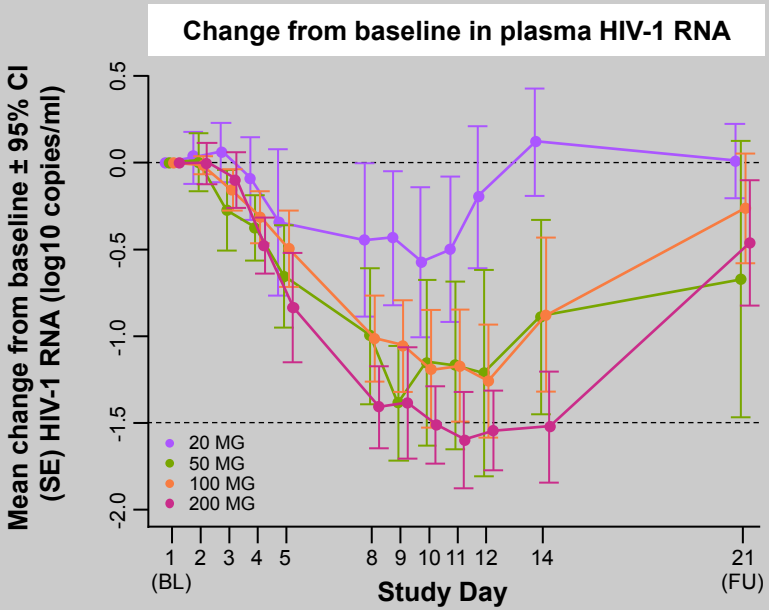
20 mg 50 mg 100 mg 200 mg

Steady state was reached by Day 8

$AUC_{(0-\tau)}$, area under the curve over the dosing interval; C_{max}, maximum observed

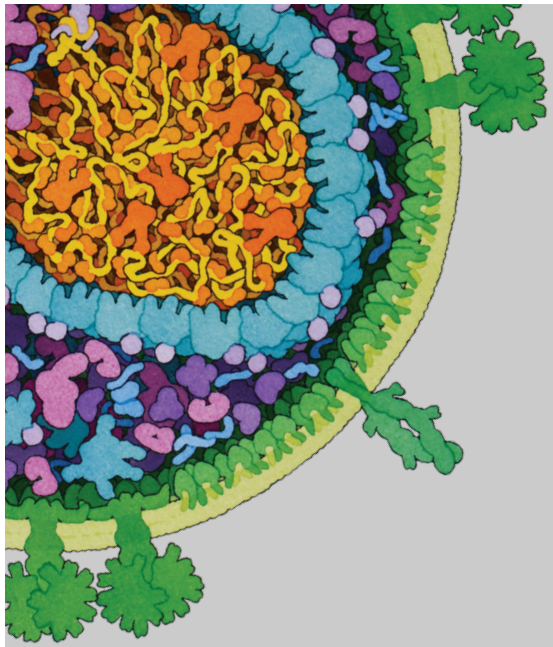
Antiviral Activity of GSK'232

Robust reductions in 50 mg, 100 mg, and 200 mg cohorts; maximal effect in 200 mg cohort



	20 mg (n=7)	50 mg (n=8)	100 mg (n=10)	200 mg (n=8)
Plasma HIV RNA (copies/mL)				
Max. decline from baseline, mean (SD)	**-42,095** (37,576)	**-49,066** (71,340)	**-32,948** (54,291)	**-33,149** (31,786)
Max. decline from baseline (log_{10}-transformed), mean (SD)	**-0.67** (0.41)	**-1.56** (0.67)	**-1.32** (0.44)	**-1.70** (0.38)
>1.5 log_{10} copies/mL decrease from baseline, n (%)	**0**	**2** (25)	**2** (20)	**5** (63)
<400 copies/mL, n (%)	**0**	**2** (25)	**2** (20)	**4** (50)
CD4 count				
Change from baseline, mean (SD)	**-1.4** (95.3)	**52.0** (145.4)	**40.7** (94.5)	**11.1** (75.2)

BL, baseline; CI, confidence interval; FU, follow-up; HIV, human immunodeficiency virus; SD, standard deviation; SE, standard error



SAFETY AND PK OF SUBCUTANEOUS GS-6207, A NOVEL HIV-1 CAPSID INHIBITOR

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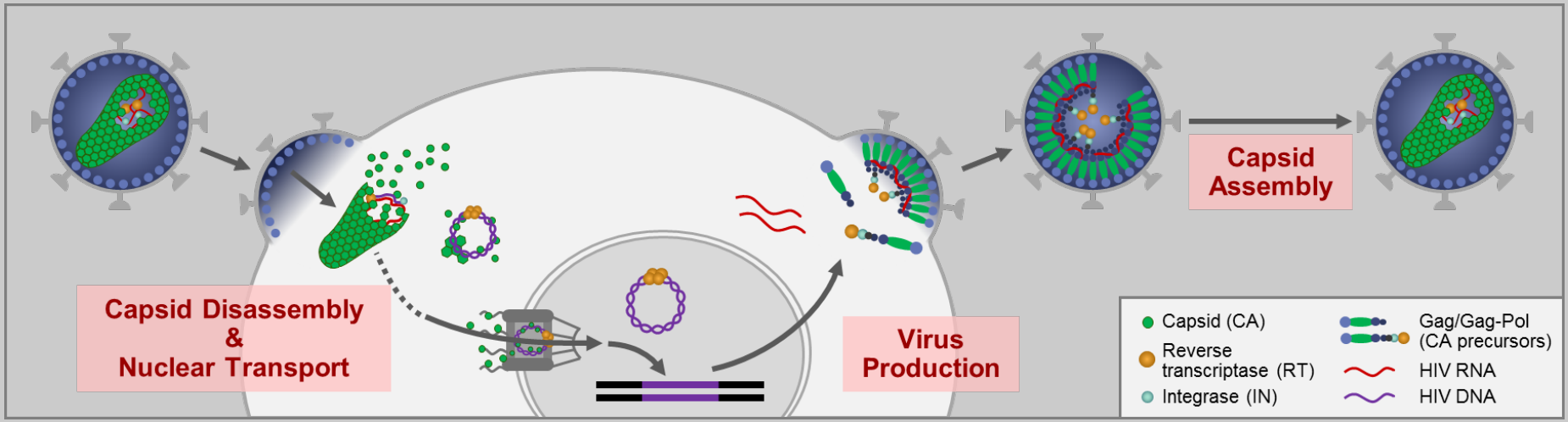
Disclosure: Self: Employment at and stock/stock options in Gilead Sciences

CROI 2019

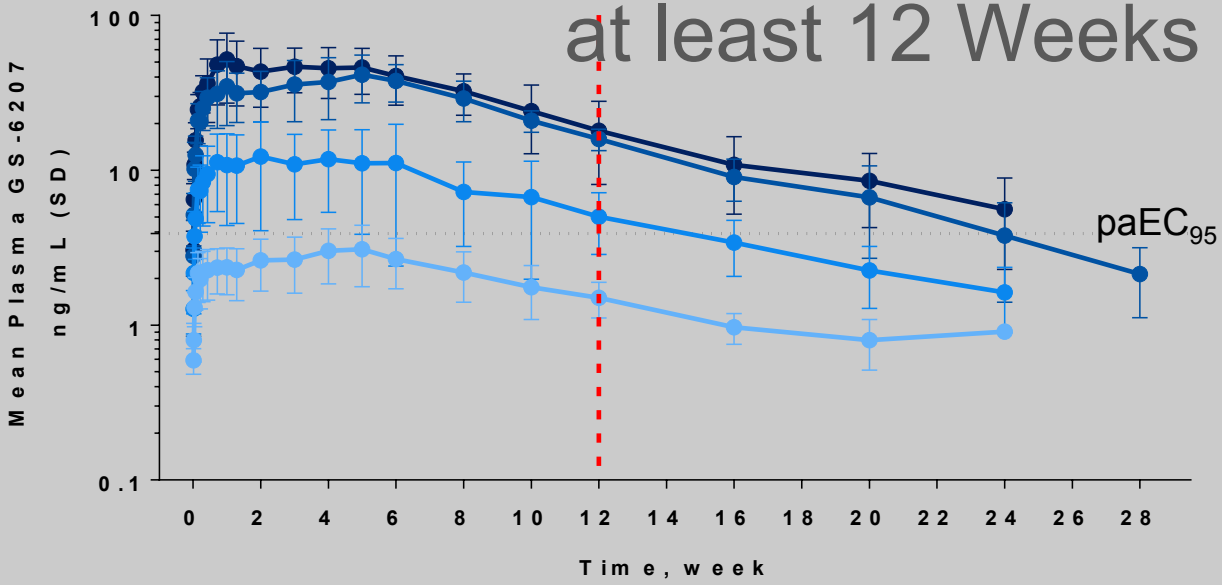
GS-6207: First-in-Class HIV Capsid Inhibitor



- HIV capsid is essential at multiple stages in the viral life cycle

Results

Sustained Delivery Supports Dosing Interval of at least 12 Weeks

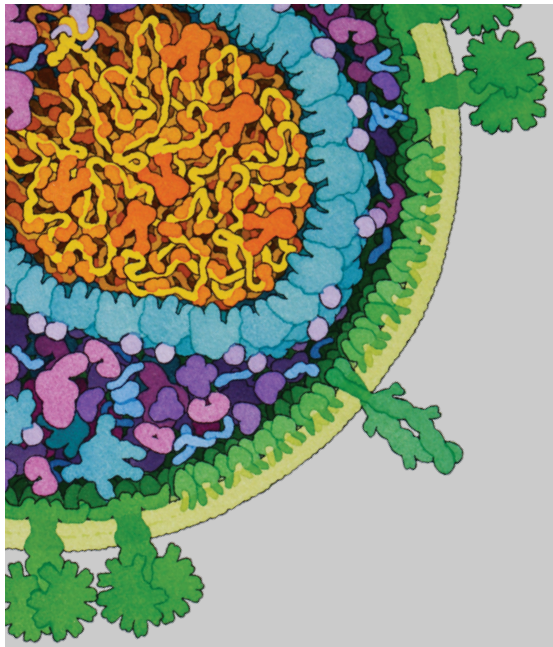


Dose	IQ at week 12
450 mg	4.7
300 mg	4.1
100 mg	1.3
30 mg	0.4

IQ = C_{w12}/ $paEC_{95}$

- At doses ≥100 mg, GS-6207 plasma concentrations at 12 weeks were above the $paEC_{95}$ of 3.87 ng/mL

