HPTN 2018
State of the Network

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)
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
  – **6 studies completed**

• 78 sites are active (22 HPTN sites)
  – >25 new protocol-specific sites launched in the last year

• 65 presentations, 47 publications

• Robust engagement of communities

• Dissemination of results/best practices

• A successful “scholars” program
HPTN STUDIES “BY THE NUMBERS”
Financial Incentives for Linkage to Care and Viral Suppression Among HIV-Positive Patients: A Randomized Clinical 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 Khareen, 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
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
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)

Treatment as Prevention Trials

- HPTN 071 (PopART)
- CDC Botswana
- ANRS Africa Center
- SEARCH Uganda

…and many smaller studies

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, Kaipana Sabapathy, Sam Griffith, Deborah Donnell, Estella Picower-Manning, Walda El-Sadr, Nulda Boyers, Helen Aykles, Sarah Fidler, for the HPTN 071 (PopART) Study Team

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

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
HPTN 073
PrEP Uptake and Use by Black Men Who Have Sex With Men in Three U.S. Cities

Darrell P. Wheeler; Sheldon Fields; LaRon E. Nelson; Leo Wilton; Lisa Hightow-Weidman; Steven Shoptaw; Manya Magnus; Geetha Beauchamp; Phaedrea Watkins; Kenneth H. Mayer for the HPTN 073 Study
HPTN 074
Integrated intervention including supported ART compared to the standard of care for PWID

• Vietnam, Ukraine, Indonesia
• 504 HIV infected PWID
• 810 PWID “partners”
• Results presented at CROI 2018
MSM: HPTN 075 and 078

Studies designed to better inform our ability to prevent HIV in hard to reach MSM … worldwide

HPTN 075 recruited MSM in SSA

Results at IAS 2018!
Pre-Exposure Prophylaxis
HPTN 082: Design & PrEP uptake

HPTN 082: Evaluation of daily oral PrEP as a primary prevention strategy for young African women

Study Population

- Uninfected women
  - Ages 16-25 yrs
- Johannesburg & Cape Town, South Africa
- Harare, Zimbabwe

Target Enrollment

- 400 women who accept PrEP at enrollment
- ≤ 200 women who decline PrEP at enrollment

Primary objectives:

Assess the proportion and characteristics of women who accept versus decline PrEP
Assess PrEP adherence using drug levels in young women

Figure 1: PrEP uptake overall and by site

- Overall: 95%
- Harare: 97%
- Cape Town: 99%
- Johannesburg: 88%

- PrEP accepted
- PrEP not accepted
HPTN 076
TMC278 LA (Rilpivirine) 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 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
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)
**HPTN 084: CAB LA 600mg**

To Prevent HIV Acquisition in Women
Delaney-Moretiwe 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>Step 2</td>
<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>
</tr>
<tr>
<td>Step 3</td>
<td>Open-label oral TDF/FTC to cover the PK tail</td>
<td>Open-label oral TDF/FTC to cover the PK tail</td>
</tr>
</tbody>
</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
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!
A Phase 1 study 2019

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
Next Generation BnAB Studies
Safety and PK/PD and Potential

- HPTN 087: VRC01-523LS
- HPTN 088: Sanofi trispecific antibody
- HPTN 089: Combination of 3 antibodies:
  Evaluation of safety, PK, antiviral activity of combinations PGT121, PDGM 1400, VRC07-523LS, 10E8 to identify the best “triple threat”
HPTN: Putting It All Together!

**POPULATIONS**
- Young Women
- MSM
- PWID
- High Prevalence Communities

**PUBLIC HEALTH IMPACT**
- Reduced HIV incidence

**HIV-INFECTED**
- Behavioral
- Structural
- Biomedical
- ART
  - Maximize ART Effectiveness

**HIV-UNINFECTED**
- Behavioral
- Structural
- Biomedical
- PREP
  - Maximize ART Effectiveness

**New PrEP Agents**

**Vanguard Study**

**Integrated Strategies**
HPTN is More Than A Series of Studies
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

2018-2019 Scholars
HPTN Scholars Program Achievements

• 43 Scholars since 2010
  – Studies: 037, 039, 043, 058, 061, 063, 064, 065, 067, 068
  – 43 Mentors have graciously provided their expertise and time
  – Just added 052, 073, and 075 (qualitative)

• HPTN involvement
  – Protocol Team Members (HPTN 073, 078)
  – Black Caucus
  – Scientific Committees
Community Cross Site Exchange of Best Practices
Cross Network Collaborations/Partnerships

The AMP Studies: Antibody-Mediated Prevention

These are landmark studies to establish whether IV infusions of VRC01, 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 089 is a safety and efficacy research study designed to test if the Injectable ARV cabotegravir, administered once every eight weeks, will prevent HIV infection among men and transgender women in clinical trials in Europe, the United States, and South Africa.

It will enroll 1,500 participants at research sites in Argentina, Brazil, Peru, South Africa, India, Thailand, Vietnam and the U.S.

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

Saturday, January 21, 8:30-10 a.m. • Ballroom 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 trials 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.
AMP Social Marketing Strategies
Community Outreach/Education
Dissemination – Best Practices
One More Thing!

Call for concepts: See HPTN Web Site
August 15, 2018
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