HPTN 2023
State of the Network
Myron S. Cohen, MD
Wafaa M. El-Sadr, MD, MPH, MPA
HPTN Principal Investigators
Network Structure – Leaders

Executive Committee (EC)
- Myron S. Cohen
- Wafaa El-Sadr
- Quarraisha Abdool Karim
- Chris Beyrer
- Sinead Delany-Moretlwe
- Deborah Donnell
- Susan Eshleman
- Sybil Hosek
- Raphael Landovitz
- Nyaradzo Mgodi
- David Serwadda
- Sten Vermund
- Nirupama Sista
- Melissa Turner
- Darrell Wheeler
- 2 NIH Representatives

Leadership and Operations Center (LOC) FHI 360
- Nirupama Sista

Statistical and Data Management Center (SDMC) SCHARP
- Deborah Donnell

Laboratory Center (LC) Johns Hopkins University
- Susan Eshleman
- Mark Marzinke
78 Trials
ongoing or completed
Study participants enrolled 172,000+
800+
Publications
UNDETECTABLE  ⇔  UNTRANSMITTABLE

Prevention Access Campaign
The impact of Fast-Track

New HIV infections in low- and middle-income countries

AIDS-related deaths in low- and middle-income countries

- Business as usual (no scale-up)
- Fast-Track results (rapid scale-up)
Forward: 2023 Clinical Research Sites

- 69 HPTN Sites
- 13 Countries
- 22 African Sites
- 5 Asian Sites
- 31 North American Sites
- 11 South American Sites

Map of clinical research sites around the world.
Two Points to Consider First

• HPTN/HVTN = The COVID Prevention Network (CovPN)
  - Moderna, Astra Zeneca, J&J, Novavax vaccines
  - mAbs from Lilly, Regeneron and Astra Zeneca

But.. Consider the HPTN/HVTN Opportunity Costs

Recent HVTN Vaccine Trials
- HIV vaccine development continues to prove VERY challenging
- Collaborative HVTN/HPTN bnAb research for next PrEP
- bnAb research informs vaccine development, long-term
Achieving Population Impact
NEXT in PrEP
CAB LA PrEP IS APPROVED in the U.S. – What’s Next?

• Open label extension (OLE) studies will estimate continued safety and protection, PK, resistance, and include pregnancy and adolescent substudies.

• CAB LA for PrEP is approved in several countries, including Botswana, Malawi, South Africa, Zambia and Zimbabwe. In addition, full EMA approval was received for use in EU countries.

-ROUND OF APPLAUSE!!!!!

• New studies in development to examine the effectiveness of CAB-LA among adolescents and PWID.

• New studies to explore different routes of administration (e.g., thigh). fewer injections/year and more.

• Combine cabotegravir-LA with contraceptives in future studies?
Pregnancy Sub-Study in HPTN 084 OLE

• Estimate the incidence of pregnancy among participants during the OLE period
• Evaluate safety and infant outcomes among pregnant participants
• Evaluate the PK of CAB LA among pregnant participants, combining blinded, unblinded and OLE periods
• Evaluate concentration in breastmilk and infants among women who receive CAB LA injections during pregnancy and/or the early post-partum period.
Lenacapavir, a first-in-class selective HIV capsid inhibitor, with subcutaneous injections every 6 months.

HPTN and Gilead will develop two companion studies in collaboration:

- **HPTN 102/Purpose 3**: A lenacapavir Phase 2 PK, safety, acceptability in cis-gender women in the US.
- **HPTN 103/Purpose 4**: A phase 2 PK, safety, acceptability of lenacapavir in people who inject drugs (PWID) in the US.
Broadly Neutralizing Antibodies for HIV Prevention
Broadly Neutralizing Antibodies

The transmitted-Founder virus

Escape virus

HIV-1

Antibody

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 Mediated Prevention Trials

VRC01 is a broadly neutralizing antibody (bNAb) which blocks the CD4 binding site on the HIV envelope.