*EC_{95} determined in MT-4 T-Cell Line with WT HIV-1 (IIIB strain). C_{w12}, GS-6207 plasma concentration on Day 84; IQ, inhibitory quotient; $paEC_{95}$, protein adjusted EC_{95}



THERAPEUTIC ACTIVITY OF PGT121 MONOCLONAL ANTIBODY IN HIV-INFECTED ADULTS

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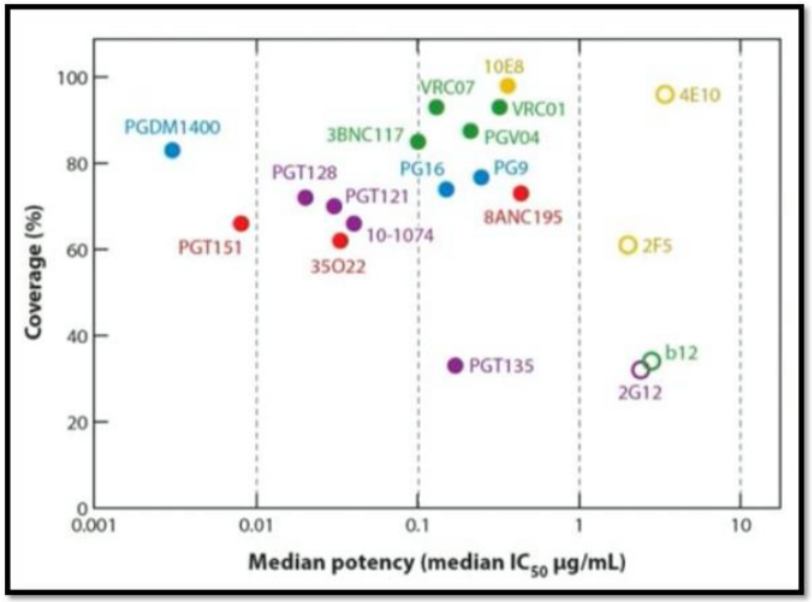
Disclosure: Nothing to Disclose

CROI 2019

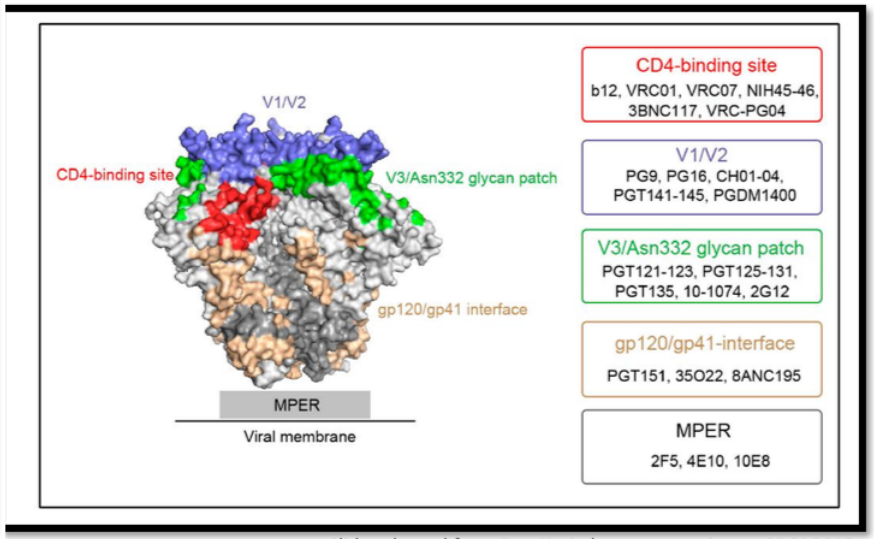
Broad neutralization by monoclonal antibodies

- bNAbs show a continuum of potency and breadth



Slide adapted from Malcolm Martin presentation at CROI 2018

- Different bNAbs target different parts of HIV-1 envelope protein (gp120)



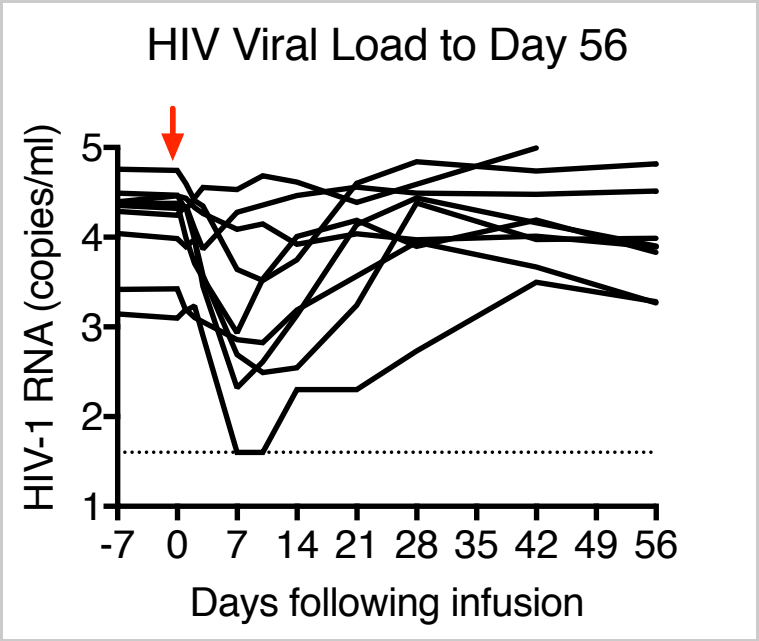
Slide adapted from Dan Kuritzkes presentation at CROI 2018

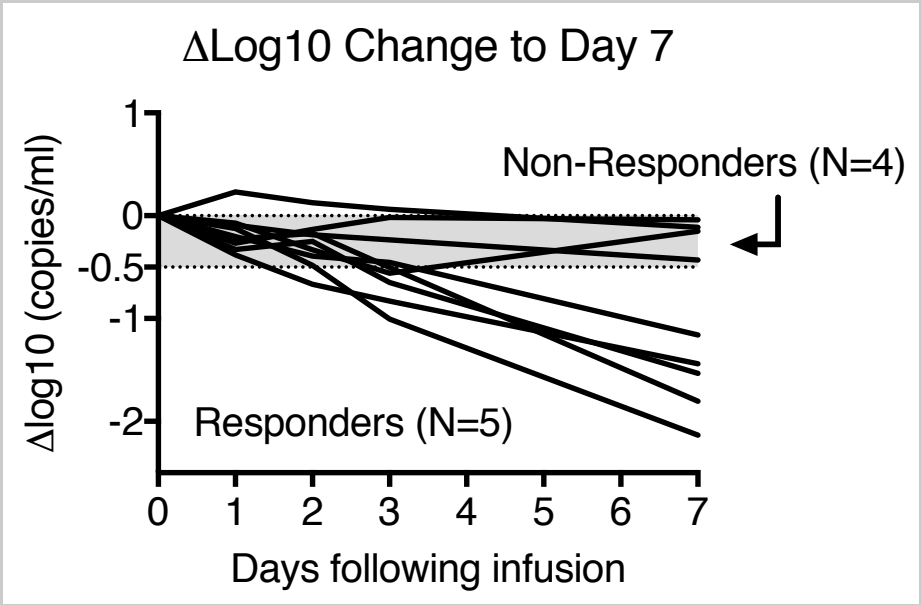
PGT121 Monoclonal Antibody

- Human IgG1 mAb targeting V3 Env epitope (IAVI, Theraclone, Scripps)
- Potent neutralizer of 60-70% of global HIV-1 viruses
- Therapeutic and preventive efficacy in rhesus monkeys:
  - Decreased viral load (VL) in SHIV-infected monkeys
  - Delayed rebound following ATI when combined with TLR7 agonist
  - Protected against SHIV challenge at <5 ug/ml concentration
- Here we present the first-in-human phase 1 clinical trial of PGT121

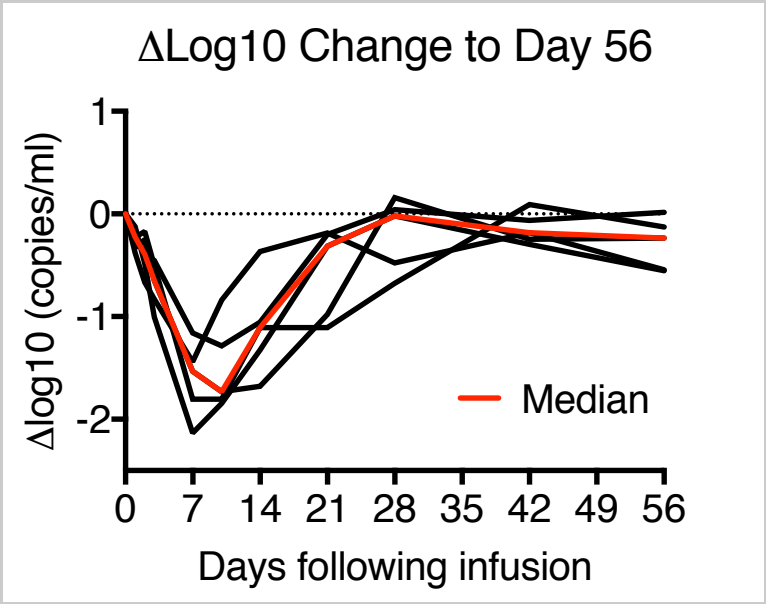
Walker et al. Nature 2011:466; Julg et al. Sci Transl Med. 2017 Sep 20;9(408); Barouch et al. Nature. 2013:224-8; Borducchi et al. Nature. 2018:360-364; Moldt et al. Proc Natl Acad Sci. 2012:18921-5.

