



ARV Therapies and Therapeutic Strategies

INDEPENDENT REPORTING ON CROI 2017

Comprehensive Expert Review and Discussion of Key Presentations

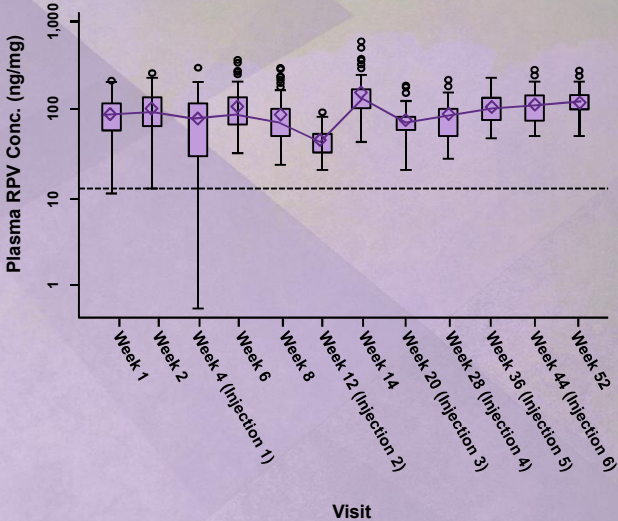
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PREVENTION UPDATE

Richard Elion, MD

HPTN 076: PK and Tolerability of Rilpivirine LA for PrEP

- Long acting injectable is appealing for Prep, due to concerns of adherence
- Four sites in South Africa, Zimbabwe, Bronx and New Jersey
- 122 women (80 active arm/42 placebo) and 64 (a) and 34 (p) received injections
- No differences seen in Aes and in those with 6 injections < 2% had RPV concentrations below PA IC-90 at any given point after 4 week induction
- >80% said injection was easier to use but 30% said it was painful and approx 1/3 had side effects, but 68% said they would they definitely use this and only 4% said they would definitely not use it



Bekker L, et al. 24th CROI; Seattle, WA; February 13-16, 2017. Abst. 421LB.

Resistance to Cabotegravir in Macaques

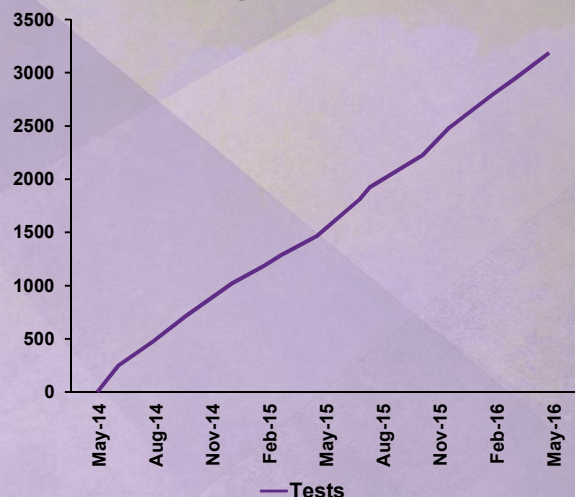
- New agents are being tested currently in clinical trials for injectable PrEP
- Cabotegravir can be injected every two months via IM injection and has been shown to have adequate pk for protection
- Study with macaques evaluated dosing similar to those in clinical trials and revealed mutations
- **Conclusion:** CAB initiation during acute infection frequently selects for mutations that are known to be associated with resistance to other INI including G118R, E92Q, and E92G
- Some of the mutations were detected as early as 8 weeks and persisted during the pharmacologic tail. The finding of G118R and E92Q in rectal and vaginal fluid highlights risks of secondary transmission of these viruses. Our results reiterate the importance of strategies to prevent CAB LA PrEP initiation during undiagnosed HIV infection

Radzio J, et al. 24th CROI; Seattle, WA; February 13-16, 2017. Abst. 84.

