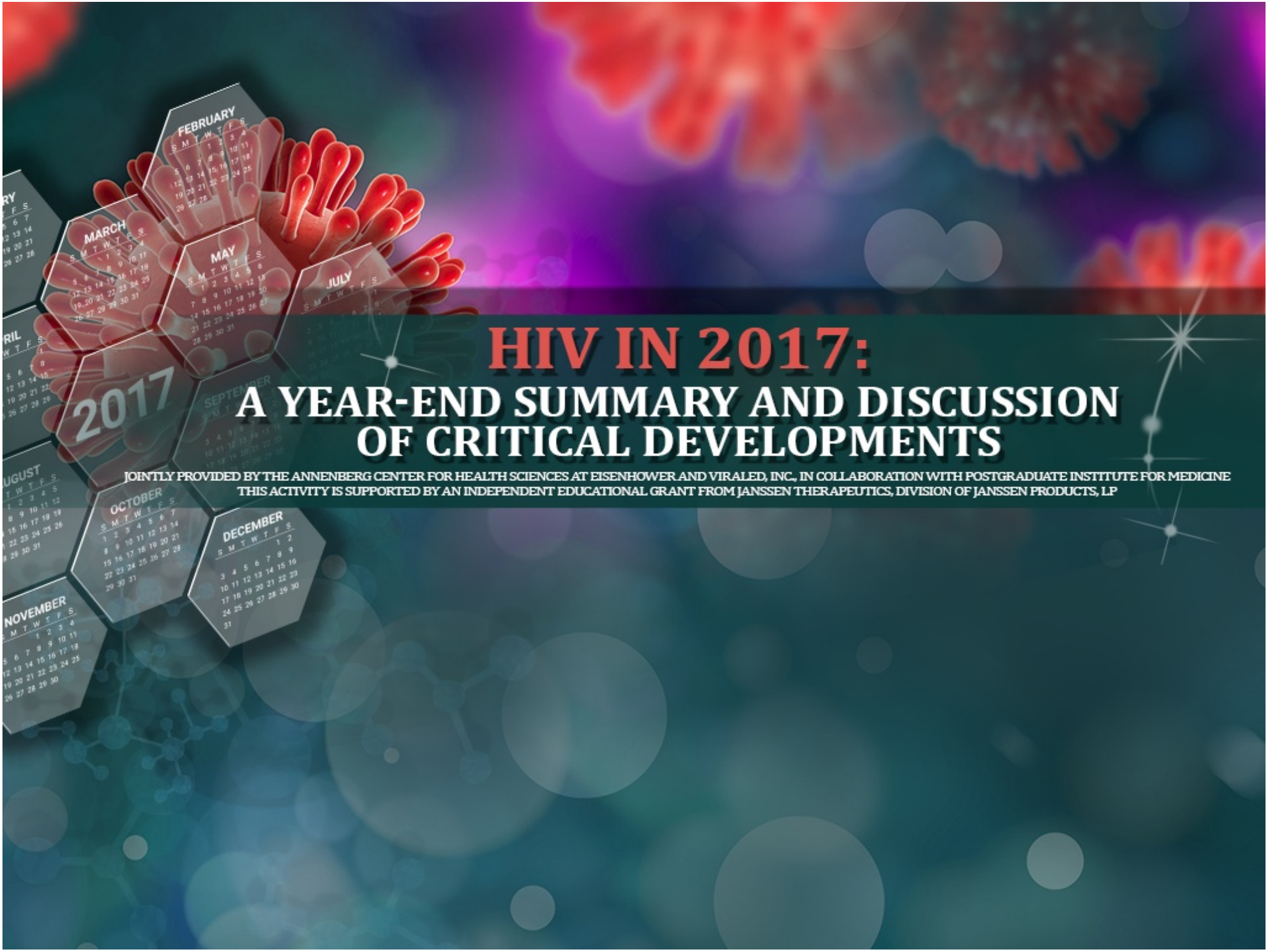


HIV IN 2017:
A YEAR-END SUMMARY AND DISCUSSION OF CRITICAL DEVELOPMENTS

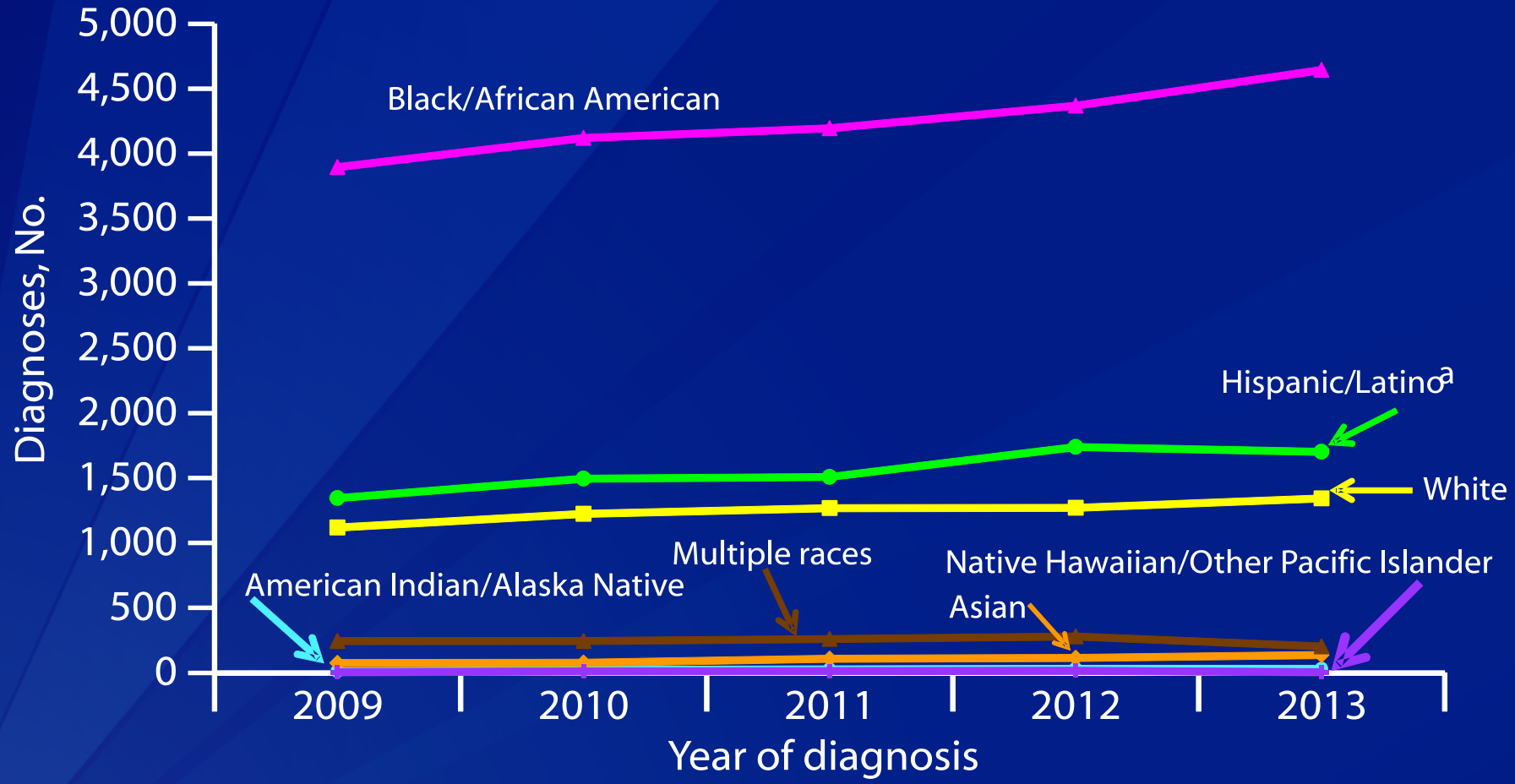
JOINTLY PROVIDED BY THE ANNENBERG CENTER FOR HEALTH SCIENCES AT EISENHOWER AND VIRALED, INC., IN COLLABORATION WITH POSTGRADUATE INSTITUTE FOR MEDICINE
THIS ACTIVITY IS SUPPORTED BY AN INDEPENDENT EDUCATIONAL GRANT FROM JANSSEN THERAPEUTICS, DIVISION OF JANSSEN PRODUCTS, LP

Main topics

- Studies in Prevention
- Overview of ART
- Studies in Treatment-Naïve Patients
- Studies on Hepatitis

Diagnoses of HIV Infection among Men Who Have Sex with Men Aged 13–24 Years, by Race/Ethnicity, 2009–2013

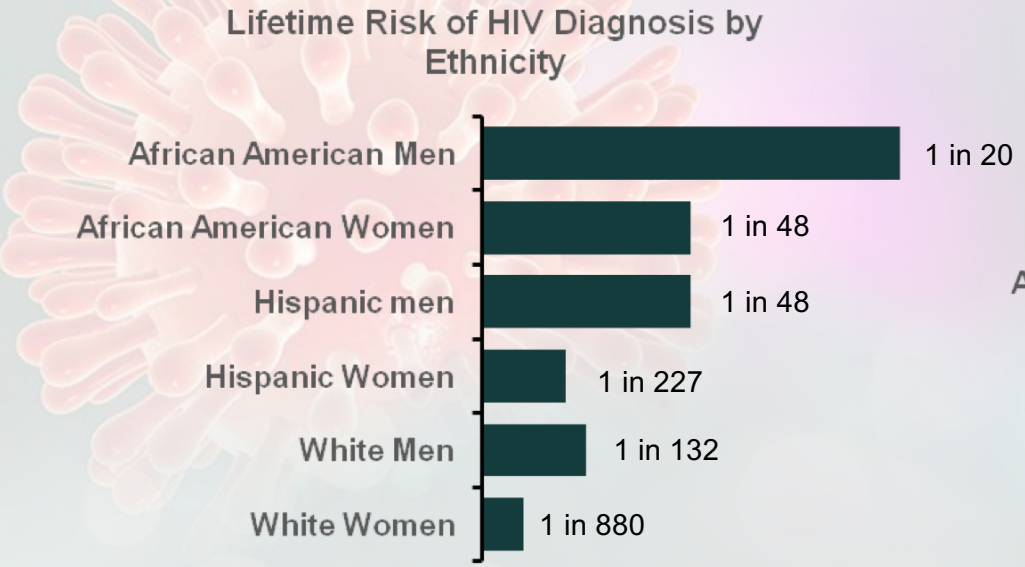
United States and 6 Dependent Areas

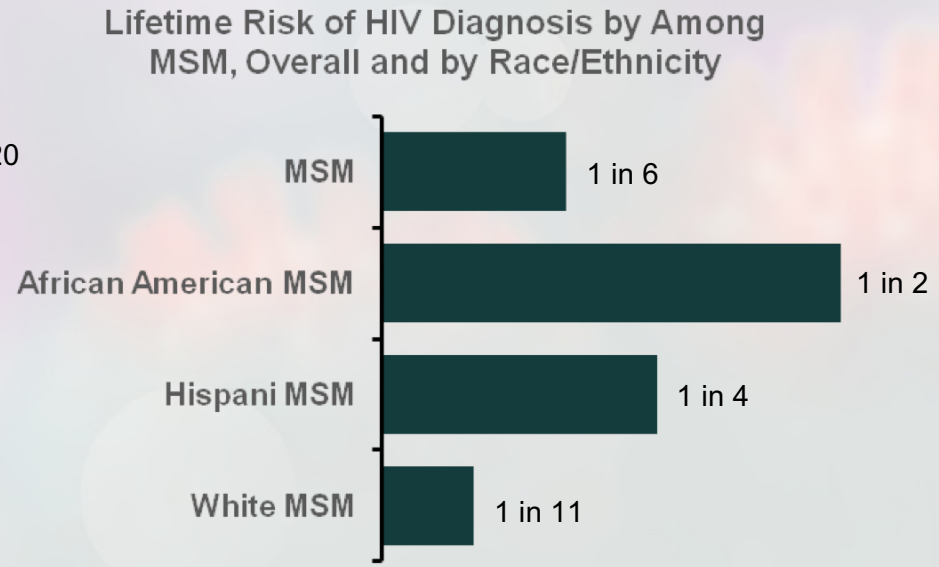


Note. Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays and missing transmission category, but not for incomplete reporting. Data on men who have sex with men do not include men with HIV infection attributed to male-to-male sexual contact *and* injection drug use.

[a] Hispanics/Latinos can be of any race.

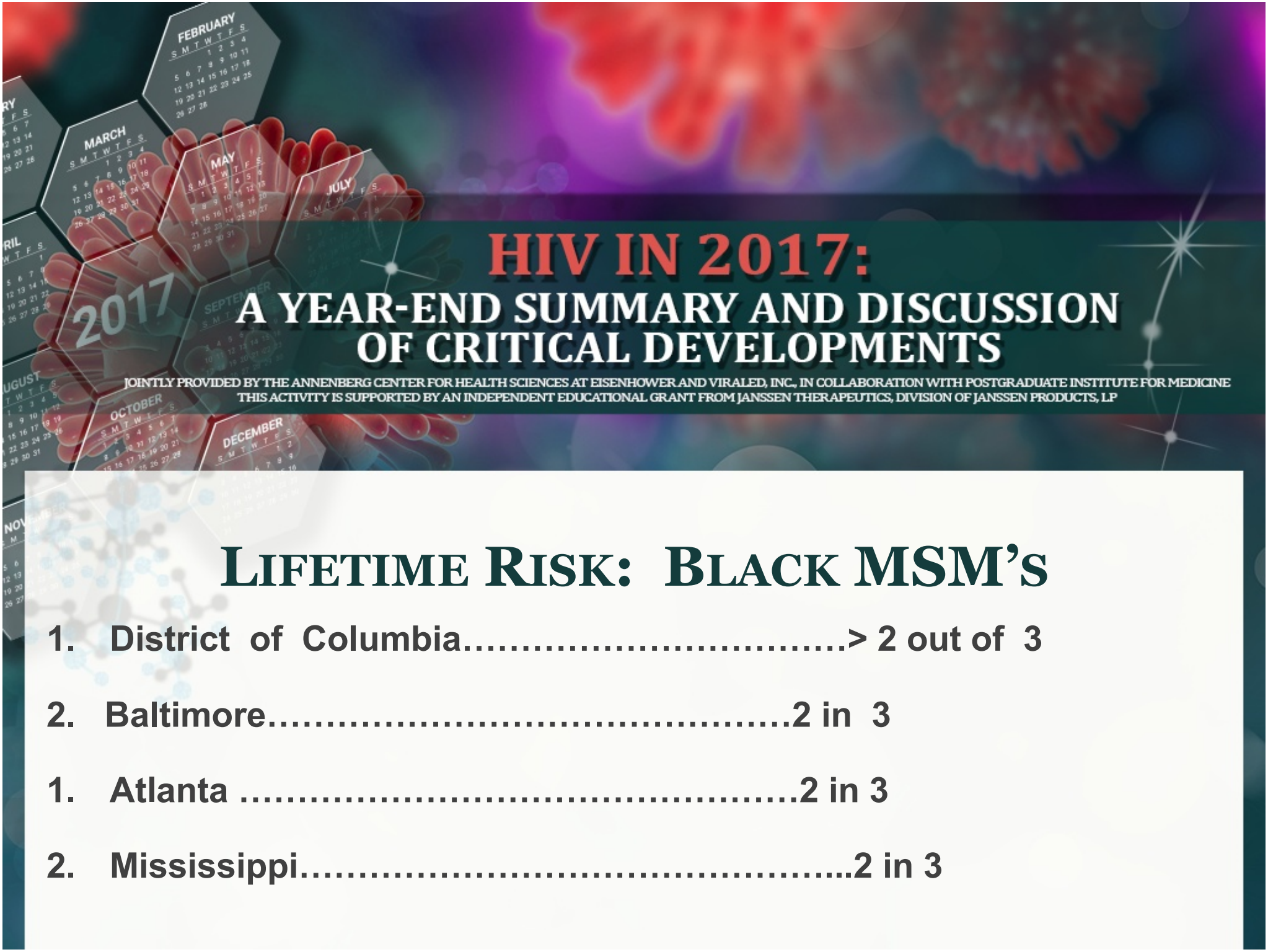
African-Americans Have the Highest Lifetime Risk of HIV Diagnosis