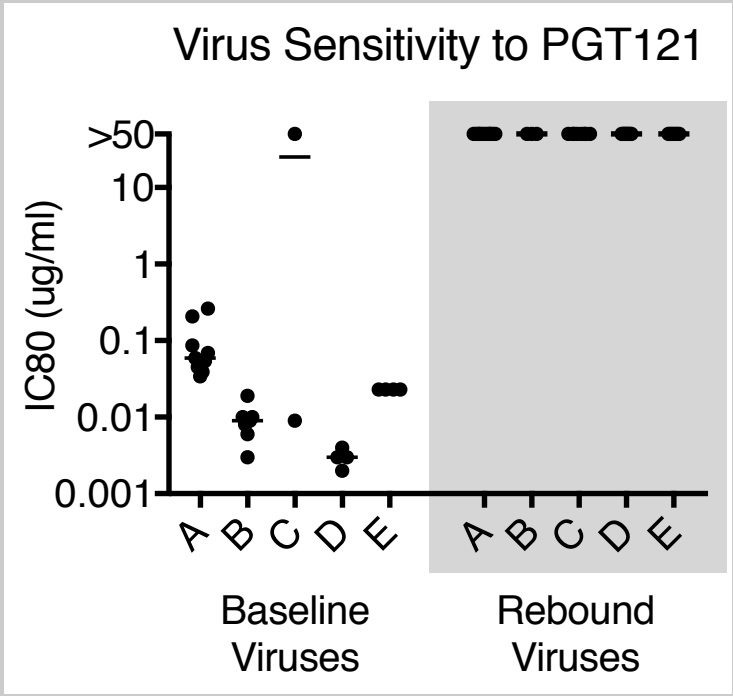
Antiviral Activity of PGT121 in High Viral Load Group (Baseline VL 3.3-5 log cp/mL, N=9)





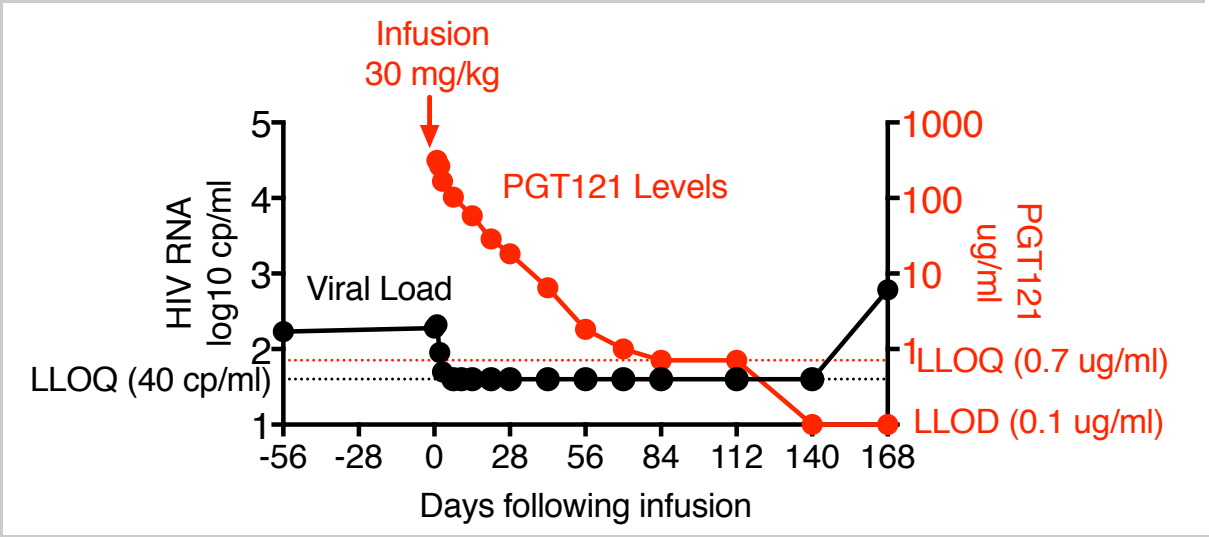
High Viral Load Group: Responders



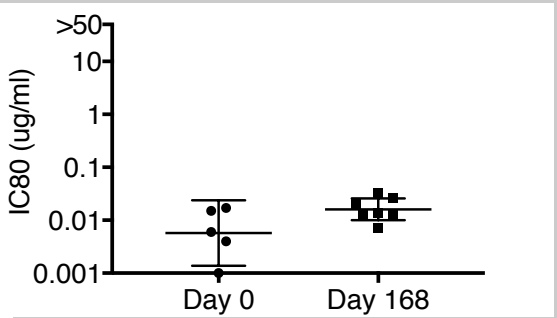


Median VL Drop = 1.7 logs

Low Viral Load Group: Participant 3D-A



Virus Sensitivity to PGT121



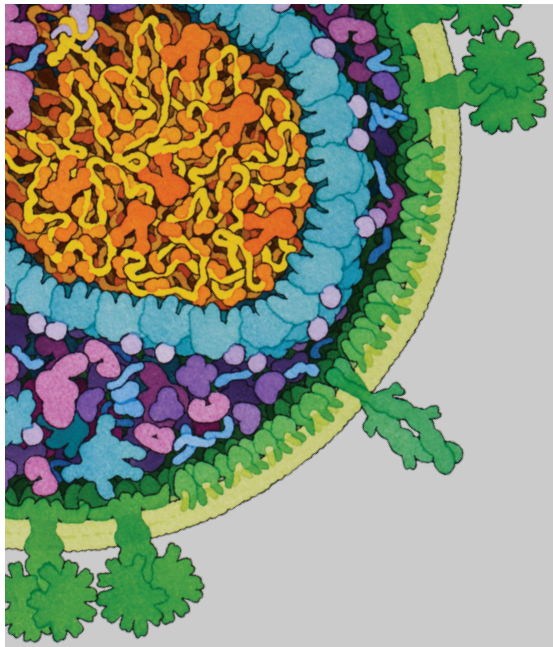
Env Sequences

Summary

- Safe and well-tolerated, including by SC route
- Half-life **23** days (13 days in viremic, HIV-infected)
- Therapeutic efficacy in individuals with baseline VL 3.3-5 log cp/ml:
  - **5/9** participants responded
  - Median **1.7** log drop in 7-10 days with rebound at 21-28 days
  - All responders had PGT121-sensitive viruses at baseline
  - All rebound viruses were PGT121-resistant
  - Detailed sequence analysis is pending

Summary

- Therapeutic efficacy in individuals with baseline VL <3.3 log cp/ml:
  - 2 participants sustained suppression for **≥ 6 months**
  - This is the longest observed suppression following a single bNAb infusion in a viremic HIV-infected individual
  - No evidence of enhanced cellular immune responses
  - Long-term virologic suppression likely due to exquisite potency of PGT121, even at levels below the limit of quantitation



RISK FACTORS FOR EXCESS WEIGHT GAIN FOLLOWING SWITCH TO INTEGRASE INHIBITOR–BASED ART

Jordan E. Lake

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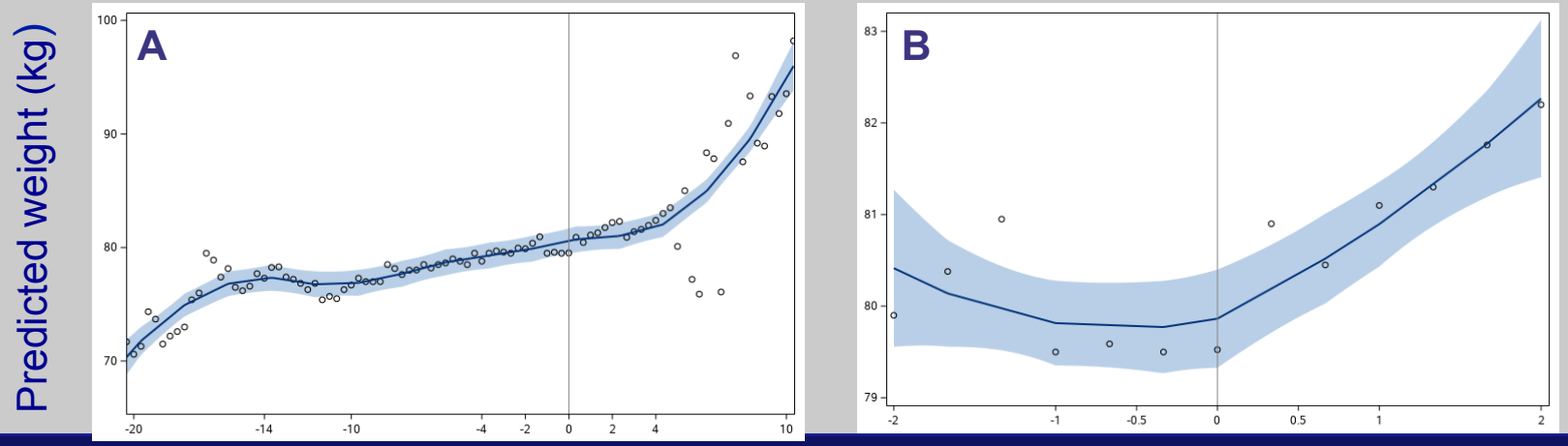
Disclosure: Self: Consulting or advisor fees from Merck & Co, Inc., Gilead Sciences
To self, paid to my institution: Research grant/grant pending from Gilead Sciences

CROI 2019

Results I

972 adults switched to INSTI at median 7.8 years after parent trial entry. 691 had suppressed HIV-1 RNA at time of switch:

- -82% male, 45% non-white
- -Median age 51 years, $CD4^+$ T cell count 610 cells/μL, and BMI 26 kg/m^2
- -63% switched from PI, 35% from NNRTI
- -289 switched to RAL, 204 to EVG and 198 to DTG (median follow-up 1.8 years)

