



HPTN
HIV Prevention
Trials Network

HPTN 2017-8

The Way Forward

Myron S. Cohen
Wafaa El-Sadr
on behalf of the HPTN



HPTN MISSION

The HIV Prevention Trials Network (HPTN) advances HIV prevention through research:

- Integrated HIV prevention strategies
- Improve pre-exposure prophylaxis (PrEP)
- New strategies for key populations

What Does this Really Mean?

- We are trying to develop tools/strategies
 - That improve public health policy/practice
 - That improve medical care
 - In a timely fashion (FAST)

Highlights

- Where have we been?
- Where are we going?
- **WE NEED YOU (!!!) to go anywhere**

The Year in Review: Metrics

- 9 ongoing studies including the HPTN 071 (PopART), the largest HIV prevention study to date
 - Many more (> 6) new studies planned
- 78 sites are active (22 HPTN sites)
 - >25 new protocol-specific sites launched in the last year
- Successful scholars program
- 65 presentations, 47 publications
- Robust engagement of communities
- Expanded global partnerships
- **6 studies completed**

JAMA Internal Medicine

Research

JAMA Internal Medicine | [Original Investigation](#)

Financial Incentives for Linkage to Care and Viral Suppression Among HIV-Positive Patients A Randomized Clinical Trial (HPTN 065)

Wafaa M. El-Sadr, MD; Deborah Donnell, PhD; Geetha Beauchamp, MS; H. Irene Hall, PhD; Lucia V. Torian, PhD;
Barry Zingman, MD; Garret Lum, MPH; Michael Kharfen, BA; Richard Elion, MD; Jason Leider, MD;
Fred M. Gordin, MD; Vanessa Elharrar, MD; David Burns, MD; Allison Zerbe, MPH; Theresa Gamble, PhD;
Bernard Branson, MD; for the HPTN 065 Study Team

El-Sadr, et al.; JAMA Intern Med. June 19, 2017



The Effect of a Conditional Cash Transfer on HIV Incidence in Young Women in Rural South Africa (HPTN 068): a Phase 3, Randomised Controlled Trial

Audrey Pettifor, Catherine MacPhail, James P Hughes, Amanda Selin, Jing Wang, F Xavier Gómez-Olivé, Susan H Eshleman, Ryan G Wagner, Wonderful Mabuza, Nomhle Khoza, Chirayath Suchindran, Immitrude Mokoena, Rhian Twine, Philip Andrew, Ellen Townley, Oliver Laeyendecker, Yaw Agyei, Stephen Tollman, Kathleen Kahn

Pettifor, et al.; Lancet Glob Health Dec 2016;4(12):e978-88



Phase 2 Study of the Safety and Tolerability of Maraviroc-Containing Regimens to Prevent HIV Infection in Men Who Have Sex With Men (HPTN 069/ACTG A5305)

Roy M. Gulick, Timothy J. Wilkin, Ying Q. Chen, Raphael J. Landovitz, K. Rivet Amico, Alicia M. Young, Paul Richardson, Mark A. Marzinke, Craig W. Hendrix, Susan H. Eshleman, Ian McGowan, Leslie M. Cottle, Adriana Andrade, Cheryl Marcus, Karin L. Klingman, Wairimu Chege, Alex R. Rinehart, James F. Rooney, Philip Andrew, Robert A. Salata, Manya Magnus, Jason E. Farley, Albert Liu, Ian Frank, Ken Ho, Jorge Santana, Joanne D. Stekler, Marybeth McCauley, and Kenneth H. Mayer

Daily and non-daily pre-exposure prophylaxis in African women (HPTN 067/ADAPT Cape Town Trial): a randomised, open-label, phase 2 trial

Prof Linda-Gail Bekker, MD, Surita Roux, MBChB, Elaine Sebastien, RNRM, Ntando Yola, PgDPH, K Rivet Amico, PhD, Prof James P Hughes, PhD, Mark A Marzinke, PhD, Craig W Hendrix, MD, Prof Peter L Anderson, PharmD, Vanessa Elharrar, MD, Michael Stirratt, PhD, James F Rooney, MD, Estelle Piwowar-Manning, MT(ASCP), Prof Susan H Eshleman, MD, Laura McKinstry, MPH, Maoji Li, MMath, Bonnie J Dye, MPH, Robert M Grant, MD, on behalf of the HPTN 067 (ADAPT) study team

Articles

A network meta-analysis of second-line therapies

See page e433

Articles

Effect of vaginal microbiota on oral PrEP efficacy

See page e449

Articles

A household survey of HIV incidence in Rwanda

See page e457

“Gaps” and Vanguard Studies

- 073-integrated strategies for MSM
- 075-Recruitment of MSM in Africa
- 078-Recruitment of MSM in the US
- 082-TDF/FTC PrEP for women in SSA