- African Americans are the most affected group with a lifetime HIV risk of 1 in 20 for men (compared to 1 in 132 for whites) and 1 in 48 for women (compared to 1 in 880 for whites)
- African American MSM and Hispanic MSM have a **1 in 2 and 1 in 4 lifetime risk of HIV infection**, respectively

http://www.cdc.gov/nchhstp/newsroom/2016/croi-2016.html#Graphics

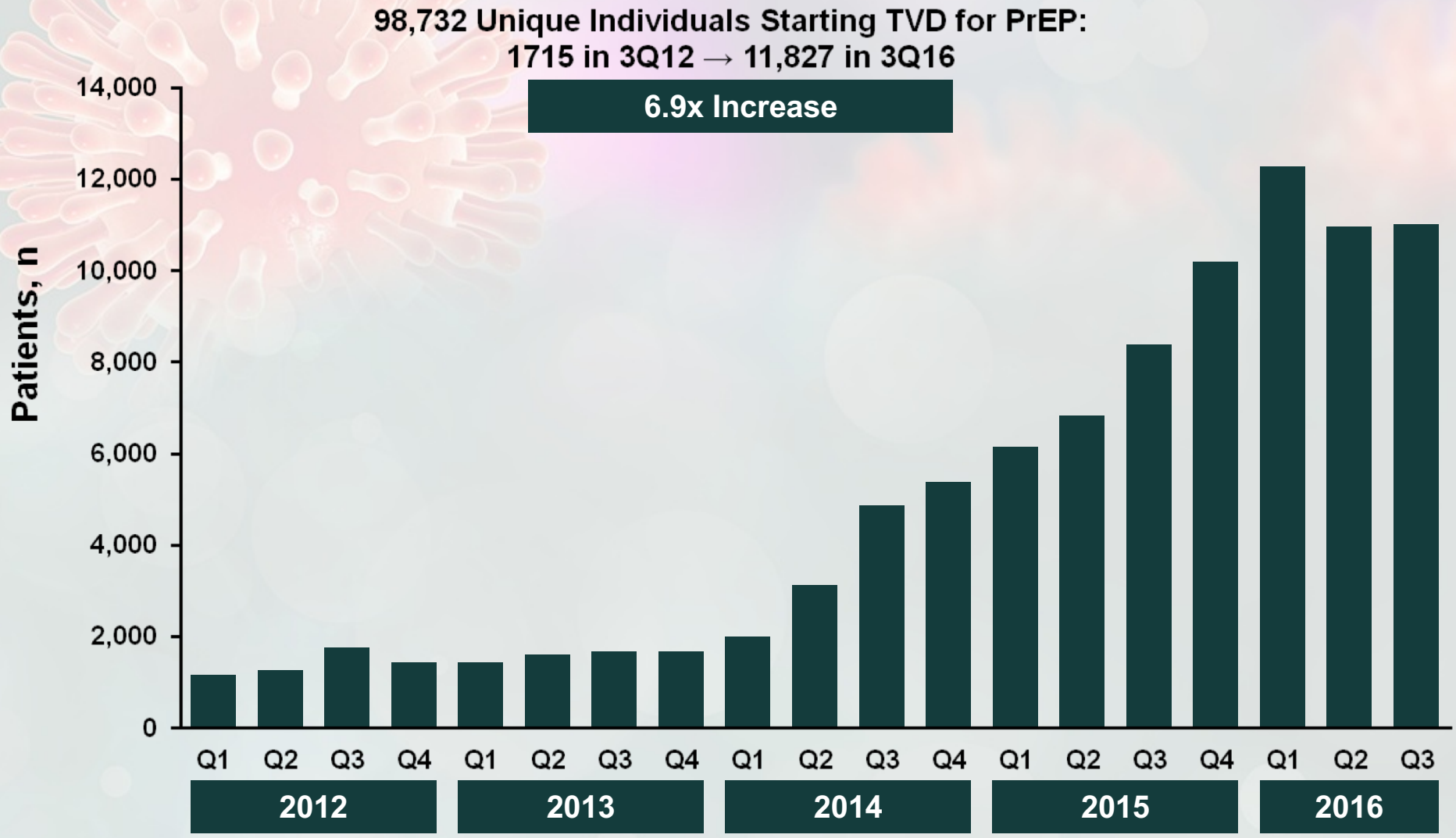


LIFETIME RISK: BLACK MSM'S

1. District of Columbia……> 2 out of 3
2. Baltimore……2 in 3
1. Atlanta ……2 in 3
2. Mississippi……..2 in 3

Utilization of TDF/FTC for PrEP in US: Number of Users

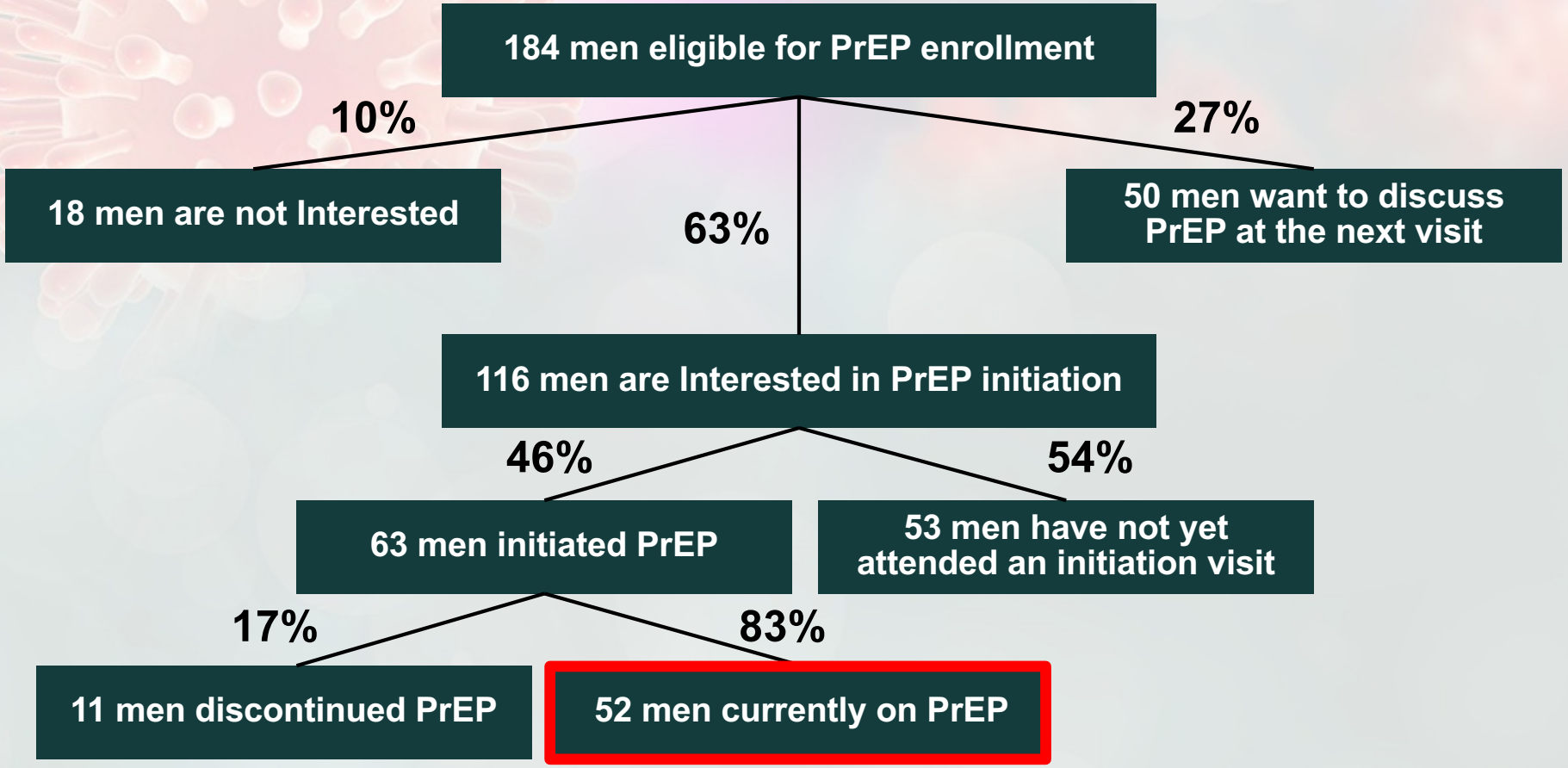
PrEP Users 2012 – Q3 2016



Mera R, et al; 9th IAS, Paris, France, July 23-26, 2017; Abst. WEPEC0919.

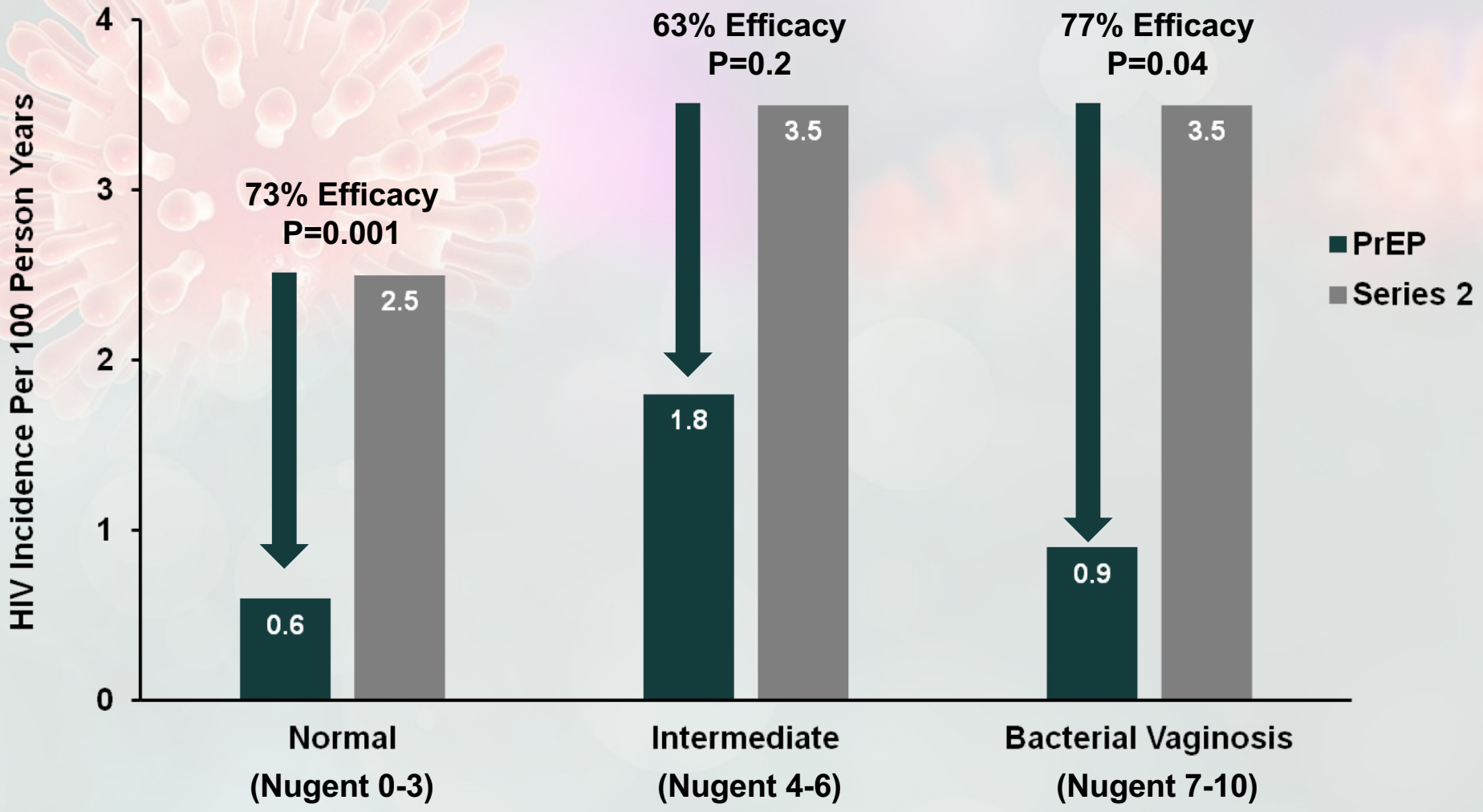
Poor PrEP Uptake Among Young Black MSM in Atlanta

Observational cohort study offering HIV prevention services to young Black MSM ages 16 - 29



Rolle C, et al. 24th CROI; Seattle, WA; February 13-16, 2017. Abst. 90.

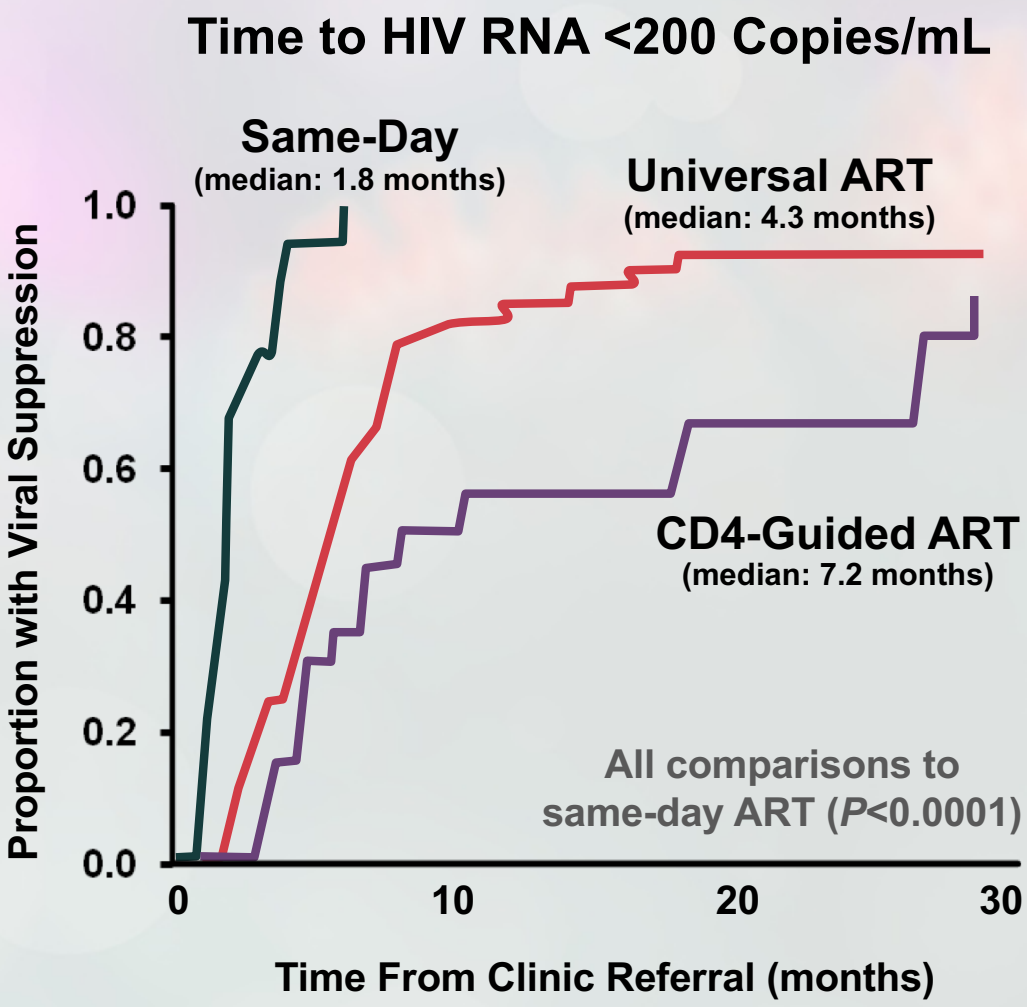
Efficacy of Oral TDF/FTC Not Diminished by Vaginal Dysbiosis



Heffron R, et al. 24th CROI; Seattle, WA; February 13-16, 2017. Abst. 85.