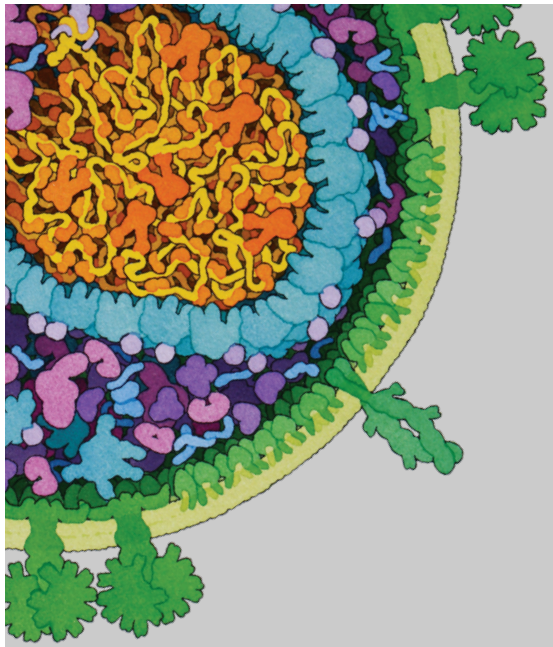


Results II

- **In sex-stratified, adjusted models:**
  - -White or black race, age ≥60 and BMI ≥30 kg/m^2 were associated with greater weight gain following switch among women
  - -Age ≥60 was the greatest risk factor among men
- **DTG associated with greatest increase in annual weight gain.**

	DTG (n=198)	EVG (n=204)	RAL (n=289)
Pre-INSTI	0.2 (0.11)	0.5 (0.008)	0.5 (<0.0001)
Post-INSTI	1.3 (<0.0001)	0.9 (<0.0001)	0.3 (0.045)
Pre-post difference	1.0 (0.0009)	0.5 (0.11)	-0.2 (0.37)

kg/year (p value)
DTG=dolutegravir, EVG=elvitegravir, RAL=raltegravir



INTEGRASE STRAND TRANSFER INHIBITORS ARE ASSOCIATED WITH WEIGHT GAIN IN WOMEN

Anne Marie Kerchberger
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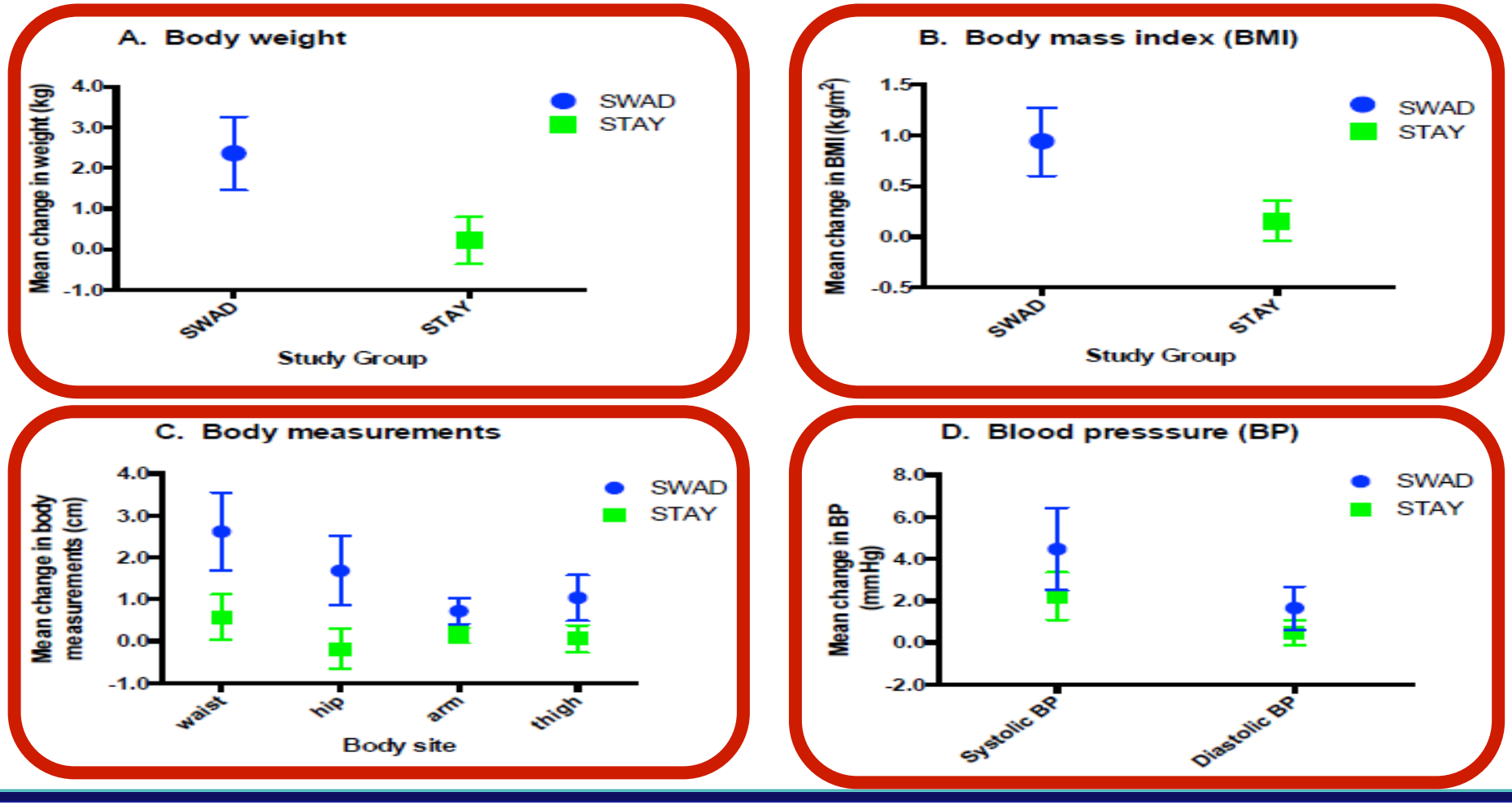
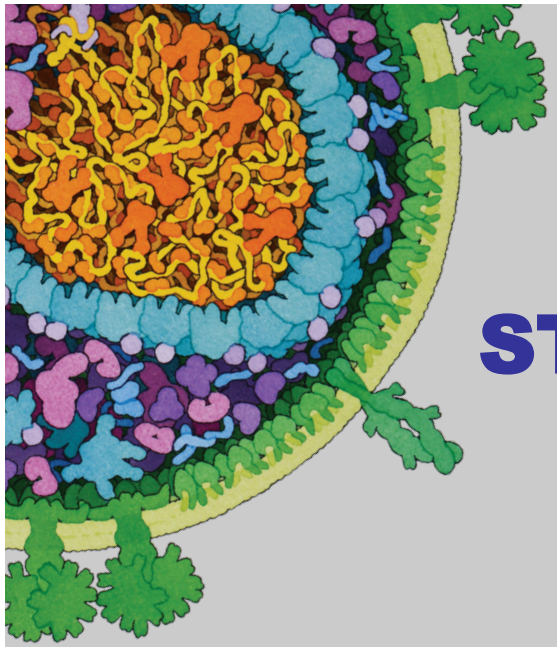
Disclosure: Nothing to Disclose

Model-adjusted change over time in outcome variables



CROI 2019: PrEP

- F/TAF vs F/TDF
- dual bNAb and penile exposure
- TAF/EVG vaginal implant
- PrEP retention/persistence in the US



THE PHASE 3 DISCOVER STUDY: DAILY F/TAF OR F/TDF FOR HIV PREEXPOSURE PROPHYLAXIS

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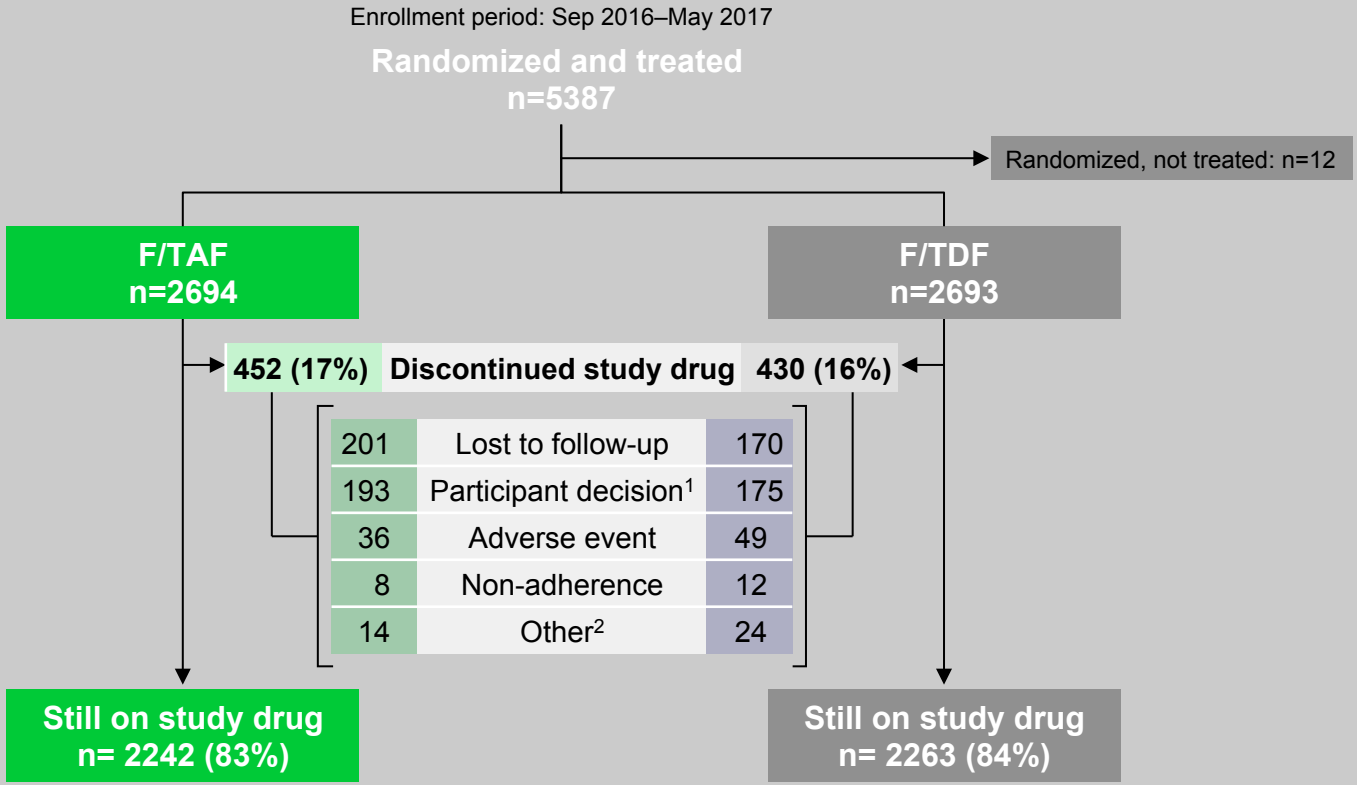
San Francisco, CA, USA

Disclosure: Nothing to Disclose

DISCOVER Participant Disposition



1. Most frequent reasons provided: withdrew consent, moved, monogamous relationship, reduced sexual risk, work/school/military obligations.
2. Investigator decision, withdrew consent, incarceration, HIV infection, death.