Innovative Efforts to Increase Testing

- June 1, 2014 - June 30, 2016, Walgreens pharmacists performed 3,221 HIV tests, including 25 positive tests, for a 0.8% positivity rate
- 46% had never been tested or were unsure, versus 31% of clients in community-based HIV testing programs
- Among HIV-positive clients in the pharmacy testing program, 64% had never been tested or were unsure, versus 17% of clients in community-based HIV testing programs
- Only 39% of tests were performed during business hours, while 61% were provided at night or over the weekend. Statewide, 61% of clients were Black or Latino, more than double the minimum selection criteria. The cost per positive test was \$4,300, versus \$14,900 in community-based HIV testing programs

HIV Testing Over Time (Cumulative)



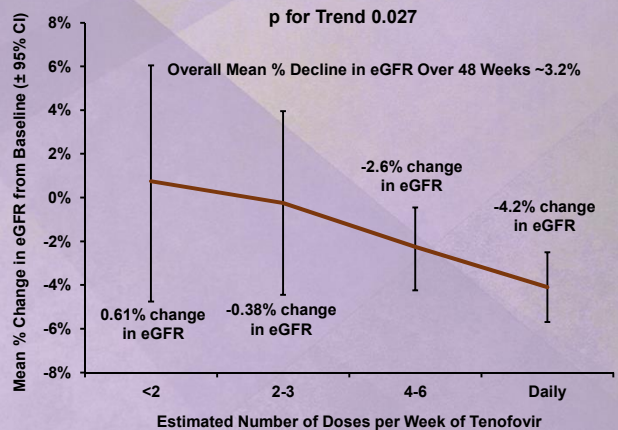
Collins B, et al. 24th CROI; Seattle, WA; February 13-16, 2017. Abst. 962.

Older Age Associated with Good Adherence and Renal Decline in PrEP

▪ **Study population:** The U.S. PrEP Demonstration Project (PrEP Demo) provided open-label PrEP to a diverse population of men-who-have-sex-with-men (MSM) and transgender women (TGW) in San Francisco, Miami and Washington DC (N=557) from Oct 2012-Jan 2014¹²

1. Predictors of PrEP adherence as measured by hair TFV levels in this real-world cohort of MSM were older age, condomless receptive anal sex with HIV+ partner and & amphetamine use
2. Predictors of renal decline include older age, lower baseline eGFR and higher concentrations of PrEP drugs in hair
3. Significant predictors of eGFR falling <70 were lower eGFR before starting PrEP and age >45
4. MSM who initiated PrEP at older ages are more adherent, but may require more frequent safety monitoring

Relationship between hair concentration of TFV and mean % change in eGFR from baseline (using all poste-baseline observations) over duration of study (up to 48 weeks)

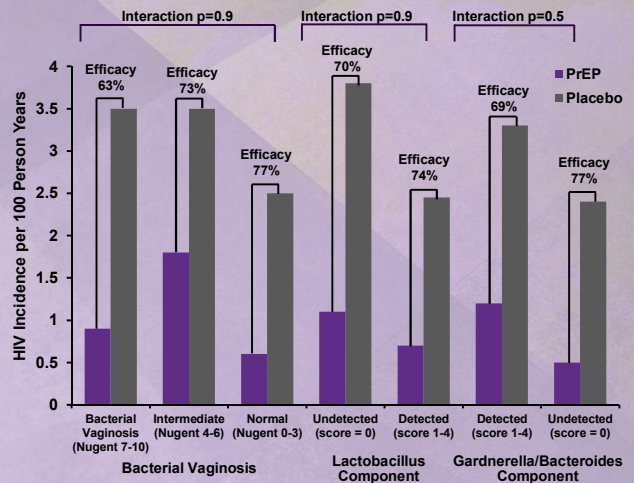


Gandhi M, et al. 24th CROI; Seattle, WA; February 13-16, 2017. Abst. 978.

Does Altered Vaginal Microbiome Impact Efficacy of PrEP?