San Francisco Experience:
Same-Day Observed ART Initiation vs. Standard of Care

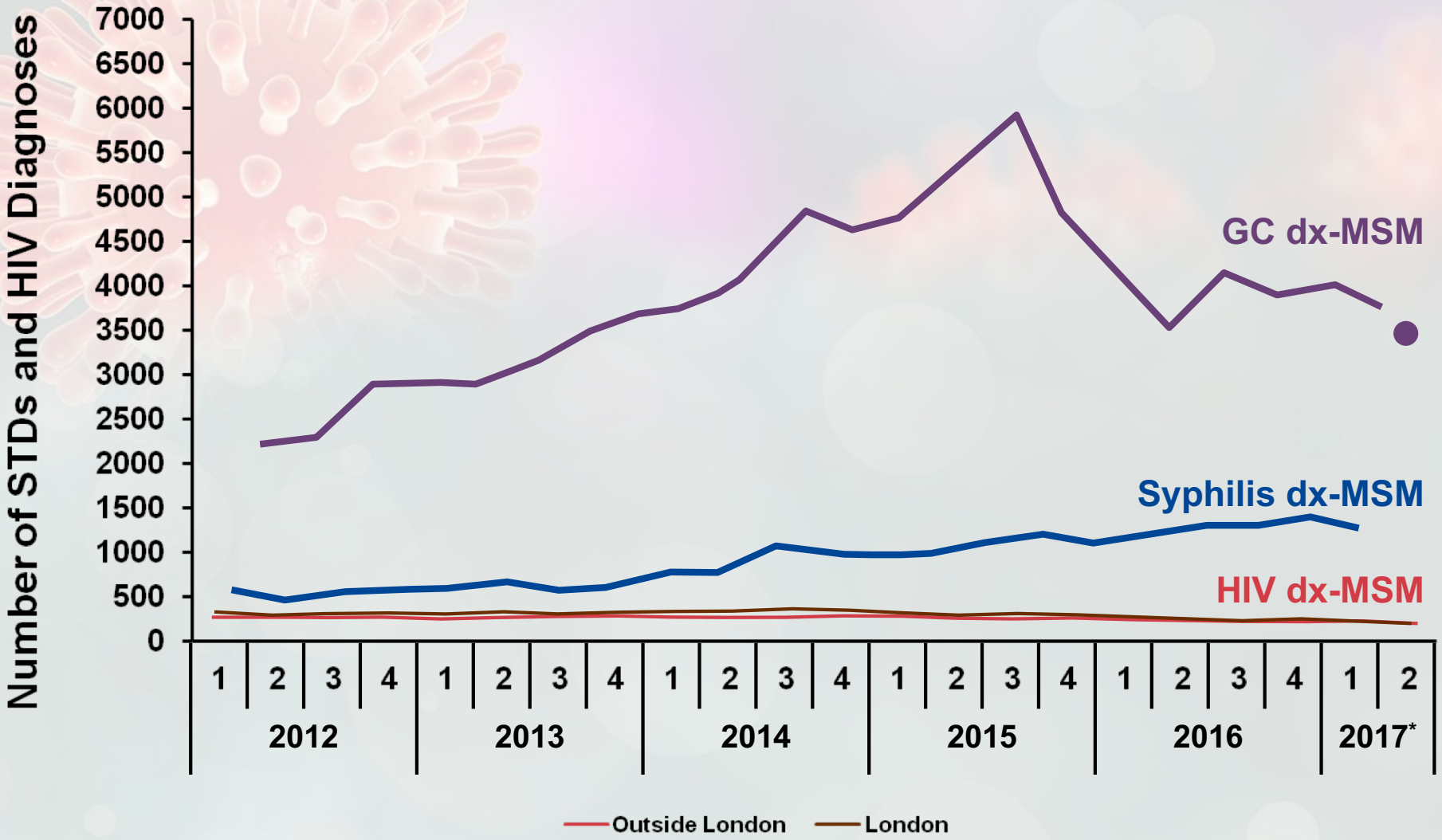
- **Significantly shorter time to viral suppression (*P*<0.0001)**
  - Same-day ART versus universal ART (2010-2013) and CD4-guided ART (2006-2009)
- **Similar rates of loss to follow-up**
  - Same-day (10%) versus non-same-day ART (15%)
- **Most same-day patients received INSTI-based regimens**
  - Similar safety and tolerability with non-same day ART
  - No regimen modifications due to virologic failure
  - No cases of treatment-emergent resistance (35% had transmitted mutations, 24% with major NNRTI mutations)



Dolutegravir (69%), elvitegravir/cobicistat (18%), darunavir/r (10%), raltegravir (2%).

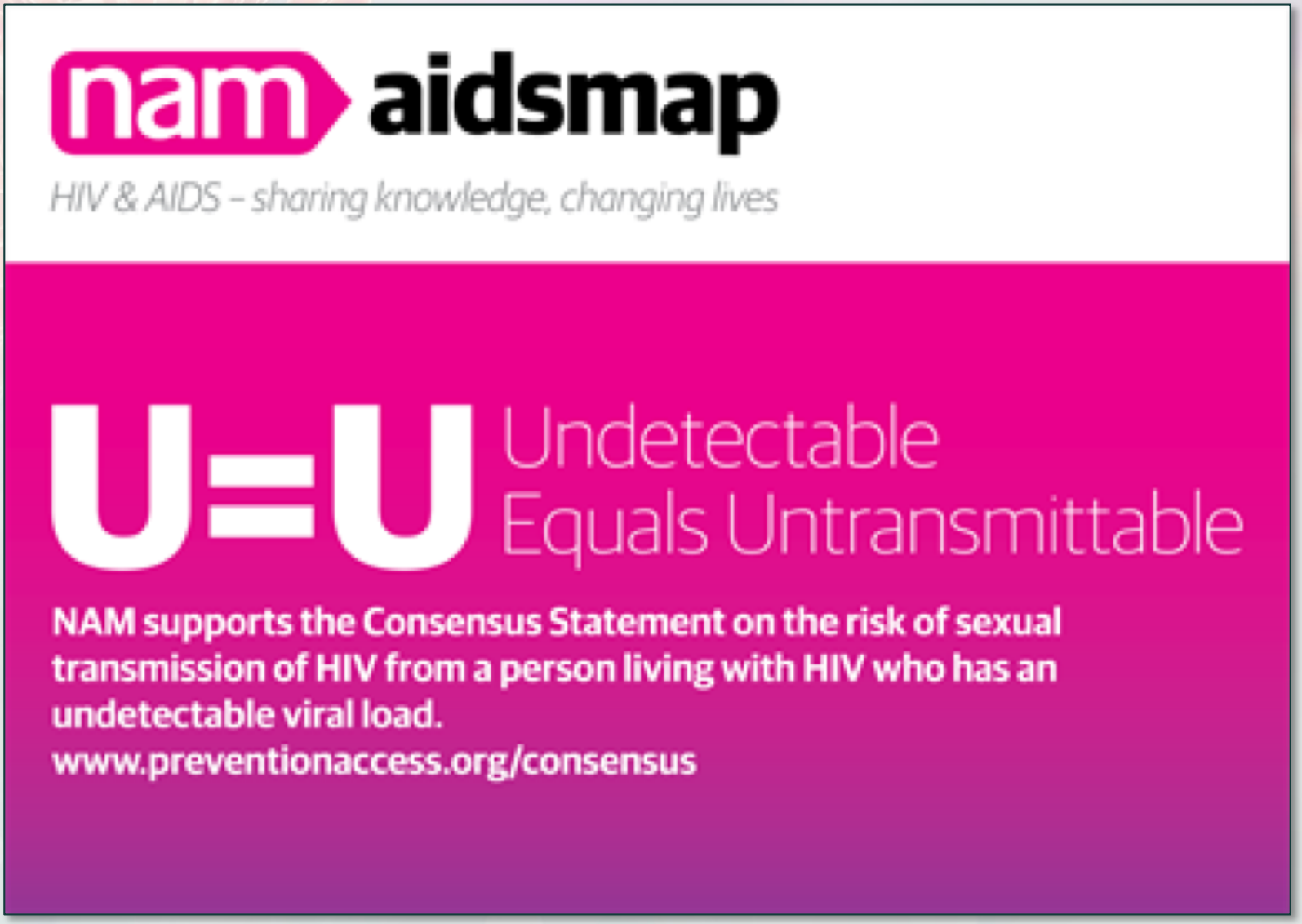
Pilcher CD, et al. JAIDS. 2017;74:44-51.

Trends in STDs and HIV Infection Among MSM in England Diagnosed at STI Clinics



Gill, N. ML3

Is U=U?


nam aidsmap
HIV & AIDS – sharing knowledge, changing lives
U=U
Undetectable
Equals Untransmittable
NAM supports the Consensus Statement on the risk of sexual transmission of HIV from a person living with HIV who has an undetectable viral load.
www.preventionaccess.org/consensus

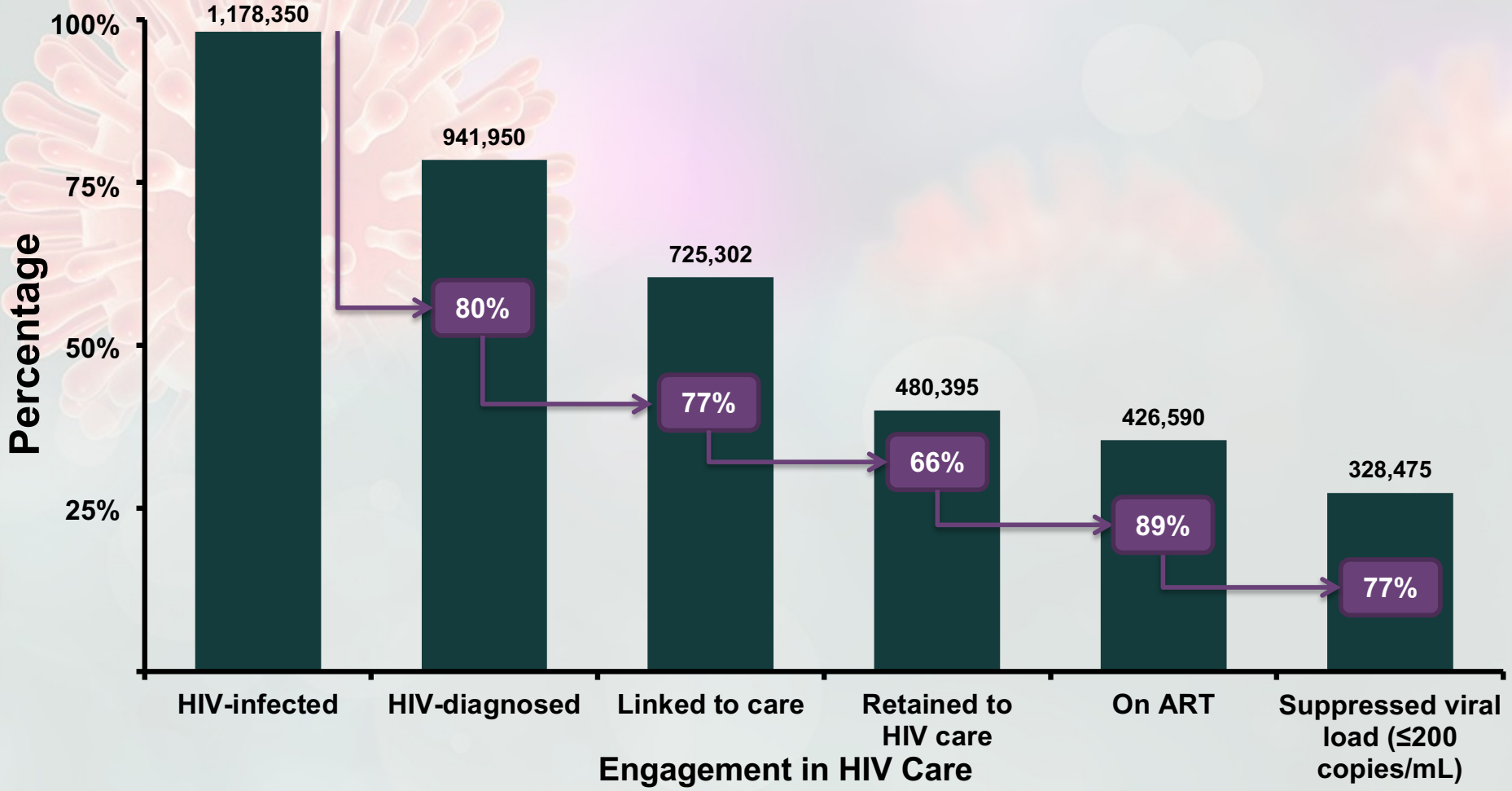


HIV IN 2017:
A YEAR-END SUMMARY AND DISCUSSION OF CRITICAL DEVELOPMENTS

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$U_S = U$

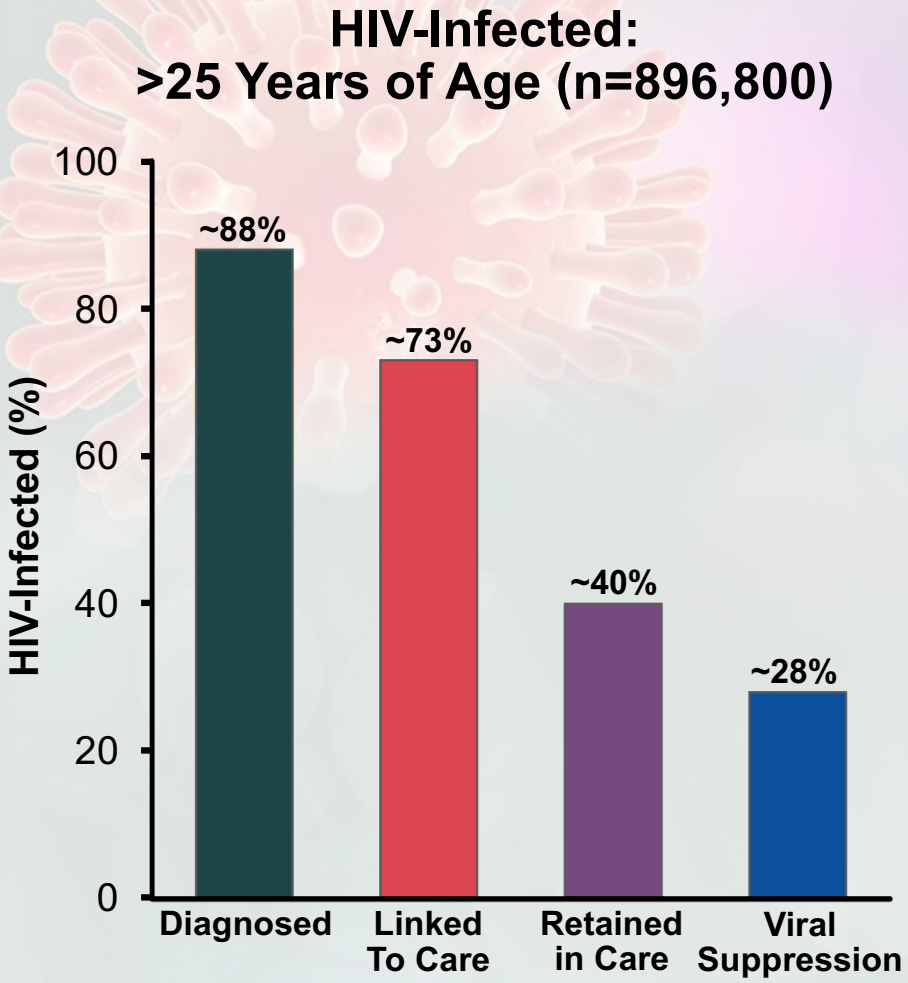
Gaps that Limit Test and Treat for HIV Prevention in US

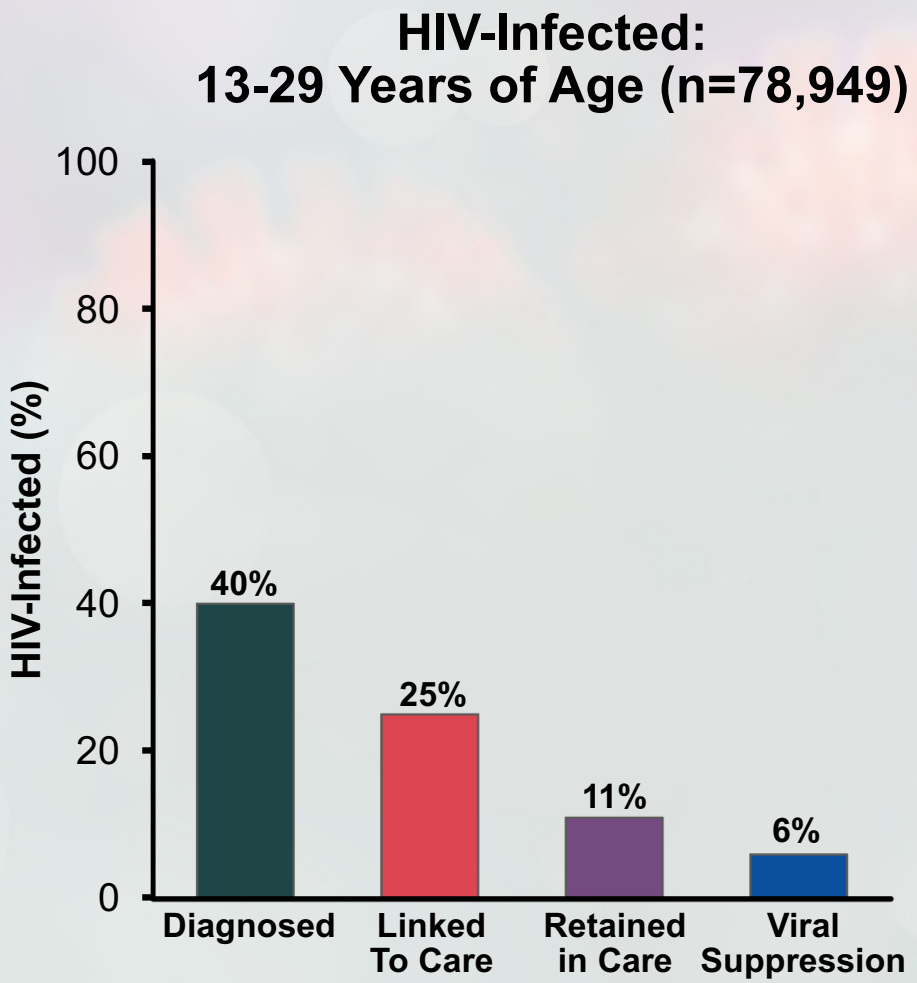


Of all with HIV infection, ~850,000 individuals do not have suppressed HIV RNA (72%)

MMWR (60), 2011.