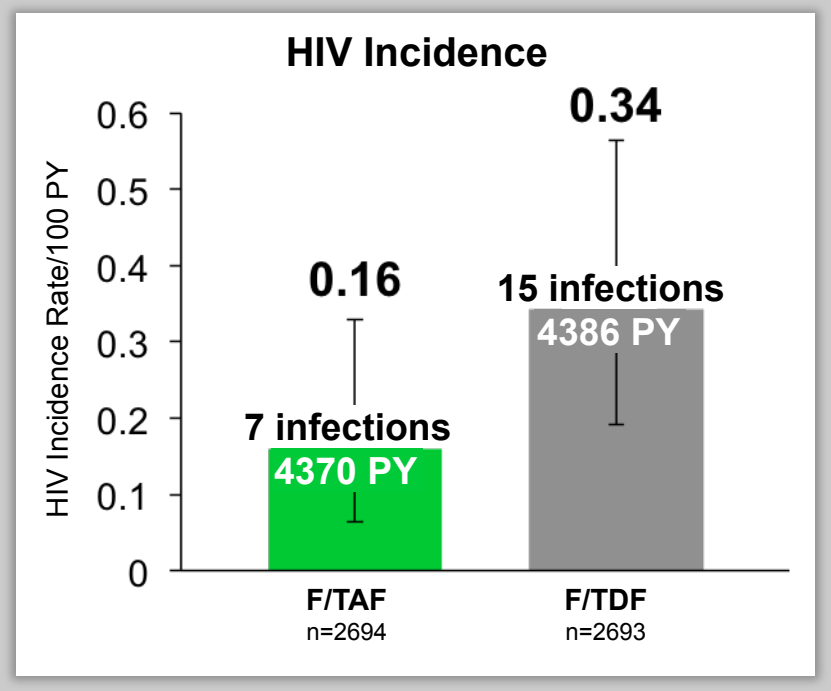
Baseline Demographics and HIV Risk Factors

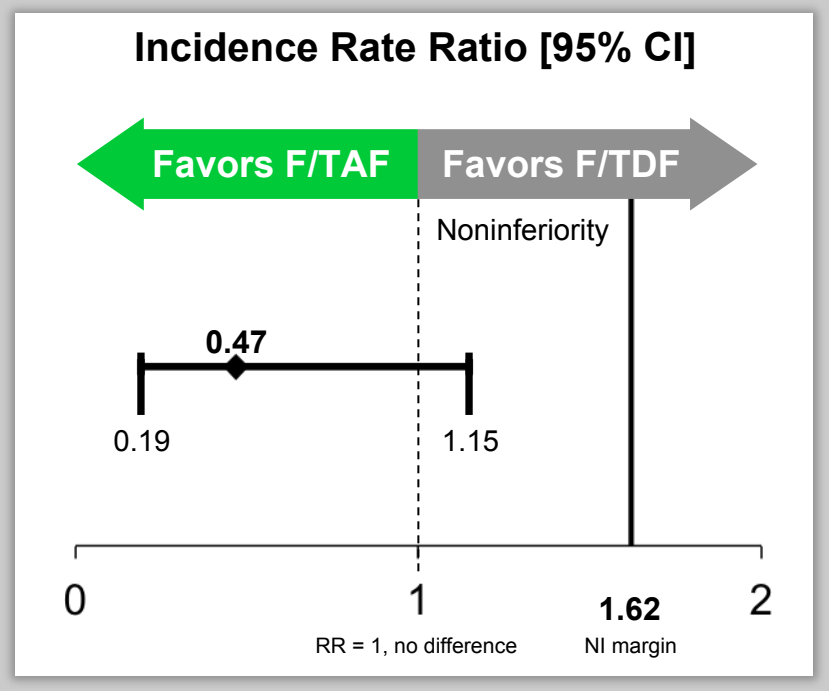
		F/TAF n=2694	F/TDF n=2693
Demographics	Median age, y (range)	34 (18–76)	34 (18–72)
	Race, n (%)		
	White	2264 (84)	2247 (84)
	Black*	240 (9)	234 (9)
	Asian	113 (4)	120 (5)
	Hispanic or Latinx ethnicity, n (%)	635 (24)	683 (25)
	Proportion TGW, n (%)	45 (2)	29 (1)
HIV risk factors, %	≥2 condomless anal sex (receptive), past 12W	60	58
	Rectal gonorrhea, past 24W	10	10
	Rectal chlamydia, past 24W	13	12
	Syphilis, past 24W	9	10
	Recreational drug use, past 12W	67	67
	Binge drinking†	23	22
	Taking F/TDF for PrEP at baseline	17	16

*Includes mixed black race; †≥6 drinks on ≥1 occasion, at least monthly.

DISCOVER Primary Endpoint Analysis: HIV Incidence

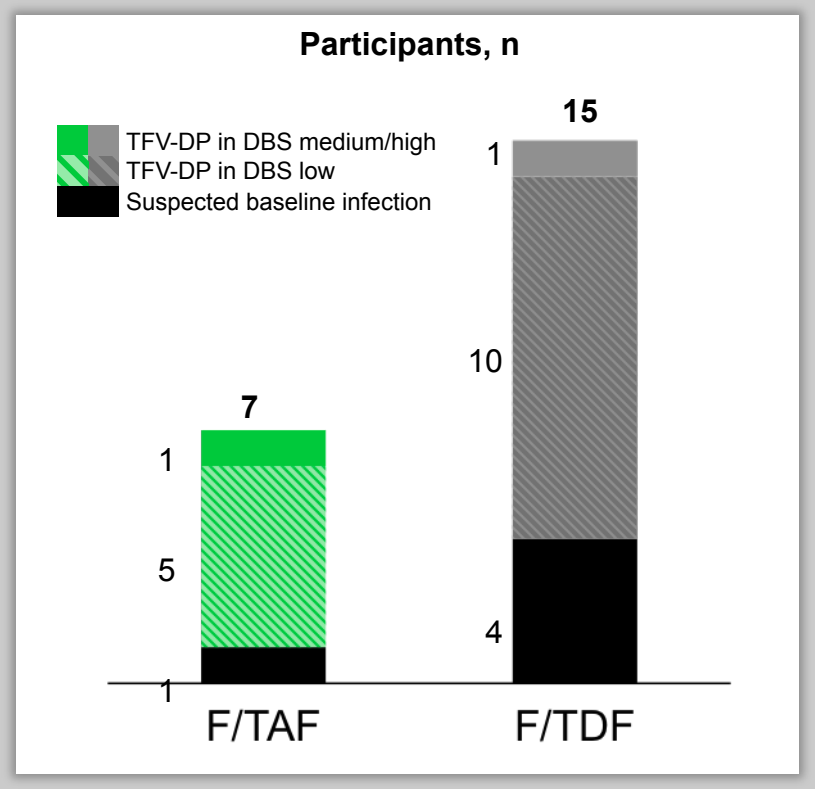
22 HIV infections in 8756 PY of follow-up





F/TAF is noninferior to F/TDF for HIV prevention

DISCOVER Adherence and Resistance Analyses of HIV Infections

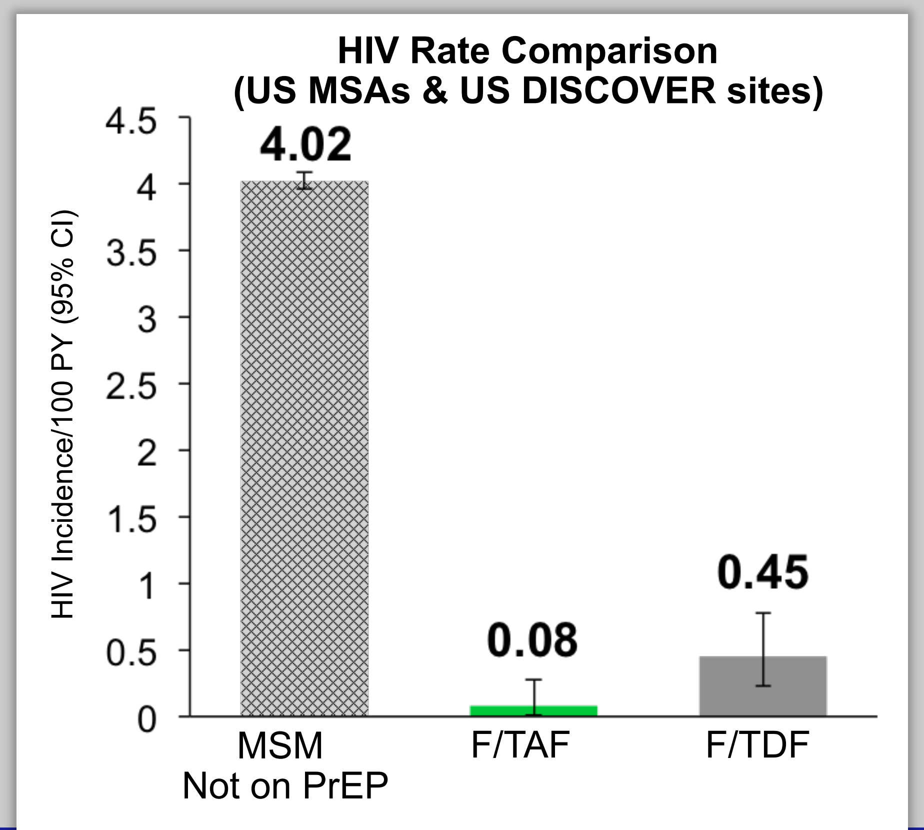


- 7 F/TAF infections: 1 suspected baseline infection, 5 low levels of TFV-DP in DBS,1 medium level
- 15 F/TDF infections: 4 suspected baseline infections, 10 low levels of TFV-DP in DBS, 1 high level
- In a sensitivity analysis that excluded suspected baseline infections, noninferiority was maintained (0.55 [0.20, 1.48])

n	F/TAF n=7	F/TDF n=15
Resistance genotyped*	6	13
Resistance to study drugs		
FTC	0	4†
TFV	0	0