- Daily oral tenofovir-based PrEP demonstrated high efficacy in clinical trials for HIV prevention among women with high adherence. Recent data suggest that vaginal tenofovir gel may not effectively prevent HIV among women with bacterial vaginosis. Those data raised concern whether daily oral tenofovir could be less effective among women with abnormal vaginal microbiota
- **Methods:** Using data from women in the Partners PrEP PrEP had comparable efficacy for HIV
- **Prevention among women with normal microbiota** (efficacy=77%), intermediate microbiota (73%), and bacterial vaginosis (63%) (interaction p-value=0.9, Figure)
- **Conclusion:** Among African women with a high prevalence of bacterial vaginosis and high PrEP adherence, the efficacy of daily oral PrEP was not different among women with abnormal versus normal vaginal microbiota. Bacterial vaginosis and other indicators of vaginal dysbiosis do not diminish the efficacy of oral PrEP for HIV prevention

Efficacy of Daily Oral PrEP for HIV Prevention in Women With and Without Vaginal Dysbiosis



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

Disparities in PrEP Uptake-Online Assessment in US

Conclusions

- In this online, national MSM sample, PrEP users had an increased odds of:
 - Engaging in condomless anal sex with 2+ partners
 - Reporting a recent bacterial STD
 - Having ever used PEP
- Those who had NOT used PrEP despite frequent condomless sex were more likely to be:
 - Younger
 - Immigrant
 - Black
 - Uninsured
- Programs to address economic and social disparities are needed to ensure wider PrEP access to those who might benefit most

Multivariable Factors Associated with Ever Using PrEP

		PrEP Use (vs. Never PrEP Use)	
		aOR (95% CI)	p
Age	18-24	1.0	
	25+	1.9 (1.3, 2.7)	0.002
Race/ethnicity	White	1.0	
	Black	0.7 (0.6, 0.9)	0.004
	Hispanic	0.8 (0.5, 1.2)	0.213
	Other	1.1 (0.8, 1.6)	0.391
Insurance status	No insurance	1.0	
	Private	3.8 (2.4, 6.0)	<0.0001
	Public	2.0 (1.2, 3.4)	0.007
	Unknown type	1.2 (0.6, 2.4)	0.558
Country of birth	Other	3.1 (1.5, 6.2)	0.002
	United States	1.0	
	Outside United States	0.7 (0.4, 0.9)	0.025
CAI acts, past 3 months	0	1.0	
	1	1.5 (1.0, 2.3)	0.039
Diagnosed with any STI, past year	2+	2.9 (2.2, 3.8)	<0.0001
	Yes	3.1 (2.4, 3.9)	<0.0001
Ever used PEP	No	1.0	
	Yes	6.5 (4.7, 9.0)	<0.0001
Percent Urban zip code area of residence		1.02 (1.01, 1.02)	<0.0001

Mayer K, et al. 24th CROI; Seattle, WA; February 13-16, 2017. Abst. 971.

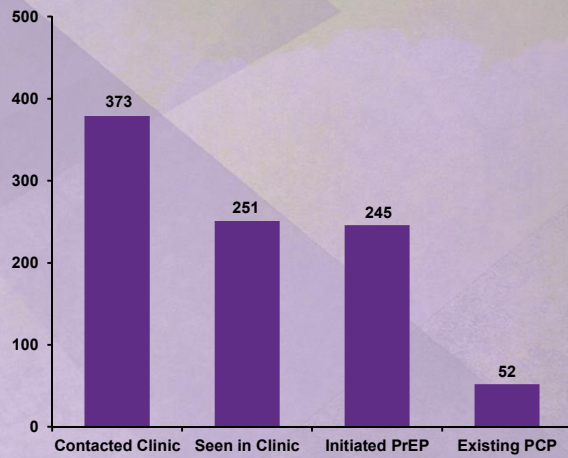
Pharmacy Based Delivery of PrEP

The aim of the project was to determine feasibility of a pharmacist-run HIV PrEP clinic in a community pharmacy setting. The specific objectives were to:

- Develop and implement a protocol for a PrEP program in a community pharmacy called One-Step PreEP®
- Assess the patient demand
- Assess patient acceptability
- Investigate whether a PrEP clinic in a community pharmacy is a financially viable program