- VRC01 was infused every 2 months x 10 to high-risk women (Africa) and MSM and transgender individuals (Americas) (n=4,600)
- Two doses of VRC01 were evaluated: 10 mg/kg and 30 mg/kg

VRC01 neutralized highly sensitive viruses, no effect on others.
HIV bnAb clinical trials in HIV-uninfected adults

**Participants**
- HVTN/HPTN 92%
- VRC, 3%
- CAPRISA, 2%
- IAVI, 1%
- Rockefeller University, 2%

**Protocols**
- HVTN/HPTN...
- VRC, 7
- Rockefeller University, 4
- IAVI, 2
- CAPRISA, 2
<table>
<thead>
<tr>
<th>Clinical Trial Participants</th>
<th>Start</th>
<th>bnAb</th>
<th>New concepts(^1)</th>
<th>Key results – the road to combo-AMP</th>
<th>Countries</th>
</tr>
</thead>
</table>
| HVTN 104 N=88               | 2014  | • VRC01 IV, SC | • Safety, PK, PD, neutralization  
• Repeat dosing up to 22 weeks | • Interim PK and neutralization data informed AMP protocol development | USA |
| HVTN 704/HPTN 085 N=2699    | 2016  | • VRC01 IV | • HIV prevention efficacy proof of concept  
• Correlate of protection | • HIV bnAb can prevent HIV acquisition  
• Correlate of protection – PT, biomarker to predict protection  
• HIV bnAbs are safe – safety profile equal to placebo | Brazil, Peru, USA, Switzerland |
| HVTN 703/HPTN 081 N=1924    | 2016  | • VRC01 IV | • HIV prevention efficacy proof of concept  
• Correlate of protection | | Botswana, Kenya, Malawi, Mozambique, South Africa, Tanzania, Zimbabwe |
| HVTN 116 N=80               | 2017  | • VRC01 IV  
• VRC01LS IV | • LS modification, longer half-life  
• Mucosa, tissue & secretions PK & activity | • VRC01LS ~3x longer half-life in serum, higher and prolonged levels in genital and rectal tissue | South Africa, USA |
| HVTN 127/HPTN 087 N=124     | 2018  | • VRC07-523LS IV, IM, SC | • IM dosing | • VRC07-523LS ~2x longer half life  
• Neutralization consistent after 5 doses | Switzerland, USA |
| HVTN 128 N=28               | 2019  | • VRC07-523LS IV | • Mucosa PK & activity | | USA |
| HVTN 130/HPTN 089 N=27      | 2019  | • VRC07-523LS IV  
• 10-1074 IV  
• PGT121 12V  
• PGDM1400 IV | • 2 bnAb combinations  
• No PK interaction  
• No loss of complementary neutralization  
• Greater neutralization coverage in 3 bnAb arms compared to 2 bnAb arms | | USA |
| HVTN 136/HPTN 092 N=32      | 2020  | • VRC07-523LS IV, SC  
• PGT121.141LS IV, SC | • 2 LS bnAb combination  
| | USA |
| HVTN 140/HPTN 101 N=95      | 2021  | • VRC07-523LS IV, SC  
• PGT121.141LS IV, SC  
• PGDM1400LS IV | • 3 LS bnAb combination  
• Fixed dose compared to weight-based dose  
• No PK interaction | • PGT121.414LS ~3x longer half-life  
• PGDM1400LS ~2.5x longer half-life | Kenya, South Africa, USA, Zimbabwe |
| HVTN 143/HPTN 109 N=77      | 2023  | • VRC01.23LS IV  
• PGT121.414LS IV  
• PGDM1400LS IV | • 3 LS bnAb combination  
• 1st of 3 LS bnAbs to be used in ‘combo AMP’ in a 3 LS bnAb combination – 1 of 3  
• No loss of neutralization  
• PK interaction | | South Africa |
| HVTN 141/HPTN 105 N=92      | 2024  | • VRC01.23LS IV  
• ePGT121v1LS IV, SC | • 2nd (and 1st) of 3 LS bnAbs combination to be used in ‘combo AMP’ in a 2 LS bnAb combination – 2 of 3  
• No PK interaction | | South Africa, USA |
| HVTN TBD/HPTN TBD N=tbd ± 92 | 2024  | • VRC01.23LS IV  
• ePGT121v1LS IV, SC  
• PGDM1400.93LS IV, SC | • 3rd (and 2nd and 1st) of 3 LS bnAbs combination to be used in ‘combo AMP’ in a 3 LS bnAb combination – 3 of 3  
• Safety run-in for combo-AMP  
• Fixed ‘combo-AMP’ dose compared to weight-based dose | | TBD, South Africa, USA |
| HVTN TBD/HPTN TBD N=tbd ± 200 | 2024  | • VRC01.23LS IV  
• ePGT121v1LS IV, SC  
• PGDM1400.93LS IV, SC | • 3rd (and 2nd and 1st) of 3 LS bnAbs combination to be used in ‘combo AMP’ in a 3 LS bnAb combination – 3 of 3  
• Safety run-in for combo-AMP  
• Fixed ‘combo-AMP’ dose compared to weight-based dose | | TBD, South Africa, USA |
| Combo-AMP studies 1. Women in SSA  
2. MSM & transgender  
N=tbd | 2025/2026 | • VRC01.23LS IV  
• ePGT121v1LS IV, SC  
• PGDM1400.93LS IV | • 3 LS bnAbs combination  
• HIV prevention efficacy proof of concept  
• Correlate of protection | | AMP countries, TBD |