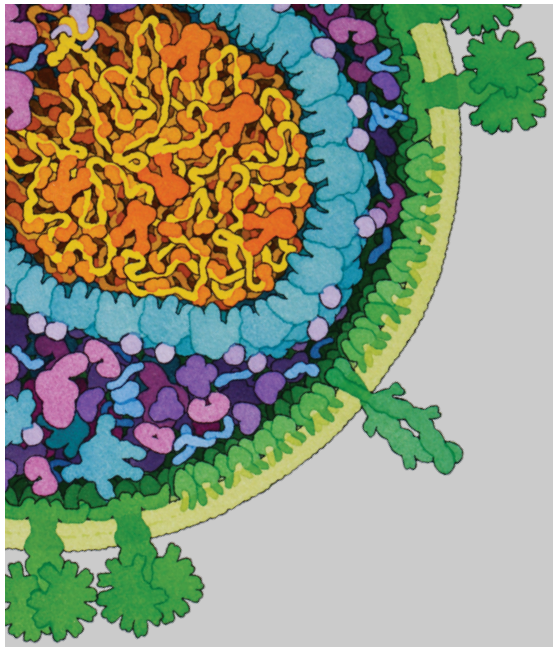
*3 samples could not be amplified; †All 4 participants with resistance were suspected baseline infections.

Comparing DISCOVER Results to HIV Infection Rate In MSM at HIV Risk but Not on PrEP



- In the absence of placebo control, we sought to contextualize the HIV incidence rates in DISCOVER to the rate in MSM not on PrEP
- Using CDC-reported HIV surveillance data, we calculated the background infection rate for MSM at HIV infection risk* in US metropolitan statistical areas (MSAs) that overlapped with DISCOVER sites[1]
- HIV infection rate for MSM not on PrEP in 2016:
  - 4.02/100 PY 95%CI [3.96, 4.09]
- HIV incidence rates in US DISCOVER sites:
  - F/TAF = 0.08/100 95%CI [0.01, 0.28]
  - F/TDF = 0.45/100 95%CI [0.23, 0.78]

*CDC-defined persons with an indication for PrEP (Smith Ann Epidemiol 2018). 1. Mera JIAS 2019, under review.



PROTECTION AGAINST PENILE OR INTRAVENOUS SHIV CHALLENGES BY bNAb 10-1074 OR 3BNC117

David A. Garber

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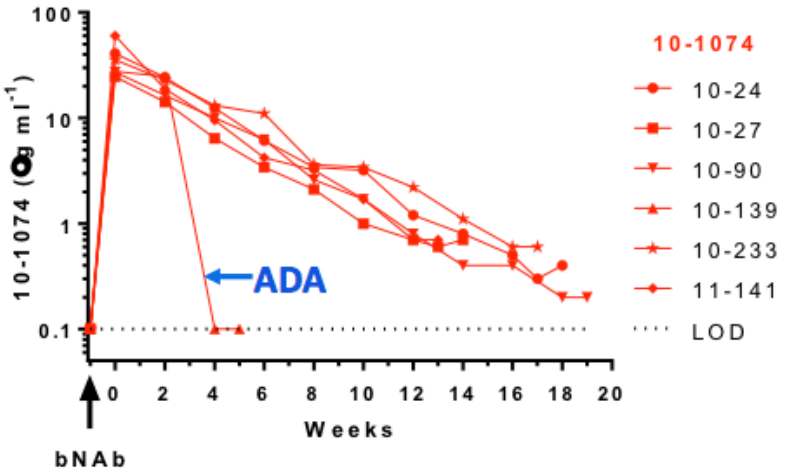
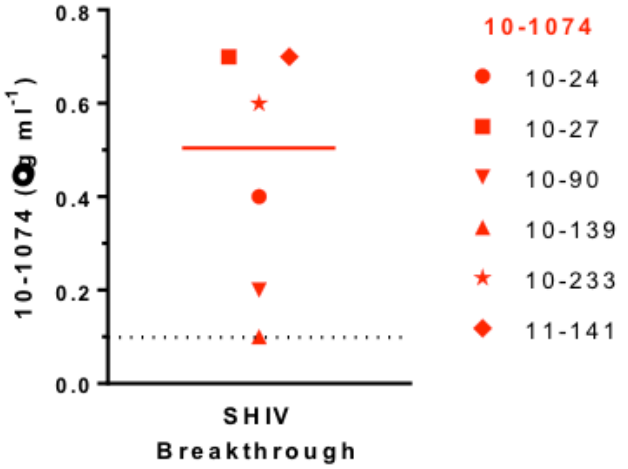
Atlanta, GA, USA

Disclosure: Nothing to Disclose

Plasma pharmacokinetics of 10-1074





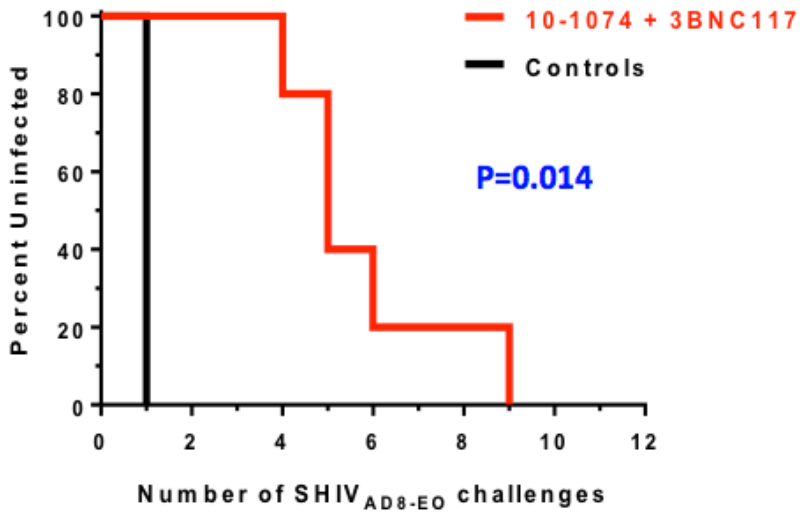
Mean C_{max} = 36 ± 13 μg/ml

Mean $T_{1/2}$ = 15.5 ± 4.0 Days

bNAb protection against intravenous SHIV infection

Group	bNAb	Dose	Route	N
1	10-1074 + 3BNC117	10mg/kg 10mg/kg	SC SC	5
2	Control	--	--	2

- No differences between groups for peak vRNA or AUC

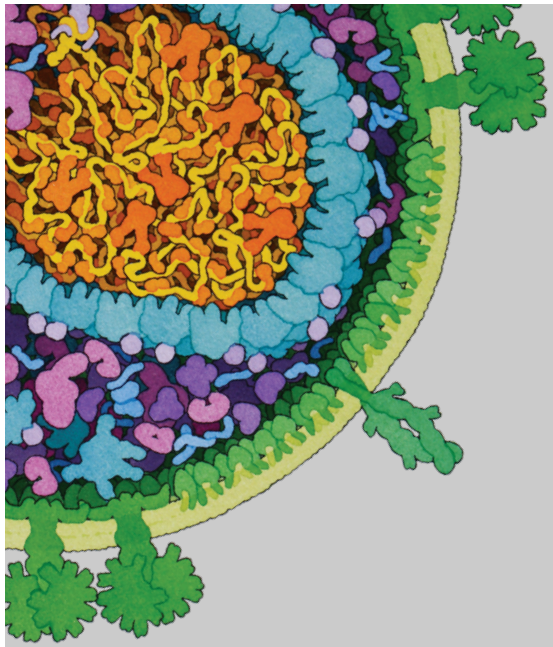


	Median	Range
10-1074 + 3BNC117	5	4 - 9
Control	1	1 - 1

Cynomolgus macaques; 150 $TCID_{50}$ challenge dose

Summary and Conclusions

- A single SC administration of 10-1074 (10mg/kg) or 10-1074 + 3BNC117 (10mg ea/kg) protected macaques against repeated penile or IV SHIV challenges for a median of 15.5 or 5 weeks, respectively.
- Protection in the 10-1074 + 3BNC117 group appears due to 10-1074, which persisted relatively longer in vivo
- The plasma levels of 10-1074 associated with breakthrough infection are similar among all major mucosal routes of HIV acquisition (0.10 – 0.5 μg/ml) and will facilitate dose selection for humans
- Higher level for IV infection (1.0 μg/ml) may reflect relatively higher challenge virus dose
- Our findings support the continued development of 10-1074 as a long-acting prevention for men, women and persons who inject drugs