Conclusion

- A pharmacist-run HIV PrEP clinic in a community pharmacy is feasible through a collaborative drug therapy agreement with a physician medical director
- A higher-than-expected response from MSM patients seeking PrEP care in a community pharmacy setting suggests that this clinic identifies an unmet need, with more-than-sufficient patient demand to support such services
- Excellent retention rates indicate high patient acceptability of this PrEP delivery model
- The clinic proves to be financially sustainable by demonstrating a return on investment at about 9 months of clinic operation



75% Retention Rate in Program

Tung E, et al. 24th CROI; Seattle, WA; February 13-16, 2017. Abst. 961.

Failure of PrEP with Good Adherence

- 50 year old male on PrEP in Amsterdam study and was neg at enrollment, and had adequate TDF-DP levels by both pill count and diary information as well as DBS levels of 2234 fmol/punch (6 months) and 2258 fmol/punch (8 months)
- 8 months after being on PrEP he had an indeterminate fourth gen HIV AG/AB test, and VL was non detectable
- 3 weeks after seroconversion VL was 40,000c/mL, and he responded to CART

Sexual Risk Behavior of PrEP User Who Seroconverted for HIV with High Tenofovir-diphosphate Levels

	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6	Month 7	Month 8
Anal sex partners ^a	75	56	56	50	38	49	66	12
Number of days he reported CAS ^a	21/31	12/30	13/31	15/31	15/29	19/31	17/30	3/20
Median [IQR] number of sex partners per day he reported CAS ^a	3 [1.7-5]	4-5 [2.25-8.5]	4 [1.5-6]	4 [1-5]	2 [1-5]	3 [1-4]	5 [2-6]	5 [1-5]
CAS partners ^b		90			51		missing	
CAS episodes ^b		100			100		missing	

a. Per month, data collected via daily diary via application for mobile phone
 b. In 12-week periods, collected through computer-assisted self-reported questionnaires
 CAS: Condomless anal sex
 Hoernegorg E, et al. 24th CROI; Seattle, WA; February 13-16, 2017. Abst. 953.

AB Prophylaxis for STIs: A New Strategy ?

THE ORAL USE OF SULFATHIAZOLE AS A PROPHYLAXIS FOR GONORRHEA

PRELIMINARY REPORT

CAPTAIN JAMES A. LOVELESS
 MEDICAL CORPS, ARMY OF THE UNITED STATES

AND

COLONEL WILLIAM DENTON
 MEDICAL CORPS, ARMY OF THE UNITED STATES

Our purpose in this study is to determine whether the prophylactic administration of sulfathiazole prevents the development of gonorrhea. The existence of an inordinately high gonorrhea rate among certain troops makes the development of an easily administered chemical prophylaxis particularly important. The following incomplete experimental data are published as

JAMA 1943

Public Health Reports

Vol. 63 • OCTOBER 29, 1948 • No. 44

Prevention of Gonorrhea With Penicillin Tablets

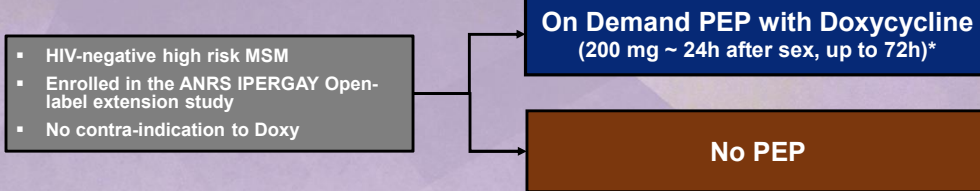
Preliminary Report

By HARRY EAGLE, *National Institutes of Health, Public Health Service*; A. V. GUDE, M. D., Lt. jg., MC, USNR; G. E. BECKMANN, M. D., Lt. jg., MC, USNR; GEORGE MAST*, M. D.; J. J. SAPERO, M. D.; Capt., MC, USN, *Research Division, Bureau of Medicine and Surgery*; and J. B. SHINDLECKER, HMC, USN.