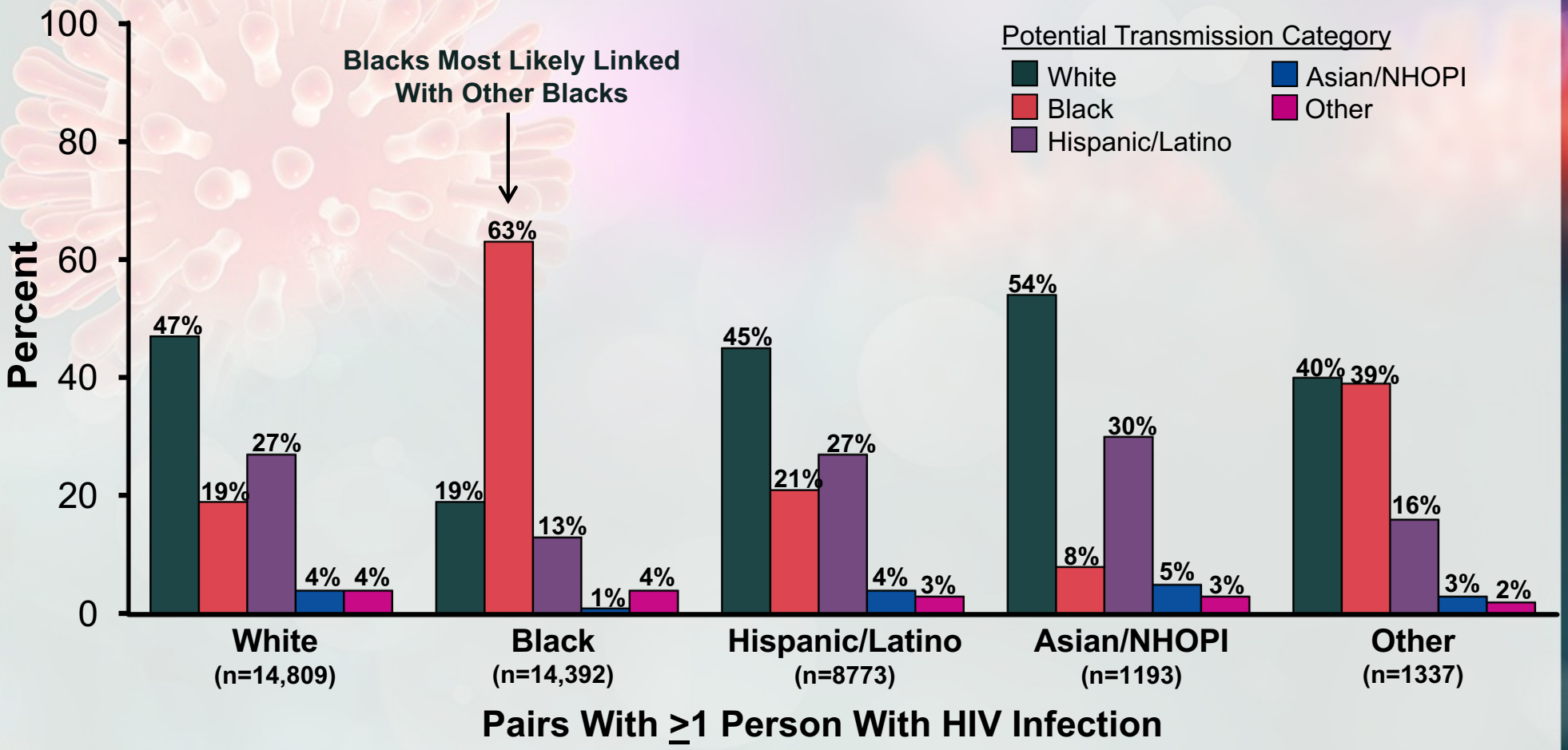
HIV Cascade of Care: Missed Opportunities in the US





Hall HI, et al. *JAMA Intern Med.* 2013;173:1337-1344.
Zanoni BC, et al. *AIDS Patient Care STDS.* 2014;28:128-135.

Transmission Category of Potential Transmission Partners (2001-2012)



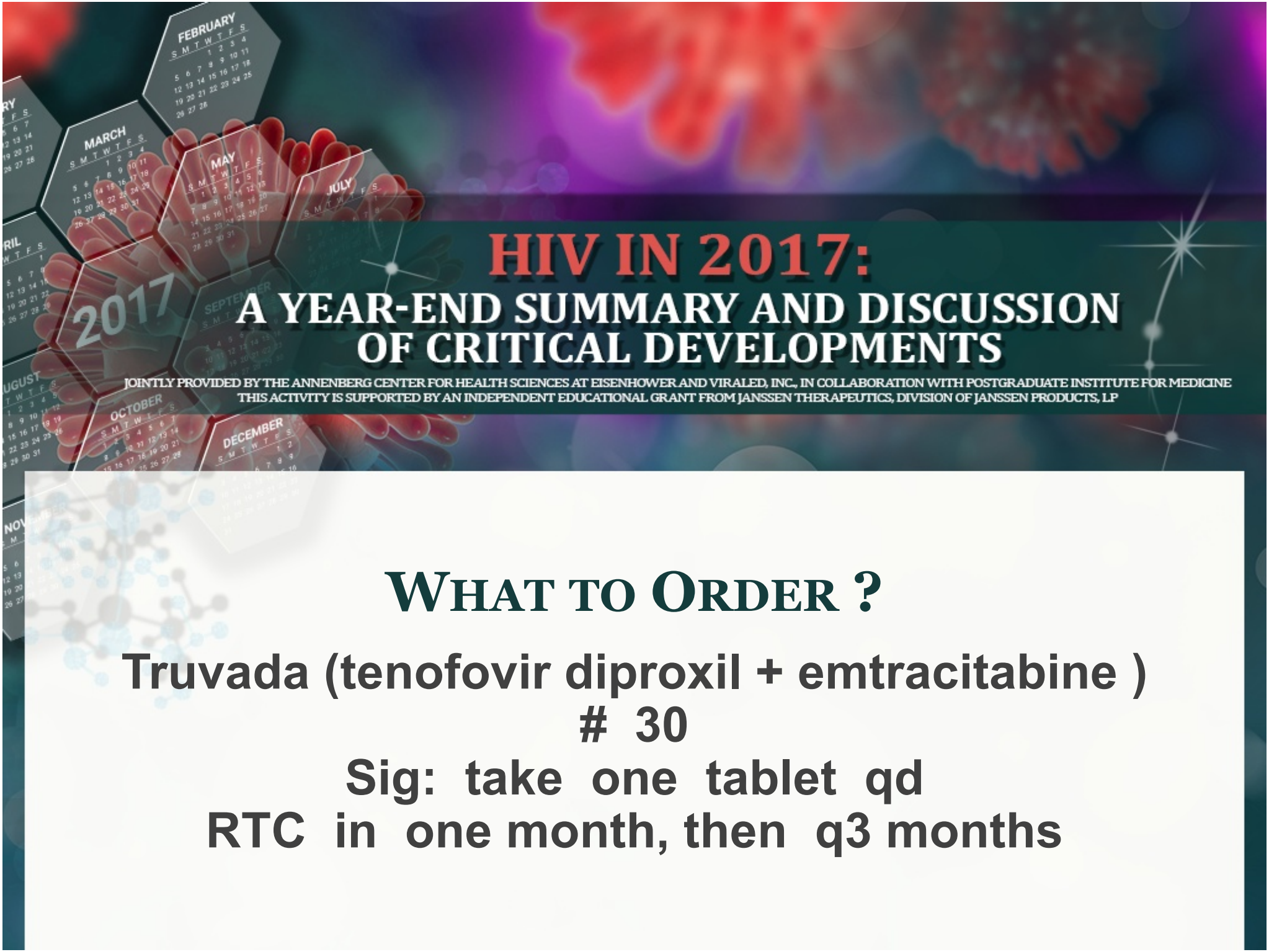
NHOPI: Native Hawaiian or other Pacific Islander.

Oster AM, et al. 21st CROI. Boston, 2014. Abstract 213.

Preventing HIV Transmission in Couples Attempting Conception When the Man has HIV Infection

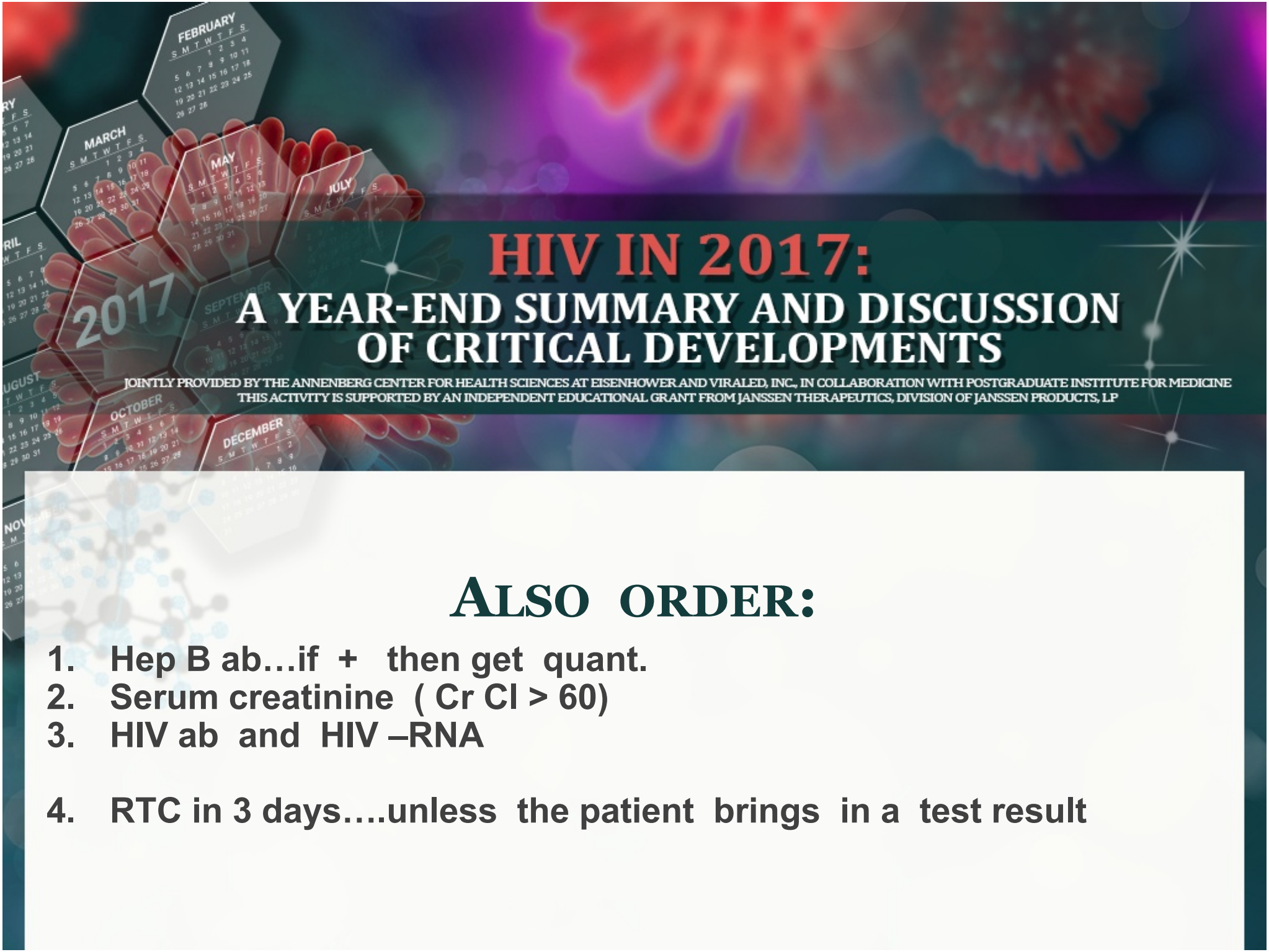
- Men with HIV infection should achieve virologic suppression with effective ART before attempting conception
- Mixed HIV-status couples attempting conception can reduce risk for transmitting HIV by decreasing frequency of sexual contact and limiting condomless intercourse to the time of ovulation
- PrEP can reduce risk for a woman who is attempting conception with an HIV+ man, especially if his viral load is not known or is detectable
- Semen processing with subsequent intrauterine insemination (IUI) or in vitro fertilization (IVF) also substantially reduces transmission of HIV from men to women
- It is important that HCPs regularly assess mixed HIV-status couples' plans for conception; considering factors such as risk tolerance, personal health, costs, and access to health care services, providers can help couples make the best decision for their personal circumstances

Brooks JT, Kawwass JF, Smith DK, et al. Effects of Antiretroviral Therapy to Prevent HIV Transmission to Women in Couples Attempting Conception When the Man Has HIV Infection – United States, 2017. MMWR Morb Mortal Wkly Rep 2017;66:859–60.



WHAT TO ORDER ?

Truvada (tenofovir diproxil + emtracitabine)
 # 30
Sig: take one tablet qd
RTC in one month, then q3 months



ALSO ORDER:

1. Hep B ab…if + then get quant.
2. Serum creatinine (Cr Cl > 60)
3. HIV ab and HIV –RNA

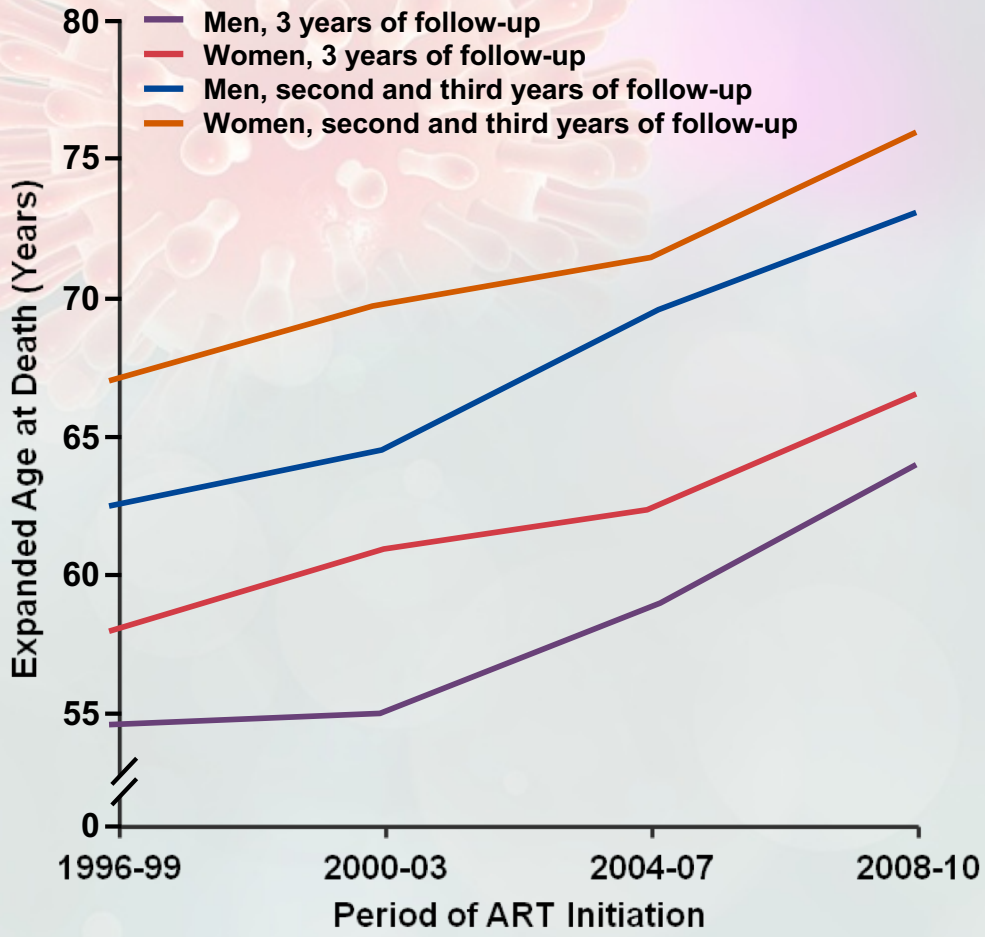
4. RTC in 3 days….unless the patient brings in a test result



Overview of ART

ART-CC: Life Expectancy for People with HIV

- Expected age at death of men and women living with HIV starting ART aged 20 years, by period of initiation*



A 20-year-old patient starting antiretroviral therapy (ART) in 2008–10, with a CD4 count >350, is projected to survive until age 78

*Estimates of life expectancy were based on mortality during the first 3 years of follow-up and the second and third years of follow-up. Data are for all regions.

