HPTN 2017-8
The Way Forward

Myron S. Cohen
Wafaa El-Sadr
on behalf of the HPTN
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)
Where have we been?
Where are we going?
WE NEED YOU (!!!) to go anywhere
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
Financial Incentives for Linkage to Care and Viral Suppression Among HIV-Positive Patients: A Randomized Clinical Trial (HPTN 065)

Wafa 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
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

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)

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

“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
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)

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

Primary outcome: HIV incidence at 36 months

**HPTN**
- **HIV Prevention Trials Network**
- **Original Trial Design**

**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

Total Population ~ 1M

12 in Zambia
9 in S. Africa

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

Primary outcome: HIV incidence at 36 months
3 arm cluster-randomised trial with 21 communities

**Arm A**
- Full PopART intervention
  - including immediate ART irrespective of CD4 count

**Arm B**
- Full PopART intervention
  - including immediate ART irrespective of CD4 count

**Arm C**
- Standard of care at current service provision levels
  - including Immediate ART irrespective of CD4 count

7 communities per arm (N=21)

12 in Zambia
9 in S. Africa

**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, Nuila Beyers, Helen Ayles, Sarah Fidler, for the HPTN 071 (PopART) Study Team

Published: May 2, 2017 • https://doi.org/10.1371/journal.pmed.1002202

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: Henva Amphitheater
Date & Time: Wednesday 26, July 07:00 - 09:30
Chairs: David Sewaika, Makerere University School of Public Health, Uganda
Alistair Reed, UNAIDS, Switzerland
Session Code: WESA01

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

Linda-Gail Bekker, Shuying S. Li, Betsy Tolley, Mark A. Marzinke, Nyaradzo Mgodi, 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

CABOTEGRAVIR: GSK126744 Long Acting (744LA)

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

HPTN 077


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*

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Daily oral CAB and TDF/FTC placebo</th>
<th>TDF/FTC and oral CAB placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CAB LA at two time points 4 weeks apart and every 8 weeks thereafter and TDF/FTC placebo</td>
<td>TDF/FTC and injectable placebo at two time points 4 weeks apart and every 8 weeks thereafter</td>
</tr>
<tr>
<td>Step 2</td>
<td>Open-label TDF/FTC to cover the PK tail</td>
<td>Open-label TDF/FTC to Cover the PK tail</td>
</tr>
</tbody>
</table>

**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*

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Daily oral CAB and TDF/FTC placebo</th>
<th>Oral TDF/FTC and oral CAB placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAB LA and oral TDF/FTC placebo at two time points 4 weeks apart and every 8 weeks thereafter</td>
<td>Oral TDF/FTC and injectable placebo at two time points 4 weeks apart and every 8 weeks thereafter</td>
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<th>Open-label oral TDF/FTC to cover the PK tail</th>
</tr>
</thead>
</table>

**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)

The initial neutralizing antibody response to HIV "autologous nAb"

Continuum with 10~20%- Broadly neutralizing antibodies

The transmitted-Founder virus

Escape virus

HIV-1

Antibody

The initial neutralizing antibody response to HIV "autologous nAb"
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 Mgodi
**AMP Studies: Safety and Efficacy of VRC01 broadly neutralizing monoclonal antibody**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>HVTN 703/HPTN 081 Cisgender Women in sub-Saharan Africa</th>
<th>HVTN 704/HPTN 085 MSM &amp; TG People in the Americas and Switzerland</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>VRC01 10 mg/kg</td>
<td>634</td>
<td>900</td>
<td>1534</td>
</tr>
<tr>
<td>VRC01 30 mg/kg</td>
<td>634</td>
<td>900</td>
<td>1534</td>
</tr>
<tr>
<td>Control</td>
<td>634</td>
<td>900</td>
<td>1534</td>
</tr>
<tr>
<td>Total</td>
<td><strong>1900</strong>*</td>
<td><strong>2700</strong></td>
<td><strong>4600</strong>*</td>
</tr>
</tbody>
</table>

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
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.

**bnAbs in epithelial mucosa**
A mixture of two bnAbs, PGDM1400 and PGT121, or a trispecific bnAb prevent infection of CD4 T cells from HIV-1.

**bnAbs in deeper tissue**
bnAbs can also protect tissues from HIV-1 infection through natural killer cells or other phagocytic cells, with no latent or persistent viral replication in lymphoid tissue.
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)
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**
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

084: LONG-ACTING INJECTABLE PrEP

084 is a safety and efficacy research study designed to test if an injectable ARV cabravir, given once every 8 weeks, will prevent HIV infection better than daily tenofovir disoproxil fumarate (Truvada) in women at risk of acquiring HIV. Around 2,200 participants are recruiting in Botswana, South Africa, Swaziland, and Zimbabwe.
The AMP Studies: Antibody-Mediated Prevention

These are landmark studies to establish whether IV infusions of VIRCO1, a broadly neutralizing antibody produced in the laboratory, will protect HIV-negative individuals against infection, and what dose is needed to achieve protection.

The AMP Studies will enroll:
- 2,700 men and transgender people who have sex with men at 25 sites in North and South America and Europe
- 1,500 heterosexual women at 15 sites in sub-Saharan Africa

HPTN 083: Long-Acting Injectable PrEP

HPTN 083 is a safety and efficacy research study designed to test if the injectable ARV cabotegravir, administered once every 8-10 weeks, will prevent HIV infection as well as daily oral Truvada in men who have sex with men and transgender women.

It will enroll 4,500 participants at research sites in Argentina, Brazil, Peru, South Africa, India, Thailand, Vietnam, and the US.

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.
Dissemination – Best Practices
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