PROTECTION AGAINST VAGINAL SHIV INFECTION WITH AN INSERT CONTAINING TAF AND EVG

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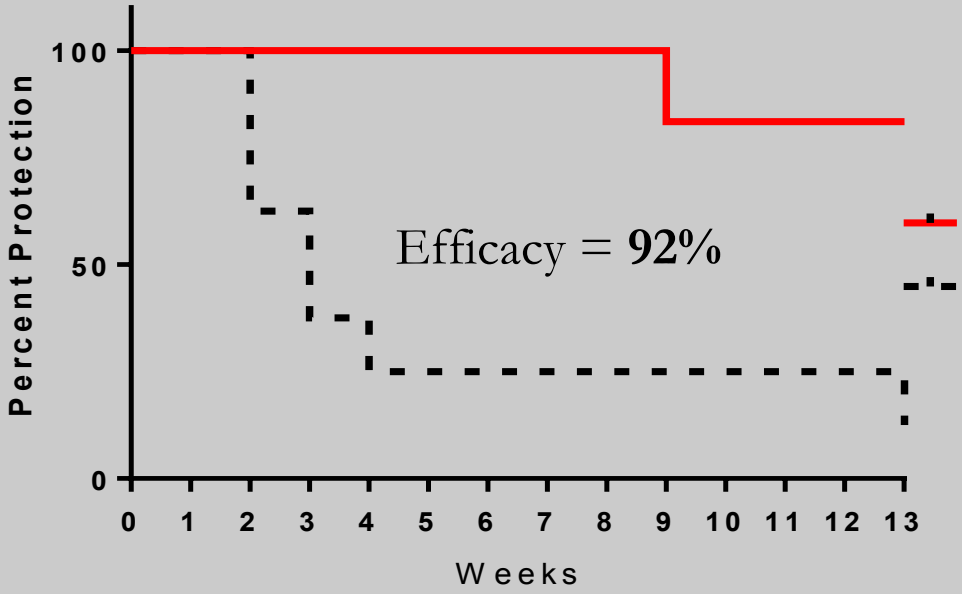
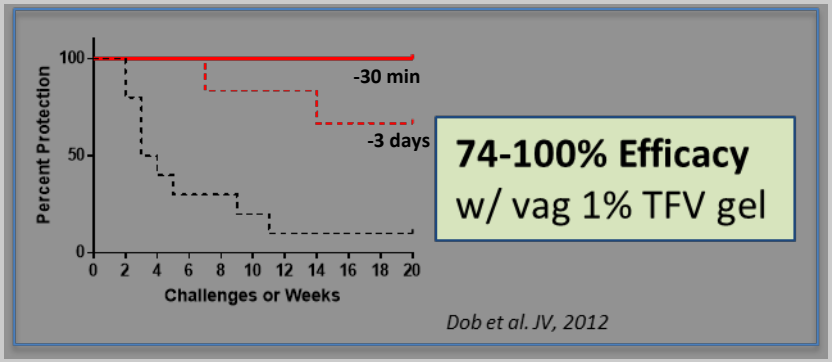
Atlanta, GA, USA

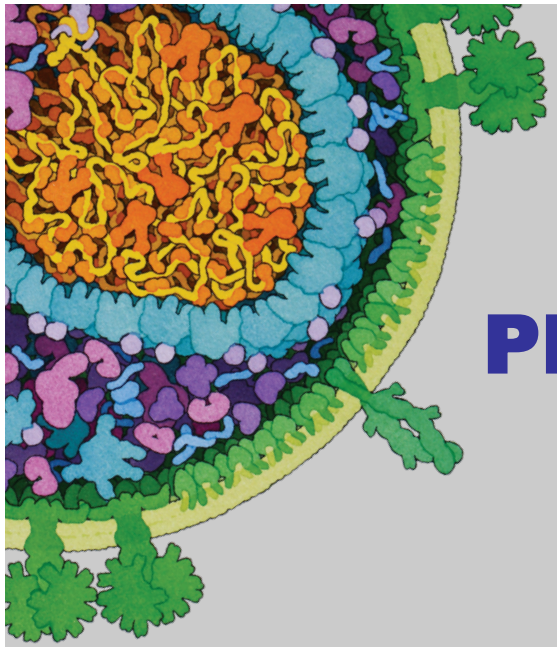
Disclosure: Nothing to Disclose

TAF/EVG inserts administered 4h prior to SHIV exposure protects macaques against vaginal infection



Hazard Ratio = 4.54 *(p = 0.008; log-rank)*





PERSISTENCE WITH HIV PREEXPOSURE PROPHYLAXIS IN THE UNITED STATES, 2012-2016

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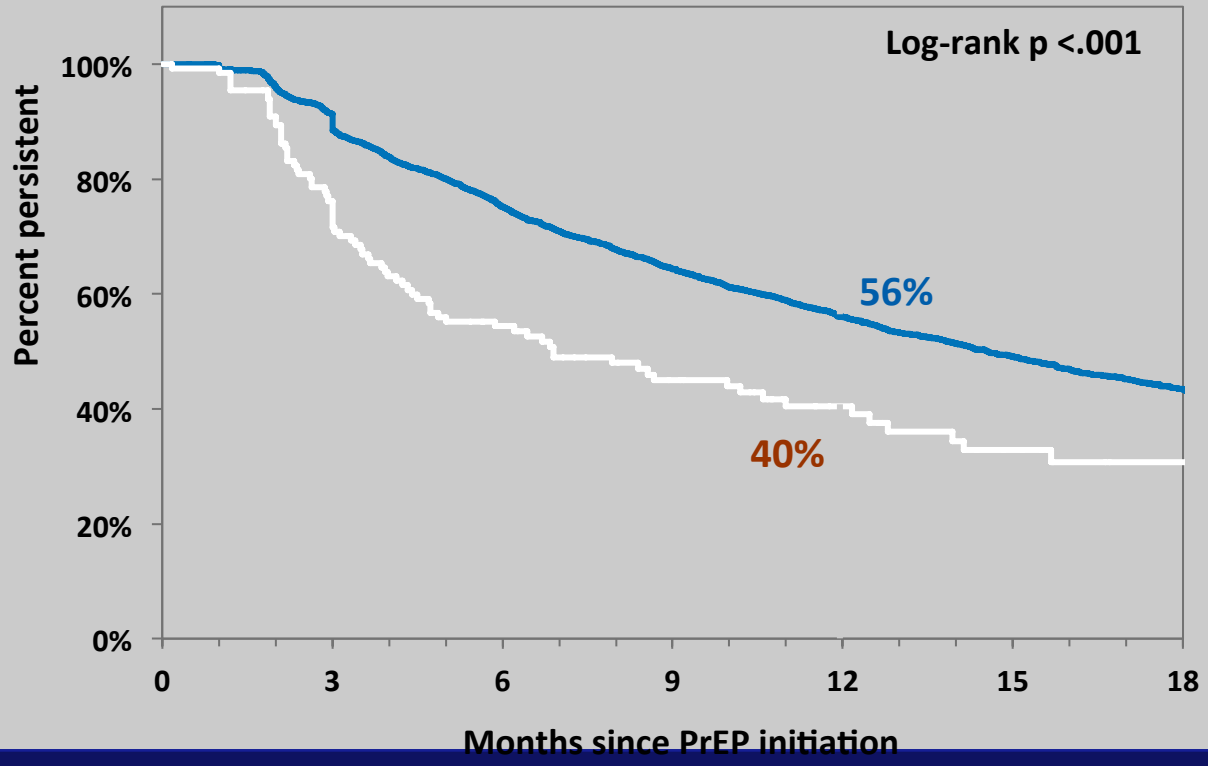
Disclosure: Nothing to Disclose

CROI 2019

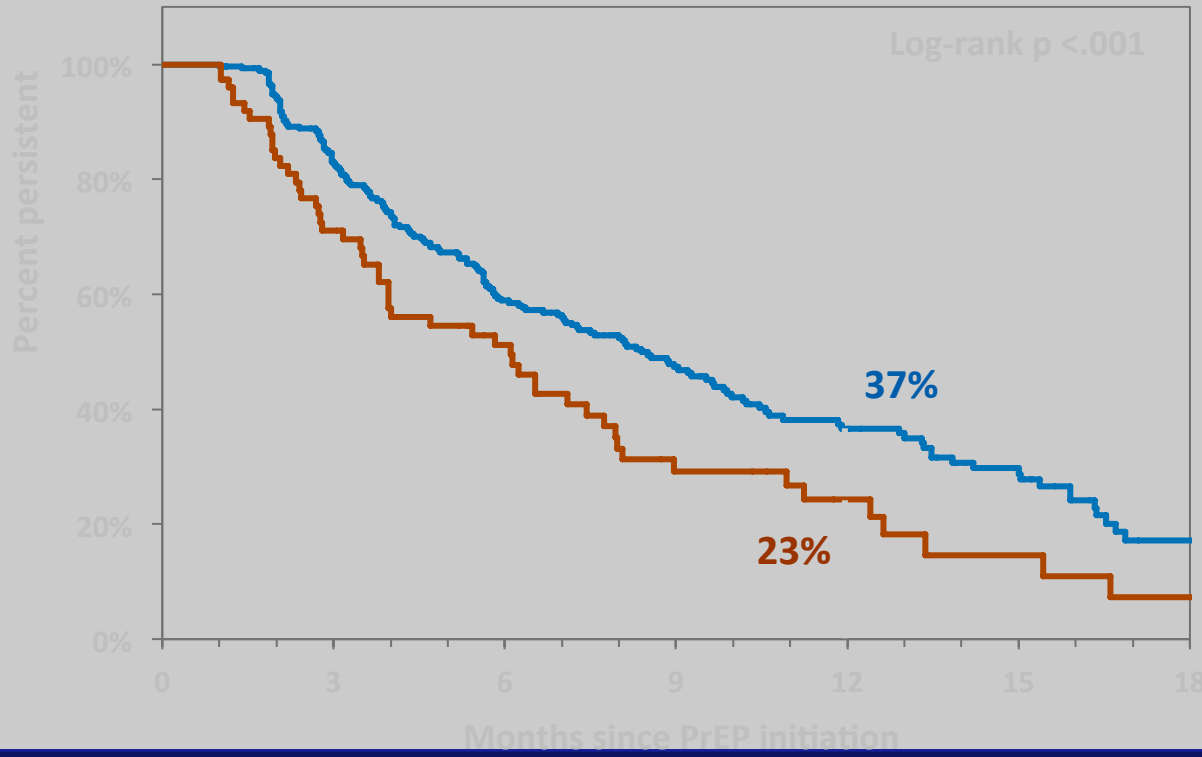
Among commercially insured PrEP users, men persisted longer than women