Antiretroviral Therapy Cohort Collaboration. Lancet HIV. 2017;4(8):e349-e356.

DHHS Guidelines: October 2017 Update

Recommended Initial Regimens for Most People with HIV

Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use

- INSTI + 2 NRTIs:DTG/ABC/3TC — if HLA-B*5701 negative
- DTG + tenofovir/FTC
- EVG/c/tenofovir/FTC
- RAL + tenofovir/FTC

https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/11/what-to-start



NEED FOR SUPPORT GROUPS

1. 46% of OASIS young MSM's become infected after their mother's "kick them out" because she can't handle their homosexuality
2. 64% of OASIS MSM's give a history of adolescent molestation



Studies in Treatment-Naïve Patients

Bictegravir: Background

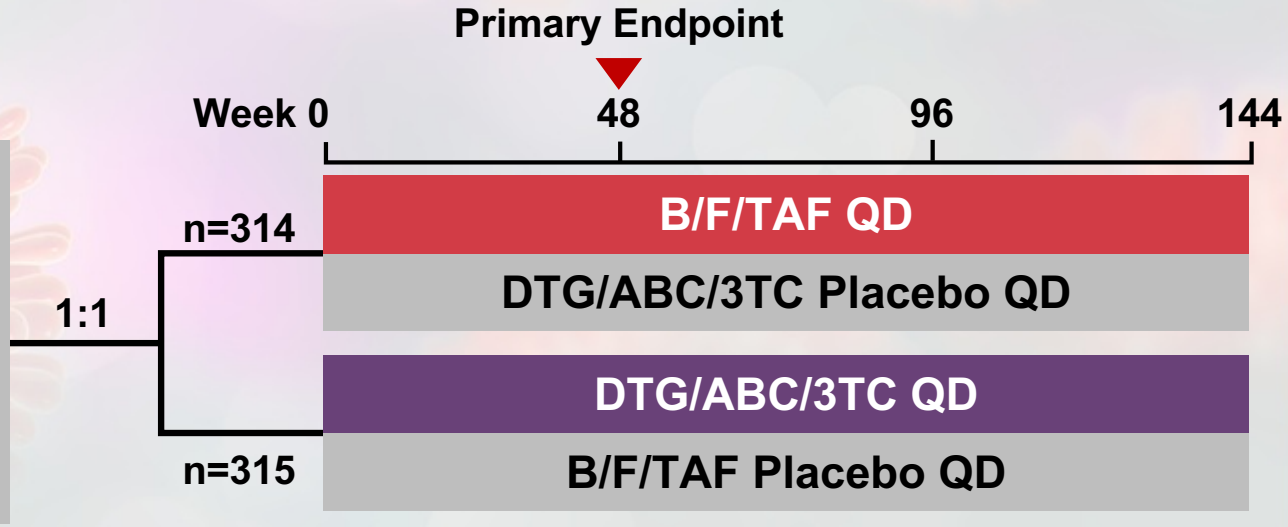
- Bictegravir (BIC; GS-9883) is a novel, once-daily, INSTI
  - Potent in vitro activity against wild-type and most INSTI-resistant variants[1–4]
  - Low potential for drug interactions
  - BIC plasma half-life approximately 18 hours without boosting
  - Long "dissociation constant" from HIV-1 integrase-DNA complexes[5]
- A 10 day study of BIC monotherapy in HIV-1 infected patients demonstrated rapid decline in HIV-1 RNA >2 $\log_{10}$ copies/mL[6]
- Currently in clinical development co-formulated with tenofovir alafenamide (TAF) and emtricitabine (FTC) for the treatment of HIV-1 infection

1. Jones G, et al. ASM Microbe 2016, poster 1673;
2. Lazerwith SE, et al. ASM Microbe 2016, poster 414;
3. Tsiang M, et al. ASM Microbe 2016, poster 1643;
4. White K, et al. 14th European Meeting on HIV & Hepatitis 2016, abstr O-01;
5. White K, et al. HIV Drug Therapy 2016, poster P025;
6. Gallant J, et al. ASM Microbe 2016, poster PW-030.

GS-1489: Study Design and Baseline Characteristics

Treatment-Naïve Adults

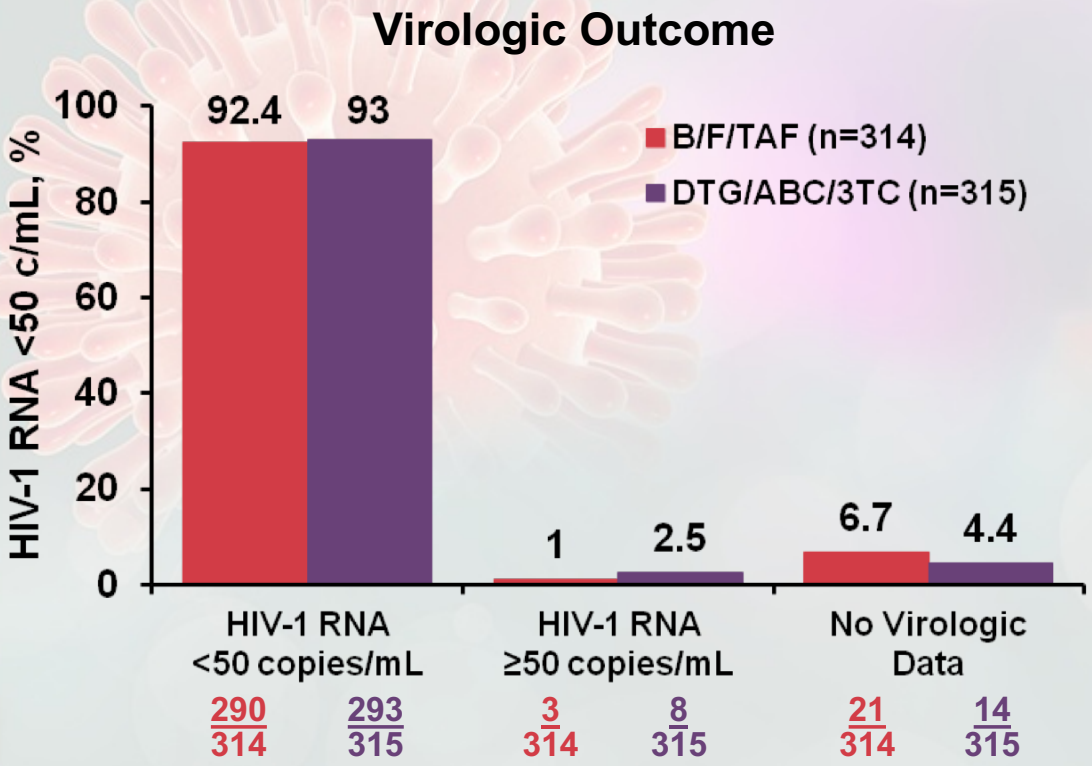
- HIV-1 RNA ≥ 500 copies/mL
- $eGFR_{CG}$ ≥ 50 mL/min
- HLA B*5701 negative
- Negative for chronic HBV

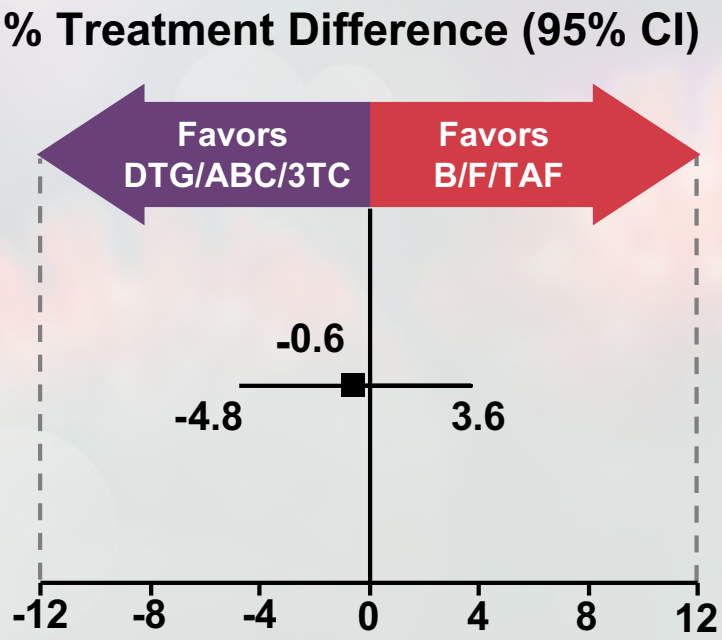


	B/F/TAF n=314	DTG/ABC/3TC n=315
Age, median years (range)	31 (18–71)	32 (18–68)
Male, %	91	90
Race/ethnicity, %		
Black or African descent	36	36
Hispanic/Latino ethnicity	23	21
HIV-1 RNA, median log_{10} c/mL (IQR)	4.42 (4.03, 4.87)	4.51 (4.04, 4.87)
HIV-1 RNA >100,000 c/mL, %	17	16
CD4 cell count, median cells/μL (IQR)	443 (299, 590)	450 (324, 608)
CD4 count <200 cells/μL, %	11	10
Asymptomatic HIV infection, %	91	91
$eGFR_{CG}$, median mL/min (IQR)	126 (108, 146)	123 (107, 144)

Gallant J, et al; The Lancet , Volume 390 , Issue 10107 , 2063 – 2072.

GS-1489 Study: Results





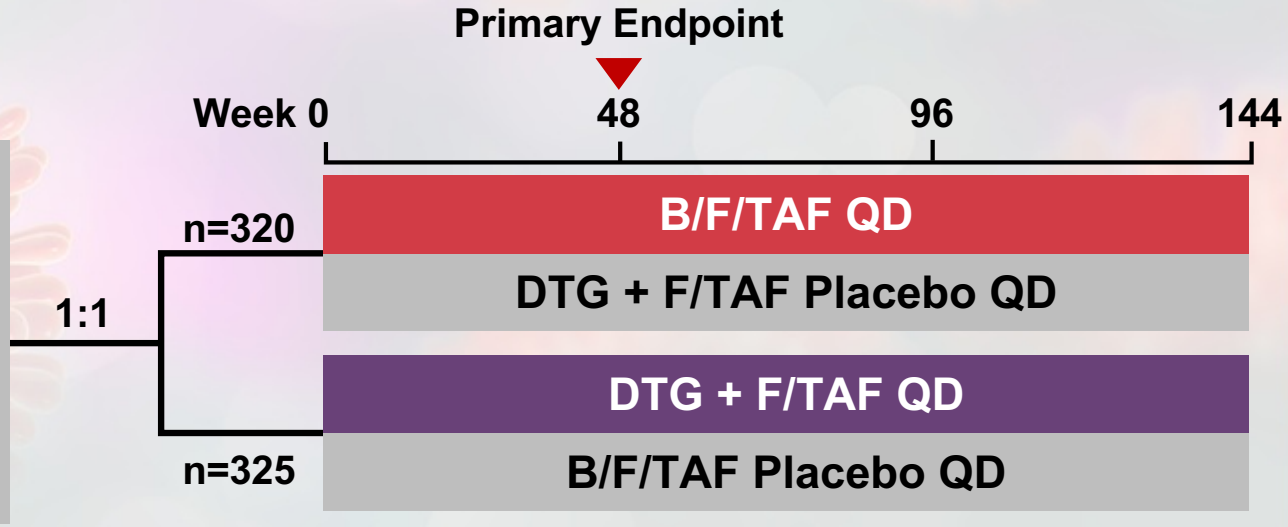
- BF-TAF non-inferior to DTG/ABC/3TC
  - No resistance in either study arm
- Lipids not significantly different
- No drug-related renal events
- Significantly less nausea and minor adverse events with BF-TAF

Gallant J, et al; The Lancet , Volume 390 , Issue 10107 , 2063 – 2072.

GS-1490: Study Design and Baseline Characteristics

Treatment-Naïve Adults

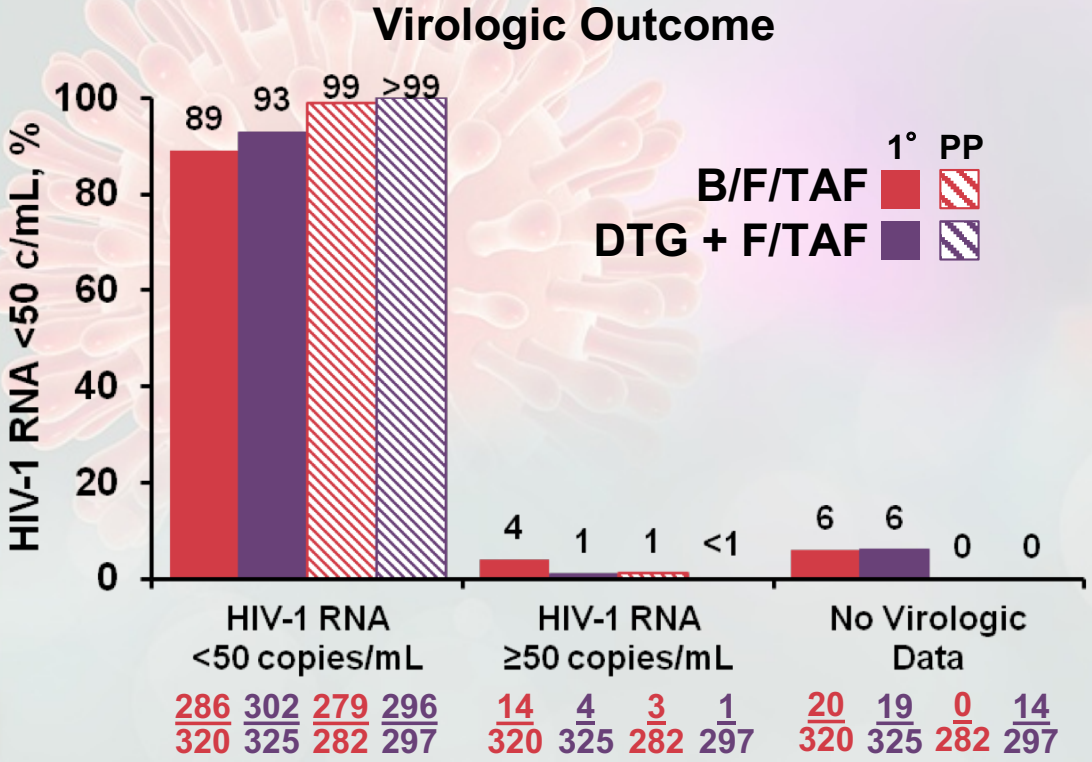
- HIV-1 RNA ≥500 copies/mL
- $eGFR_{CG}$ ≥30 mL/min

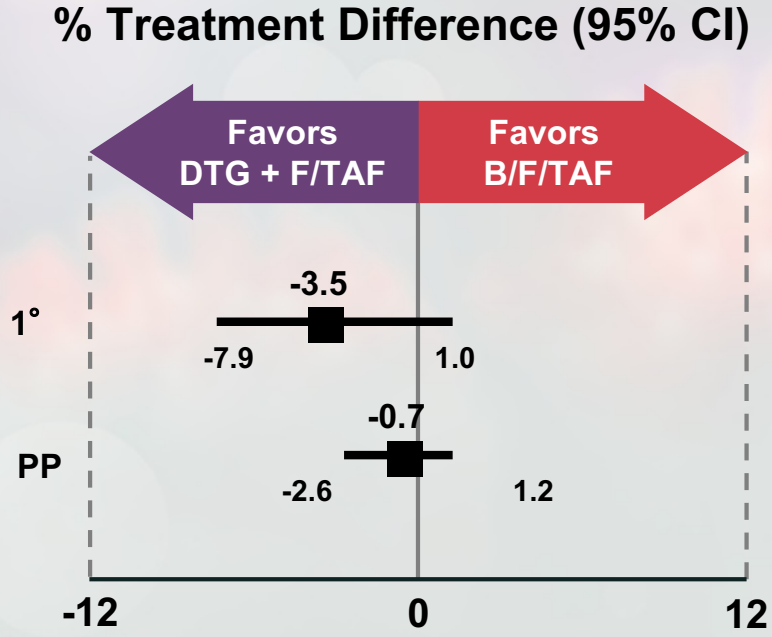


	B/F/TAF (n=320)	DTG + F/TAF (n=325)
Median age, y (range)	33 (18–71)	34 (18–77)
Male, %	88	89
Race/ethnicity, %		
Black or African descent	30	31
Hispanic/Latino	26	25
Median HIV-1 RNA, log_{10} copies/mL (Q1, Q3)	4.43 (3.95, 4.90)	4.45 (4.03, 4.84)
HIV-1 RNA >100,000 copies/mL, %	21	17
Median CD4 cell count, cells/μL (Q1, Q3)	440 (289, 591)	441 (297, 597)
CD4 count <200 cells/μL, %	14	10
HBV*/HCV† coinfection, %	3/2	2/2
Median $eGFR_{CG}$, mL/min (Q1, Q3)	120.4 (100.8, 141.8)	120.6 (102.8, 145.1)

Sax P, et al; The Lancet , Volume 390 , Issue 10107 , 2073 - 2082 .