Sulfathiazole was very effective: not a single case of chancroid in 450 men and a single case of gonorrhea **which proved to be refractory to treatment with sulfonamides!**

STI Prophylaxis with Doxycycline: Study Design

Randomized Open-Label Trial



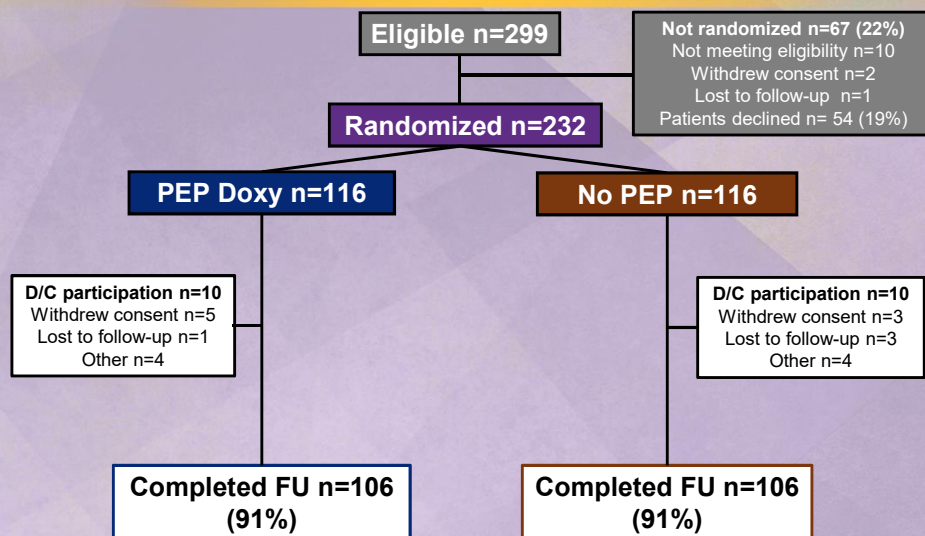
* No more than 6 pills/week to limit AB exposure and selection pressure

- ▲ With 276 subjects enrolled: 80% power to detect a 55% relative decrease in incidence of a first STIs with PEP (expected incidence: 40/100 PY with no PEP)
- ▲ Visits: **Baseline and every two months** with serologic assays for HIV and syphilis and PCR assays for CT and NG in urine samples, anal and throat swabs

www.ipergay.fr

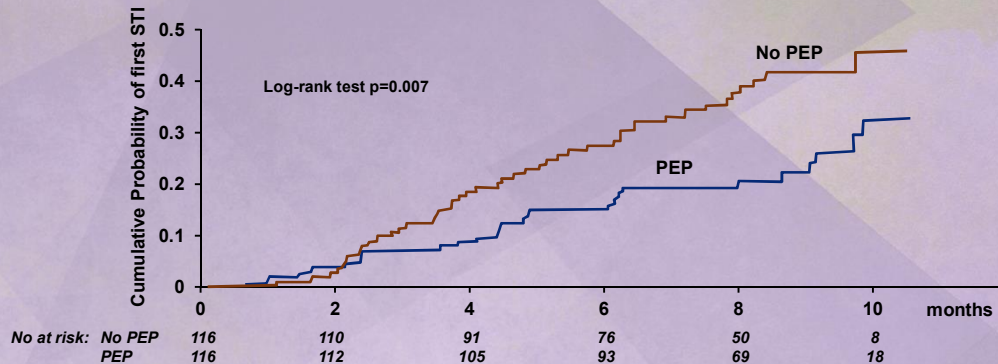
Molina J, et al. 24th CROI; Seattle, WA; February 13-16, 2017. Abst. 91LB.

STI Prophylaxis with Doxycycline: Flow-Chart



Molina J, et al. 24th CROI; Seattle, WA; February 13-16, 2017. Abst. 91LB.