Integrated Prevention Trials

HPTN 071 (PopART) Population effects of antiretroviral therapy to reduce HIV transmission

Meeting with UNAIDS/WHO/GFATM
Geneva, May 2017
Richard Hayes and Sarah Fidler



U.S. NATIONAL INSTITUTES OF HEALTH:
National Institute of Allergy and Infectious Diseases
National Institute of Mental Health
National Institute on Drug Abuse

3 arm cluster-randomised trial with 21 communities

Arm A

Full PopART
intervention

including

immediate ART
irrespective of CD4
count

Arm B

PopART intervention

except

ART initiation
according to current
national guidelines

Arm C

Standard of care at
current service
provision levels

including

ART initiation
according to current
national guidelines

7 communities
per arm (N=21)



Total Population ~ 1M

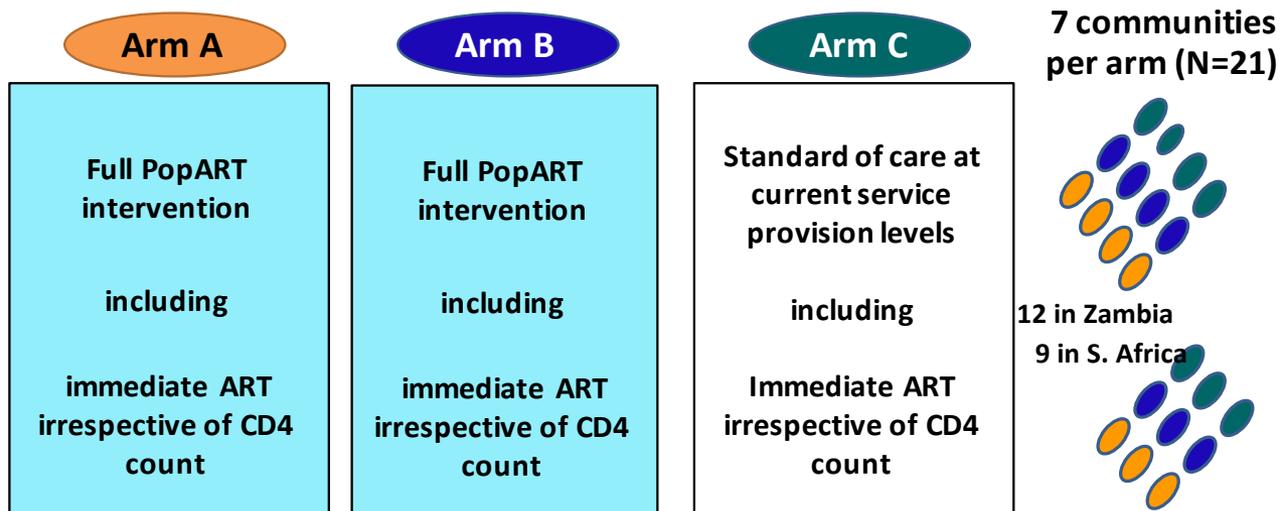
~ 2,000 random sample
from each community :
Population Cohort
N ~ 43,000

Primary outcome:
HIV incidence at 36 months

PopART intervention package

- Annual rounds of Home Based Voluntary HIV Testing by Community HIV-care Providers (CHiPs)
- Health promotion, Active Referral and/or Retention in Care support by CHiPs for the following:
 - Voluntary Medical Male Circumcision (VMMC) for HIV negative men
 - Prevention of Mother to Child Transmission (PMCT) for HIV positive women
 - HIV treatment and care for all HIV positive individuals
 - Promotion of sexual health and TB services
 - Condom provision
- ART irrespective of CD4-count or immune-status provided at the local health centre in Arm A

3 arm cluster-randomised trial with 21 communities



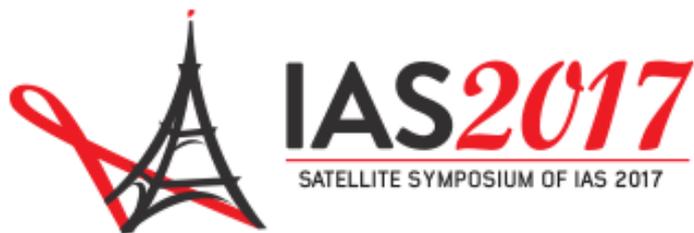
Key difference between Arms A&B vs Arm C is the community-based activities:

- Regular house-to-house HIV testing and re-testing
- Active linkage and follow-up for HIV+
- Adherence support for HIV+
- Condom promotion/distribution, VMMC referral, STI counseling, PMTCT referral
- Active case finding and follow-up for TB