GS-1490 Study: Results





- Bictegravir non-inferior to dolutegravir
- Results consistent in sensitivity analyses

Sax P, et al; The Lancet , Volume 390 , Issue 10107 , 2073 - 2082 .

DORAVIRINE

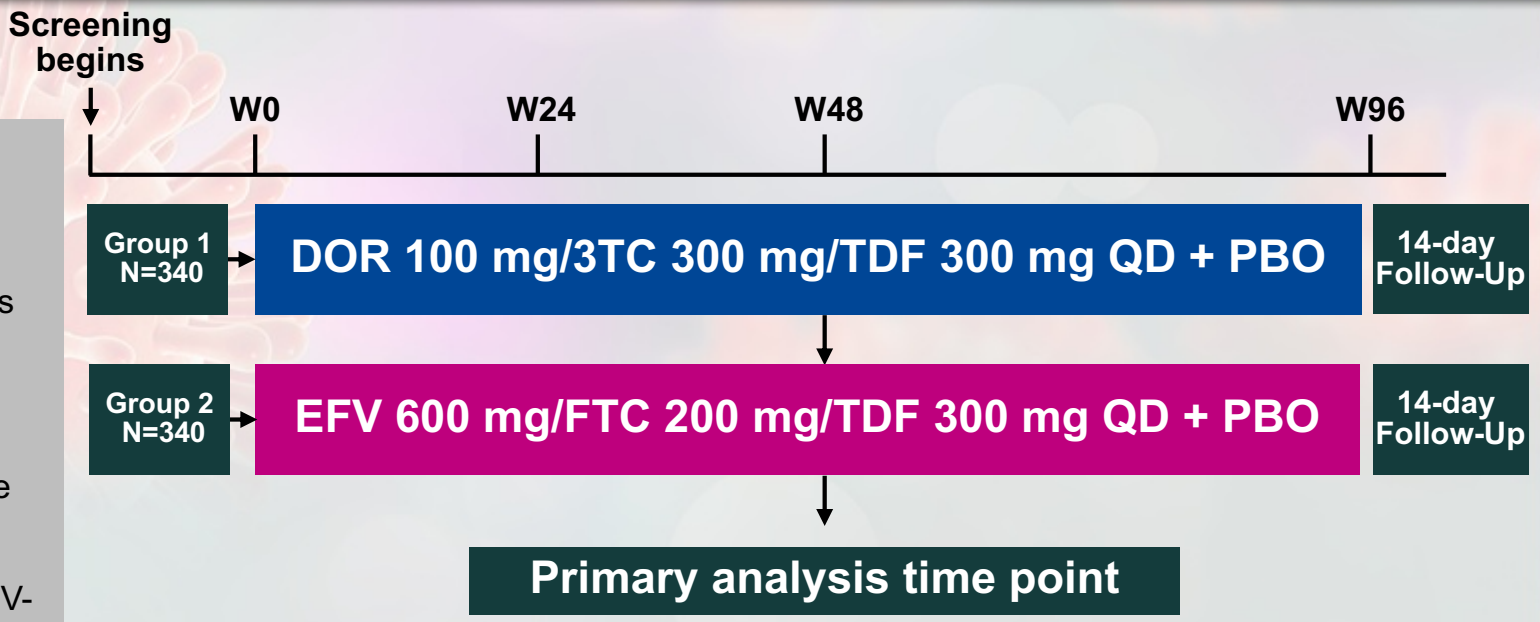
- Doravirine is a novel, next generation non-nucleoside reverse transcriptase inhibitor (NNRTI)
  - Unique resistance profile with in vitro activity against wild-type HIV-1 and the most prevalent NNRTI resistance mutations (RT K103N, Y181C, G190A, K103N/Y181C, and E138K)[1]
  - Low potential for drug-drug interactions[2]
  - Dosed once daily without regard to food[3]
  - Being developed as a single entity and fixed-dose combination with tenofovir disoproxil fumarate (TDF) and lamivudine (3TC)
- Doravirine 100 mg demonstrated favorable efficacy and a superior neuropsychiatric profile vs efavirenz 600 mg QD in Phase 2b[4]

1 Feng et al, Antimicrob Agents Chemother. 2016 Mar 25;60(4):2241-7.
2 Anderson et al, Antivir Ther. 2015;20(4):397-405.
3 Behm et al ICAAC 2015, Abstract H-778.
4 Gatell et al, J Int AIDS Soc. 2014; 17(4Suppl 3): 19532.

DRIVE-AHEAD: STUDY DESIGN

Key Entry Criteria:

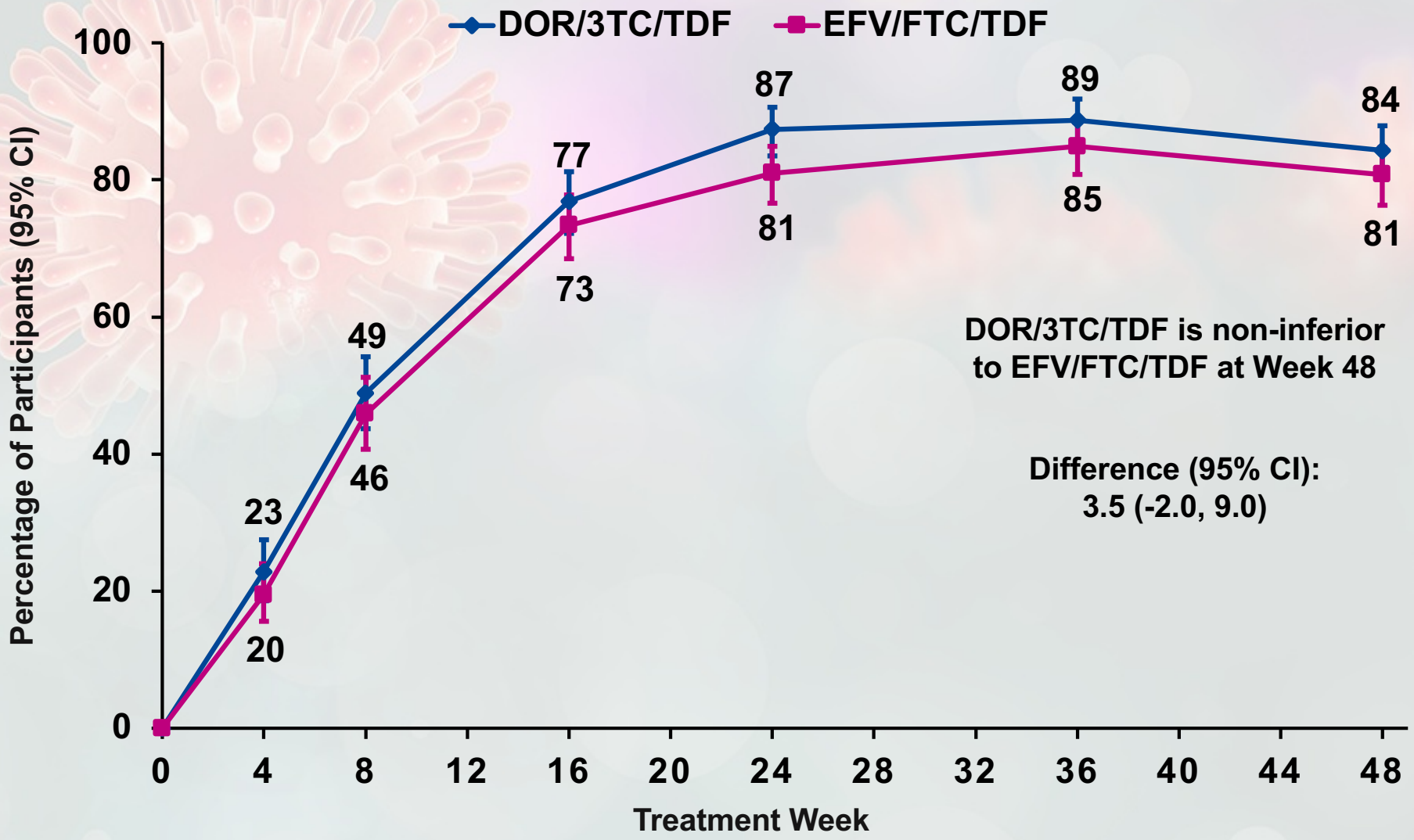
- HIV-1 RNA ≥1000 copies/mL within 45 days before Day 1
- Antiretroviral-naïve
- No genotypic resistance to any study drugs
- Stratification factors: HIV-1 RNA >100,000 copies/mL and chronic hepatitis B or C infection status



- Early discontinuation and/or virologic failure confirmation visits if applicable
- At Week 96, eligible patients may opt to continue for additional 96 weeks (study extension phase)

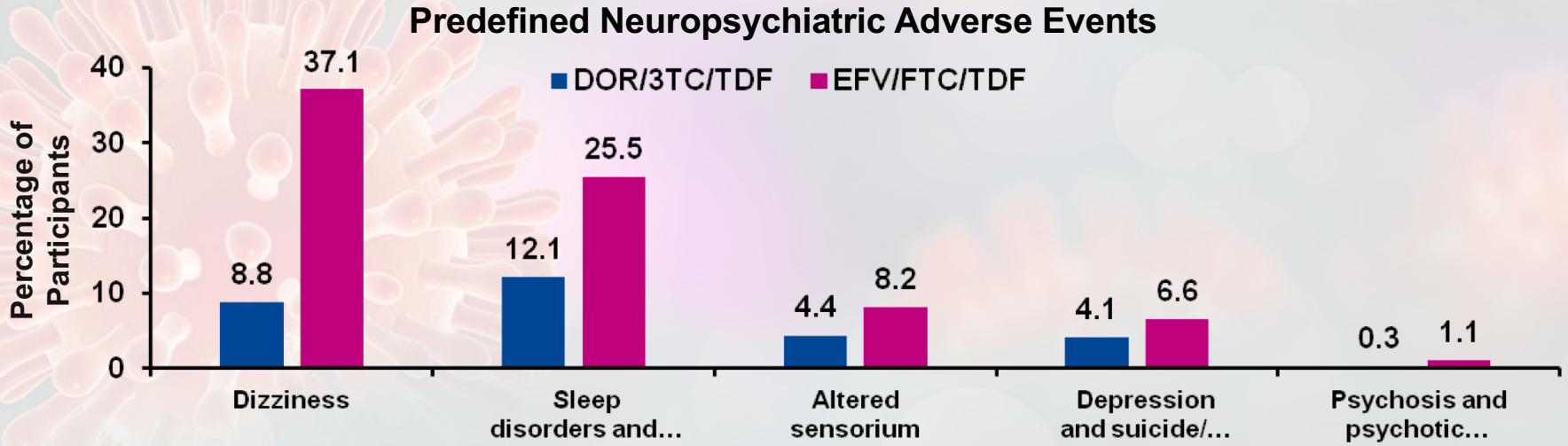
Squires K, et al; 9th IAS, Paris, France, July 23-26, 2017; Abst. TUAB0104LB.

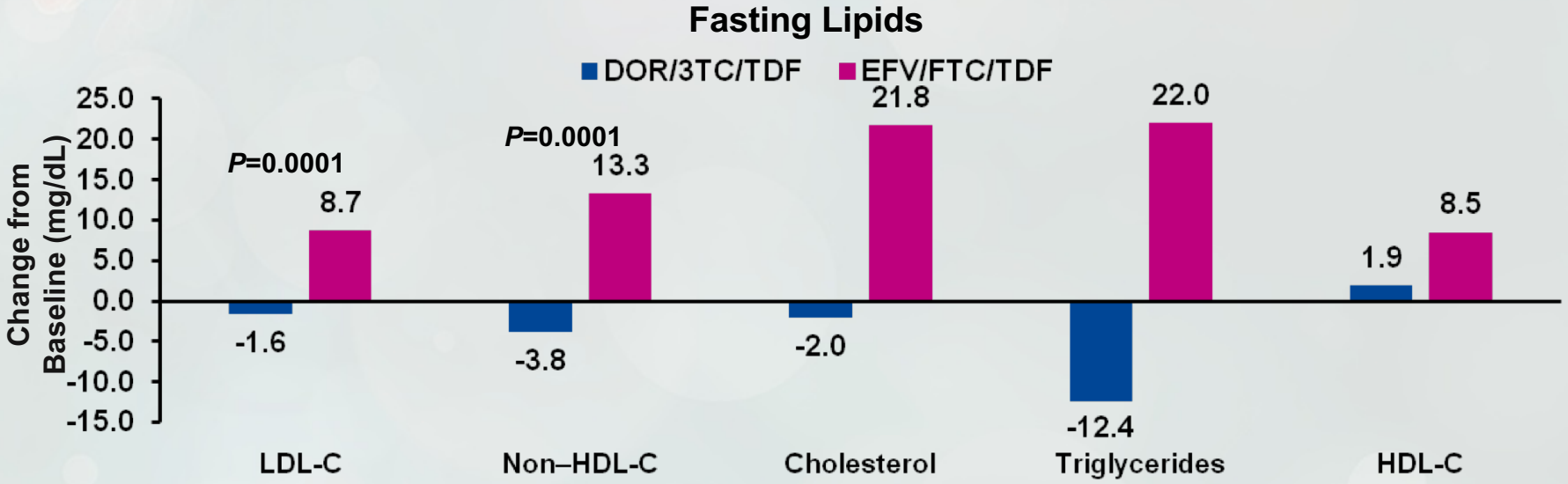
DRIVE-AHEAD STUDY: EFFICACY



Squires K, et al; 9th IAS, Paris, France, July 23-26, 2017; Abst. TUAB0104LB.

Drive-Ahead Study: Tolerability and Safety at Week 48





DOR/3TC/TDF is superior to EFV/FTC/TDF

Squires K, et al; 9th IAS, Paris, France, July 23-26, 2017; Abst. TUAB0104LB.

ACTG 5353: Study Design and Baseline Characteristics

- Single-arm study of DTG + 3TC in treatment-naïve study subjects
- Eligible:
  - HIV RNA < 500,000; minimum 25% with HIV RNA >100,000
  - No resistance to any ART drug class (including integrase) on screening
  - Negative hepatitis B surface antigen
- Baseline characteristics:

		Baseline HIV-1 RNA Category	
		>100,000 cpm (N=37)	≤100,000 cpm (N=83)
Age (years)	Median (Q1, Q3)	30 (25, 40)	30 (24, 42)
Sex	Male	89%	86%
Race/Ethnicity	White Non-Hispanic Black Non-Hispanic Hispanic	27% 32% 35%	29% 43% 23%
CD Count (cells/mm^3)	Median (Q1, Q3) <200	350 (173, 458) 30%	413 (328, 671) 6%
HIV-1 RNA (log_{10} cpm) (cpm)	Median (Q1, Q3) <10,000 10,000 -99,999 100,000 – 200,000 >200,000	5.23 (5.09, 5.46) -- -- 62% 38%	4.23 (3.82, 4.65) 42% 58% -- --

Taiwo B, et al; 9th IAS, Paris, France, July 23-26, 2017; Abst. MOAB0107LB.