STI Prophylaxis with Doxycycline: KM Estimates of Time to a First STI (ITT Population)



Median follow-up of 8.7 months (IQR: 7.8-9.7): 73 subjects infected
45 in No PEP arm (incidence: 69.7/100 PY), **28 in PEP arm** (incidence: 37.7/100 PY)

Hazard Ratio: 0.53 (95% CI: 0.33-0.85, p=0.008)

Molina J, et al. 24th CROI; Seattle, WA; February 13-16, 2017. Abst. 91LB.

Conclusions

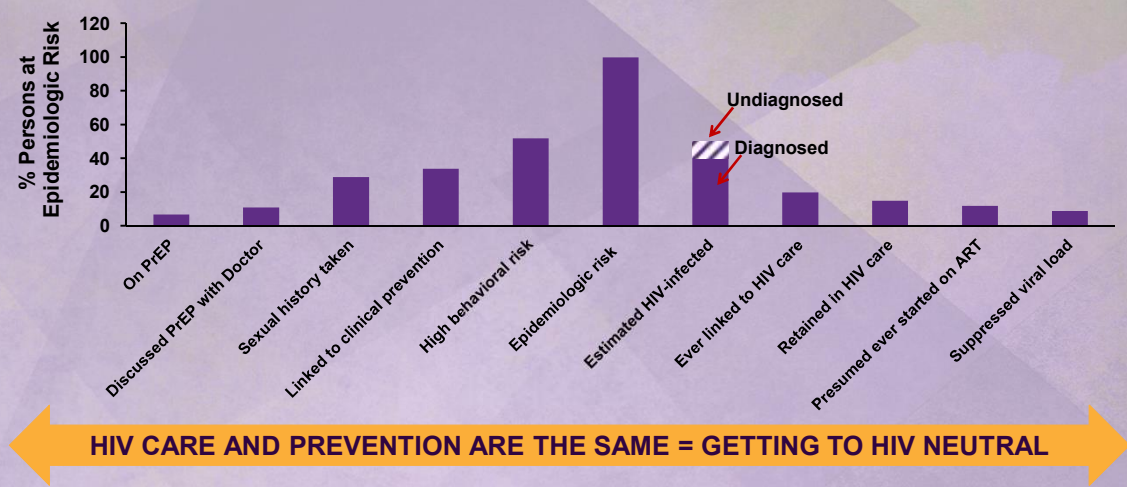
- PEP with doxycycline reduced the overall incidence of bacterial STIs by 47% in MSM on PrEP (8.7 months of FU)
- No effect on Gonorrhea but strong reduction (70-73%) in Chlamydia and Syphilis incidence
- Acceptable safety profile with mild/moderate GI AEs leading to D/C in only 7% of participants
- No evidence of risk compensation
- Analysis of antibiotic resistance pending
- Long-term benefit of PEP yet unknown
- Antibiotic prophylaxis for STIs still **NOT recommended**
- More research needed in the field of STIs

Why the Sexual Health Clinics Matter in EtE Strategy

HIV POSITIVE	HIV NEGATIVE
<p>10% of new HIV in NYC diagnosed there</p>	<p>65% of patients surveyed at STD clinics would start PrEP at STD clinics</p>
<p>20% of NYC Acute HIV diagnosed there</p>	<p>STD clinic data demonstrates that patients diagnosed with syphilis and rectal STIs are at very high risk for HIV</p>
<p>Safety net for some PLWHA not connected to care</p>	<p>Potentially thousands of PrEP candidates seen annually in STD clinics</p>
<p>Existing models of immediate ARV starts for newly diagnosed ideal for this setting</p>	<p>Multi-domain diversity of clients</p>
<p>Data support treatment is prevention</p>	<p>Service delivery environment supports STD clinics as gateway to primary care and biomedical prevention</p>
<p>STD clinics with proven track record for connection to care</p>	



The HIV Neutral Continuum of Care v 1.0



Hootenborg H, et al. 24th CROI; Seattle, WA; February 13-16, 2017. Abst. 963.