A universal testing and treatment intervention to improve HIV control: One-year results from intervention communities in Zambia in the HPTN 071 (PopART) cluster-randomised trial

Richard Hayes  Sian Floyd, Ab Schaap, Kwame Shanaube, Peter Bock, Kalpana Sabapathy, Sam Griffith, Deborah Donnell, Estelle Piwowar-Manning, Wafaa El-Sadr, Nulda Beyers, Helen Ayles, Sarah Fidler, for the HPTN 071 (PopART) Study Team 

Published: May 2, 2017 • <https://doi.org/10.1371/journal.pmed.1002292>



HPTN 071 (PopART)

Cross-Disciplinary Approaches to Understand Successes and Challenges of Implementing a Community-Wide Universal Test and Treat Programme in Sub-Saharan Africa



Organizer: HIV Prevention Trials Network (HPTN)
Location: Havana Amphitheater
Date & Time: Wednesday 26, July 07:00 - 08:30
Chairs: David Serwadda, Makerere University School of Public Health, Uganda
Alasdair Reid, UNAIDS, Switzerland
Session Code: WESA01

Breakfast will be served



Have We Reached the 90-90-90 Targets After Two Years of the PopART Intervention?
Richard Hayes, London School of Hygiene & Tropical Medicine, United Kingdom

PrEP Research Summary

Optimize the use of TDF/FTC

- Pharmacology and adherence (HPTN 066, 067)
- Vanguard (pilot) studies directed toward:
 - Acceptability in MSM in the US (HPTN 073)
 - Recruitment of MSM in Africa (HPTN 075)
 - PrEP uptake in women in Africa (HPTN 082)

Develop new PrEP/ drugs/delivery methods for PrEP

- Long-acting ART (HPTN 076, 077, 083, 084, 086)
- Broadly neutralizing antibodies (HPTN 081, 085, 087, 088)

New PrEP Agents

HPTN 076

Safety and Acceptability of TMC278 LA for PrEP



HPTN 076: TMC278 LA Safe, Tolerable, And Acceptable for HIV Pre-exposure Prophylaxis

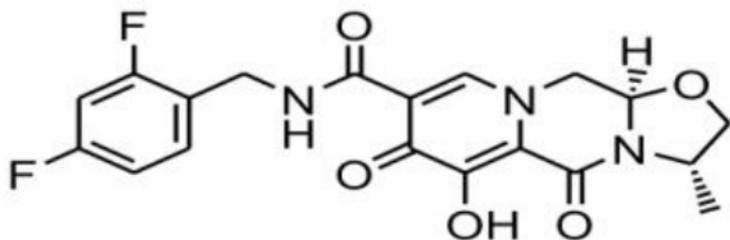
Linda-Gail Bekker, Shuying S. Li, Betsy Tolley, Mark A. Marzinke, Nyaradzo Mgodzi, Jessica E. Justman, Shobha Swaminathan, Adeola Adeyeye, Jennifer H. Farrior, Nirupama Sista

HPTN 076: Safety and Pharmacokinetics of Rilpivirine LA Through Week 76 in HIV-uninfected Women

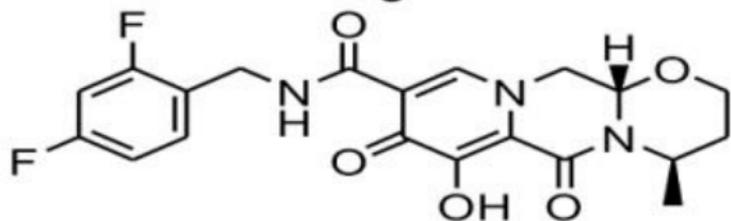
N.D. Sista, S. Li, M. Marzinke, N. Mgodzi, J. Justman, S. Swaminathan, A. Adeyeye, E. Piwowar-Manning, S. Pathak, J. Farrior, L.-G. Bekker, and the HPTN Study Team

CABOTEGRAVIR: GSK126744 Long Acting (744LA)

**GSK1265744
(GSK744)**



Dolutegravir



Favorable attributes for PrEP:

- High genetic barrier to resistance
- PK profile – half life of 21-50 days -- allows once-daily oral or 1-3 month injectable dosing using nanosuspension formulation

*Muller et al, European Journal of Pharmaceutics and Biopharmaceutics, 2011
Spreen, 7th IAS, 2013; Min, ICAAC, 2009
Taoda, International Congress on Drug Therapy in HIV Infection, 2012*



HPTN

HIV Prevention
Trials Network

Safety, Tolerability, and Pharmacokinetics of Long-Acting Injectable Cabotegravir in Low-Risk HIV-uninfected Women and Men