Men (n=7,118)
Median persistence=14.5 months

Women (n=132)
Median persistence=6.9 months

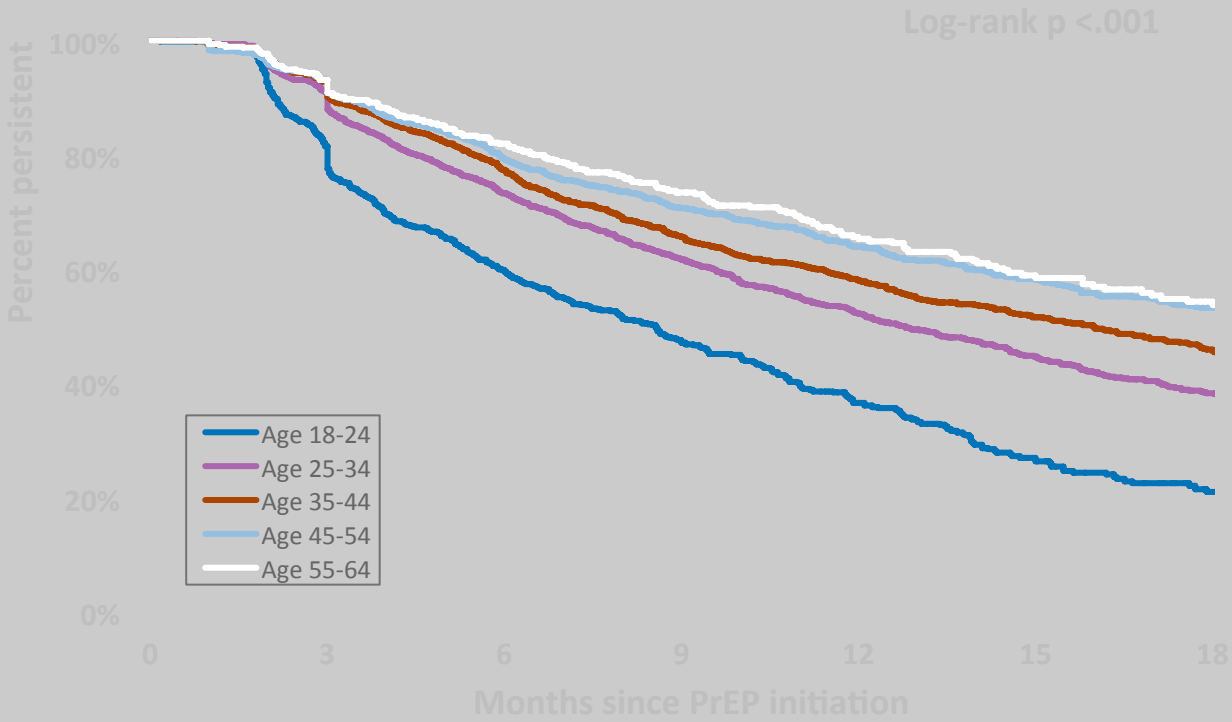
Among Medicaid insured PrEP users, men persisted longer than women



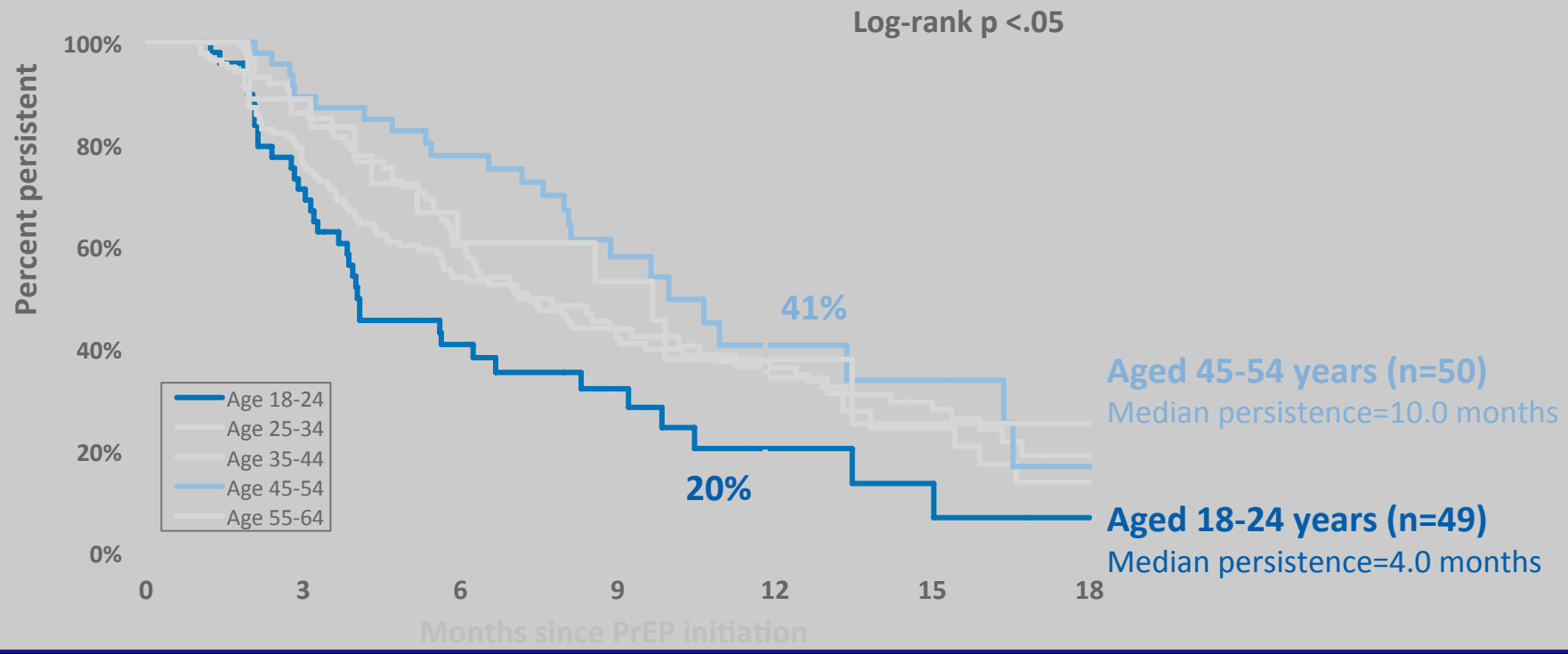
Men (n=273)
Median persistence=8.4 months

Women (n=76)
Median persistence=5.8 months

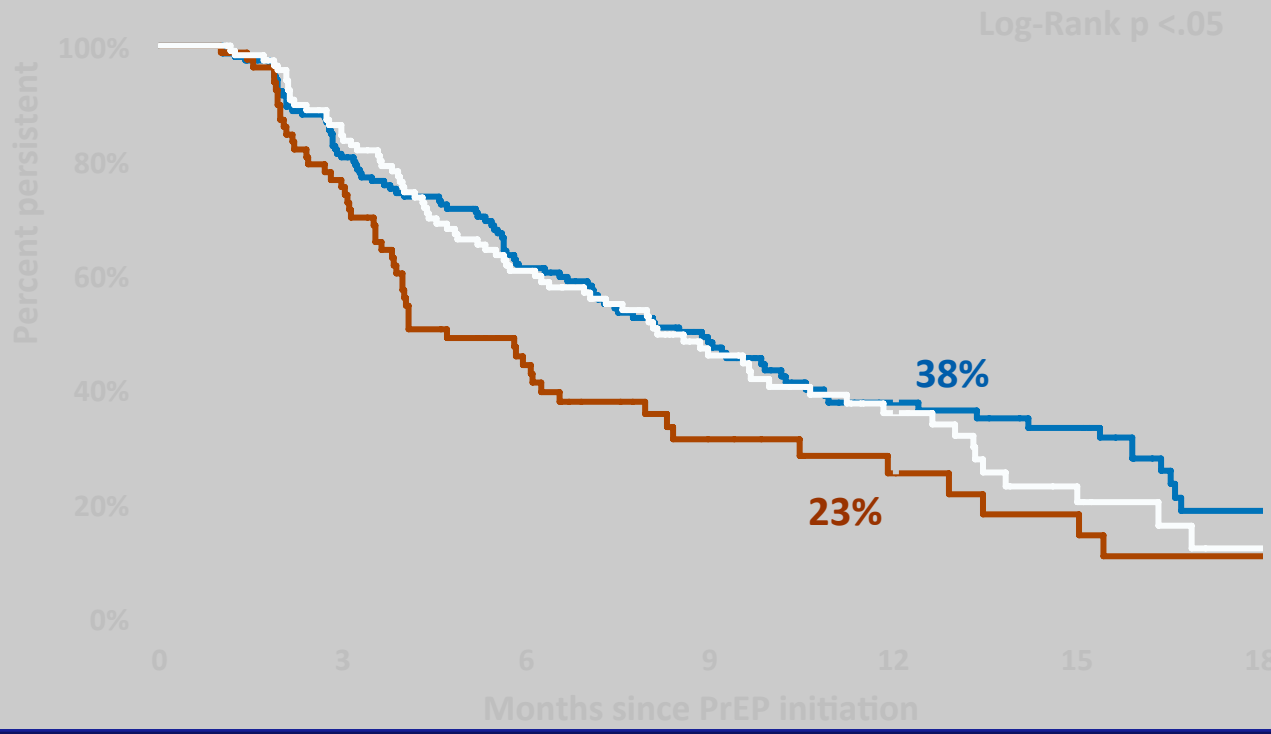
Among commercially insured PrEP users, persistence increased with age



Among Medicaid insured PrEP users, younger users persisted for less time than older users



Among Medicaid insured PrEP users, black users persisted for less time than white users



White (n=151)
Median persistence=8.5 months

Other (n=117)
Median persistence=8.1 months

Black (n=81)
Median persistence=4.1 months

Thanks

Questions...