\(^1\)All trials evaluate safety, PK, & serum neutralization; additional protocol-specific evaluations noted here.
## HIV bnAb clinical trials in HIV-uninfected adults

<table>
<thead>
<tr>
<th>Year</th>
<th>Study</th>
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<tbody>
<tr>
<td>2013</td>
<td>VRC 602 – VRC01</td>
</tr>
<tr>
<td>2014</td>
<td>VRC 606 – VRC01LS</td>
</tr>
<tr>
<td>2015</td>
<td>VRC 605 – VRC07-523LS, VRC 609* – NL65</td>
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<tr>
<td>2017</td>
<td>VRC 611 – CAP254VLS</td>
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<tr>
<td>2018</td>
<td>VRC 615 – VRC01-20S</td>
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</tr>
<tr>
<td>2029</td>
<td>VRC 615 – VRC01-20S</td>
</tr>
</tbody>
</table>

### Study Details

- **Legend**
  - Single antibodies
  - Single antibodies, LS versions
  - Antibody combinations
  - Next-generation ebNAbs
  - Phase 1 = black font
  - Phase 2 = red font
  - combo-AMP antibodies
    - **BLUE** = 1st choice
    - **YELLOW** = back-up candidate

- **Study start dates** will depend on product availability and other factors

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10 September 2023
NIH Criteria for a bNab PreP Trial

• Pharmacology leads to a stable combination (i.e. no “tails”)
• A product manufacturer
• A commercial partner
• An ethical trial design
• Feasible implementation
Phase 2b, open label, randomized crossover study of DPP (co-formulated F/TDF+ ethynyl estradiol/levonorgestrel oral contraceptive pill (OCP), compared with the two tablets with daily oral F/TDF + OCP (2PR) for PrEP and pregnancy prevention in HIV-uninfected women

**Sample Size:** ~300 women 16-39 years (100 adolescents) for 48 weeks per participant

**Regulatory Sponsor:** Viatris

**Primary Objective:**
Compare PrEP adherence to the DPP versus 2PR during a randomized crossover period

Pivotal Bioequivalence results to be submitted to US FDA 2023

**Speculation:** Study launched 2024. Aspiration {US FDA approval 2025!!
Among cases with reported HIV status, 44% among MSM were HIV+, compared with 38% among men with unknown sex of sex partners, 7.1% among men who have sex with women only, and 3.9% among women.