HPTN 077

**R. Landovitz, S. Li, B. Grinsztejn, H. Dawood, A. Liu, M. Magnus, M.
Hosseini-pour, R. Panchia, L. Cottle, G. Chau, P. Richardson, M.
Marzinke, C. Hendrix, B. Tolley, A. Adeyeye, D. Burns, A. Rinehart,
D. Margolis, MB McCauley, J Eron**

**IAS 2017 - Paris, France
July 25, 2017**

HPTN 083: CAB LA 600mg

To Prevent HIV Acquisition in MSM and TGW

Landovitz and Grinsztejn, *Protocol Chairs*

Step 1	Daily oral CAB and TDF/FTC placebo	TDF/FTC and oral CAB placebo
Step 2	CAB LA at two time points 4 weeks apart and every 8 weeks thereafter and TDF/FTC placebo	TDF/FTC and injectable placebo at two time points 4 weeks apart and every 8 weeks thereafter
Step 3	Open-label TDF/FTC to cover the PK tail	Open-label TDF/FTC to Cover the PK tail



Primary Objective: Reduce HIV Incidence (non-inferiority**, double blind, double dummy design)**

N=4500; Study duration: Enrollment 24-30 months; follow-up ~ 4.5 years

Enrollment goals:

- *Minimum* 50% of US enrollment Black MSM (~ 950)
- Overall minimum 10% TGW (~ 450)
- Overall > 50% under age 30

HPTN 083 Research Sites

43 Sites in 7 Countries



**Study started in December 2016 in U.S.
1252 Enrolled! (as of March 21 2018)**

Status of Site Activation – 43 Sites

- All US sites activated (27)
- South America (11)
 - Brazil: One of 4 sites activated (Rio de Janeiro)
 - Argentina/Peru: Pending
- Asia(4)
 - Thailand: All 3 Sites Activated
 - Vietnam: Activated
- Africa (1)
 - Cape Town Activated

HPTN 084: CAB LA 600mg

To Prevent HIV Acquisition in Women
Delaney-Moretlwe and Hosseinipour, *Protocol Chairs*

Step 1	Daily oral CAB and TDF/FTC placebo	Oral TDF/FTC and oral CAB placebo
Step 2	CAB LA and oral TDF/FTC placebo at two time points 4 weeks apart and every 8 weeks thereafter	Oral TDF/FTC and injectable placebo at two time points 4 weeks apart and every 8 weeks thereafter
Step 3	Open-label oral TDF/FTC to cover the PK tail	Open-label oral TDF/FTC to cover the PK tail

Primary Objective: Reduce HIV Incidence (superiority**, double blind, double dummy design)**

Study duration: Enrollment 24 months; follow-up up to 4.5 years, N=3200

Study Population

- 20 research sites in 7 countries in Sub-Saharan Africa
- 3,200 women who have sex with men
- Expected HIV incidence $>3/100$ person years



Status of Study

- ✓ **6 Sites Activated**
- ✓ **Remaining 14 to be activated after the next protocol training in April 2018**
- ✓ **86 enrolled (as of March 20 2018)**

Subcutaneous PrEP Implants?