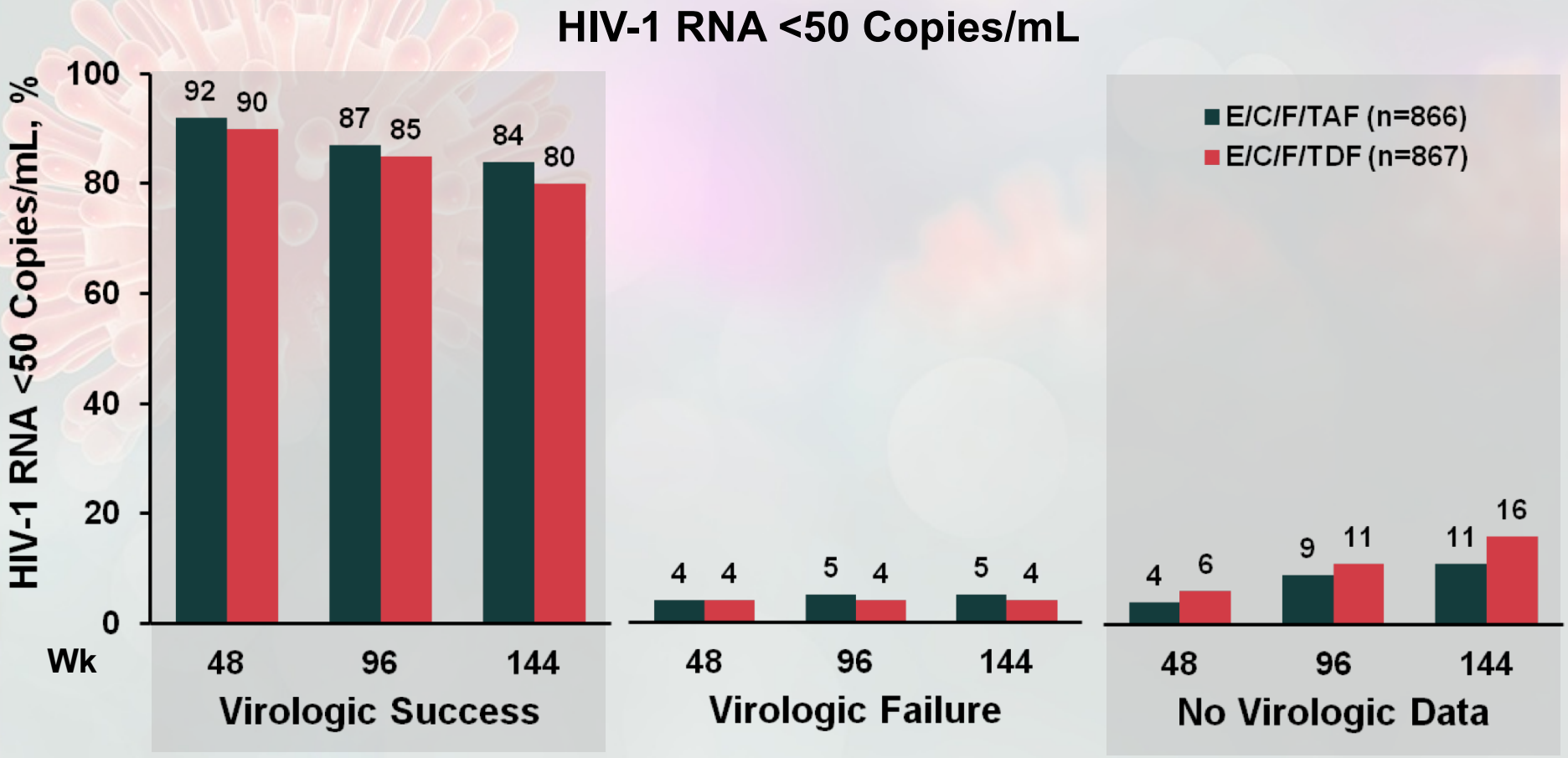
ACTG 5353: Results at 24 Weeks

	Baseline HIV-1 RNA		
	>100,000 cpm N=37	**≤100,000 cpm N=83**	**Total N=120**
Virologic success HIV-1 RNA <50 cpm **[95% CI]**	**33 (89%)** **[75%, 97%]**	**75 (90%)** **[82%, 96%]**	**108 (90%)** **[83%, 95%]**
Virologic non-success HIV-1 RNA ≥50 cpm Discontinued study treatment for other reasons while HIV RNA ≥50	**3 (8%)** 3 0	**2 (2%)*** 0 2	5 (4%) 3 2
No virologic data in window Discontinued study treatment for other reasons On study but missing data in window	**1 (3%)** 1 0	**6 (7%)** 5 1	**7 (6%)** 6 1

*One study subject with poor adherence developed M184V, and R263R/K mixture

Taiwo B, et al; 9th IAS, Paris, France, July 23-26, 2017; Abst. MOAB0107LB.

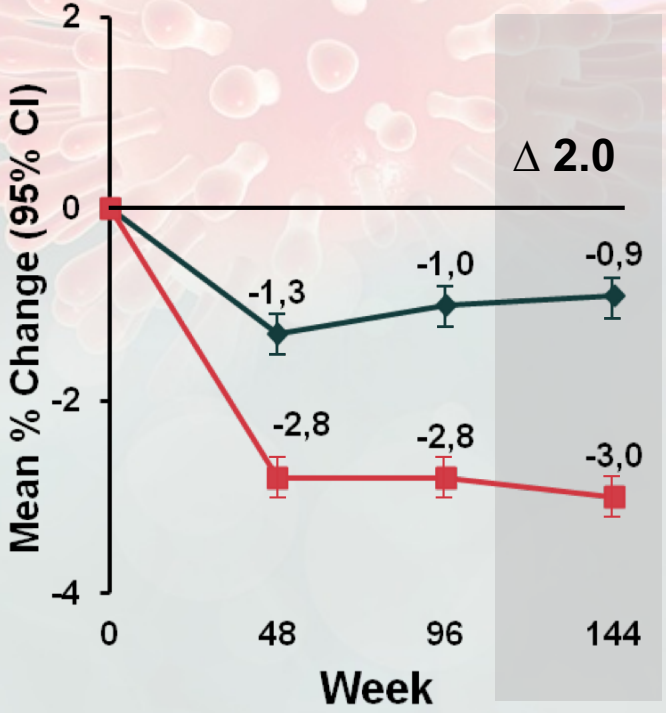
TAF vs. TDF (FTC/EVG/c) in Treatment-Naïve: 144 Weeks



- At Week 144, E/C/F/TAF was superior to E/C/F/TDF in efficacy difference at both <50 copies/mL; 4.2% (95% CI 0.6%, 7.8%; p=0.02) and <20 copies/mL: 5.4% (95% CI 1.5%, 9.2%; p=0.01)

Arribas J, et al. 24th CROI; Seattle, WA; February 13-16, 2017. Abst. 453.

TAF vs. TDF (FTC/EVG/c) in Treatment-Naïve: Bone and Renal Endpoints

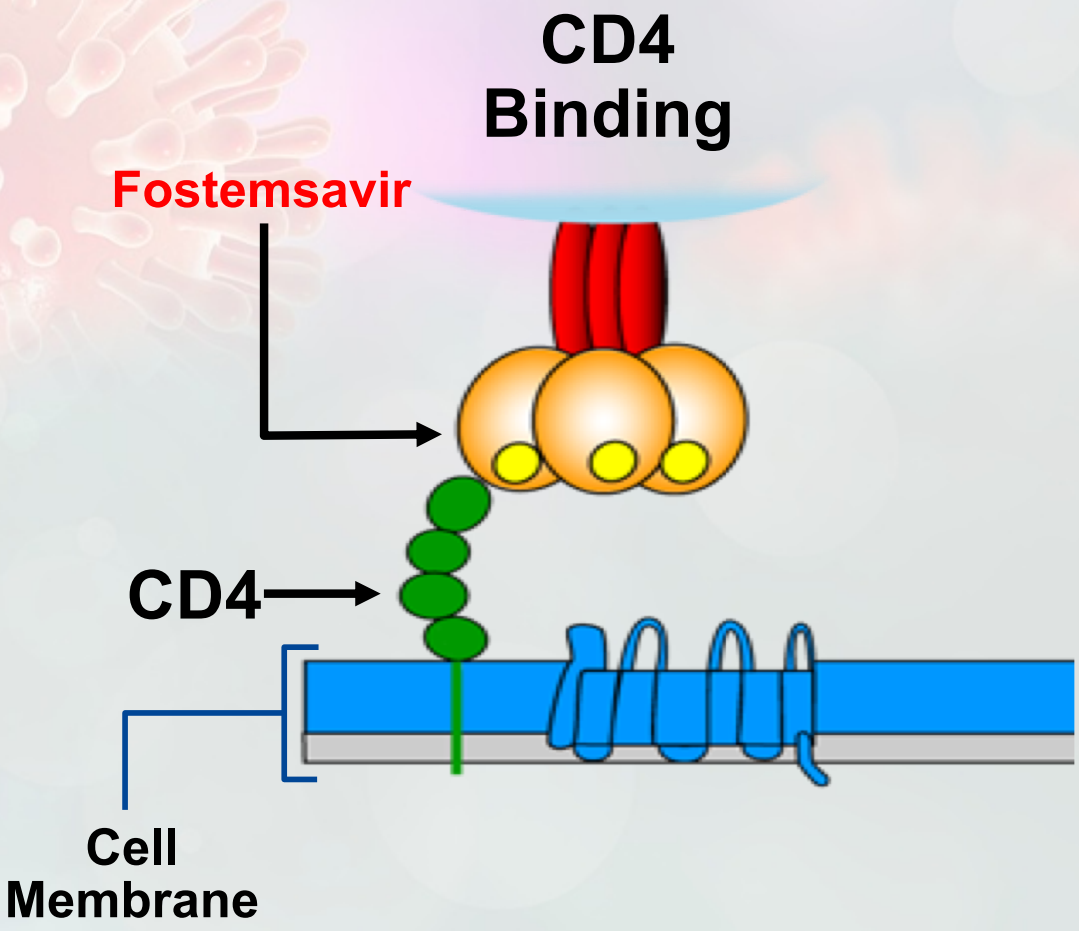


Renal AE D/C, n	E/C/F/TAF n=866	E/C/F/TDF n=867
Total	**0**	**12**
Proximal renal tubulopathy	0	4
Increased creatinine/decreased eFGR	0	3
Renal failure	0	2
Nephropathy	0	1
Proteinuria	0	1
Bladder spasm	0	1

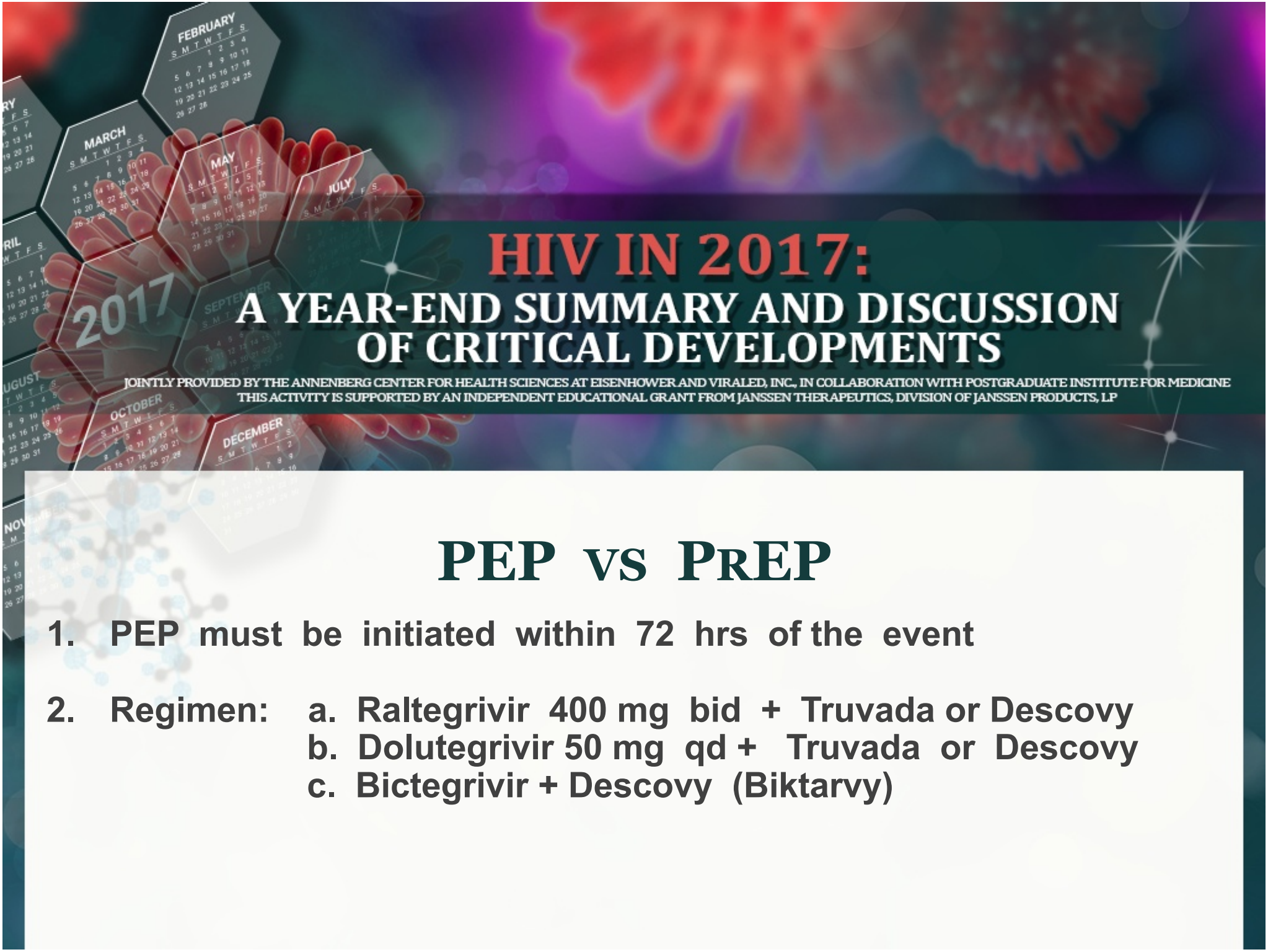
6 patients discontinued due to decrease in BMD

Arribas J, et al. 24th CROI; Seattle, WA; February 13-16, 2017. Abst. 453.

FOSTEMSAVIR:
ATTACHMENT INHIBITOR



Lataillade M, et al; 16th EACS, Milan, Italy, October 25-27, 2017; Abst. PS8/5.