Percent with primary and secondary syphilis was higher for HIV+ compared with those not (12% vs 4.9%), similar to urogenital chlamydia (6.2% vs 5.4%) and gonorrhea (12% vs 7.8%)
A Phase II randomized, observer-blind, placebo-controlled study to assess efficacy of meningococcal **Group B vaccine MenB+OMV NZ (Bexsero)** in preventing gonococcal infection (DMID Protocol 19-0004/HPTN 108)

### Study design
Phase II, randomised, observer-blind, placebo-controlled trial (USA and Thailand)

### Primary objective
Bexsero efficacy in preventing urogenital and/or anorectal gonococcal infection

#### Subjects at risk of *N. gonorrhoeae* infection
N=~2200, aged 18–50 years

#### Randomised
1:1

0  1  2  3  6  9  12  15 months

**Bexsero**

**Placebo**

### Key:
- Treatment dose
- Phone call to assess safety
- Clinic visit

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**Recruiting** estimated completion **2024**

**Target enrolment** 2,200 to achieve 202 incident infections

**Current enrolment** 667 across 11 sites

**3 HPTN Sites in the US and (soon) Malawi**

US Vanguard Integrated Strategies

HPTN 091: HIV Prevention, Gender-Affirmative Medical Care, and Peer Health Navigation for Transgender Women in the Americas

HPTN 094: A Study of Health Service Delivery in a Mobile Health Delivery Unit to Link Persons who Inject Drugs to Integrated Care and Prevention for Addiction, HIV, HCV and Primary Care

HPTN 096: Getting to Zero among Black MSM in the American South: Testing the Efficacy of an Integrated Strategy
• **HPTN 111**: Uptake of HIV Self-testing and Linkage to Prevention and Care among Heterosexual Men Attending Barbershops in Uganda: A Cluster Randomized Trial

• **HPTN 112**: Improving HIV Prevention Among Heterosexual Men Seeking STI Services in Sub-Saharan Africa: Examining the Feasibility, Acceptability, and Associated Costs of a Systems-Navigator-Delivered Integrated Prevention Package

• **HPTN 113**: Double Prevention: A Vanguard Study of an Integrated Strategy of HIV PrEP and STI PEP for Young Latino Sexual Minority Men (SMM) in the Americas
Community Engagement
Community Engagement

Community Engagement is pivotal part of all HPTN studies.

A few examples:

• Advocacy for affordable post-trial access to CAB LA in countries where HPTN 083 and HPTN 084 are being conducted

• Participating in the development of all forthcoming HPTN research initiatives

• Contributed “Including pregnant and breastfeeding people in trials of novel LAED PrEP agents – perspectives from sub-Saharan Africa community stakeholders” in JIAS Special Issue
Domestic Program established in 2010
  • 48 Scholars to date

International Program established in 2015
  • 15 Scholars to date

60+ Scholars since 2010 (some were in multiple cohorts)
  • 34% men; 66% women
  • 20 datasets: HPTN 037-HPTN 082
  • 50+ mentors

HPTN involvement
  • Protocol Team Members (HPTN 073, 078, 094, 096)
  • Protocol Team Leadership (HPTN 091, HPTN 096)
  • Memberships/Observerships: Black Caucus, Scientific Committees, and Working Groups
2022-2023 HPTN Scholars

Dr. Tina Herrera  Dr. David Zelaya  Dr. Donte Boyd  Dr. Waru Gichane

Dr. Sophia Zamudio-Haas  Dr. Victoria Ndyanabangi  Kudzai Hlahla
Acknowledgments

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- National Institute on Drug Abuse (NIDA)
- National Institute of Mental Health (NIMH)
- Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)
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