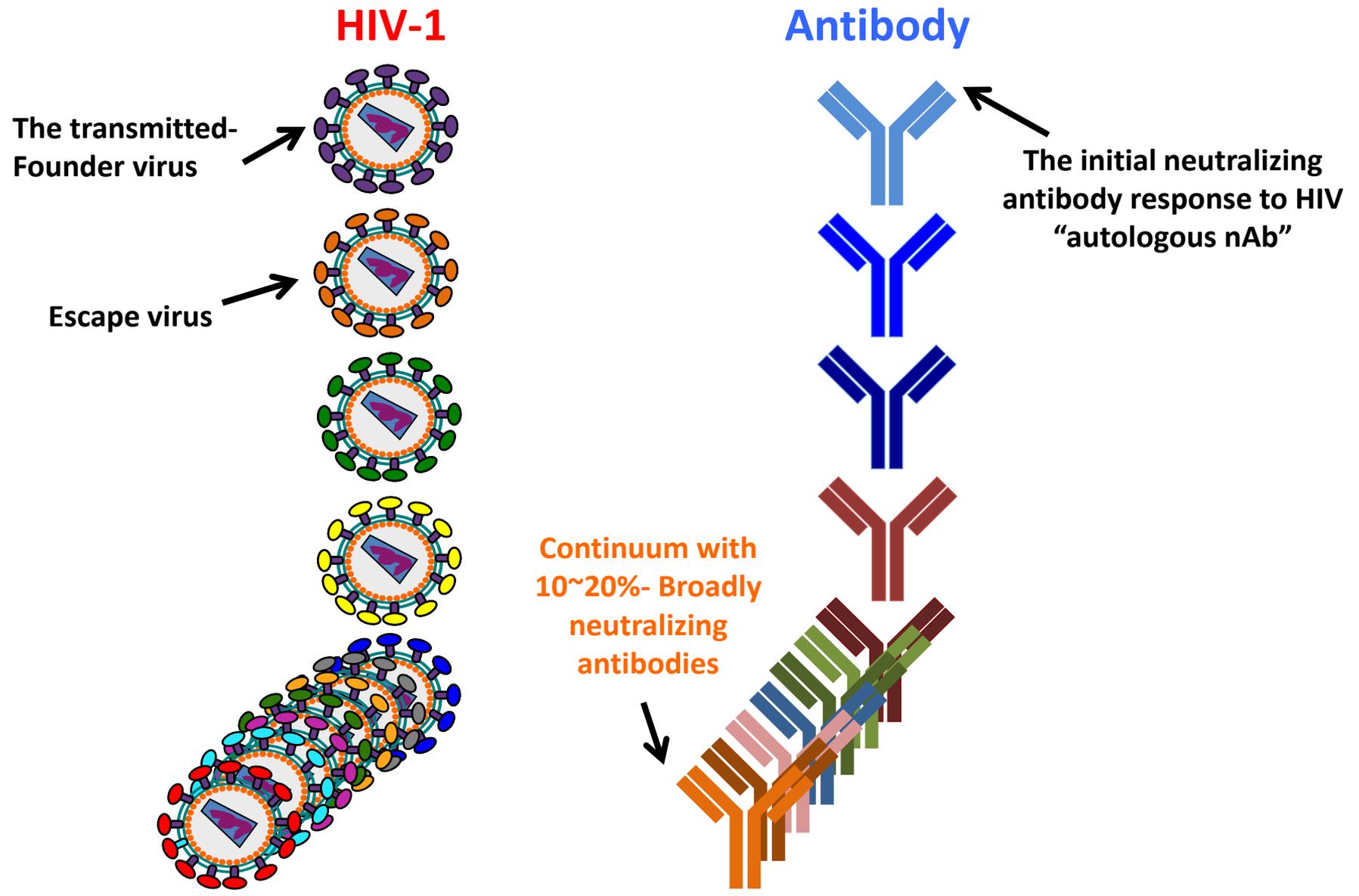
Like Implanon/Nexplanon Contraception



- Simple insertion AND removal
- Long-acting (months to years)
- PrEP + contraception?
- Current development:
 - TAF, EFdA (MK-8591), Cabotegravir

Partnerships established!
Phase 1 studies 2019

Development of Broad Neutralizing Antibodies (BnABs)



Passive Antibody Prevention Phase IIB Efficacy Studies

AMP = Antibody Mediated Prevention

Can a passively infused monoclonal antibody
prevent HIV-1 infection in high risk adults:
MSM in Americas & Heterosexual Women in sub-Saharan Africa?

Chairs: Lawrence Corey, HVTN
Myron S. Cohen, HPTN

Co-chairs: Srilatha Edupuganti
Nyaradzo Mgodzi

AMP Studies: Safety and Efficacy of VRC01 broadly neutralizing monoclonal antibody