PEP vs PrEP

1. PEP must be initiated within 72 hrs of the event

2. Regimen:
   a. Raltegrivir 400 mg bid + Truvada or Descovy
   b. Dolutegrivir 50 mg qd + Truvada or Descovy
   c. Bictegrivir + Descovy (Biktarvy)



OCCUPATIONAL VS NON-OCCUPATIONAL

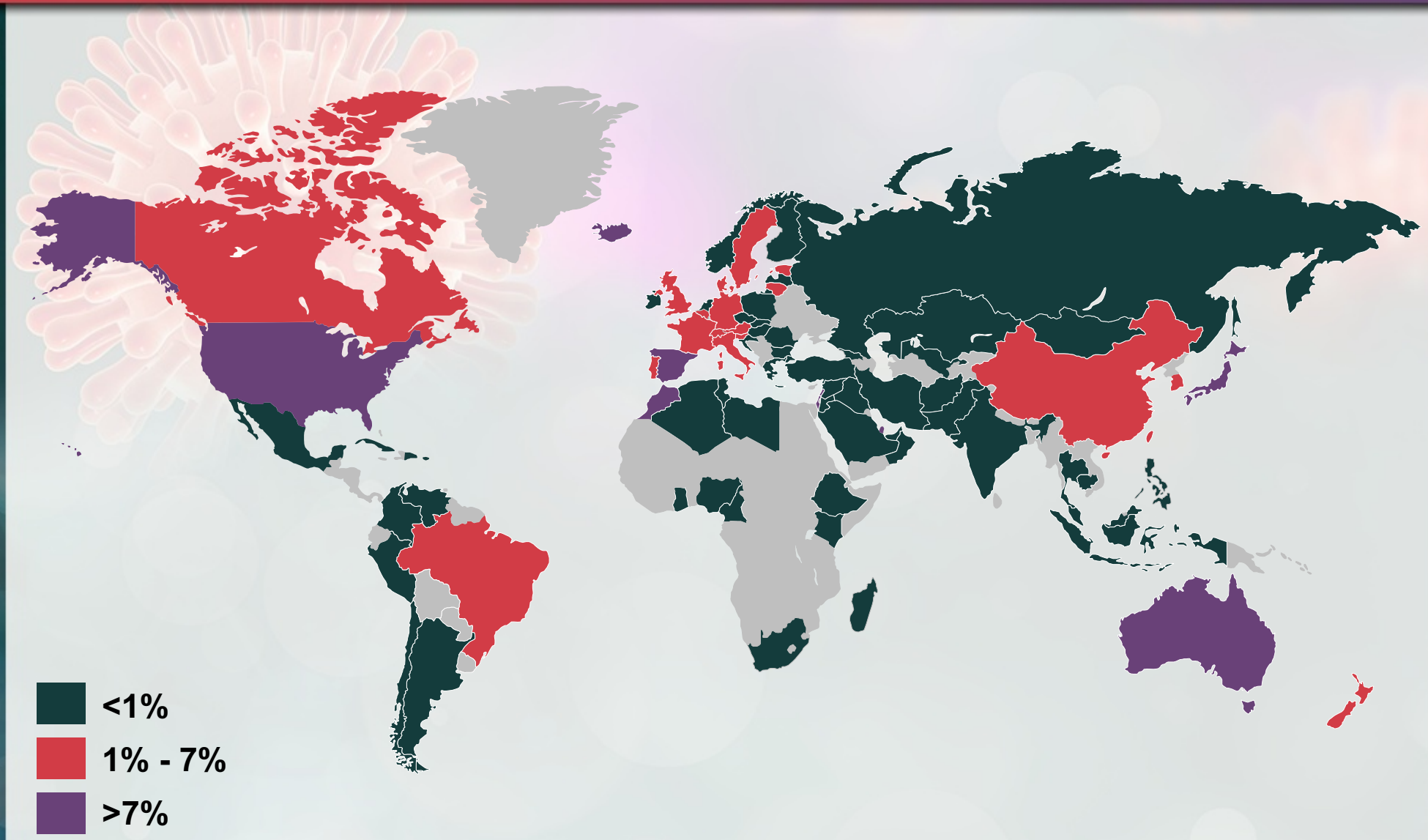
1 Occupational is usually covered by Workmen's Comp

2. Non-Occupational…….+/- the Individual's insurance
LA County …but they need to be seen within 72 hrs



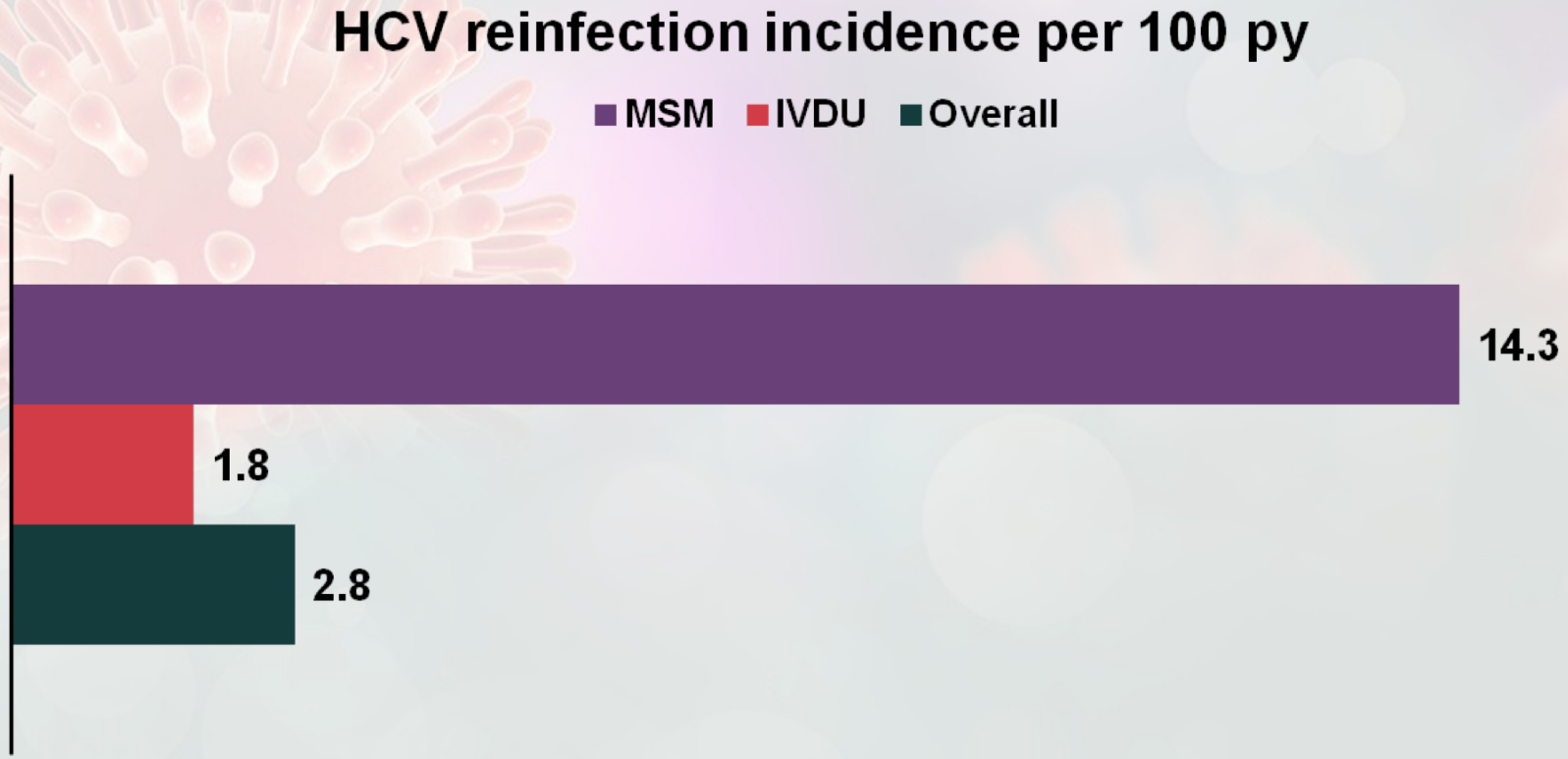
Studies in Hepatitis

Hepatitis C: Net Cure Rates in 2016, by Country SVR + Deaths – New Infections



Hill et al. J Vir Erad, July 2017, 3: 117-123; Hill A et al. IAS Paris; 23-26 July 2017; Paris, France; Abst. MOSA0808.

HCV Reinfection Incidence

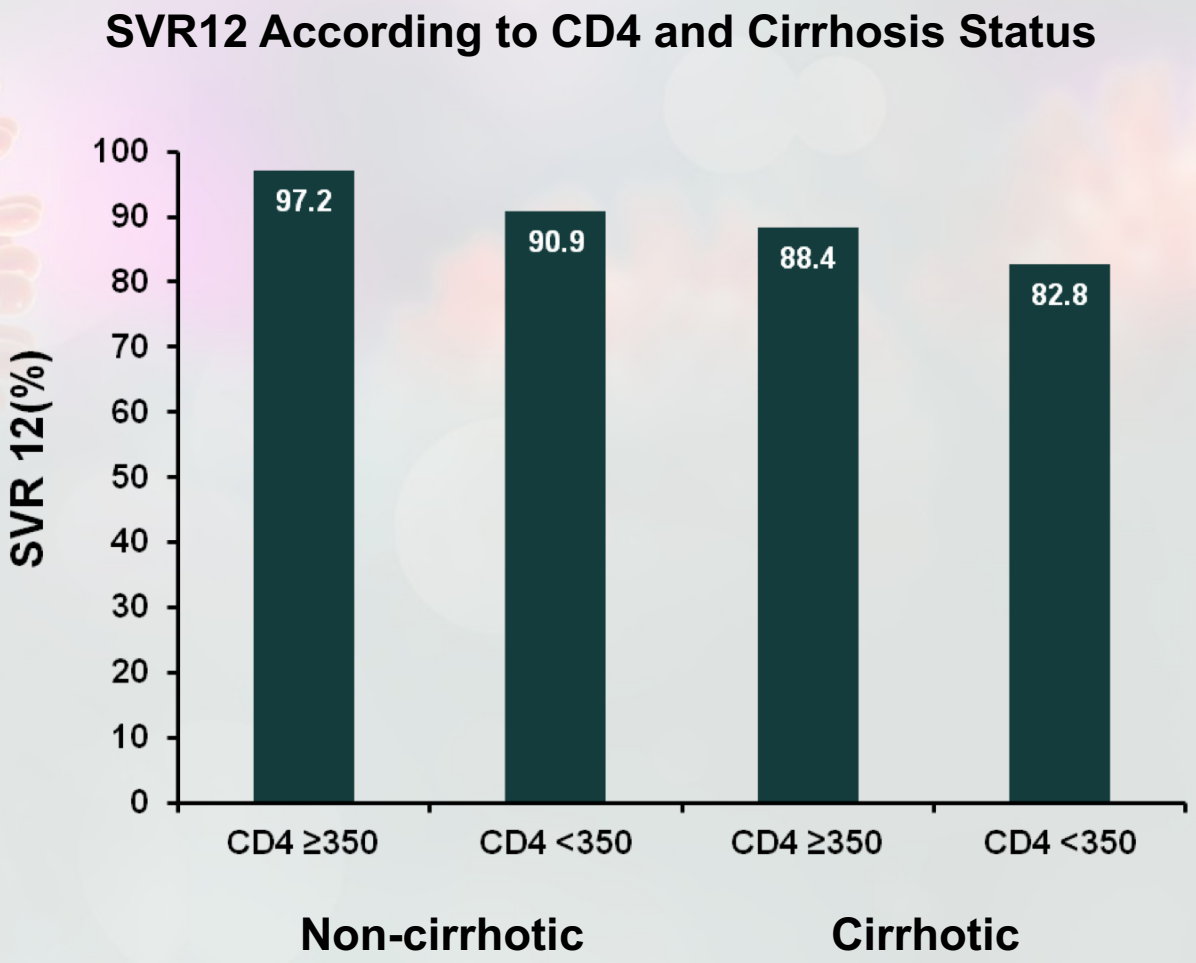


Follow-up time was 1141 person-years overall (median: 26 weeks per patient; range 4-205 weeks)
390 py in IVDU, 175 py in MSM

Ingiliz P, et al; 16th EACS, Milan, Italy, October 25-27, 2017; Abst. PS9/5.

DAA Similarly Effective in HIV Coinfection?

- GECCO Cohort (9 German centres)
- n=1,505
- 1,156 mono-, 349 coinfected
- Liver cirrhosis 29% (31% vs. 22%)
- Overall-SVR 95%, 95% monoinfected, 94% coinfected



Boesecke C, et al. 24th CROI; Seattle, WA; February 13-16, 2017. Abst. 551.

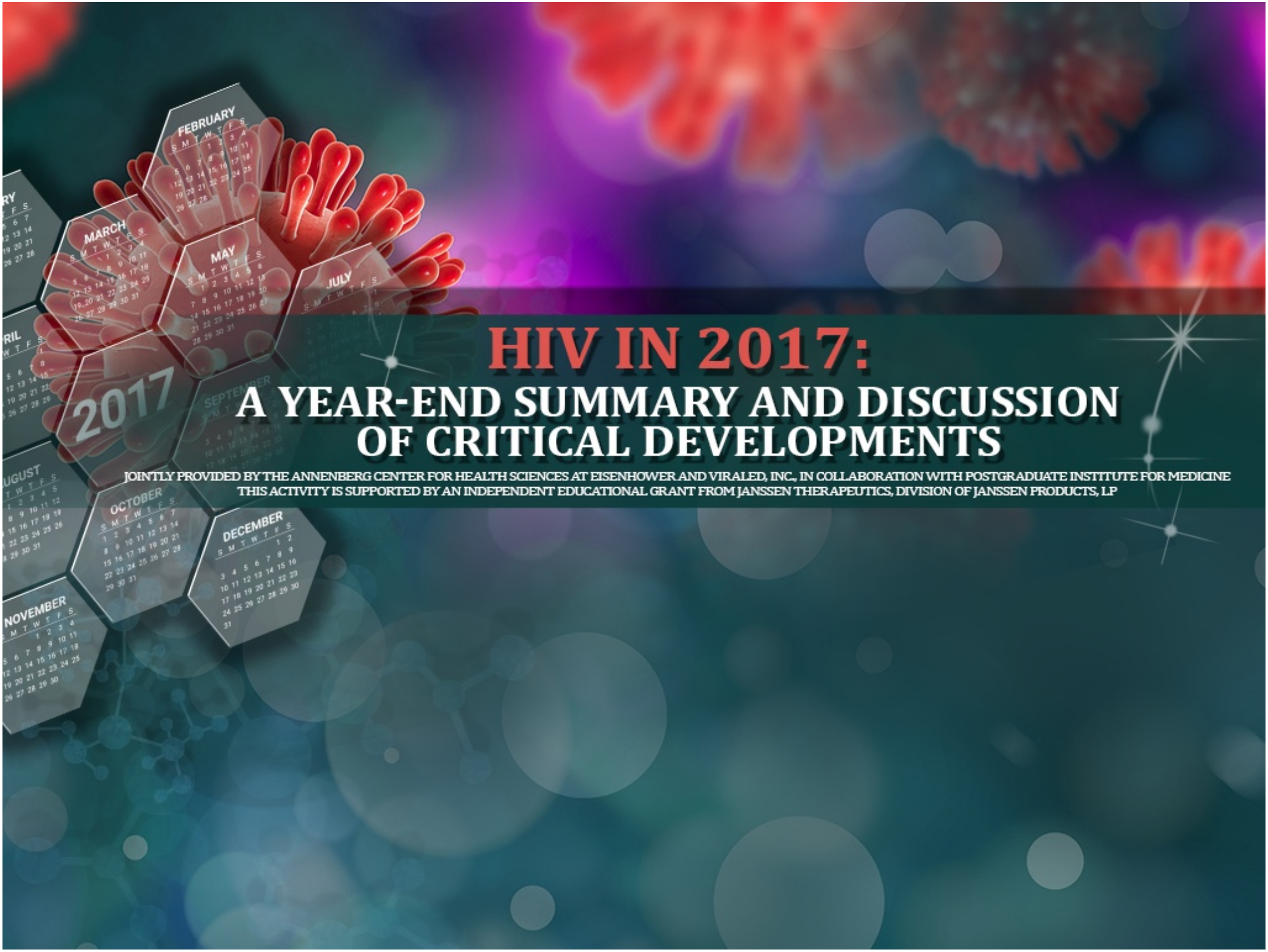
DDI Summary by HIV ARV and DAA Regimen

Agent	OBV/PTV/r + DSV	LDV/SOF	SOF/VEL	EBR/GZR	SOF/VEL/ VOX	GLE/PIB
Abacavir	◊	◊	◊	◊	◊	◊
Atazanavir	□	◊	◊	x	x*	x
Darunavir (boosted)	□	◊	◊	x	◊	○
Dolutegravir	◊	◊	◊	◊	◊	◊
Efavirenz	x	□	○	x	○*	○
Elvitegravir/cobi	x	◊	◊	◊	◊	◊
Emtricitabine	◊	◊	◊	◊	◊	◊
Lamivudine	◊	◊	◊	◊	◊	◊
Lopinavir	x	□	◊	x	○*	○
Raltegravir	◊	◊	◊	◊	◊	◊
Rilpivirine	□	◊	◊	◊	◊	◊
TAF	□	◊	□	◊	◊	◊
TDF	◊	□	□	◊	□	◊

*Expected based on DDI with similar mechanism	◊ - No dose adjustment	□ - Dose adjustment or caution	○ - Not recommended	x - Contraindicated

Coding based on present or anticipated Liverpool database classification

Rockstroh J, et al; 9th IAS, Paris, France, July 23-26, 2017; Abst. MOAB0303.



HIV IN 2017:
A YEAR-END SUMMARY AND DISCUSSION OF CRITICAL DEVELOPMENTS

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