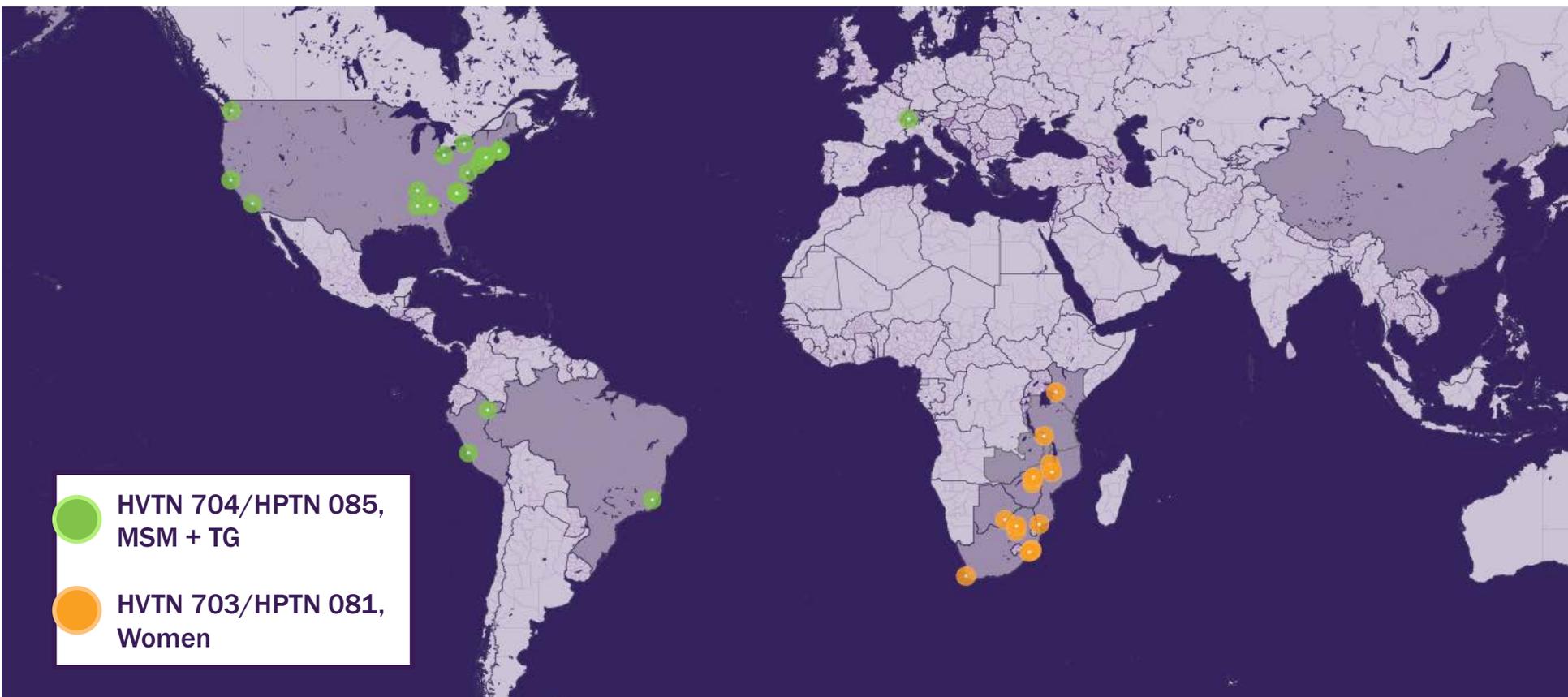
Regimen	 HVTN 703/HPTN 081 Cisgender Women in sub-Saharan Africa	 HVTN 704/HPTN 085 MSM & TG People in the Americas and Switzerland	Total
VRC01 10 mg/kg	634	900	1534
VRC01 30 mg/kg	634	900	1534
Control	634	900	1534
Total	1900*	2700	4600*

10 infusions total; Infusions every 8 weeks. Study duration: 24 months

***Due to randomization scheme the number of active product and control recipients may vary slightly.**

AMP Research Sites

47 sites in 11 countries



Enrollment and Retention Updates

703/081

African Women

1,512 enrolled
80%

95% retention
through 15,034
clinic visits

99% adherence
of 7,672
infusions

704/085

MSM + TG

2,224 enrolled
82%

94% retention
through 25,169
clinic visits

100% adherence
of 12,460
infusions

The tree hugger who now
embraces logging p. 24

Piecing together the proton
size puzzle pgs. 30 & 79

Price tags influence pain
perception pgs. 44 & 105

Science

315
6 OCTOBER 2017
science.org

AAAS

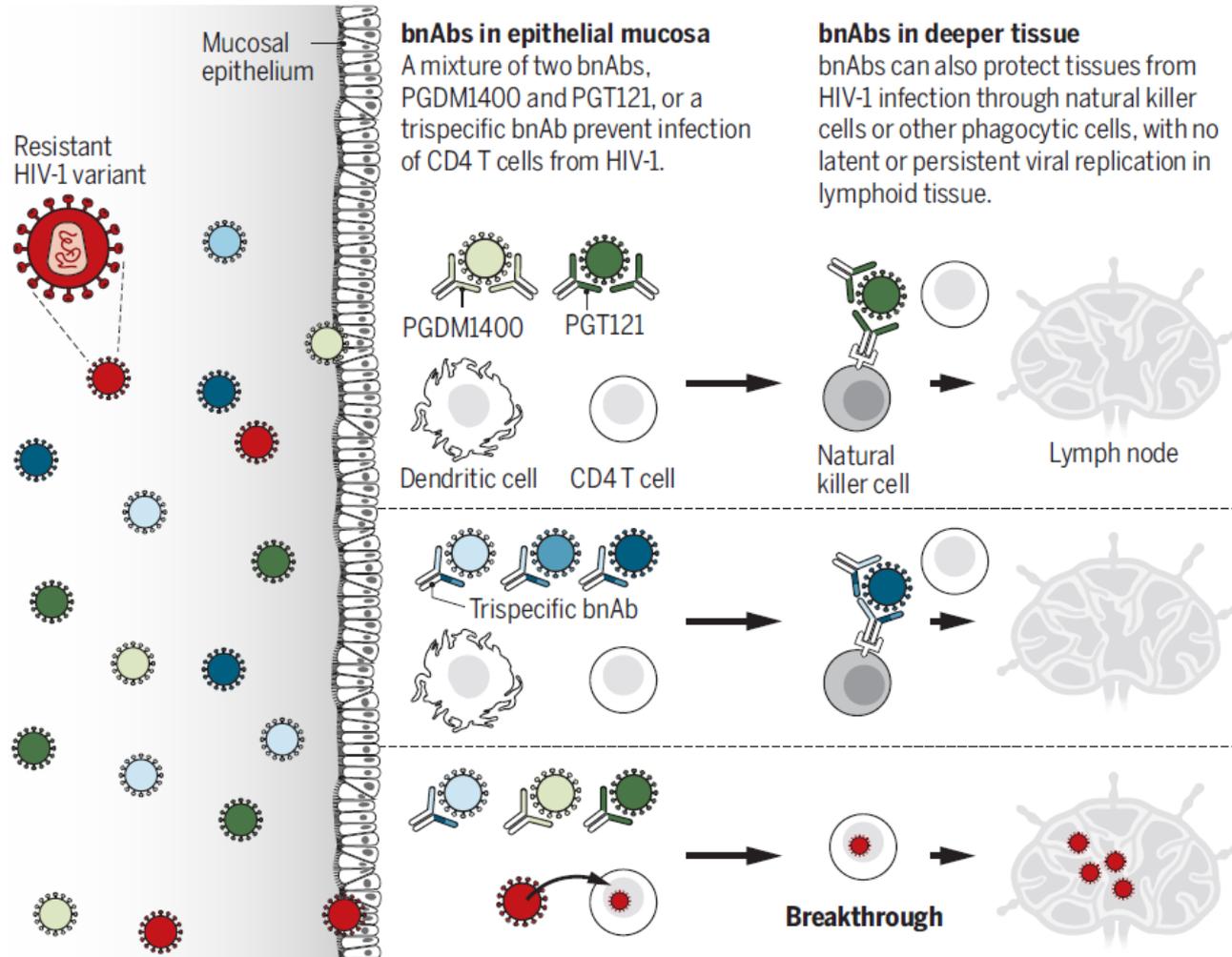
Broadly neutralizing antibodies to prevent HIV-1

Studies show the potential of synthetic and
Combinations of broadly neutralizing antibodies.

By Myron S. Cohen *and* Lawrence Corey

bnAbs prevent HIV-1

Combinations of bnAbs and a trispecific antibody can bind to virions and prevent HIV-1 mucosal infection and elicit antiviral responses in deeper tissue. It is hoped this multitarget approach will prevent resistant breakthrough.



Next Generation BnAB Studies Safety and PK/PD and Potential

- HPTN 087: VRC01-523LS
- HPTN 088: Sanofi trispecific antibody
- HPTN 089: Combination of 2-3 antibodies:
 - *PGT121, PDGM 1400, VRC07-523LS, 10E8:*
neutralization at peak/trough in vivo?

....and BnABS for treatment and cure

“Gaps” and Vanguard Studies

- 073-integrated strategies for MSM
- 075-Recruitment of MSM in Africa
- 078-Recruitment of MSM in the US
- 082-TDF/FTC PrEP for women in SSA

HPTN Scholars Program

Goal: To develop the next generation of HIV prevention scientists from under-represented racial/ethnic communities

- Scholars utilize HPTN data to develop analytic skills, conduct reviews, give presentations, write publications

To date:

- 26 scholars completed program
- 31 mentors engaged
- K & U awards, R01, R03s, R21s, faculty positions
- 18 publications
(+ 2 in press, 1 under review)



Second Cohort of Int'l Scholars



Community Engagement Activities

- **Good Participatory Process**
 - Five HPTN 083 presentations at national conferences engaging community advocates, CBOs, ASOs, MSM & TG-specific service providers, and health departments
 - One HPTN 083 community webinar engaging U.S. national community advocates and providers
- **Scientific Literacy**
 - “Understanding Clinical Research Process and Principles of Clinical Research” workshop for the HPTN 071/PopART Zambia National CAB

Community Engagement Activities

- **Community partnerships**
 - Five, study-specific national stakeholder consultations (including HPTN 081 and HPTN 084)
 - SA AIDS booth, photo campaigns
- **Social Media**
 - #GivePrEPaShot social marketing campaign and website for HPTN 083
- **Dissemination of Results**
 - Webinars, at sites, brochures, posters, presentations, etc.

Cross Site Exchange of Best Practices



Community Outreach/Education

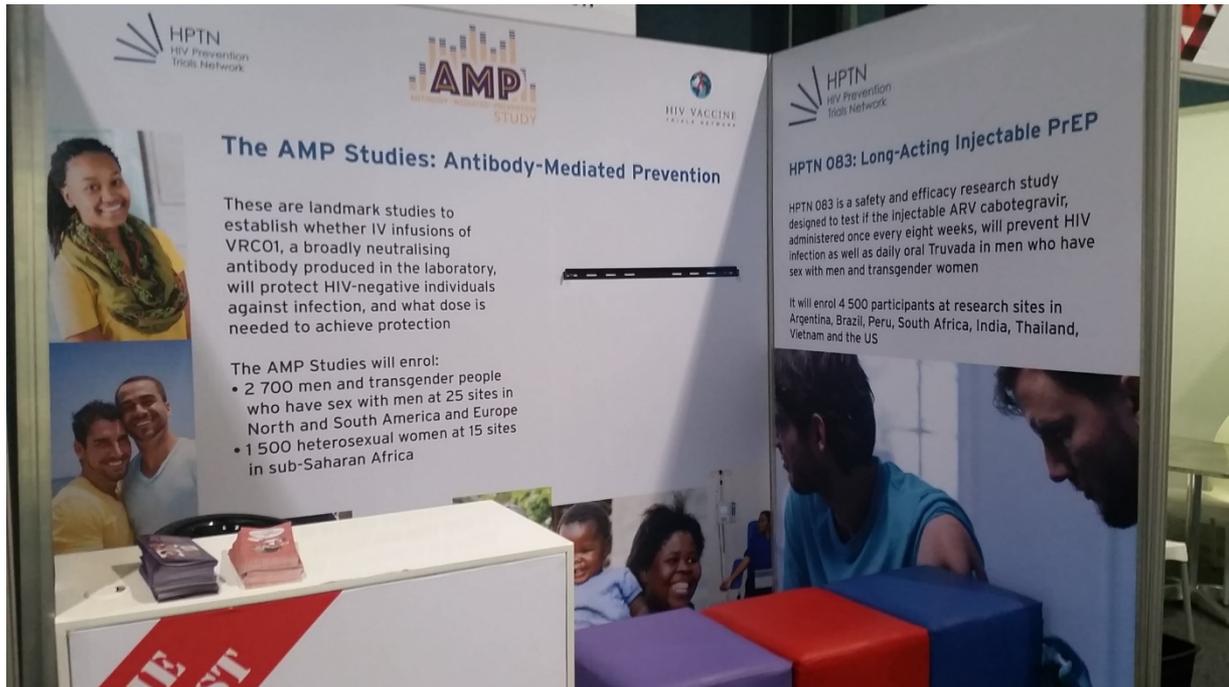




Community Outreach/Education



Dissemination - Cross Network Collaboration




**PLEASE JOIN US FOR
AN EXCITING BREAKFAST
PLENARY AT THE
2017 NAESM MEETING!**

Saturday, January 21, 8:30-10 a.m. • Bent Tree 1-2
Dallas/Addison Marriott Quorum by the Galleria • Dallas, Texas

**HIV Prevention Research Studies Engaging
Black MSM and Transgender Persons**

Presenters will provide updates on two biomedical HIV prevention research studies that seek to advance HIV prevention options available for Black MSM, and transgender men and women who have sex with men, with the ultimate goal of reducing the HIV epidemic among these groups.




Women and Adolescent Subjects

- ~40,000 women in HPTN clinical trials
- A rapidly growing and exciting adolescent research agenda team
- Consideration of ethical bridging studies

The Way Forward

When we complete our current studies we will have:

- A long-acting PrEP agent
- Strategies to deliver HIV testing and universal access to ART to decrease HIV incidence
- Methods for optimizing uptake of TDF/FTC
- Advanced BnABS for prevention of HIV infection

THE HPTN IS DETERMINED TO GENERATE RESEARCH RESULTS THAT INFORM AND GUIDE HIV PREVENTION STRATEGIES WORLDWIDE

The Team

- **Study participants and participating communities**
- **Site investigators, staff, and community representatives**
- BMGF, USAID, PEPFAR/OGAC, ViiV, Gilead, VRC, PANGEA, and many other partners
- NIH Institutes (NIAID, NIMH, NIDA) and OAR
- HPTN Scientific Committees, Working Groups, Executive Committee, and Scientific Advisory Group